Treatment effect of guided tissue regeneration on the horizontal and vertical components of furcation defects: A retrospective study

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One sentence summary: This study showed that guided tissue regeneration using an absorbable membrane with allogeneic bone graft improves tooth retention and clinical outcomes in furcation defects.

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Abstract

Background and Aim: Identifying factors affecting the treatment outcomes of guided tissue regeneration (GTR) in furcation defects is imperative in order to obtain predictable regeneration outcomes. The aims of this study were to evaluate the clinical outcomes and survival of furcation-involved teeth treated with GTR, and potential factors affecting the results.

Materials and methods: Furcation defects treated with GTR using an allogeneic cancellous bone graft and covered by an absorbable membrane with at least 1-year follow-up were selected. All data relative to the clinical outcomes were recorded. Analyses were conducted to evaluate the

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immediate (1-year post-op) clinical outcomes and the long-term (the last assessment time) survival of the treated teeth. The effect of variables on the 1-year post-op clinical attachment level (CAL) changes and the tooth survival were assessed via multi-level regression analyses and Cox Proportional-Hazards Models.

Results: Ninety-eight treated defects were selected. The average follow-up was 5.3 ± 4.3 years. At the 1-year post-surgical recall, 1.23 ± 1.48 mm CAL gain was observed ($p<0.05$). The 5- and 10-year survival rates of the treated teeth were 86.5% and 74.3%, respectively. The vertical component of the defect and the location of the furcation were significantly related to the post-surgical 1-year CAL gain, whereas membrane exposure significantly affected tooth survival.

Conclusion: Within the limitations of this study, data suggests GTR using allogeneic cancellous bone graft and absorbable collagen membrane to be a viable option for treating furcation-involved teeth if the defect morphology and the location of the defect are favorable.

Keywords

furcation defect, guided tissue regeneration, periodontitis, smoking, survival analysis

INTRODUCTION

Furcation involvement (FI) has been classified as one of the most important factors determining the complexity of periodontitis.[1] This can develop once the periodontal disease reaches the root separation area of a multirooted tooth.[2] If left untreated, the disease will disseminate in a horizontal pattern towards the interior part of the furcation,[3] as well as in a vertical pattern towards the apices of the roots,[4] rendering the maintenance of the teeth more challenging due to the unique anatomy of the area, that allows only limited access for cleaning.[5]

Several long-term studies have shown that there is a high risk of tooth loss when a furcation involved tooth is left untreated,[6] or even when periodontal maintenance is performed.[7] In particular, Nibali et al. found that the presence of FI increases the risk of tooth loss for molars undergoing periodontal maintenance by two folds (in a 15-year period).[8]

Several strategies have been proposed for the treatment of FI in teeth, including osseous resection, root amputation, tunneling and regeneration[9-12] to name a few. Among the regenerative procedures, guided tissue regeneration (GTR) using absorbable barrier membranes has shown improvements in CAL gain and probing depth (PD) reduction.[13-16] Furthermore, with the addition of bone graft more predictable outcomes have been demonstrated.[13, 17-20]

Studies looking at the predictability and prevalence of complications following GTR treatment in furcation defects are limited.[21-24] Although factors affecting the success of GTR in furcation defects have been examined previously,[25, 26] in-depth assessment of factors that may influence and predict the long-term treatment outcomes are still lacking.[17, 27-31]

Furthermore, most studies have evaluated the effect of regeneration in furcations only on the horizontal component and not on the vertical aspect of the furcation defect.[23, 29, 32, 33] The vertical component of furcation defect has been linked to the long-term survival of furcation-involved teeth.[7, 34]

Therefore, the aims of this study were to evaluate the clinical outcomes and survival of furcation-involved teeth treated with GTR, and to evaluate potential factors affecting the results. Specifically, the following study aims were examined: 1) the immediate short-term (1-year) clinical outcomes, 2) the long-term survival of the treated teeth, 3) the factors influencing both the immediate treatment outcomes, and the long-term survival of the treated dentition, and 4) the impact of GTR on the horizontal as well as the vertical components of the furcation defect.

2.MATERIALS AND METHODS

2.1. Study design

The current investigation was designed according to the principles presented in the Helsinki Declaration of 1975, as revised in 2000 for biomedical research involving human patients. The study was approved by the Institutional Review Board for Human Studies, School of Dentistry, University of Michigan, Ann Arbor, MI, (HUM00154408) to be conducted at the Department of Periodontology within the same institution.

This retrospective cohort study selected all patients that had undergone treatment for furcation defects with GTR using an allogeneic cancellous bone graft then covered with an absorbable membrane in the time period between January 1980 and December 2017 at the School of Dentistry, University of Michigan, Ann Arbor, MI. All paper files and digital charts of patients treated with GTR were carefully scanned and analyzed by two independent and pre-calibrated investigators (JM, SB). At every stage, after examining the gathered data, in case of a disagreement, discussion was held by the two reviewers to reach consensus. If resolution was not possible, a third investigator (LT) or a senior author (HLW) was consulted and his decision was decisive. As no patients were treated as a direct result of this research, the study required no additional informed consent for the included patients. Furthermore, all patient data and charts were anonymized since the data were retrieved without any identifiable information.

2.2. Inclusion criteria

(1) A patient who had previously received GTR therapy for at least one furcation defect on either a first or second molar.

(2) Prior to the GTR procedure, all individuals must have previously received a comprehensive periodontal treatment (including oral hygiene instructions, scaling/root planing, prophylaxis, etc.).

(3) GTR procedures must have included utilization of an allogeneic cancellous bone graft then covered with an absorbable membrane

(4) Patient records must have had at least 1-year of follow-up following the GTR procedure.

(5) Patients charts should have contained complete clinical data including radiographs at baseline (pre-surgical stage) and at 1 year after the surgical procedure.

2.3. Exclusion criteria

(1) Patients without a post-surgical follow-up data reaching 12 months.

(2) The use of barrier membranes for procedures other than GTR (such as sinus lift, guided bone regeneration, socket augmentation, etc.).

(3) GTR procedures in non-furcation associated defects (such as pure infrabony defects).

(4) The sole use of bone graft without utilization of a barrier membrane, or the utilization of a membrane without placement of a bone graft material.

(5) Placement of a non-resorbable membrane.

(6) A medically compromised patients or those taking medications that are known to interfere with the normal healing response process (e.g., bisphosphonates, anti-cancer therapy, etc.).

2.4. Data collection and Classification

The following information were obtained for all qualified patients**: 1)** patient related factors (such as age, gender, etc.) **; 2)** medical history (including documentation of smoking, diabetes, other systemic or local diseases); **3)** location of the treated defect (mandible/maxilla – buccal/lingual, mid-facial/mesio-palatal/disto-palatal); **4)** clinical parameters of the furcation defect: probing depth (PD), gingival recession (REC), clinical attachment level (CAL) and horizontal FI ; **5)** occurrence of post-surgical complications (such as membrane exposure); **6)** follow-up time (until tooth extraction or last maintenance appointment); **7)** frequency of maintenance appointments throughout the entire follow-up; and **8)** baseline and 1-year post-surgical patient radiographs.

2.5. Study outcomes

The study outcomes of the present project were three folds:

2.5.1 Clinical outcomes of GTR

The changes in the clinical parameters (PD, CAL, REC) were compared from baseline (pre-surgical treatment) to the 1-year post-surgical appointment. Additionally, the influence of other recorded variables was assessed on the CAL outcomes obtained 1 year following the GTR procedure.

2.5.2 Survival

The survival of all treated teeth was assessed according to the Kaplan-Meier analysis. The final follow-up of any treated tooth was the last recorded appointment at the University of Michigan,

School of Dentistry. A tooth was considered lost if it was extracted due to periodontal reasons. If a tooth was extracted for any other reason (decayed, fractured, endodontic or prosthodontic reasons), this tooth was excluded from the analysis. Additionally, the effect of the recorded variables on the treated teeth were assessed for their potential effect on tooth retention/survival.

2.5.3 The effect of GTR on the vertical and horizontal components of furcation defects

The vertical furcation subclassification was determined from peri-apical radiographs that were collected at baseline and 1-year following the surgery according to Tonetti 2017.[34] Briefly, the vertical component was calculated based on the amount of bone loss in the furcation defect, subclass A was designated when bone loss reached the coronal third (≤33%) of the furcation region, subclass B was when the bone loss reached the middle third (33%–67%) of the furcation region and subclass C was assigned when the bone loss reached the apical third (≥67%) of the furcation region.[4, 7, 21, 34] When multiple root areas of a single tooth were involved, the area with the greatest vertical component was used to determine the subclass of the tooth.[34] The values obtained at baseline were then compared to the values obtained from radiographs taken at the 1-year post-op follow-up (Fig. 1).

The horizontal subclassification of the furcation was based on assessment with the use of a Naber's probe†*, as extracted from clinical records.[3] Briefly, this was measured based on a horizontal probe penetration in the furcation region of a multirooted tooth; degree 0 was assigned when there was no probable horizontal furcation involvement; degree 1 was assigned when the horizontal loss of periodontal tissue support was less than 3 mm; degree 2 was assigned when there was a horizontal loss of support that had exceeded 3 mm but not the total width of the furcation area; and degree 3 was assigned when a horizontal through-and-through destruction of the periodontal tissue in the furcation area had been observed.[3] The values obtained at baseline were then compared to the values obtained at the 1-year post-surgical recall.

2.6. Data management and statistical analysis

The collected data were entered into prefabricated spread sheets. Descriptive statistics were used for presenting the retrieved data at baseline as means ± standard deviations (SD), and range.

The treated furcation defects served as the unit of analysis. The changes in clinical parameters from baseline to the 1-year outcome were assessed with dependent t-tests. Mixed-effects Uni- and Multi-level Regression analyses were performed to identify prognostic factors for CAL gain at the 1-year post-surgical appointment. Kaplan-Meier survival probabilities were calculated, and the curves were subsequently plotted. Multi-variate Cox Proportional Hazard models were used for assessing correlations between independent variables and tooth loss, accounting for the fact that an individual may have attributed to multiple treated furcation defects (shared frailty was accounted for by including random effects). Step-wise regression analyses were performed using likelihood ratio tests, with variables presenting a *p* value of <0.05 in the initial univariate analysis. Exponentiated regression coefficients (Hazard ratios) and corresponding 95% confidence intervals (CI) were produced, and a *p* value threshold of 0.05 was set for the statistical significance. All analyses were performed by an author with experience in biostatistics (SB) using Rstudio[†], the survminer,[35] survival,[36] and ggplot2[37] packages.

3.RESULTS

3.1. Study population

A total of 83 patients [(45 Males and 38 females), mean age of 52.5 ± 13.8 (16 - 79) years] with 98 GTR-treated furcation defects were included in this study (see Supplementary Figure S1 in online Journal of Periodontology). In all GTR procedures, the combination of an allograft material and a collagen membrane was used. The utilized bone grafts were all allogeneic cancellous in nature either Freeze-dried bone allograft[‡] (in 23 defects), or Solvent-dehydrated bone allograft[§] (in 75 defects). The utilized membranes were of two types, both collagenous in nature: one type[**] in 86 defects, and another type[††] in 12 cases. The mean follow-up for the selected cases was 5.29 ± 4.3 years. The average maintenance visits for the included patients was 2.11 ± 1.08 times per year (range: 1 - 4). Table 1 presents details on the characteristics of the selected patients.

3.2. Clinical outcomes of GTR

At baseline, 55.10% of sites presented with BOP, a mean PD of 3.14 ± 0.94 mm, REC of 1.21 ± 0.76 mm, and CAL of 4.36 ± 1.13 mm. At the 1-year post-surgical recall, the BOP dropped to 28.57%,

an average of 1.35 ± 1.43 mm PD reduction and 1.23 ± 1.48 mm of CAL gain were observed, changes that were all statistically significant (p<0.001). In addition, an increase of 0.16 ± 1.13 mm in REC was also observed; however, this change lacked statistical significance (p=0.18).

Univariate analyses demonstrated a significant correlation with smoking (-0.77 (95% CI [-1.5, -0.04], p=0.03)), and post-op membrane exposure (-0.98 (95% CI [-1.88, -0.08], p=0.03)), to lower amounts of CAL gain. In addition, when cases with furcation defects of subclass B and C were combined (B + C), a significantly less amount of CAL gain was observed, compared to teeth with subclass A (-1.59 (95% CI [-2.23, -0.95], p<0.001)). Finally, when regeneration attempts were performed in the buccal furcation defects of mandibular molars a higher CAL gain was noted compared to the lingual furcation defects of mandibular molars (-1.20 (95% CI [-2.11, -0.30], p=0.01)), the buccal (-1.51 (95% CI [-2.5, 0.51], p=0.003)), the mesio-palatal (-1.76 (95% CI [-2.82, -0.70], p=0.001)), and the disto-palatal (-1.66 (95% CI [-3.02, -0.30], p=0.01)) furcations of the maxillary molars.

The multivariate analysis including the above mentioned statistically significant variables displayed that, vertical subclassification of B + C compared to A (-1.43 (95% CI [-2.12, -0.76], p<0.001)), as well as GTR in the buccal (-1.55 (95% CI [-2.41, -0.69], p<0.001)), mesio-palatal (-1.01 (95% CI [-1.98, -0.05], p=0.03)), and disto-palatal (-1.40 (95% CI [-2.65, -0.14], p=0.02)) furcations of maxillary molar were significantly associated with lower CAL gain at 1 year when compared to the buccal furcation of the mandibular molar. Lastly, gender, age, diabetes, previous endodontic treatment, initial PD, initial CAL, and the horizontal component of the furcation defect were not found to statistically significant in relation to observed CAL gain at the 1-year recall (p>0.05). Table 2 depicts the results of these regression models in detail.

3.3. Survival analysis

From baseline until the final gathered follow-up appointment (5.29 ± 4.3 years), 12 teeth in 11 patients were lost. The 5- and 10-year survival rates were 86.5% and 74.3%, respectively. Figure 2 demonstrates the survival curves of the treated molars, with the respective number of followed

molars, and the life table analysis presents the number of followed, censored, and extracted teeth at the respective timepoints (see Supplementary Table S1 in online Journal of Periodontology).

Univariate analyses showed that the occurrence of membrane exposure significantly affected the survival of the GTR-treated molars (5.14 (95% CI [1.65, 16], p=0.005)). The frequency of maintenance appointment was also significantly and inversely correlated to tooth loss, (0.28 (95% CI [0.12, 0.65], p=0.003)). In addition, teeth that presented with higher levels of initial attachment loss displayed lower survival rates (1.81 (95% CI [1.02, 3.22], p=0.04)). When the effect of the horizontal component was evaluated 1 year after the GTR surgery, it was shown that teeth with degrees 2 and 3, presented with lower survival rates compared with teeth that had non-probable FI (12.27 (95% CI [1.47, 102.6], p=0.02)), and 24.15 (95% CI [2.73, 213.3], p=0.004)), respectively. However, teeth with degree 1 were not statistically different in terms of survival than teeth with non-probable FI. Regarding the vertical component of the defect, it was observed that the baseline subclass for all teeth that were lost remained the same 1 year after the treatment, and was significantly associated to lower survival rates in subclass B + C defects, when furcation subclass A served as the reference (3.84 (95% CI [1.03, 14.28], p=0.04)). Membrane exposure however was the only factor that maintained its significance in the multi-variate model (7.77 (95% CI [1.4, 43.14], p= 0.01)).

Factors such as gender, age, smoking, diabetes, endodontic treatment, initial PD and the location of the treated furcations were not statistically associated to the survival of the treated teeth (Table 3).

3.4. Effect of the site topography of the furcation defect on regeneration

3.4.1. Effect of the vertical component of the furcation defect on regeneration

Out of 98 treated teeth that presented, at baseline, 61 were classified as subclass A, 30 as subclass B and 7 as subclass C (Table 4). One-year following the GTR treatment, 44.3% of the teeth that presented with subclass A had no detectable FI (as assessed with peri-apical radiographs), 47.5% remained subclass A, and 8.2% became subclass B. Teeth that presented with subclass B majorly remained the same (63.3%), however some teeth improved to subclass A (20%), and other become undetectable on peri-apical radiographs (6.7%) and 10% worsened to a subclass C. When GTR was

attempted in subclass C, out of the 7 treated teeth, 6 remained subclass C while only one improved to become subclass B.

3.4.2. Effect of the horizontal component on regeneration of the furcation defect

Overall, GTR was attempted on 29 degree 1, 65 degree 2, and, 4 degree 3 defects (Table 3). One year after the surgery out of the defects that presented with degree 1, 37.9% did not have a probable furcation, 41.4% remained degree 1, 13.8% became degree 2, and 6.9% worsened to degree 3. It was also found that 1 year after the surgery, in degree 2 defects, 63.1% did not exhibit a probable furcation, 10.8% improved to degree 1, 20.0% remained degree 2 and 6.1% worsened to degree 3. When GTR was attempted in degree 3 furcation defects, out of 4 defects, 3 remained degree 3 and 1 showed moderate improvement by becoming degree 2.

3.4.3. Membrane exposure

In total, membrane exposure occurred in 15 treated teeth, out of which 3 had been classified as degree I, 11 had been classified as degree II and one was classified as having a degree III horizontal furcation involvement. Regarding the location of the treated defect, membrane exposure had occurred on the buccal and lingual of 3, and 5 defects of mandibular molars, respectively, and 3 buccal, 2 disto-palatal and 2 mesio-palatal furcation defects in the maxillary molars.

4. DISCUSSION

The main outcome of the present study was the survival of furcation-involved molars that had been treated with GTR. FI has been widely established as a risk factor for tooth loss.[38-42].Results from this study found survival rates of 86.5% and 74.3% for molars treated with an allogeneic cancellous bone graft and a collagen membrane at 5, and 10 years, respectively. It is important to highlight that most of the studies evaluating the survival of FI teeth treated with GTR had only included molars with degree 2 furcation defects.[28-30, 43-45] Eickholz and colleagues, when evaluating the long-term outcomes of GTR treatment in FI teeth over a period of 10 years, found that 2 out of 18 teeth were lost leading to 83.3% survival rate at 10 years.[43] Our analyses however, consisted of furcation defects with diverse horizontal (degree 1, 2 and 3)[3] and vertical (subclass A, B and C)[34] components. Therefore, an exact and direct comparison of our results to previous studies may not be feasible. In

the current study, when factors affecting the survival rate were evaluated, membrane exposure was shown to be of utmost importance, affecting the long-term maintenance of the treated dentition. In fact, 50% of all extracted teeth in this study had experienced this complication. A major reason associated to the occurrence of this complication in furcation defects is the location of the bone at the mesial and distal aspects of the tooth. It has been suggested that when the furcation defect is a keyhole defect (where interproximal bone is coronal to the furcation fornix), coronal positioning of the flap would allow adequate coverage and stabilization of the barrier membrane.[21, 24, 46]

Regarding the clinical parameters, a statistically significant CAL gain of 1.23 ± 1.48 mm was achieved one year after the procedure. This finding is in line with a prospective study reporting on treatment of 86 furcation defects, where on average 1.33 mm of CAL gain was achieved 1 year after GTR treatment with expanded polytetrafluoroethylene membranes combined with an allograft.[25] Additionally, in a split-mouth randomized clinical trial Wang et al observed 1.67 ± 0.22 mm of CAL gain at 1 year, using collagen membranes alone for the treatment of mandibular molars with degree 2 FI.[45] Whether this CAL gain is clinically superior to the CAL gain obtained after open flap debridement surgery [47] remains debatable; In fact, in a systematic review with meta-analysis, Graziani and colleagues reported that open flap debridement in the treatment of degree 2 furcation involvement resulted in 0.55 mm CAL gain. [47]

We found that the location of the treated furcation defect was shown to be highly associated with CAL gain at 1 year (Table 4). It was observed that compared to the buccal furcation of mandibular molars, the mid-facial, disto-palatal and mesio-palatal furcations of upper molars were significantly associated with lower levels of CAL gain. Whereas, no significant difference was observed when comparing the buccal and the lingual furcations of mandibular molars. This could be attributed to the fact that the distance from the CEJ to the furcation entrance is typically larger in maxillary molars and that the anatomy in the mandibular molar furcation is more contained.[5, 48, 49]

So far, the effect of the anatomical topography of the furcation defect has mostly been based on the horizontal component of the defect. Agreements have been made on the hypothesis that periodontal regeneration in furcation defects seems to be predictable in degree 2 (Table 4) as well as degree 1 in certain scenarios.[17, 23] However, due to the heterogeneity in the studies with GTR

attempts in furcation defects, a strict strategy leading to a predictable outcome when treating different types of furcation defects may not be feasible.[17, 23] In the present study, 1-year following the GTR surgery, an undetectable FI (degree 0) was reported in 37% of the defects that had presented with degree 1 at baseline, 63% which had presented with degree 2 at baseline and none of the 4 defects that were degree 3 at initial evaluation. Our results show that GTR is indeed most predictable in degree 2 furcation defects. This could be attributed to the containment of the space in degree 2 furcation involvement, where more than 3 mm of horizontal space is available to contain the bone graft that is packed against a bony wall, and then covered with a membrane. This type of defects would provide a high level of stability.[50] In addition, 11% of the remaining defects that presented with a degree 2 FI improved to a degree 1 furcation defect and molars with degree I FI have been shown to have a better long-term prognosis than molars with degree II defects.[51, 52] In fact, our study confirmed that degree 1 FI teeth do not have a higher chance of tooth loss than teeth with non-probable FI. Nonetheless, our results still support that a considerable amount of degree 1 FI could benefit from GTR. Finally, in agreement with the literature,[21, 27, 53] as the 4 degree 3 FI defects included in this study did not show any benefit from GTR. This implies for management of degree 3 FI, other treatment options such as extraction, alveolar ridge preservation and implant placement might be considered. [54-56]

The importance of the vertical component of furcation defect has been highlighted recently. In a retrospective study, Tonetti et al.[34] evaluated 200 subjects having molars with degree II defects with different subclasses (A, B and C). The included subjects were only undergoing periodontal maintenance due to an unfavorable cost-effectiveness profile. They found that the 10-year survival rate for molars with subclass A was 91%, for subclass B it was 67%, and for subclass C they found it to be 23%. They concluded that the subclass seems to be a viable predictor of survival of degree 2 FI molars.[34] Similarly, in another publication with a larger sample size (633 FI molars with periodontal maintenance for at least 5 years) that had included teeth having a diverse horizontal and vertical defect components, Nibali and co-workers found that that FI molars were 5 times more likely to be lost than teeth without FI, and that the vertical component significantly increased the risk of tooth loss.[7] Thus, the vertical defect component is a critical aspect as this could broaden the indication for regeneration in furcation defects, as improvement in the vertical component could enhance the

longevity of the treated tooth, regardless of obtaining a complete furcation closure.[34] In fact, Cortellini et al[21] recently evaluated the effect of papilla preservation flaps with the use of enamel matrix derivatives in severely compromised molars by a combination of furcation and infrabony defects on the vertical component of the furcation defect. The authors found that the vertical sub-classification improved 1-year after periodontal regenerative surgery in over 84% of the treated molars.[21] In our study, the subclass of the included FI teeth was evaluated at baseline and 1-year after the GTR procedure, aiming to evaluate the effect of GTR on the vertical component. Teeth that presented originally with type A furcation defects, were re-evaluated after 1 year, and it was observed that 91.8% of these defects either had no detectable vertical component on peri-apical radiographs or remained with furcation type A (44.3%, and 47.5%, respectively). Additionally, only 8.2% declined to type B and none became type C. The majority of the teeth that had presented with type B FI at baseline, remained type B (63.3 %), with some improving (26.7 %) while others worsening (10 %). Finally, 7 teeth presented with type C at baseline, and almost no improvement was noticed in these cases. Therefore, it seems that GTR is the most predictable in furcation defects with vertical subclassification A. Thus, understanding the 3-dimensional anatomy of the furcation defect is fundamental in order to establish the correct treatment suggestion for this specific defect.

Limitations

Among the limitations of this study are the retrospective nature of this project, such as lack of a control group for comparison of GTR with other treatment options for furcation defects, and absence of standardization protocols for the radiographic assessment which would have increased the reliability and precision of our measurements. Additionally, the unequal and relatively reduced sample size of the defects, particularly in some of the subclassifications, may limit the ability to generalize our results. Furthermore, although the change in the incidence of bleeding on probing provides a general idea about the oral hygiene of the patients,[57, 58] full-mouth bleeding and local plaque scores were not available to evaluate the influence of oral hygiene status on the outcomes of GTR. Lastly, it would have been beneficial to have had access to treatment of furcation involved teeth with non-regenerative approaches (i.e. open flap debridement) to provide a direct comparison to regeneration therapy. Future studies in this area are strongly encouraged.

CONCLUSION

Within the limitations of the present study, the following conclusions could be drawn: i) GTR with the use of an allogeneic cancellous bone graft and then covered with a collagen membrane is a viable treatment for the management of teeth with furcation defects; ii) Membrane exposure, the vertical component of furcation, and the location of the furcation defect significantly affects the outcomes of GTR.

Conflict of interest

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper.

Conflict of interest and source of funding

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Author Contributions

J. Majzoub, contributed to conception, design, data acquisition, and interpretation, drafted and critically revised the manuscript;

S. Barootchi, contributed to conception, design, data acquisition, statistical analysis, drafted and critically revised the manuscript;

L. Tavelli, contributed to conception, design, data acquisition, and interpretation, drafted and critically revised the manuscript;

C-W Wang, contributed to data interpretation, critically revised the manuscript;

S. Travan, contributed to data interpretation, critically revised the manuscript;

H.L. Wang, contributed to conception and design, data interpretation and critically revised the manuscript.

All authors gave final approval and agree to be accountable for all aspects of the work.

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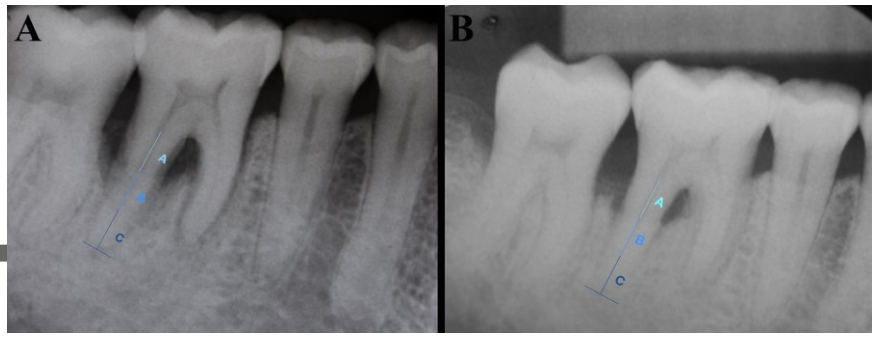

FIGURE 1 Radiographic evaluation of an included furcation defect at (A) baseline, and (B) 1-year post-surgical re-evaluation showing the enhancement of radiographic bone support from the apical (subclass C) third, to the middle (subclass B) third of the root length

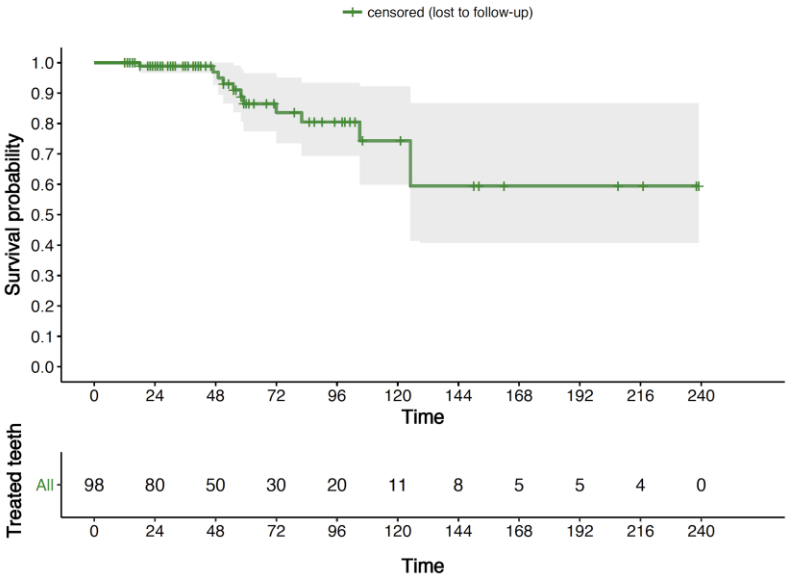

FIGURE 2 Kaplan-Meier survival curve for the entire follow-up period. Each event represents a tooth loss. The grayish hue represents the upper and lower limit of the 95% confidence bands

TABLE 1 Characteristics of the included patients/defects at baseline

Characteristic	**Frequency**
Subject level data	
Males (N, %)	45, 54.2%
Age	52.5 ± 13.9
Diabetics (N, %)	4, 4.82%
Smoker (N, %)	17, 44.57 %
Stage 3 grade A Periodontitis[1] (N, %)	17, 20.48%
Stage 3 grade B Periodontitis[1] (N, %)	23, 27.71%
Stage 3 grade C Periodontitis[1] (N, %)	27, 32.53%
Stage 4 grade A Periodontitis[1] (N, %)	2, 2.41%
Stage 4 grade B Periodontitis[1] (N, %)	7, 8.43%
Stage 4 grade C Periodontitis[1] (N, %)	7, 8.43%
Tooth level data	
Maxilla (N, %)	41, 41.84%
Mandible (N, %)	57, 58.16%
Endodontically treated (N, %)	12, 12.24%
Clinical attachment level [CAL (mm)]	4.36 ± 1.12 mm
Pocket depth [PD (mm)]	3.14 ± 0.94 mm
Recession [REC (mm)]	1.21 ± 0.76 mm

Data are expressed as mean ± standard deviation; or N, numbers, percentages

TABLE 2 Results of the regression models evaluating the effect of different variables on the CALs of the treated defects at the 1-year recall

Variable		Univariate analysis				Multivariate analysis			
		Estimate	Std. Error	95% CI	*p*-value	Estimate	Std. Error	95% CI	*p*-value
Gender (Male)		0.24	0.38	-0.52, 0.99	0.54				
Age		-0.002	0.01	-0.03, 0.03	0.89				
Smoking		**-0.77**	**0.36**	**-1.5, -0.04**	**0.03**	-0.18	0.32	-0.83, 3.39	0.58
Diabetes		-0.95	0.88	-2.71, 0.81	0.28				
Membrane exposure		**-0.98**	**0.45**	**-1.88, -0.08**	**0.03**	-0.28	0.38	-1.05, 0.49	0.46
Endodontic treatment		-0.13	0.57	-1.27, 1.01	0.82				
Initial PD		0.09	0.20	-0.31, 0.49	0.66				
Initial CAL		0.20	0.17	-0.14, 0.53	0.24				
Horizontal component (Hamp 1975) – ref: none									
	degree 2	-0.684	0.41	-1.51, 0.14	0.1				
	degree 3	-0.184	0.81	-1.81, 1.44	0.82				
Vertical component (Tarnow and Fletcher 1984) – ref: class A									
	vertical B + C	**-1.59**	**0.32**	**-2.23, -0.95**	**<0.001**	**-1.43**	**0.34**	**-2.12, -0.76**	**<0.001**
Furcation location (ref: Buccal Lower)									
upper mid-facial		**-1.51**	**0.50**	**-2.5, -0.51**	**0.003**	**-1.55**	**0.43**	**-2.41, -0.69**	**<0.001**
disto-palatal		**-1.66**	**0.68**	**-3.02, -0.30**	**0.01**	**-1.40**	**0.63**	**-2.65, -0.14**	**0.02**
lower lingual		**-1.20**	**0.45**	**-2.11, -0.30**	**0.01**	-0.73	0.41	-1.54, 0.08	0.08

mesio-Palatal	**-1.76**	**0.53**	**-2.82, -0.70**	**0.001**	**-1.01**	**0.48**	**-1.98, -0.05**	**0.03**

Bold signifies statistical significance; CI, confidence intervals

TABLE 3 Results of the multilevel cox proportional hazard models evaluating the effect of different variables on the survival of the treated teeth

Variable		Univariate analysis				Multivariate analysis			
		HR	Std. Error	95% CI	*p*-value	HR	Std. Error	95% CI	*p*-value
Gender (Male)		0.7	0.60	0.22, 2.26	0.55				
Age		1.02	0.02	0.97, 1.07	0.4				
Smoking		2.04	0.68	0.54, 7.71	0.29				
Diabetes		0.000001	10180	0, Inf	0.99				
Membrane exposure		**5.14**	**0.58**	**1.65, 16**	**0.005**	**7.77**	**0.87**	**1.40, 43.14**	**0.01**
Maintenance/year		**0.28**	**0.43**	**0.12, 0.65**	**0.003**	0.33	0.80	0.07, 1.56	0.16
Endodontic treatment		2.18	0.78	0.47, 9.99	0.32				
Initial PD		1.41	0.47	0.56, 3.54	0.47				
Initial CAL		**1.81**	**0.30**	**1.02, 3.22**	**0.04**	1.58	0.33	0.83, 3.02	0.16
Horizontal component (Hamp 1975) – ref: none									
	Hamp degree 1	0.000001	10390	0, Inf	0.99				
	hamp degree 2	**12.27**	**1.084**	**1.47, 102.6**	**0.02**	1.26	1.18	0.13, 12.73	0.84
	hamp degree 3	**24.15**	**1.112**	**2.73, 213.3**	**0.004**	4.12	1.47	0.23, 73.72	0.37

Vertical component (Tarnow and fletcher 1984) – ref: Class A									
	vertical B + C	**3.84**	**0.67**	**1.03, 14.28**	**0.04**	3.79	1.09	0.45, 32.04	0.22
Furcation location (ref: lower buccal)									
upper buccal		2.63	1.00	0.37, 18.73	0.33				
disto-palatal		3.10	1.012	0.43, 22.55	0.26				
lower lingual		2.23	0.87	0.41, 12.18	0.36				
mesio-Palatal		2.45	1.00	0.35, 17.47	0.37				

Bold signifies statistical significance; HR, hazard ratio; CI, confidence intervals

TABLE 4 Characteristics of the treated furcation defects

Furcation site	Furcation location		Total	Tooth loss (%)	CAL gain (mm)	
	Buccal furcation of mandibular molars		31 (100)	5 (16.1)	2.35 ± 1.65	
	Lingual furcation of mandibular molars		24 (100)	8 (33.3)	1 ± 1.03	
	Mid-facial furcation of maxillary molars		16 (100)	3 (18.75)	0.75 ± 1.42	
	Mesio-palatal furcation of maxillary molars		13 (100)	5 (38.46)	0.5 ± 1.17	
	Disto-palatal furcation of maxillary molars		10 (100)	4 (40)	0.5 ± 1.73	
			Post-op Vertical classification			
Pre-op Vertical classification	Subclass	Total	None	A	B	C
	A	61 (100)	27 (44.3)	29 (47.5)	5 (8.2)	0 (0)
	B	30 (100)	2 (6.7)	6 (20)	19 (63.3)	3 (10)
	C	7 (100)	0 (0)	0 (0)	1 (14.3)	6 (85.7)
			Post-op Horizontal classification			
Pre-op Horizontal classification	Degree	Total	0	1	2	3
	1	29 (100)	11 (37.9)	12 (41.4)	4 (13.8)	2 (6.9)
	2	65 (100)	41 (63.1)	7 (10.8)	13 (20)	4 (6.1)

	3	4 (100)	0 (0)	0 (0)	1 (25)	3 (75)

[*] Hu-Friedy Mfg. Co. Inc.
[†] Rstudio Version 1.1.383, RStudio, Inc., Boston, Massachusetts, USA
[‡] Salvin Dental Specialties, Charlotte, NC, USA
[§] Puros, Zimmer Biomet, Carlsbad, CA, USA
[**] BioMend, Zimmer BioMet, Carlsbad, CA, USA
[††] Bio-Gide, Geistlich Pharma, Wolhusen, Switzerland