Furcation Therapy with Bioabsorbable Collagen Membrane: A Clinical Trial

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Abstract

This study compared the effectiveness of 2 barrier membranes, expanded polytetrafluoroethylene (e-PTFE) and collagen, in treating Class II furcation defects of mandibular molars in humans. Seventeen nonsmoking subjects with no history of systemic disease each presenting with Class II furcation defects in 2 mandibular molars were selected and underwent initial therapy. At the time of the surgery and at 8-month follow-up, soft-tissue measurements consisting of the gingival index, vertical and horizontal probing depth, recession and clinical attachment level were obtained at the midfurcation level. At the time of membrane placement and at 12-month re-entry, horizontal midfurcation probing depth and hard-tissue measurement of vertical fill (from the crown to the depth of the pocket) were also obtained. According to the surgical protocol, both membranes were completely covered with a coronally positioned flap, and in all cases healing was uneventful. Data were analyzed first by comparing baseline measurements (at surgery) with measurements at 8-month follow-up and 12-month re-entry for both e-PTFE and collagen membranes according to repeated-measures analysis of variance. The changes from surgery to follow-up and re-entry were then compared between the 2 treatment modalities with paired Wilcoxon rank-sum tests. No statistically significant differences were found between e-PTFE and collagen membranes with respect to gingival index, reduction in probing depth, gain in clinical attachment or filling of the horizontal defect. However, the improvement in vertical fill at 12-month re-entry was more substantial for the teeth treated with collagen membrane than those treated with e-PTFE ($p < 0.05$). Within the limits of this study, it appears that collagen is a beneficial material for regenerative therapy of Class II furcation defects in humans, yielding results that are similar to or better than (vertical fill) those for e-PTFE membrane.

MeSH Key Words: *collagen/metabolism; furcation defects/surgery; guided tissue regeneration/methods*

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Treatment of furcation lesions is one of the most challenging tasks in periodontal therapy today. The anatomical features of the furcation area, which include numerous small ridges, peaks and pits forming convexities and concavities,[1–3] offer limited access for routine periodontal debridement. The presence of accessory canals in the furcation region (the actual furcation area plus 4 mm apically on the internal aspect of the root surfaces) in up to 25% of permanent molars,[4] as well as the presence of enamel projections in 29% of mandibular and 17% of maxillary molars,[5] further complicates the management of furcation invasions.

Attempts to treat inaccessible furcation lesions have led to therapies ranging from surgical flap debridement to root resection and hemisection and, more recently, regenerative therapy. Surgical access significantly enhances removal of calculus from molars with furcation invasion; however, in most cases residual calculus has been detected even after open-flap surgery,[6] and there is clinically significant loss of attachment within the furcation area during at least the first 2 years of maintenance care.[7] Root resection combined with conservative root canal preparation and use of the remaining root(s) as bridge abutments was successful in up to 70% of cases over a 10-year period, with most failures occurring within 5 years of the resection procedure and involving

catastrophic root fracture leading to loss of the bridge.[8,9] Therefore, it is generally believed that root resection should be carried out only on teeth with large roots and that it should be combined with conservative access and canal preparation, along with optimal periodontal maintenance and judicious prosthetic rehabilitation to minimize failure.[10]

Class II furcation lesions have traditionally been treated by closed scaling or resection techniques, but over the past decade, guided tissue regeneration (GTR) has become more common. GTR involves first a periodontal flap surgical procedure, followed by the creation of an environment that allows the cells from the periodontal ligament to repopulate the debrided root surface and form a new periodontal attachment. The rationale for GTR is to exclude gingival epithelium and connective tissue from the alveolar bone and root surfaces, thus creating areas into which progenitor cells from the periodontal ligament or alveolar bone (or both) can migrate.[11–13] The GTR technique has many indications in periodontal therapy, among the most important being treatment of Class II furcation lesions in molars. It is well established that the efficacy of GTR procedures using expanded polytetrafluoroethylene (e-PTFE) membrane in treating Class II mandibular furcations is much better than that of debridement alone,[14–16] and human studies using e-PTFE membrane for the treatment of furcation defects have reported significant and predictable gains in new attachment.[16,17] However, during the postsurgical periodontal healing period, use of the e-PTFE barrier can lead to clinical complications such as acute or chronic inflammation and early membrane exposure,[18,19] and a second surgical procedure (to remove the membrane) 4 to 6 weeks after the initial procedure is always required. The use of a resorbable membrane eliminates the need for the second-stage surgery. The resorbable materials most commonly used in both animal studies and human clinical trials have been collagen, polyglycolic acid, polylactic acid and their copolymers.[20–26] For example, these materials have been used in the management of periodontal osseous defects, and collagen membranes have been successful in GTR studies in dogs, maintaining their integrity, preventing epithelial migration and supporting new connective tissue attachment in experimental defects.[21,22] Collagen is a natural protein that lends itself to GTR procedures because the body's own enzymes eventually break it down into its constituent amino acids. Type I collagen of bovine tendon origin has been effective in GTR procedures in animals and humans.[20–24]

The study reported here compared e-PTFE membranes with processed type I collagen from bovine tendon in GTR of periodontal Class II mandibular molar furcation defects over a 12-month healing interval, with clinical assessments at 8 months and re-entry at 12 months.

Materials and Methods

Seventeen nonsmoking subjects (8 women and 9 men), ranging in age from 35 to 75 years (mean ± standard deviation 56.5 ± 13.3 years) who were receiving periodontal care at the faculty of dentistry, University of Manitoba, Winnipeg, Manitoba, and who had no history of systemic disease participated in the study. The investigation was approved by the Committee on Ethics Involving Human Subjects of the University of Manitoba. Before acceptance into the study, each patient received a brief description of the investigation and provided signed informed consent.

Each subject had undergone initial periodontal therapy without occlusal adjustment (as such adjustment was not indicated in any of the cases) and had been re-evaluated at 6 to 8 weeks. The primary inclusion criterion for each subject was presence of 2 teeth with Class II mandibular first and second molar furcation defects. In 13 patients the affected teeth were contralateral, and in 4 patients the affected teeth were located on the same side of the mouth. Both teeth in each subject were treated by GTR, one with an e-PTFE membrane (standard Gore-Tex periodontal material; W.L. Gore & Associates Inc., Flagstaff, Arizona) and the other with a bioabsorbable collagen membrane (CollaTec Corporation, Plainsboro, New Jersey), with the type of membrane assigned randomly before surgery. There was no control group (i.e., no teeth underwent debridement only).

All measurements were completed by 2 experienced examiners (VKP and SCG). A simple classification system for assessing the severity of furcation was used.[27] Measurements before surgery consisted of the gingival index of Loe[28] and vertical probing depths relative to the gingival margin, horizontal probing depth, recession and clinical attachment level were obtained at the midfurcation level. After administration of adequate local anesthesia, full-thickness envelope flaps were raised buccally and lingually at least one tooth mesial and one tooth distal to the test tooth, and soft-tissue debridement and root planing were performed with hand instruments. No osteoplasty or ostectomy was performed. Hard-tissue measurements at the time of surgery consisted of horizontal probing depth and vertical depth from the occlusal surface of the crown to the base of the defect without an acrylic stent (determined with a manual periodontal probe, PCP UNC15 Hu-Friedy, Hu-Friedy Mfg. Co. Inc., Chicago, Illinois) and midfurcation horizontal probing depth from the tooth surface into the furcation from the buccal to the lingual direction (determined with a Nabers furcation colour-coded probe, Hu-Friedy Mfg. Co. Inc.).

The membrane for each tooth was trimmed to cover the furcal opening and overlap 3 to 4 mm over adjacent tooth and bone. The collagen membrane was held in place with chromic gut (4-0) sling sutures and the e-PTFE membrane

Table 1 **Vertical midfurcation measurements[a]**

	Mean measurement ± SD (mm)	
Variable	**e-PTFE**	**Collagen**
Pocket depth		
At surgery	4.53 ± 1.77	4.73 ± 1.16
At 8-month follow-up	3.60 ± 1.30	3.33 ± 0.90
At 12-month re-entry	3.47 ± 1.41	3.20 ± 0.94
Change from surgery to 8-month follow-up	0.93 ± 0.88	1.40 ± 0.98
Change from surgery to 12-month re-entry	1.12 ± 1.36	1.47 ± 1.01
Recession		
At surgery	1.87 ± 1.46	1.80 ± 1.42
At 8-month follow-up	2.33 ± 1.59	2.33 ± 1.84
At 12-month re-entry	2.73 ± 1.87	2.20 ± 1.74
Change from surgery to 8-month follow-up	–0.40 ± 1.18	–0.73 ± 1.03
Change from surgery to 12-month re-entry	–0.47 ± 1.18	–0.65 ± 1.32
Clinical attachment level		
At surgery	6.47 ± 2.33	6.33 ± 1.75
At 8-month follow-up	5.93 ± 1.79	5.67 ± 1.95
At 12-month re-entry	6.20 ± 2.14	5.40 ± 1.68
Change from surgery to 8-month follow-up	0.53 ± 1.64	0.67 ± 1.05
Change from surgery to 12-month re-entry	0.47 ± 1.81	1.00 ± 1.22
Vertical fill[b]		
At surgery	11.12 ± 2.19	11.62 ± 2.06
At 12-month re-entry	12.12 ± 2.42	10.81 ± 2.46
Change from surgery to 12-month re-entry	–1.00 ± 2.03	0.81 ± 1.80

SD = standard deviation, e-PTFE = expanded polytetrafluoroethylene

[a] *Two subjects missed the 8-month follow-up.*

[b] *Statistically significant difference between treatment groups* ($p < 0.05$)

Table 2 **Horizontal midfurcation measurements**

	Mean furcal score ± SD (mm)	
Time	**e-PTFE**	**Collagen**
At surgery	2.00 ± 0.00	2.00 ± 0.00
At 8-month follow-up[a]	1.60 ± 0.51	1.85 ± 0.36
At 12-month re-entry	1.60 ± 0.63	1.67 ± 0.62
Change from surgery to 8-month follow-up[a]	0.36 ± 0.50	0.14 ± 0.36
Change from surgery to 12-month re-entry	0.41 ± 0.62	0.41 ± 0.71

SD = standard deviation, e-PTFE = expanded polytetrafluoroethylene

[a] *Two subjects missed the 8-month follow-up.*

was sutured with Gore-Tex material. Finally, the flaps were positioned coronally over the membrane (either type) and closed with interrupted silk (4-0) sutures.

Periodontal dressing was placed and the subject was given a prescription for doxycycline (200 mg on the first day and 100 mg daily for the subsequent 13 days), oral analgesics as needed and 0.12% chlorhexidine rinse (twice daily for 4 weeks). Patients were seen for professional removal of supragingival plaque at 1, 2 and 4 weeks, and the e-PTFE membrane was removed 4 to 6 weeks after the initial surgery. All patients were seen every 3 months for periodontal maintenance.

Soft-tissue measurements were repeated at 8 months and a re-entry procedure was carried out at 12 months. At the time of re-entry, a vertical incision was used to raise a small flap at the surface of each treated tooth, and hard-tissue measurements were obtained. The decrease in probing depth, gain in clinical attachment level and increase in horizontal midfurcation attachment level (horizontal and vertical fill) were analyzed in 2 ways. First, comparisons were made individually for the 2 types of membrane between baseline (at surgery) and 8-month follow-up (soft-tissue measurements) and 12-month re-entry (soft- and hard-tissue measurements) according to repeated-measures analysis of variance. Second, the changes from surgery to follow-up and re-entry were compared between the 2 treatment modalities by means of paired Wilcoxon rank-sum tests.

Vertical and horizontal midfurcation measurements are presented in **Tables 1** and **2**, respectively. Pocket depths were measured from the gingival margin to the depth of the pocket, recession was measured from the cemento-enamel junction (CEJ) to the gingival margin, and clinical attachment levels were measured from CEJ to the depth of the pocket. Vertical fill (from the crown to the base of the defect) was measured in each subject at 12-month re-entry.

Table 3 **Mean gingival index scores (± SD), at the time of surgery, at 8-month follow-up and at 12-month re-entry**

Treatment	At surgery	8-month follow-up[a]	12-month re-entry
e-PTFE	0.20 ± 0.41	0.33 ± 0.72	0.20 ± 0.56
Collagen	0.33 ± 0.72	0.00 ± 0.00	0.13 ± 0.35

SD = standard deviation, e-PTFE = expanded polytetrafluoroethylene

[a] *Two subjects missed the 8-month follow-up.*

Results

Of the 17 subjects who completed the study, 2 missed the 8-month follow-up but were not excluded from the final analysis. The results were not analyzed according to buccal and lingual lesions because the experiment paired 2 available mandibular teeth in each patient, one tooth being treated with the e-PTFE membrane and the other with the collagen membrane. In 11 subjects, both defects were buccal, in 1 subject both were lingual, and 5 subjects had one buccal and one lingual defect.

The gingival health of the 2 groups of teeth, as measured by the gingival index, is shown in **Table 3**. A decline in the gingival index was observed for the teeth treated with collagen membrane, whereas the gingival index was consistent over the study period for the e-PTFE teeth. However, the difference between the 2 groups of teeth was not statistically significant.

Both treatments resulted in a significant decrease in probing depths from surgery to 8-month follow-up ($p < 0.01$) and from surgery to 12-month re-entry ($p < 0.005$), but the changes were not statistically different between the 2 groups of teeth. Recession increased equally for the 2 treatment groups from the time of the surgery and reached statistical significance ($p < 0.05$) at 12-month re-entry. Clinical attachment level, the composite of pocket depth and recession, remained fairly consistent within each treatment group over time and did not differ between the 2 treatment groups.

The mean measurement from the crown to the base of the defect (vertical fill), determined at baseline and re-entry, increased from 11.12 mm to 12.12 mm ($p < 0.005$) for the teeth treated with e-PTFE membrane, but decreased from 11.62 mm to 10.81 mm ($p < 0.05$) for the teeth treated with collagen; this difference between the 2 treatments was statistically significant ($p < 0.05$). Both treatment groups showed a decrease in horizontal measurements from surgery to 8 months ($p < 0.005$) and from surgery to re-entry ($p < 0.0005$), but there was no statistically significant difference between the 2 treatments.

Discussion

This study compared the effectiveness of a collagen membrane with that of the gold standard, e-PTFE membrane, in treating Class II mandibular molar furcation defects in humans. Our study did not include a control group receiving debridement only, because previous studies have shown the e-PTFE membrane is more effective than debridement alone.[14–16] We used type 1 collagen derived from bovine tendon. Type 1 collagen is the major structural protein in the periodontal ligament as well as most extracellular organic matrices and connective tissues throughout the body. The properties of collagen that favour its use as a biomaterial are numerous.[29–31] It is biodegradable and when implanted in the body is absorbed at a rate that can be controlled by the degree of cross-linking to which it is subjected.[30] As a membrane, it is semipermeable and is a good support for cell growth.[32] For all practical purposes, collagen is immunologically inert and safe.[26,33]

Researchers have compared the effectiveness of collagen membrane with a control procedure consisting of flap-approach curettage in treating Class II furcation defects. Statistically significant improvements in horizontal and vertical fill, relative to control, occurred over a 12-month period, whereas treatment with debridement alone afforded little or no improvement.[23,24,29] The results of the study reported here indicate the clinical effectiveness of bioabsorbable collagen membrane in achieving reduction in pocket depth, gain in attachment and horizontal filling of the defect over a 12-month period similar to what can be attained with e-PTFE membrane. Interestingly, significantly better vertical fill at 12-month re-entry was observed for the collagen membrane than for the e-PTFE membrane. With regard to vertical fill, we obtained different results from those obtained by Yukna and Yukna.[34] This difference could have resulted, in part, from the exposure of the e-PTFE membrane during the healing process, which might have accounted for the less encouraging results with this type of membrane in terms of vertical probing depths in our study. Conversely, the collagen membrane proved easy to use, it was biocompatible, and it resulted in no adverse healing in any of the patients.[26,33] Similar results were obtained by Blumenthal,[23] who reported that sites treated with a different collagen membrane gained vertical open-probing new attachment at 12-month re-entry. Our results also agree with those of Wang and others,[29] who demonstrated significant improvement at 12-month re-entry in terms of reduction of pocket depth, gain in attachment and

filling of horizontal defect. Similar findings were reported by Chung and others[35] in their 1-year study.

A limitation of this study was the small sample size, and this shortcoming might have some effect on the power and significance of the statistical analysis. Future investigations should involve a larger sample and longer follow-up time to determine the long-term effect of treatment with collagen membrane. In retrospect, it would have been helpful to use an acrylic stent and a more accurate measurement system amenable to photographic recording.

Within the limits of this study, the following conclusions can be drawn. No significant differences were observed between bioabsorbable collagen membrane and e-PTFE membrane in terms of reduction of pocket depth, gain in attachment gain or filling of horizontal defects over a 12-month period. Only partial closure of the furcations was observed, and the furcations appeared clinically healthy. From a statistical point of view, the results with collagen membrane appeared similar to or better than (vertical fill) those obtained with commercially available e-PTFE membrane. Mandibular molar furcations are easier to treat because there is much better access to these teeth than to the maxillary molars; therefore, these results probably do not apply to mesial and distal furcations. Because bioabsorbable collagen is a natural protein of the human body that is degraded by host enzymes, there is no need for second-stage retrieval surgery. The collagen membranes were easier to manipulate than the e-PTFE membranes and resulted in no adverse healing. Overall, treatment with barrier membranes improves Class II mandibular molar furcation defects in humans. After such treatment, teeth with questionable prognosis are more easily maintained. ◆

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References

1. Svardstrom G, Wennstrom JL. Furcation topography of the maxillary and mandibular first molars. *J Clin Periodontol* 1988; 15(5):271–5.

2. Gher ME, Vernino AR. Root morphology — clinical significance in pathogenesis and treatment of periodontal disease. *J Am Dent Assoc* 1980; 101(4):627–33.

3. Bower RC. Furcation morphology relative to periodontal treatment. Furcation root surface anatomy. *J Periodontol* 1979; 50(7):366–74.

4. Gutmann JL. Prevalence, location, and patency of accessory canals in the furcation region of permanent molars. *J Periodontol* 1978; 49(1):21–6.

5. Masters DH, Hoskins SW. Projection of cervical enamel into molar furcations. *J Periodontol* 1964; 35(1):49–53.

6. Fleischer HC, Mellonig JT, Brayer WK, Gray JL, Barnett JD. Scaling and root planing efficacy in multirooted teeth. *J Periodontol* 1989; 60(7):402–9.

7. Kalkwarf KL, Kaldahl WB, Patil KD. Evaluation of furcation region response to periodontal therapy. *J Periodontol* 1988; 59(12):794–804.

8. Buhler H. Evaluation of root-resected teeth. Results after 10 years. *J Periodontol* 1988; 59(12):805–10.

9. Langer B, Stein SD, Wagenberg B. An evaluation of root resections. A ten-year study. *J Periodontol* 1981; 52(12):719–22.

10. Erpenstein H. A 3-year study of hemisectioned molars. *J Clin Periodontol* 1983; 10(1):1–10.

11. Gottlow J, Nyman S, Karring T, Lindhe J. New attachment formation as the result of controlled tissue regeneration. *J Clin Periodontol* 1984; 11(8):494–503.

12. Aukhil I, Simpson DM, Suggs C, Pettersson E. In vivo differentiation of progenitor cells of the periodontal ligament. An experimental study using physical barriers. *J Clin Periodontol* 1986; 13(9):862–8.

13. Magnusson I, Nyman S, Karring T, Egelberg J. Connective tissue attachment formation following exclusion of gingival connective tissue and epithelium during healing. *J Periodontal Res* 1985; 20(2):201–8.

14. Lekovic V, Kenney EB, Kovacevic K, Carranza FA Jr. Evaluation of guided tissue regeneration in Class II furcation defects. A clinical re-entry study. *J Periodontol* 1989; 60(12):694–8.

15. Mellonig JT, Seamons BC, Gray JL, Towle HJ. Clinical evaluation of guided tissue regeneration in the treatment of grade II molar furcation invasions. *Int J Peridontics Restorative Dent* 1994; 14(3):254–71.

16. Pontoriero R, Lindhe J, Nyman S, Karring T, Rosenberg E, Sanavi F. Guided tissue regeneration in degree II furcation-involved mandibular molars. A clinical study. *J Clin Periodontol* 1988; 15(4):247–54.

17. Wallace SC, Gellin RG, Miller MC, Mishkin DJ. Guided tissue regeneration with and without decalcified freeze-dried bone in mandibular class II furcation invasions. *J Periodontol* 1994; 65(3):244–54.

18. Metzler DG, Seamons BC, Mellonig JT, Gher ME, Gray JL. Clinical evaluation of guided tissue regeneration in treatment of maxillary class II molar furcation invasions. *J Periodontol* 1991; 62(6):353–60.

19. Schallhorn RG, McClain P. Combined osseous composite grafting, root conditioning, and guided tissue regeneration. *Int J Periodontics Restorative Dent* 1988; 8(4):8–31.

20. Pitaru S, Tal H, Soldinger M, Azar-Avidan O, Noff M. Collagen membranes prevent the apical migration of epithelium during periodontal wound healing. *J Periodont Res* 1987; 22(4):331–3.

21. Pitaru S, Tal H, Soldinger M. Partial regeneration of periodontal tissues using collagen barriers. Initial observations in the canine. *J Periodontol* 1988; 59(6):380–6.

22. Blumenthal NM. The use of collagen membranes to guide regeneration of new connective tissue attachment in dogs. *J Periodontol* 1988; 59(12):830–6.

23. Blumenthal NM. A clinical comparison of collagen membranes with e-PTFE membranes in the treatment of human mandibular buccal class II furcation defects. *J Periodontol* 1993; 64(10):925–33.

24. Van Swol RL, Ellinger R, Pfeifer J, Barton NE, Blumenthal N. Collagen membrane barrier therapy to guide regeneration in class II furcations in humans. *J Periodontol* 1993; 64(7):622–9.

25. Gottlow J, Laurell L, Nyman S, Hugosson A, Ravald N, Fornell J, and other. Treatment of furcation degree II involvements in humans with bioresorbable and nonresorbable GTR devices. *J Dent Res* 1993; 72(Spec Issue):207(IADR Abstr #825).

26. Polson AM, Southard GL, Dunn RL, Polson AP, Billen JR, Laster LL. Initial study of GTR in class II furcation defects after using a biodegradable barrier. *Int J Peridont Res Dent* 1995; 15(1):43–55.

27. Hamp SE, Nyman S, Lindhe J. Periodontal treatment of multirooted teeth. Results after 5 years. *J Clin Periodontol* 1975; 2(3):126–35.

28. Loe H. The Gingival Index, the Plaque Index and the Retention Index Systems. *J Periodontol* 1967; 38(6)Suppl:610–6.

29. Wang HL, O'Neal RB, Thomas CL, Shyr Y, MacNeil RL. Evaluation of an absorbable collagen membrane in treating Class II furcation defects. *J Periodontol* 1994; 65(11):1029–36.

30. Chvapil M, Kronenthal RL, Van Winkle WJr. Medical and surgical applications of collagen. *Int Rev Connect Tissue Res* 1973; 6:1–61.

31. Postlethwaite AE, Seyer JM, Kang AH. Chemotactic attraction of human fibroblasts to type I, II, III collagens and collagen-derived peptides. *Proc Natl Acad Sci U S A* 1978; 75(2):871–5.

32. Grinnell F, Bennett MH. Fibroblast adhesion on collagen substrata in the presence and absence of plasma fibronectin. *J Cell Sci* 1981; 48:19–34.

33. Johns LP, Merritt K, Agarwal S, Ceravolo FJ. Immunogenicity of a bovine collagen membrane used in guided tissue regeneration. *J Dent Res* 1992; 71(Spec Issue):298(AADR Abstr #1538).

34. Yukna CN, Yukna RA. Multi-center evaluation of bioabsorbable collagen membrane for guided tissue regeneration in human Class II furcations. *J Periodontol* 1996; 67(7):650–7.

35. Chung KM, Salkin LM, Stein MD, Freedman AL. Clinical evaluation of a biodegradable collagen membrane in guided tissue regeneration. *J Periodontol* 1990; 61(12):732–6.