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Original Article

The use of guided tissue regeneration in endodontic Microsurgery: Setting a threshold

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ABSTRACT

Aim: We aimed to compare the radiographic outcomes of conventional and regenerative approaches in endodontic microsurgery (EMS) and set a critical defect size for healing in conventional and regenerative therapies.
Methodology: The study evaluated 53 root canal-treated teeth (33 patients) with periapical lesions. Among them, 19 teeth (35.8 %) were treated with regenerative treatment, whereas 34 teeth (64.1 %) were managed with the conventional approach. Conventional and regenerative approaches were performed by endodontic and periodontic residents under consultants' supervision. Healing was evaluated after a minimum period of 6 months by comparing pre- and post-operative cone-beam computed tomography (CBCT) findings. The radiographic interpretation was conducted by a single examiner who was not participating in the surgeries and was blind on the type of treatment prior to CBCT evaluation. New healing criteria were proposed owing to the limitations on the present criteria in evaluating endodontic surgery after regenerative treatment. Critical measurements were calculated for each approach based on periapical lesion dimensions.
Results: The regenerative approach presented significantly better healing than conventional treatment (mean, 1.21 and 1.59, respectively; $p = 0.047$). Based on the critical-point calculations, the conventional approach was effective in lesions of up to 3 mm depth and height, whereas the regenerative approach resulted in better healing rates in lesions with 3–9 mm depth and 3–6 mm height.
Conclusions: Performing the regenerative approach in EMS resulted in better healing rates than those of the conventional approach. The conventional approach is recommended for small periapical lesions, whereas the first had better results in larger lesions.

1. Introduction

Endodontic microsurgery (EMS) is a newer version of the traditional root-end surgical intervention for managing a tooth that uderwent failed endodontic treatment and cannot be managed with the orthograde endodontic approach. Although the osteotomy site is considerably small, the bone loss around the root can be significant, and the healing of the periapical lesion may be challenging (Kim and Kratchman, 2006). The main objective of EMS is to optimise the healing environment for the *peri*-radicular tissue by effectively eliminating persistent pathogens and directly accessing the root apices and periapical area (European Society of Endodontology, 2006).

Tissue regeneration is defined as the reproduction or reconstruction of a lost or injured tissue by completely restoring its structure and function (Karring, 2000). This is performed by using a barrier over the osseous defect to prevent or retard the fast proliferation of the oral epithelium and gingival connective tissue and allow the repopulation of cells with osteogenic potential (Gottlow and Nyman, 1996).

Several human and animal studies have compared the healing rates after EMS with or without performing the regenerative approaches (Apaydin and Torabinejad, 2004; Garrett et al., 2002; Pantchev et al., 2009; Yoshikawa et al., 2002). The outcomes after using calcium sulfate were compared with those obtained after conducting the conventional treatment in beagle dogs. The results indicated that adding calcium sulfate had no benefits in some studies but significantly better healing rates in others (Apaydin and Torabinejad, 2004; Murashima et al.,

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2002). When evaluating human clinical trials, radiographic evaluation showed complete healing in 100 % of the cases received resorbable hydroxyapatite filler with an expanded polytertafluoroethylene (e-PTFE) membrane compared to 77.8 % and 88.9 % in the second group (e-PTFE membrane only) and the third group, respectively (conventional therapy) (Garrett et al., 2002).

The outcomes of applying guided tissue regeneration (GTR) during EMS were investigated. However, several limitations were found. Most of the studies did not consider the three-dimensional size of the defect. Assessing the lesions based on two-dimensional periapical radiographs may not reflect the actual healing (Garrett et al., 2002; Pantchev et al., 2009; Pecora et al., 1995; Stassen et al., 1994; Taschieri et al., 2007; Tobón et al., 2002). Evaluating the outcomes of apical surgery using periapical radiographs significantly overestimated the success rate compared to that after using CBCT (Schloss et al., 2017). Conversely, when comparing the measurements taken intraoperatively with CBCT measurements, a strong correlation was found, indicating the accuracy of CBCT measurements (Grimard et al., 2009). Although some studies have used CBCT in pre-operative evaluation (Kim et al., 2016; Kurt et al., 2014), no study has compared the outcomes of the EMS in CBCT pre- and post-operatively after regenerative treatment. Additionally, many studies have evaluated surgically created periapical defects, which may have a different healing mechanism than that of bacterially infected defects in humans (Maguire et al., 1998; Murashima et al., 2002; Yoshikawa et al., 2002). Another limitation is the use of alloplast or xenograft materials in most of the studies (Pantchev et al., 2009; Taschieri et al., 2007; Yoshikawa et al., 2002). Although new bone formation may occur using these materials, they are primarily used as fillers, and the remaining particles will not resorb within an extended period. The mean percentage of new bone formation when using allograft is 65 % compared to 45 % and 49 % when using xenograft and alloplast, respectively (Nappe et al., 2016).

Therefore, in this study, we aimed to compare the radiographic outcomes after using the conventional and regenerative approaches in patients who underwent EMS and set a critical defect size for healing in conventional and regenerative therapies.

2. Materials and methods

This retrospective study was conducted at Riyadh Elm University, from January 2021 to January 2022. It was approved by the Institutional Review Board of Riyadh Elm University (number FPGRP/2019/449/138/273), and was conducted in accordance with the tenets of the Helsinki Declaration.

The patients' records were retrieved retrospectively for those who underwent EMS. Patients' data and the surgery details were obtained from the patients' records as well as from pre- and post-operative CBCT findings. As the university clinic is an educational centre, consent forms were usually signed before any provided treatment for using the patients' data for educational and research purposes; therefore, no new consent forms were needed. Surgical interventions were conducted by endodontic and periodontic residents with supervision of specialists or consultants or by endodontic specialists and consultants alone. The use of the microscope and endodontic microsurgery is considered the standard of care in the centre. Patients with complete data were not recalled, whereas those with only pre-operative CBCT findings and detailed surgical records were recalled to undergo post-operative CBCT examination. The post-operative CBCT examination was conducted voluntarily. The exclusion criteria were as follows: missing detailed surgical information in the record that prevent proper statistical analysis; absence of pre-operative CBCT; Refusal to undergo post-operative CBCT examination; presence of through-and-through lesion; and healing period < 6 months.

CBCT measurements were conducted before checking the records for the type of treatment performed.

2.1. Radiographic measurements

The CBCT measurements included the height, width, depth, and volume of the lesion; presence or absence of buccal or palatal perforation; and buccal plate length. These measurements were taken as follows (Fig. 1):

1) Height: from the sagittal section, the deepest point considered in a parallel line with the tooth long axis
2) Width: from coronal section, the deepest point of the lesion considered in a line perpendicular to the tooth long axis
3) Depth: from the sagittal section, the deepest point considered in a line perpendicular to the long axis of the tooth
4) Volume: calculated by multiplying the height x width x depth of the defect
5) Buccal or palatal perforation: marked as present or absent
6) Buccal plate length: from the sagittal section, the distance from alveolar crest level till the buccal or palatal perforation

2.2. Records data retrievement

Once the CBCT measurements were taken, patients' data were retrieved. Patient age, sex, tooth type (single-rooted, multi-rooted), tooth position (maxilla, mandible), type of treatment (conventional, GTR), type of retrograde filling (bioceram, mineral trioxide aggregate, or zinc oxide eugenol cement), and the skills of the operator (resident, specialist/ consultant) were recorded.

2.3. Healing criteria

Although the healing criteria have been found in the literature using CBCT (Estrela et al., 2008; Kang et al., 2020; von Arx et al., 2016), these are based mainly on conventional treatment and will not be applicable for evaluating GTR treatment outcomes. Therefore, new criteria have been proposed to evaluate the study outcomes. Table 1 shows the proposed healing criteria.

2.4. Data analysis

The sample size calculation was executed. The considered test power was 0.80, and the marginal error was 0.2. This yielded a sample size of 42 patients. The tooth was considered the unit of evaluation in this study. Additionally, intra-examiner calibration was calculated. The statistical analysis was performed using the Statistical Package For The Social Sciences (SPSS) program. Descriptive statistics, simple linear regression for comparing two variables, and multiple linear regression for more than two variables were conducted. Additionally, cross-tabulation was used to specify the critical points in this study. A p-value of < 0.05 was considered significant.

3. Results

In total, 53 teeth of 33 patients had complete examination data after EMS.

To check the reliability of the measurements, CBCT examinations were conducted twice with 2-week time gap in the group of patients who were not included in the study. The intraclass correlation coefficient was 0.98 showing excellent reliability.

Table 2 shows the descriptive analysis of treated teeth in this study. A smoking habit cannot be assessed owing to incomplete data in most records. The mean age of the treated patients was 37.1 (range, 16–69). The mean follow-up period was 1.47 years, whereas the longest follow-up period was 3.29 years. Among the group treated with GTR, all cases had been treated with a collagen membrane. Allograft placement was performed in 78.9 % of the cases, whereas the rest did not receive any bone grafting.

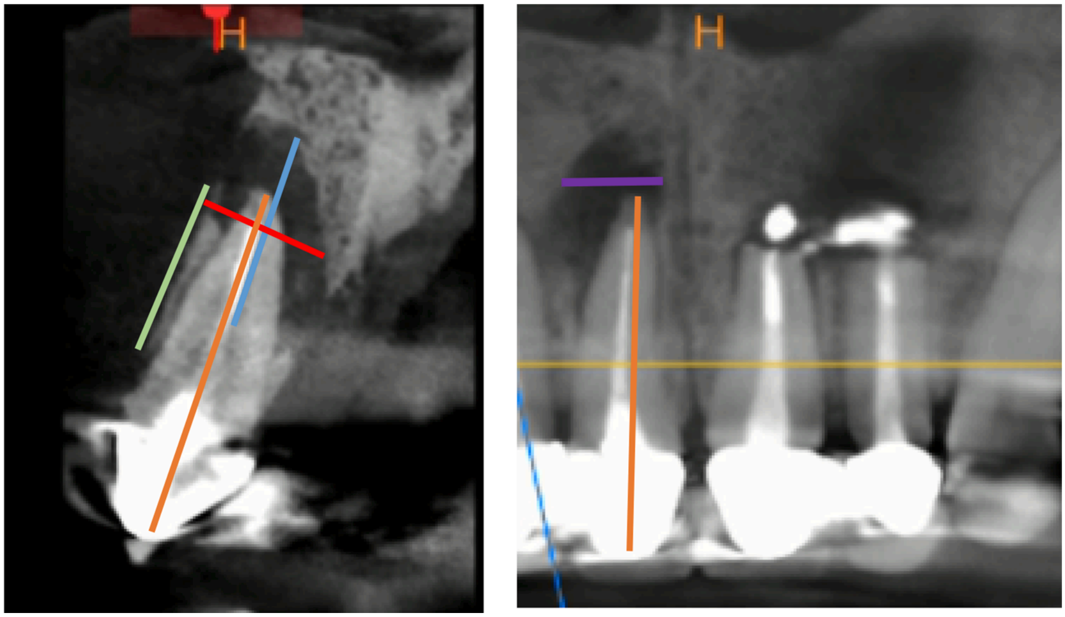

Fig 1. A sagittal and coronal section of CBCT showed the measurements taken Orange = tooth long axis, Blue = height of the lesion, Red = depth of the lesion, Green = buccal plate length, Purple = width of the lesion. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Proposed healing criteria.

	Periapical defect	Around the resected root	The buccal window
Complete healing	Complete absence of periapical defect with bone fill of similar density or more radiopaque than surrounding natural bone	Presence or absence of periodontal ligament around the sectioned tooth apex	Filled with bone with or without cortical bone plate or overbuild with lateral ridge augmentation
Partial healing	Reduction in the size of the defect in pre and post-operative CBCT measurements without complete bone fillPresence of radiopaque bone fill with radiolucent rim around the defect separating natural bone from the lesion	Presence or absence of periodontal ligament around the sectioned tooth apex	Decreased on size but not necessary closed with bone
Failed	no change or increase in the size of periapical defect	Absence of periodontal ligament around resected tooth	no change or increase in the size of buccal window

Table 2
Descriptive analysis of the treated teeth.

Type of treatment	N	%
Conventional treatment	34	64.1
GTR treatment	12	22.6
Gender		
Male	23	43.4
Female	30	56.6
Tooth type		
Single rooted	41	77
Multi-rooted	12	22.6
Arch		
Maxilla	41	77
Mandible	12	22.6
Type of retrograde filling		
MTA	11	34
Bioceram	20	54.7
IRM	1	1.9
Buccal or palatal plate perforation		
Yes	19	36.5
No	33	63.4
Skills		
Resident	24	45.3
Consultant/ specialist	29	54.7

The simple linear regression analysis (Table 3) showed a statistically significant difference in healing between cases treated with GTR compared to conventional treatment. There was no statistically significant effect of the width and volume of the periapical lesion on healing among those treated with GTR and conventional treatment.

The multiple linear regression analysis indicated that the depth of the defect had a statistically significant effect on healing among the two treated groups (Table 4). The deeper the defect, the less likely the site to show complete healing. Based on cross-tabulation, 75 % of the sites with a depth of 1–3 mm had healed completely or presented with partial healing in conventional treatment. The healing dropped to 30.6 % when the depth increased to 3–6 mm. Based on that, the critical depth for using conventional treatment is 3 mm.

In comparison, all patients treated with GTR presented complete or partial healing when the site depth ranged between 1 and 9 mm. This indicated that the critical depth of the lesion for GTR treatment is 9 mm. Failure was found when the defect was deeper than 9 mm.

Similarly, the height of the periapical lesion had a statistically significant effect on the healing among patients treated with conventional and GTR approaches (Table 4). On sites with 1–3 mm height, both treatments showed a high percentage of complete healing. This percentage decreased to 16.7 % and 37.5 %, respectively, for conventional and GTR approaches with defects ranging between 3 and 6 mm. Based on that, the critical height for periapical defect healing is 3 mm for the conventional treatment and 6 mm for the GTR approach.

Prognostic factors, such as the tooth type (single or multi-rooted), arch position (maxilla or mandible), type of retrograde filling, presence of buccal or palatal bone perforation, and crestal bone level, which indicated apicomarginal communication, as well as the skills of the

Table 3
The effect of the type of treatment on healing.

	N	Mean (±SD)		Sum of squares	Df	Mean of squares	F	*p*-Value
Conventional Treatment	34	1.59 (±0.7)	Between groups	1.739	1	1.739	4.145	0.047*
GTR treatment	19	1.21 (±0.53)	Within groups	21.393	51	0.419		
			Total	23.132	52			

Complete healing = 1, partial healing = 2, failed = 3.
* *p*-value is statistically significant < 0.05.

Table 4
The multiple linear regression showing statistically significant measurements that affect the healing among patients treated with conventional approach and GTR.

Variable	B	Std. Error	*p*-value
Healing (Constant)	1.607	0.284	0
Depth of the defect	0.069	0.025	0.009*
Type of treatment (conventional VS GTR)	−0.372	0.175	0.038*
Healing (Constant)	1.809	0.289	0
Height of the defect	−0.382	0.184	0.043*
Type of treatment (conventional VS GTR)	0.032	0.032	0.177

* *p*-value is statistically significant < 0.05.

operator (resident or specialist/consultant) did not show a statistically significant effect on the healing rates in the studied sample.

4. Discussion

The introduction of GTR therapy and bone augmentation in EMS aimed to increase the ability of the area to heal with regeneration instead of fibrous connective tissue and epithelial migration (Maguire et al., 1998). This study was conducted to specify the critical defect measures beyond which the healing might be affected in conventional and GTR approaches.

Several studies have compared the effects of conventional treatment and with those of GTR. Based on the defect type, a review article found that GTR had better performance in through-and-through lesion (von Arx and Alsaeed, 2011). However, no conclusion can be drawn for the apicomarginal defect, and limitations were found in isolated defects; this explained why these two types of defects were included in our study. Some studies have reported better results using GTR (Pantchev et al., 2009; Yoshikawa et al., 2002), in agreement with our results. In contrast, others have reported the absence of significant differences after using the two approaches (Garrett et al., 2002; Taschieri et al., 2007).

With the introduction of CBCT in the dental field, studies have reported that CBCT is superior in assessing post-operative healing compared to periapical radiographs (Kruse et al., 2018; Schloss et al., 2017). To the best of our knowledge, no study has compared the CBCT findings before and after EMS among patients treated with the GTR approach.

In contrast, the effect of defect size was assessed by CBCT evaluation among patients treated with conventional treatment in previous studies.

This study showed that the lesion's depth significantly affected the healing for patients treated with conventional and GTR approaches. Von Arx et al. (von Arx et al., 2007) showed that healed lesions had a smaller depth (mean: 7.15 mm) than non-healed lesions (mean: 8.1 mm) among those treated with the conventional approach, whereas Kim et al. (Kim et al., 2016) indicated that the depth of the defect had no effect on healing.

Evaluating the height of the defect had a significant effect on healing among the studied population. This was in contrary to the findings of Kim et al. and Von Arx et al. (Kim et al., 2016; von Arx et al., 2007).

When comparing the defect size critical measurements that influence the healing in conventional treatment and GTR, our data indicated that the conventional approach is effective in lesions with a depth up to 3 mm. Using the GTR approach may improve the healing in lesions ≥ 3 mm. The likelihood of complete or partial healing will decrease among patients treated with GTR in > 9 mm depth lesions. Similarly, there was a significant difference in healing between lesion height and treatment approaches. Conventional treatment is effective in lesions up to 3 mm in height. The probability of complete healing decreased with conventional treatment in lesions > 3 mm. Sites with 3–6 mm height may have higher complete healing rates when applying the GTR approach. Areas that showed > 6 mm height had a low healing probability even with GTR treatment. To the best of our knowledge, no study to date has examined the critical points for healing among the two treatment approaches.

In this study, the prognostic factors, such as tooth type (single or multi-rooted), arch position (maxilla or mandible), type of retrograde filling, presence of buccal or palatal bone perforation, and crestal bone level, which indicated apicomarginal communication, as well as the skills of the operator (resident or specialist/consultant), had no significant effect on healing regardless of the treatment type, in consistency with the findings of previous studies (Li et al., 2014; Shinbori et al., 2015).

However, our study had some limitations. First, it had a limited sample size and there was a possibility of attrition bias. Especially, although the sample size calculation indicated that 42 individuals were needed, only 33 participants were enrolled owing to the unavailability of the cases. As this study was based on voluntary participation, many patients refused to undergo the post-operative CBCT examination, specifically those with no signs and symptoms, even after explaining the benefice of such investigation. The additional radiation dose and the extra cost were other factors that prevented the patients from undergo post-operative CBCT examination; this can cause an underestimation of the effectiveness of the treatment provided. In addition, as this was a retrospective study, controlling all relevant variables was not possible and post-operative signs and symptoms were not evaluated.

Finally, this study was based solely on radiographic interpretation. In an attempt to mask the type of treatment, radiographic measures were taken prior to retrieving the data from the patients' files; however, the type of treatment provided can be identified based on CBCT appearance most of the time owing to the experience of the author in that field.

5. Conclusions

The GTR approach in isolated and apicomarginal periapical lesions seemed to result in significantly better healing rates than that of the conventional treatment. Further studies are needed to generalise our findings and overcome the shortage of this article. Clinical guidelines can be recommended based on the findings that conventional treatment is effective in periapical lesions with a depth and height of ≤ 3 mm and using the GTR approach has a higher probability of complete healing in lesions with a depth of 3–9 mm and height of 3–6 mm. Lesions with a periapical lesion deeper than 9 mm and a height of > 6 mm had a lower likelihood of healing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

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