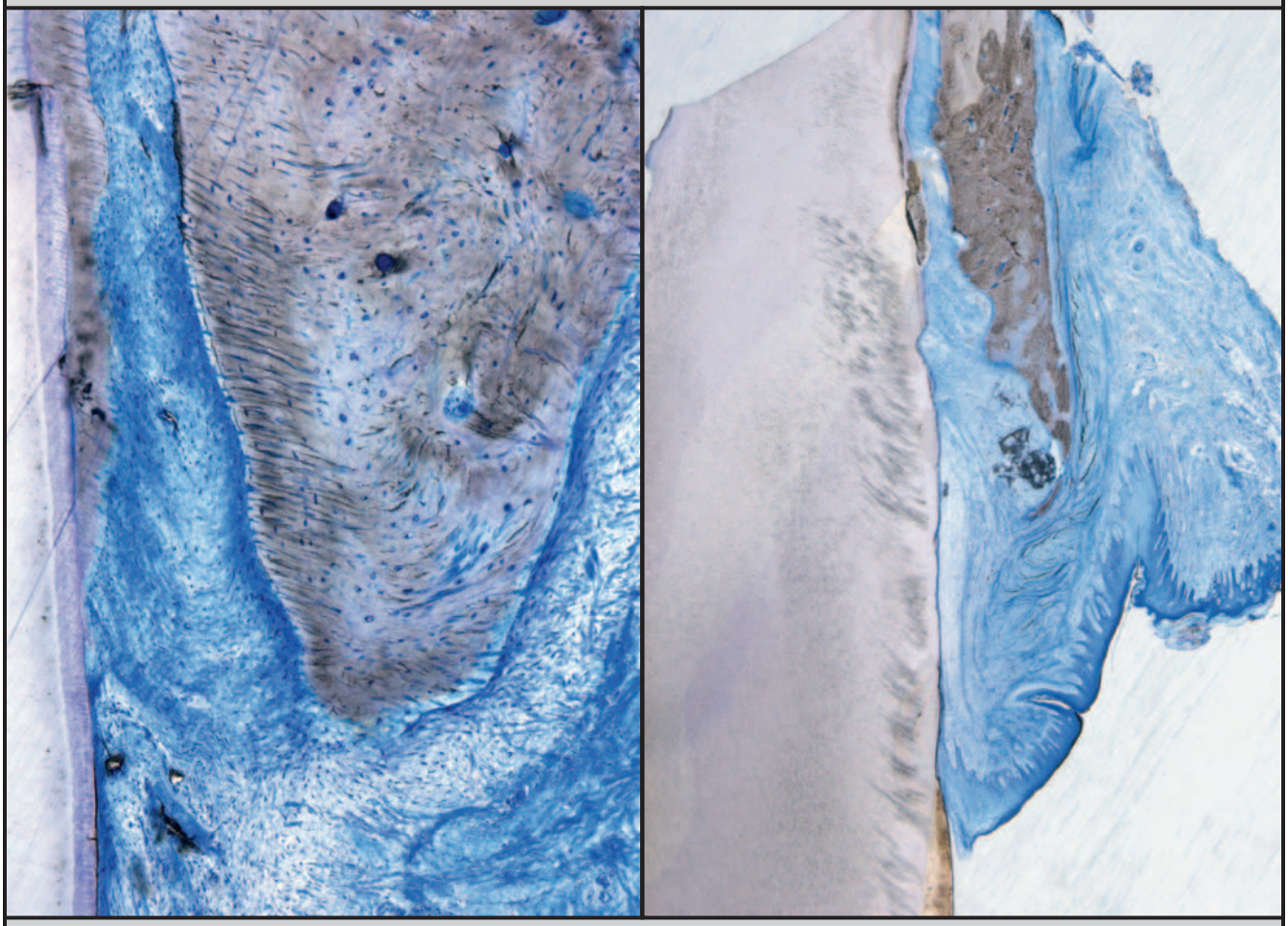
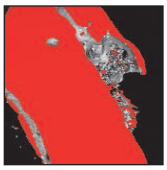


Evaluation of Human Recession Defects Treated with Coronally Advanced Flaps and Either Purified Recombinant Human Platelet-Derived Growth Factor-BB with Beta Tricalcium Phosphate or Connective Tissue: A Histologic and Microcomputed Tomographic Examination



Michael K. McGuire, DDS/E. Todd Scheyer, DDS, MS**
*Myron Nevins, DDS**/Peter Schupbach, PhD****

The current study examined the histologic and microcomputed tomographic (micro CT) outcomes of the treatment of gingival recession defects with either a subepithelial connective tissue graft (CTG) or 0.3 mg/mL recombinant human platelet-derived growth factor (rhPDGF-BB) on a beta tricalcium phosphate (β-TCP) matrix. Gingival recession defects were surgically created in six premolar teeth with no more than 3 mm of keratinized marginal tissue, an osseous crest 2 to 3 mm apical to the newly created gingival margin, and recession depth of at least 3 mm. The defects were left untouched for 2 months; then, four defects were grafted with rhPDGF-BB + β-TCP + a wound healing dressing, and two defects received CTGs. A coronally advanced flap covered each grafted site. Nine months later, sections were obtained for examination. All four sites treated with rhPDGF-BB + β-TCP showed connective tissue fibers (Sharpey fibers) perpendicularly inserting into newly formed cementum and alveolar bone. In the two sites treated with CTGs, a long junctional epithelium was seen coronal to the osseous crest and connective tissue fibers ran parallel to the adjacent root surfaces, with no evidence of insertion into cementum or bone. There was no evidence of regeneration of cementum, inserting connective tissue fibers, or supporting alveolar bone. Regeneration of the periodontium in gingival recession defects is possible through growth factor–mediated therapy. (Int J Periodontics Restorative Dent 2009;29:7–21.)

*Private Practice, Houston, Texas.
**Private Practice, Swampscott, Massachusetts.
***Adjunct Professor, School of Dental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

Correspondence to: Dr Michael K. McGuire, 3400 S. Gessner, Suite 102, Houston, TX 77063; fax: +713-952-0614; e-mail: mkmperio@swbell.net.

Improved esthetics and plaque control, reduced sensitivity, and prevention of root surface caries are primary reasons clinicians have sought predictability in root coverage for gingival recession defects. Trombelli stated that the goal of root coverage grafts was twofold: (*1*) to recreate the functional and esthetic morphology of the mucogingival complex, and (*2*) to regenerate the lost attachment apparatus, including the formation of new cementum with inserting connective tissue fibers and supporting alveolar bone.[1] Two recent systematic reviews of randomized controlled clinical trials verified that current soft tissue augmentation procedures are generally effective in obtaining root coverage.[2,3] In both reviews, the connective tissue graft (CTG) technique proved more effective than guided tissue regeneration (GTR) in reducing gingival recession. Less clear, however, is the effectiveness of all current root coverage procedures to regenerate the lost attachment apparatus with new cementum, inserting connective tissue fibers, and alveolar bone.

The periodontal literature is replete with articles examining the

effectiveness of accepted recession-related therapies to potentially regenerate tissues of the lost attachment apparatus. In reviewing the regenerative potential of GTR, variable and inconsistent results, from moderately robust regeneration of the periodontium to the establishment of a long junctional epithelium (LJE) or a connective tissue attachment, have been seen.[4–7] Studies examining acellular dermal matrix, on the other hand, have consistently failed to document positive regenerative results, finding instead a consistent histologic pattern of fibrous adhesion to adjacent root surfaces or a combination of parallel-oriented connective tissue fibers and an LJE.[8,9] More positive evidence of regenerative potential, however, has emerged from histologic studies examining enamel matrix derivative, with definitive, albeit somewhat limited, evidence for regeneration of cementum, periodontal ligament (PDL), and supporting alveolar bone.[10–12] Finally, although a few studies have suggested that CTGs seem to be capable of leading to limited regeneration, most suggest that healing occurs through either an LJE or connective tissue adhesion with the root surface.[9,13–17]

Although the CTG may be the most predictable technique for root coverage, several limitations with its use exist: (*1*) obtaining a CTG requires a remote harvest site, (*2*) limited amounts of donor tissue are available for any given procedure, and (*3*) an invasive donor site surgery may lead to increased morbidity. Given these very real limitations with the CTG and its questionable potential for regenerating missing cementum, PDL, and supporting alveolar bone, current advances in tissue engineering may offer possible therapeutic alternatives for the effective treatment of gingival recession defects, including regeneration of all three tissues of the attachment apparatus.

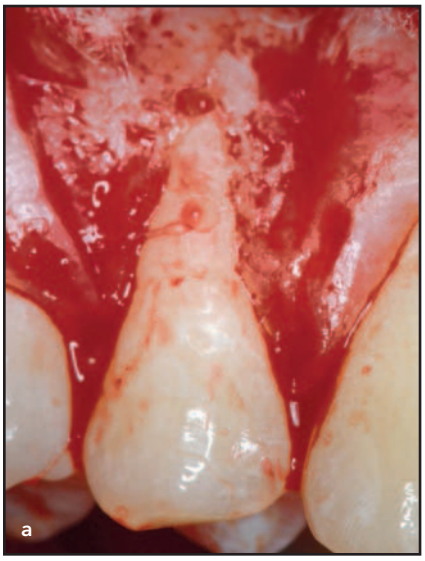
A recently published pivotal trial comparing the clinical effectiveness and safety of beta tricalcium phosphate (β-TCP) alone or with recombinantly produced platelet-derived growth factor-BB (rhPDGF-BB) in the treatment of significant intrabony and Class I and II furcation defects led to U.S. Food and Drug Administration approval of rhPDGF-BB 0.3 mg/mL on a β-TCP matrix (GEM 21S, Osteohealth) for the treatment of intrabony defects, Class I and II furcation defects, and gingival recession defects.[18] Since the late 1980s, when it was first discovered that PDGF promoted regeneration of cementum, periodontal ligament, and bone, nearly 100 studies have been published on the stimulatory effects of PDGF on chemotaxis and proliferation of PDL and alveolar bone cells in both animals and humans.[19,20] Several recent studies have closely documented the ability of PDGF to promote histologic evidence of complete periodontal regeneration in severe human intrabony and Class II furcation defects.[21–23]

Given the positive chemotactic and proliferative effects of rhPDGF-BB on PDL and alveolar bone cells as well as the ability of rhPDGF-BB to regenerate the periodontium, McGuire and Scheyer recently examined the clinical outcomes of rhPDGF-BB with β-TCP and a collagen membrane in the treatment of a series of gingival recession defects, comparing the growth factor–mediated results to those of the current clinical gold standard for root coverage, the subepithelial CTG.[24] Both procedures achieved root coverage with no more than 1 mm of residual recession at the end of 6 months. The positive results observed with the PDGF-mediated treatment, especially when compared to the CTG outcomes, supported the initiation of a larger, properly powered clinical trial.

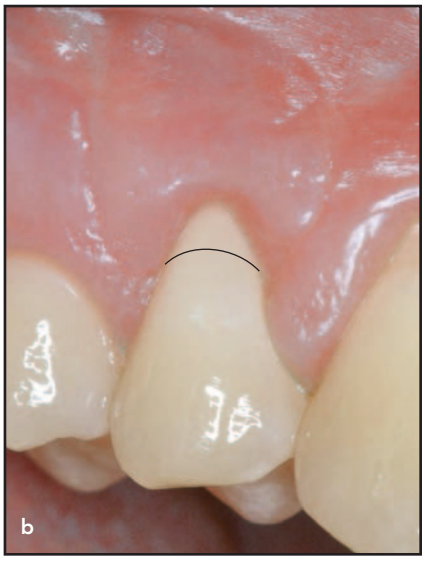
Given the potential of rhPDGF-BB on appropriate matrices to induce periodontal regeneration in significant intrabony and furcation defects, the primary objective of the current study was to determine whether it is possible to achieve similar periodontal regeneration in gingival recession defects using rhPDGF-BB placed on β-TCP and collagen wound dressing matrices. A secondary objective was to compare the regenerative responses of this tissue-engineered approach to possible regenerative responses associated with the subepithelial CTG.

Method and materials

The current study was part of a larger trial that compared multiple clinical endpoints in treating recession defects achieved with rhPDGF-BB or CTG-mediated therapies. The clinical results of the current subtrial were not included in the data of the larger trial; the sole intent of the current study was to examine the histologic regenerative responses achieved with either CTGs or a growth factor–mediated regimen.



Figs 1a and 1b (a) *Surgically created gingival recession defect with osseous crest 2 to 3 mm apical to the newly created gingival margin.* (b) *Following 2 months of healing, gingival margin is approximately 3 mm apical to the CEJ (outlined in black).*



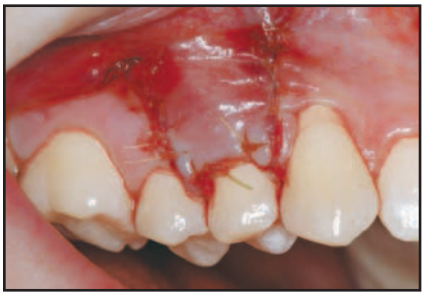
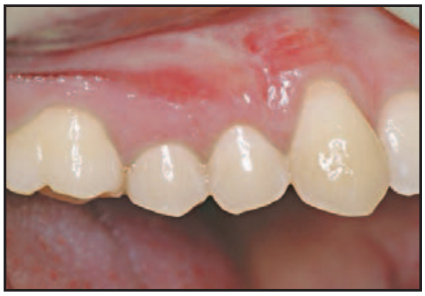


Fig 2 (left) *Gingival recession corrected 2 months following defect creation with either rhPDGF-BB +β-TCP or CTG, each with a coronally advanced flap.*

Fig 3 (right) *Nine months following correction of the recession defect.*



Patient population

The gingival recession defects required for this study were surgically induced in first premolars slated for extraction in two patients undergoing orthodontic treatment. The two patients in this subtrial were referred by an orthodontist to two of the authors' private practice in June 2006. The nature of the study, including potential risks, as well as the understanding that no clinical benefit would be gained by recession-related surgeries, was discussed with patients, after which informed consents were signed and institutional review board approval obtained. For participating in the study, the patients, who could not otherwise afford orthodontic care, were given orthodontic treatment at no cost to them.

Overall study design

First premolar teeth designated for extraction had recession defects surgically created with the following characteristics: (*1*) no more than 2 to 3 mm of keratinized marginal tissue; (*2*) osseous crest 2 to 3 mm apical to the newly created gingival margin; (*3*) recession depth of at least 3 mm (Fig 1). To duplicate a normally contaminated exposed root surface, the surgically created defects were left untouched for 2 months. After this time, four of the six defects were grafted with rhPDGF-BB + β-TCP + a wound healing dressing, and two were treated with CTGs. In each case a coronally advanced flap was used to cover the grafted site (Figs 2 and 3). Nine months later, en bloc resections were obtained for histologic and micro-computed tomographic (micro CT) examination and the resulting alveolar defects grafted with rhPDGF-BB + FDBA (Fig 4). Orthodontic treatment commenced 3 months later.

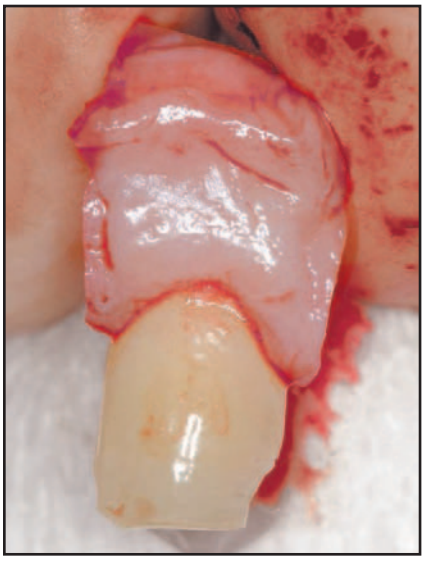
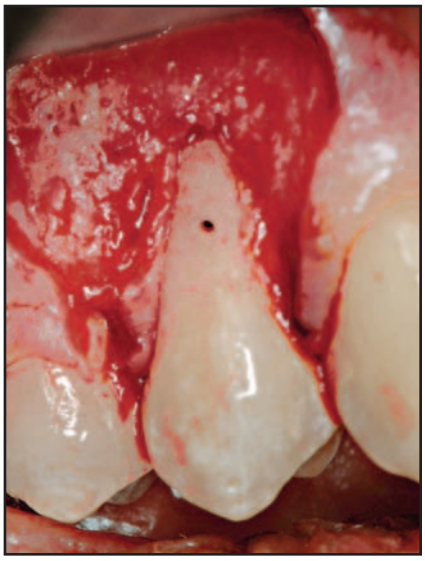


Fig 4 (left) *En bloc resection was performed 9 months following surgical correction of the gingival recession defects.*

Fig 5 (right) *Reference notches are seen at the preoperative gingival margin and alveolar crest in the surgically created defects prior to correction of the recession defect with either rhPDGF-BB + β-TCP or a CTG with coronally advanced flaps.*



Surgically creating the recession defect

Following administration of local anesthesia, all but 2 to 3 mm of keratinized marginal tissue was removed via a gingivectomy. An intrasulcular incision connected to mesial and distal vertical releasing incisions allowed a full-thickness flap to be elevated. Where necessary, the coronal portion of the buccal cortical plate was removed through ostectomy to reposition the osseous crest 2 to 3 mm apical to the newly created gingival margin (Fig 1). The mucoperiosteal flap was then apically repositioned to create a recession defect of at least 3 mm and sutured with 5-0 gut sutures.

Surgical treatment of test and control sites

Two months after creation of the gingival recession defects, both test and control sites were treated as recently described by McGuire and Scheyer[24] with the following exceptions. In place of a collagen barrier membrane, a collagen wound healing dressing (CollaTape, Integra LifeSciences) saturated with rhPDGF-BB was placed over the test root surfaces and sutured to adjacent deepithelialized papillae. In the control group, CTGs were placed in the usual manner without placement of an overlying collagen wound healing dressing. The collagen dressing helps contain the β-TCP particles, limiting their migration, and serves as an additional reservoir for the attachment and release of PDGF. However, unlike traditional GTR procedures, which require occlusive barrier membranes to exclude migration of unwanted cell types into the grafted defect, PDGF-mediated procedures potentially benefit from the osteoblast and mesenchymal cell–rich environment of the overlying periosteum by actively recruiting these cell types into the underlying graft site.[25–27] The use of a porous PDGF-saturated collagen dressing allows for both recruitment and chemotactic-mediated migration into the grafted site of the tissue-regenerating cells found in the overlying periosteum. In addition, unlike the earlier feasibility study,[23] reference notches were placed at the preoperative free gingival margin and at the alveolar bone crest of all test and control sites (Fig 5). A randomization schedule was used to identify which teeth would receive the growth factor–mediated therapy and which would receive the CTG.

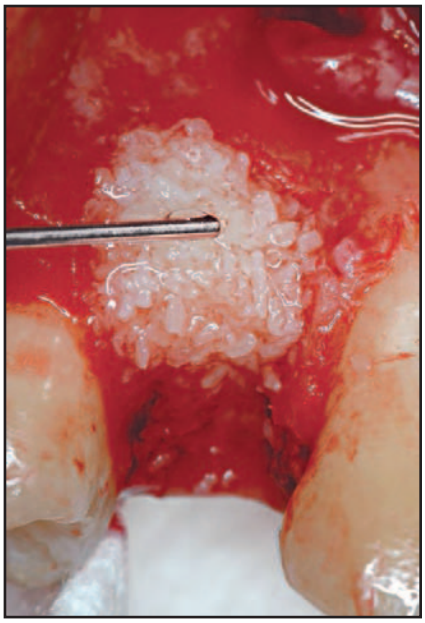


Fig 6 *Following en bloc resection of the treated areas, test and control sites were grafted with rhPDGF-BB + freeze-dried bone allograft.*

Resections of sites and grafting of residual defects

Nine months after correction of the recession defects, conservative en bloc resection of all teeth was accomplished as described previously by McGuire and Cochran in their histologic evaluation of recession sites treated with enamel matrix derivative or CTG.[11] Unlike this latter study, however, the current en bloc resection was accomplished with piezosurgical techniques (Fig 4). The specimens were immediately placed into separate containers filled with 10% neutral buffered formalin.

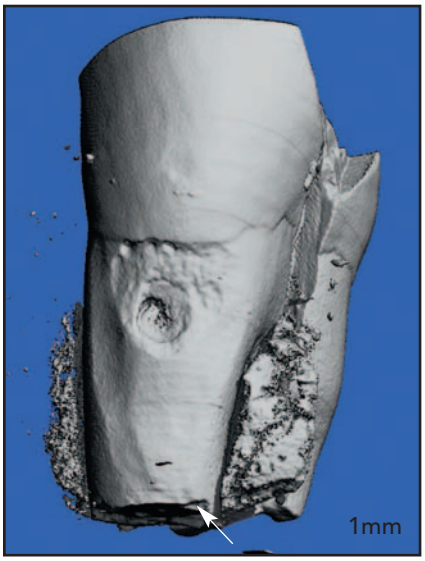
Immediately following the en bloc resection, each resected site was grafted with freeze-dried bone allograft (Life Net) saturated with rhPDGF-BB (Fig 6). Three months later, orthodontic closure of all test and control extraction sites was initiated and continued uneventfully. No postoperative complications were observed in any of the test or control locations.

Preparation of ground sections

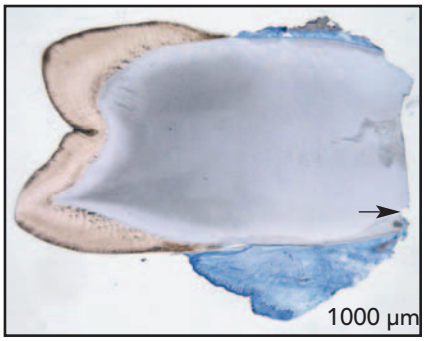
Fixed samples were dehydrated in a graded series of ethanols using a dehydration system with agitation and vacuum. The blocks were infiltrated with Kulzer Technovit 7200 VLC resin. Infiltrated specimens were placed into embedding molds, and polymerization was performed under ultraviolet light. Polymerized blocks were sliced longitudinally on a cutting unit (Exakt). The slices were reduced by microgrinding and polished using an Exakt grinding unit to a uniform thickness of 30 to 40 µm. Sections were stained with toluidine blue/pyronine G and examined using a Leica MZ16 stereomicroscope and a Leica 6000DRB light microscope.

Micro CT analysis

The specimens were scanned using a high-resolution micro CT system (µCT 40, Scanco Medical) in multislice mode. Each image data set consisted of approximately 600 micro CT slice images. The specimens were scanned in high-resolution mode with an x-, y-, and z-axis resolution of 16 µm. By application of special software (Scanco Medical), the image data sets were used to produce three-dimensional (3-D) views of the specimens.



Figs 7a and 7b *Control site images. Both the micro CT (*left*) and the ground section (*right*) show no evidence of new bone formation. The arrows indicate the osseous reference notch.*



Micro CT analysis was used to study the 2-D and 3-D structure of preexisting bone and of newly regenerated bone in the vicinity of the root. The 3-D contour of the PDL space was evaluated and adjacent new bone connected by a PDL space was examined in relation to the osseous and gingival margin reference notches to verify histologic findings of periodontal regeneration.

Results

Nine months after correction of the surgically created recession defects, both the CTG- and PDGF-mediated treatments resulted in 100% root coverage at all six sites. Both procedures led to the restoration of the functional and esthetic morphology of the mucogingival complex. However, histologic and micro CT examination of the en bloc specimens revealed distinct differences in each treatment's ability to regenerate new cementum with inserting connective tissue fibers and supporting alveolar bone. The histologic ground sections as well as the micro CT images shown in this paper represent specimens from multiple sites and are representative of the findings seen for all grafted sites in this study.

CTG-treated sites

Neither of the CTG-treated sites exhibited signs of periodontal regeneration. No evidence of new bone was evident in either the ground sections or the samples subjected to micro CT (Fig 7). In each CTG-treated site, an LJE and parallel running connective tissue fibers were seen coronal to the osseous crest (Fig 8). Other than an isolated image of reactive reparative cementum within one of the gingival notches, regenerated cementum was not seen (Fig 8). Close examination of ground histologic sections on one tooth also revealed evidence of dentinal resorption adjacent to the previously placed CTG (Fig 9).

Sites treated with rhPDGF-BB + β-TCP

In contrast to the CTG-treated sites, all four sites grafted with rhPDGF-BB + β-TCP exhibited signs of regeneration of cementum, PDL, and supporting alveolar bone. Significant amounts of newly regenerated bone coronal to the osseous reference notches were seen in both ground sections and micro CT. Significantly, at several sites this newly regenerating bone extended just apical to the gingival

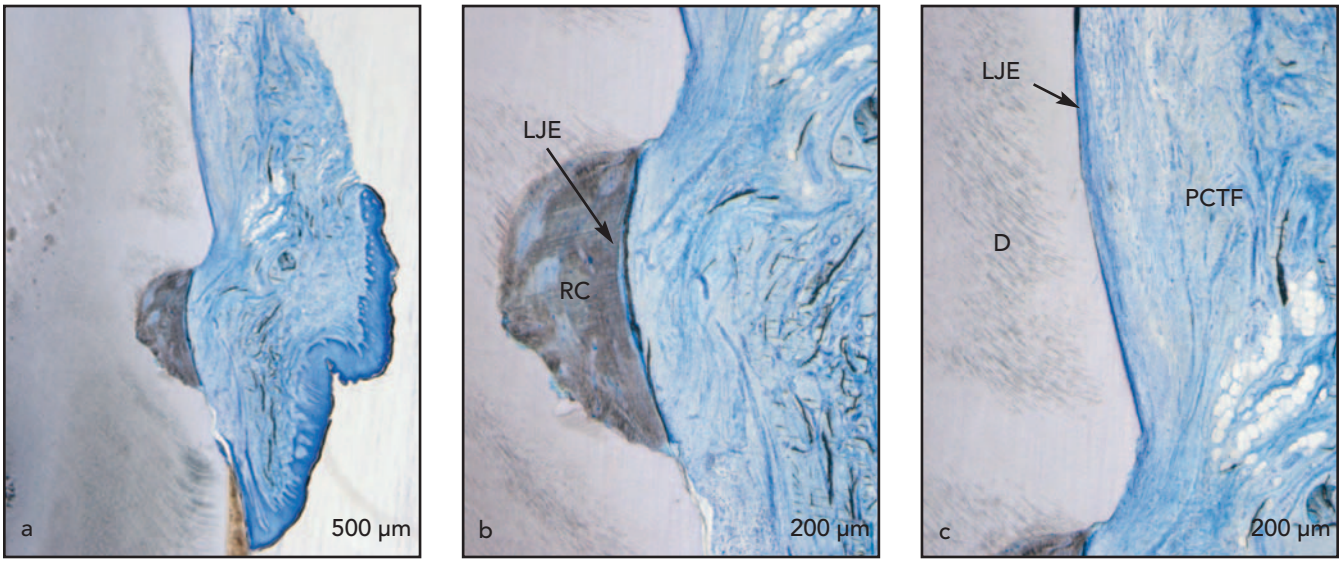
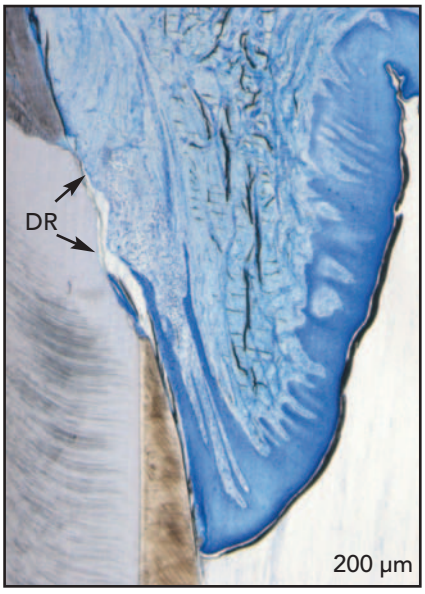


Fig 8 *Control site images. The low-power image* (a) *reveals primarily parallel-oriented CT fibers adjacent to the root surface. The gingival notch* (b) *is filled with reactive reparative cementum covered with an LJE. The high-power view* (c) *reveals a connective tissue adhesive attachment with no evidence of cementum or supporting bone and parallel-oriented connective tissue fibers. LJE = long junctional epithelium; D = dentin; PCTF = parallel connective tissue fibers; RC = reparative cementum.*

Fig 9 *Control site. Dentinal resorption (DR) is seen adjacent to the CTG.*



notch (Figs 10 and 11). In addition, the regenerated bone seen in the micro CT images is mature lamellar tissue analogous to the lamina dura observed in dental periapical radiographs. Residual particles of β-TCP are sometimes seen in both micro CT and ground section images inferior to this dense cortical regenerated bone and appear to be inhibiting the more robust bone formation apparent in areas where the β-TCP has already been resorbed (Fig 12).

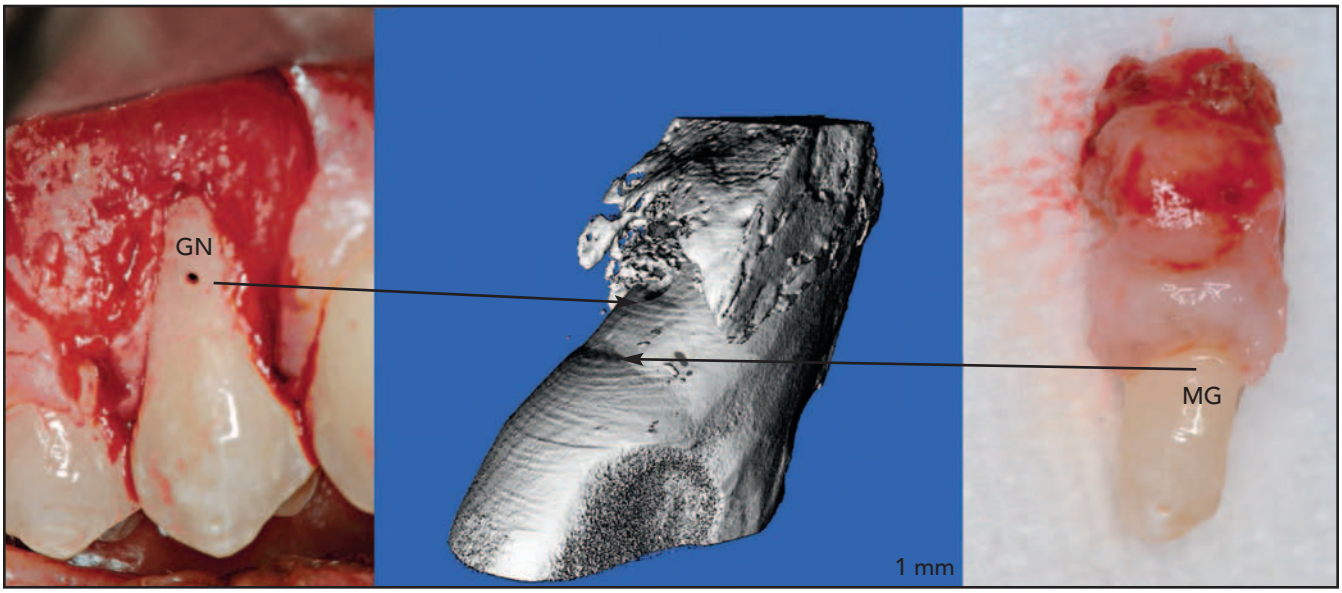


Fig 10 (left) *Clinical view of test site immediately before treatment with rhPDGF-BB + β-TCP, a collagen wound healing dressing, and a coronally advanced flap. The osseous and gingival reference notches were placed 2 months following creation of the recession defect. GN = gingival notch.* (center) *Micro CT image obtained 9 months after treatment with the growth factor demonstrates significant coronal bone formation almost to the gingival notch.* (right) *Complete root coverage has been maintained 9 months after treatment with rhPDGF-BB + β-TCP. MG = marginal gingiva.*

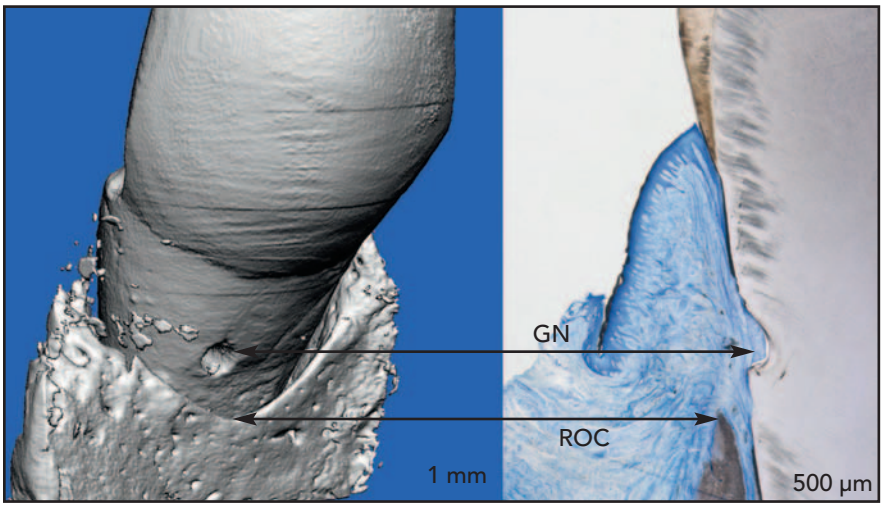


Fig 11 (left) *Nine months following growth factor–mediated treatment, dense cortical bone is seen regenerated just apical to the gingival reference notch (GN). ROC = regenerated osseous crest.* (right) *In this ground section, both new bone and PDL have formed almost to the gingival reference notch (GN), confirming the micro CT findings. ROC = regenerated osseous crest.*

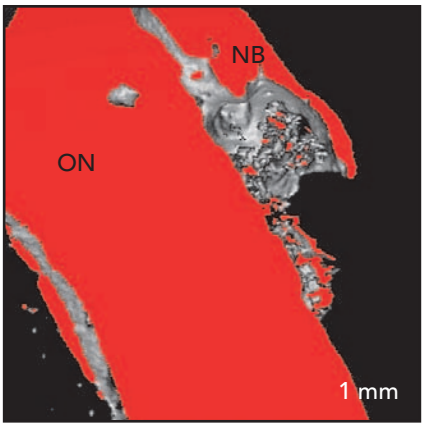


Fig 12 *In this tranverse micro CT image of a test site, new bone (NB) has formed coronal to the osseous reference notch (ON). Coronally, new bone is seen forming superior to residual particles of β-TCP.*

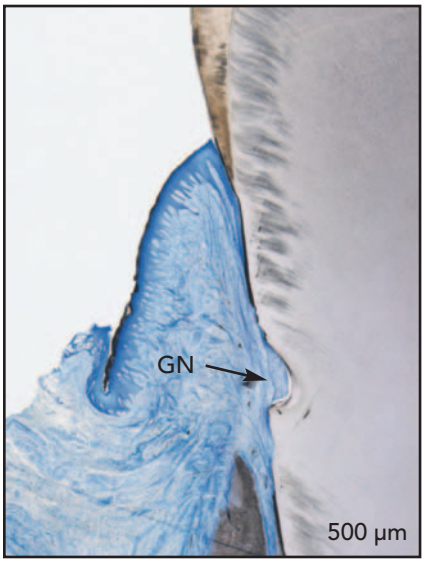


Fig 13a *A well-defined PDL space is seen in this low-power view of a test site just apical to the gingival reference notch (GN).*

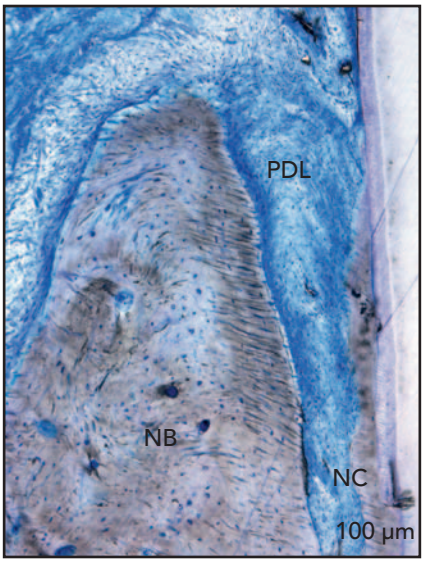


Fig 13b *At higher power, perpendicularly oriented connective tissue fibers are seen inserting into newly regenerated bone (NB) and cellular cementum (NC). PDL = periodontal ligament.*

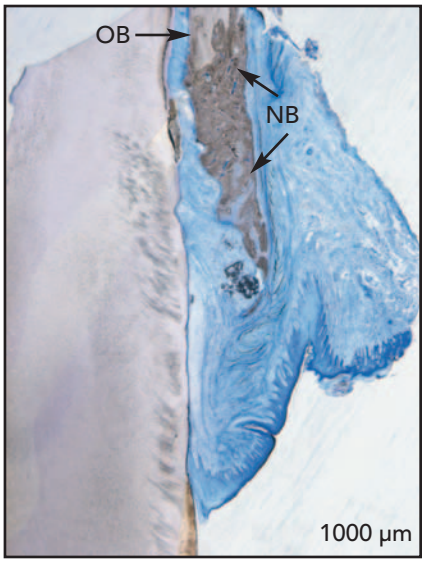


Fig 14 *In this low-power image, newly formed cementum, PDL, and bone are observed 9 months following grafting with rhPDGF-BB + β-TCP. Note the clear demarcation between old bone (OB) and newly regenerated bone (NB), with the latter extending from the original alveolar crest.*

In addition to supporting alveolar bone, regenerated PDL and cellular cementum were evident in all four sites grafted with rhPDGF-BB + β-TCP. Multiple ground sections demonstrate a uniform PDL space with connective tissue fibers inserting perpendicularly into newly regenerated cellular cementum and bone (Figs 13 and 14).

At 9 months following grafting with rhPDGF-BB + β-TCP, regeneration of tissues of the attachment apparatus was clearly apparent under ground section examination. Within one of the osseous reference notches, different stages of cementum regeneration could be seen. Cementoblasts were observed actively forming highly cellular, nonmineralized cementum, or cementoid. Adjacent to the cementoid, newly mineralized cementum has formed (Fig 15).

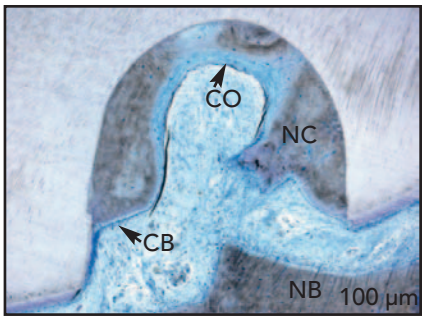
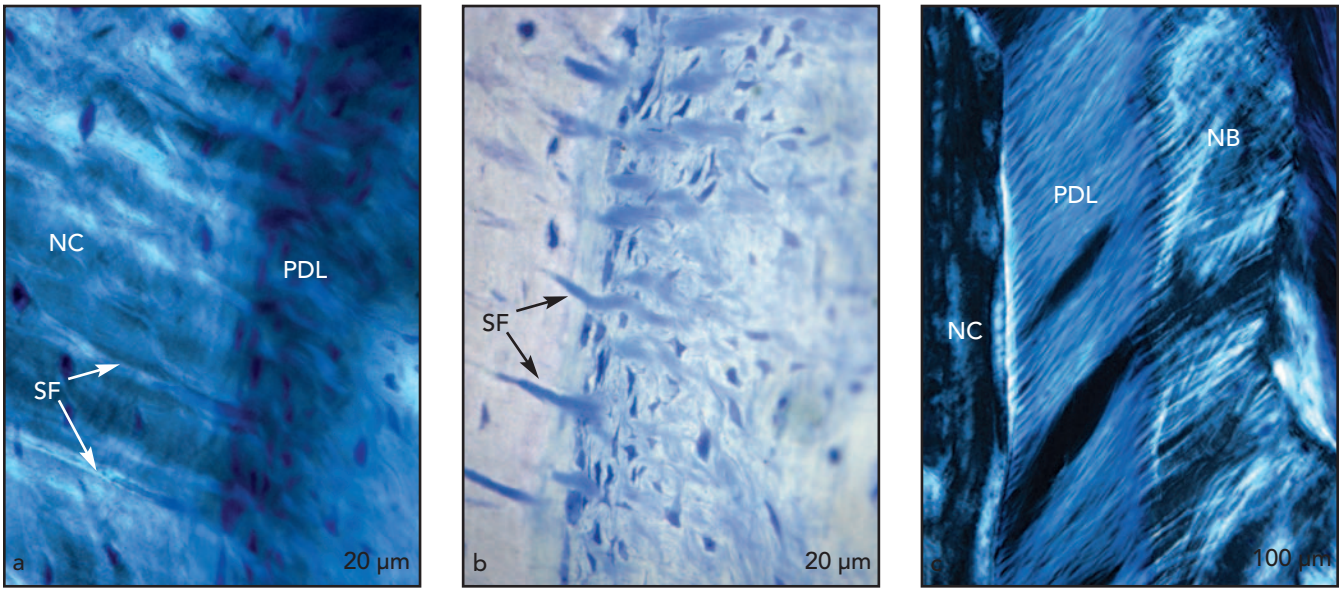


Fig 15 *Test site. Different stages of cementum formation are seen within an osseous reference notch. Cementoblasts (CB) are actively forming cellular nonmineralized cementum (cementoid; CO). Adjacent to the cementoid, mineralized cementum (NC) has formed. NB = new bone.*



Figs 16a to 16c *Test site. Under polarized light, Sharpey fibers (SF) are seen inserting into newly regenerated bone (NB) and cementum (NC). In the ground section, well-defined connective tissue fibers are also seen inserting into regenerated cementum. PDL = periodontal ligament.*

By definition, periodontal regeneration requires PDL fibers to insert into both cementum and bone. Under polarized light, Sharpey fibers were seen inserting into newly formed cementum and bone in the region of the osseous reference notch (Fig 16). Well-defined connective tissue fibers were also seen in ground sections inserting into regenerated cementum and bone (Fig 17).

Discussion

As noted, the goals of treatment for gingival recession defects can be divided into three main categories: (*1*) restoration of the protective functional morphology of the mucogingival complex, (*2*) recreation of the esthetic anatomic balance between marginal tissues and the adjacent tooth root and crown, and (*3*) regeneration of the lost attachment apparatus, including the formation of new cementum with inserting connective tissue fibers and supporting alveolar bone.[1] Numerous published reports, including two recent systematic reviews of randomized controlled clinical trials, have verified the general effectiveness of current soft tissue augmentation procedures to restore the functional and esthetic morphology of the mucogingival complex

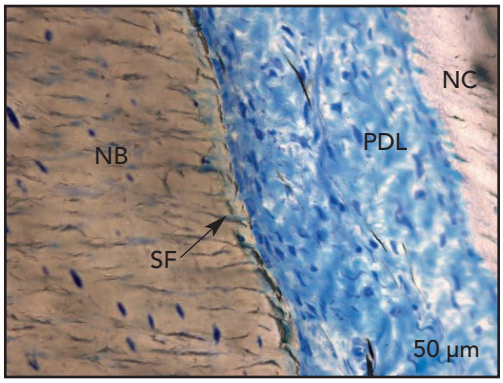


Fig 17 *Test site. In a high-power ground section, connective tissue fibers are seen inserting into newly formed cementum (NC) and bone (NB). SF = Sharpey fibers; PDL = periodontal ligament.*

in recession defects.[2,3] Significantly, in both systematic reviews the subepithelial CTG proved more effective than GTR in reducing gingival recession. As such, the CTG is viewed by many clinicians as the gold standard of treatment for recession defects. Less certain, however, is the ability of CTGs to satisfy the other major goal of recession therapy, regeneration of the complete attachment apparatus. Although a few reported cases have suggested that CTGs seem to be capable of leading to limited regeneration, most suggest that healing occurs through either an LJE or connective tissue adhesion with the root surface.[9,12–16]

In the current study, both the CTG and PDGF-mediated therapies resulted in 100% root coverage at 9 months following defect correction for all six sites. Both procedures led to restoration of the protective functional morphology of the mucogingival complex as well as recreation of the esthetic anatomic balance between marginal tissues and the adjacent tooth root and crown. However, clear and significant differences were seen in their respective ability to regenerate new cementum with inserting connective tissue fibers and supporting alveolar bone.

Neither CTG-treated site exhibited signs of true periodontal regeneration. In both cases an LJE was seen coronal to the osseous crest. In one specimen, the LJE was seen covering reparative cementum that formed within the gingival reference notch. Neither site exhibited any signs of new bone or cementum formation. Abundant connective tissue had formed coronal to each osseous notch. However, the collagen fibers ran parallel to the adjacent root surface with no signs of inserting connective tissue fibers; this was suggestive of a connective tissue adhesive attachment at both treated areas. Of particular note was the evidence of dentinal root resorption seen in a ground section of one of the sites treated with a CTG. Although infrequent, findings of external root resorption following CTG treatment have been reported in the literature. Carnio et al reported a case of severe labial root resorption 2 years after a clinically successful root coverage procedure with a CTG and a coronally advanced flap.[28] Following en bloc resection of the tooth, which was removed for prosthetic reasons, the authors found evidence of "replacement resorption," ie, root resorption followed by direct deposition of bone against the resorbed surface. In a second case report, Hokett et al demonstrated severe root resorption and labial bone loss at reentry 1 year following CTG.[29] Given the lack of positive radiographic findings as well as maintenance of stable root coverage

and no patient-generated symptoms, the authors would not have been aware of this resorption had the tooth not been evaluated histologically. Additionally, there is no way to definitively prove that the CTG was directly responsible for the resorption.

In contrast to the CTG-treated sites, all four recession sites treated with β-TCP saturated with 0.3 mg/mL rhPDGF-BB exhibited signs of true periodontal regeneration. Multiple ground sections of different teeth demonstrated significant amounts of new cellular cementum coronal to the osseous reference notches. Significant amounts of newly regenerated bone coronal to the osseous notches, and in several cases extending just apical to the gingival reference notches, were seen. Importantly, connective tissue fibers representative of a regenerated PDL were seen under polarized and nonpolarized light inserting perpendicularly into both newly formed bone and cementum.

Information from micro CT 2-D and 3-D imagery amplified information obtained from the histologic ground sections. Newly regenerated bone often appeared as mature cortical bone suggestive of a newly formed lamina dura seen in dental radiographs. Osseous and gingival reference notches were clearly identified in the transverse micro CT sections, allowing appreciation of the coronal extent of bone formation and often extending close to the gingival notch. A well-defined, uniform space was often seen in transverse images between newly regenerated cementum and bone representing the micro CT equivalent of the PDL seen in the ground sections. Residual β-TCP particles are also seen in a number of images inferior to newly regenerated bone. As noted in a recently published study of Ridgway et al[23] examining rhPDGF-BB on β-TCP for the treatment of severe intrabony defects, residual particles of the bioceramic carrier may serve to inhibit a more robust regenerative response initiated by PDGF.[23] As in the Ridgway et al study, new bone formation, while present, appeared diminished in areas occupied by remaining β-TCP particles.

Three-year follow-up

To the authors' knowledge, the current study is the first to provide definitive histologic evidence of periodontal regeneration of recession defects using a growth factor–mediated treatment. While the regenerative results of this study suggest that treatment of recession defects with PDGF may predictably lead to formation of new cementum, inserting connective tissue fibers, and supporting alveolar bone, long-term results in naturally occurring recession defects would further support evidence of regeneration following growth factor therapy. As part of a long-term follow-up of the earlier feasibility clinical trial, permission was granted for reentry 3 years following treatment with rhPDGF-BB + β-TCP (Fig 18). As noted in the clinical photographs, 8 mm of labial bone loss existed prior to treatment. Three years later, a gain of 2 to 3 mm of supporting labial bone demonstrates the potential for a positive regenerative result following growth factor–mediated therapy. In addition, the positive gains in root coverage seen at the 6 months study time point had been sustained at the end of three years from initial corrective surgery, further suggesting the potential of rhPDGF-BB + β-TCP as a viable alternative to the CTG and other therapies in the treatment of gingival recession defects.

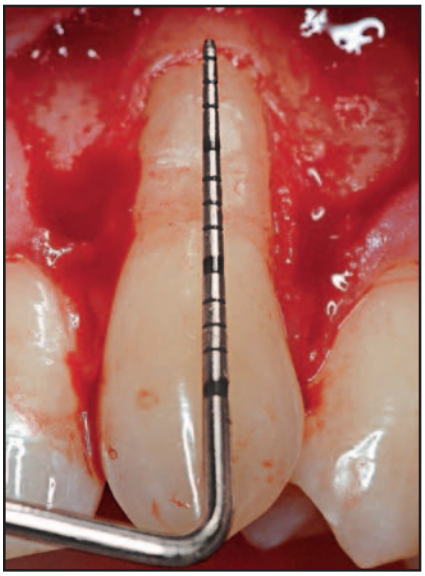
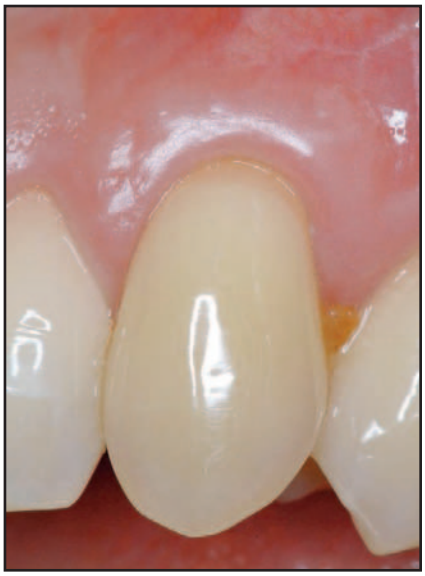


Fig 18 *Reentry at 3 years after treatment with rhPDGF-BB + β-TCP for a significant gingival recession defect demonstrates 3 mm of labial bone growth.*

Fig 18a (left) *Presurgical intraoperative measurements.*

Fig 18b (right) *Soft tissue root coverage 6 months following surgical correction.*



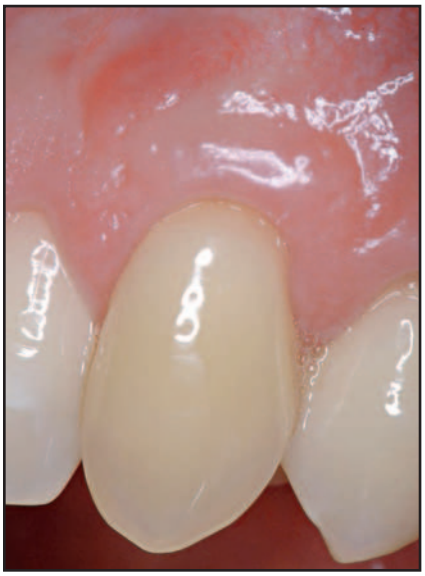
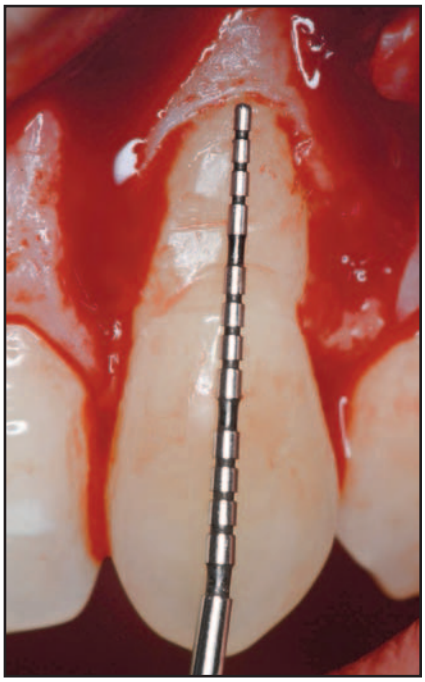


Fig 18c (left) *Soft tissue root coverage 3 years following surgical correction.*

Fig 18d (right) *Clinical evidence of bone growth over previously denuded root surface at 3 years.*



Acknowledgments

The authors would like to acknowledge the following individuals for their help in this project: Carol Waring, RDH, Cindy Wainscott, CDA, and Jacqueline A. Campbell, DDS (Perio Health Professionals, Houston, TX), for their assistance with the clinical trial and manuscript; Jennifer Gramazio (Osteohealth, Shirley, NY) for her assistance with the images; and Dr Marc Nevins (Boston, MA) for his guidance with the bloc sections. Special thanks to Dr Stuart Kay (Huntington, NY) for his help with the organization and production of the manuscript.

References

1. Trombelli L. Periodontal regeneration in gingival recession defects. Periodontol 2000 1999;19:138–150.
2. Roccuzzo M, Bunino M, Needleman I, Sanz M. Periodontal plastic surgery for treatment of localized gingival recessions: A systematic review. J Clin Periodontol 2002;29(Suppl 3):178–194.
3. Oates TW, Robinson M, Gunsolley JC. Surgical therapies for the treatment of gingival recession. A systematic review. Ann Periodontol 2003;8:303–320.
4. Cortellini P, Clauser C, Pini Prato G. Histologic assessment of new attachment following the treatment of a human buccal recession by means of a guided tissue regeneration procedure. J Periodontol 1993;64:387–391.
5. Parma-Benfenati S, Tinti C. Histologic evaluation of new attachment utilizing a titanium-reinforced barrier membrane in a mucogingival recession defect. A case report. J Periodontol 1998;69:834–839.
6. Vincenzi G, De Chiesa A, Trisi P. Guided tissue regeneration using a resorbable membrane in gingival recession-type defects: A histologic case report in humans. Int J Periodontics Restorative Dent 1998;18: 24–33.
7. Harris RJ. Histologic evaluation of root coverage obtained with GTR in humans: A case report. Int J Periodontics Restorative Dent 2001;21:240–251.
8. Richardson CR, Maynard JG. Acellular dermal graft: A human histologic case report. Int J Periodontics Restorative Dent 2002;22:21–29.
9. Cummings LC, Kaldahl WB, Allen EP. Histologic evaluation of autogenous connective tissue and acellular dermal matrix grafts in humans. J Periodontol 2005;76: 178–186.
10. Rasperini G, Silvestri M, Schenk RK, Nevins ML. Clinical and histologic evaluation of human gingival recession treated with a subepithelial connective tissue graft and enamel matrix derivative (Emdogain): A case report. Int J Periodontics Restorative Dent 2000;20:269–275.
11. McGuire MK, Cochran DL. Evaluation of human recession defects treated with coronally advanced flaps and either enamel matrix derivative or connective tissue. Part 2: Histological evaluation. J Periodontol 2003;74:1126–1135.
12. Heijl L. Periodontal regeneration with enamel matrix derivative in one human experimental defect. A case report. J Clin Periodontol 1997;24:693–696.
13. Goldstein M, Boyan BD, Cochran DL, Schwartz Z. Human histology of new attachment after root coverage using subepithelial connective tissue graft. J Clin Periodontol 2001;28:657–662.
14. Harris RJ. Successful root coverage: A human histologic evaluation of a case. Int J Periodontics Restorative Dent 1999;19: 439–447.
15. Bruno JF, Bowers GM. Histology of a human biopsy section following the placement of a subepithelial connective tissue graft. Int J Periodontics Restorative Dent 2000;20:225–231.
16. Harris RJ. Human histologic evaluation of root coverage obtained with a connective tissue with partial thickness double pedicle graft. A case report. J Periodontol 1999;70:813–821.
17. Majzoub A, Landi L, Grusovin MG, Cordioli G. Histology of connective tissue graft. A case report. J Periodontol 2001;72: 1607–1615.

18. Nevins M, Giannobile WV, McGuire MK, et al. Platelet-derived growth factor stimulates bone fill and rate of attachment level gain: Results of a large multicenter randomized controlled trial. J Periodontol 2005;76:2205–2215.

19. Lynch SE, Williams RC, Polson AM, et al. A combination of platelet-derived and insulin-like growth factors enhances periodontal regeneration. J Clin Periodontol 1989;16:545–558.

20. Matsuda N, Lin WL, Kumar MI, Cho MI, Genco RJ. Mitogenic, chemotactic, and synthetic responses of rat periodontal ligament fibroblastic cells to polypeptide growth factors in vitro. J Periodontol 1992;63:515–525.

21. Camelo M, Nevins ML, Schenk RK, Lynch SE, Nevins M. Periodontal regeneration in human Class II furcations using purified recombinant human platelet-derived growth factor-BB (rhPDGF-BB) with bone allograft. Int J Periodontics Restorative Dent 2003;23:213–225.

22. Nevins M, Camelo M, Nevins ML, Schenk RK, Lynch SE. Periodontal regeneration in humans using recombinant human platelet derived growth factor-BB (rhPDGF-BB) and allogenic bone. J Periodontol 2003;74: 1282–1292.

23. Ridgway HK, Mellonig JT, Cochran DL. Human histologic and clinical evaluation of recombinant human platelet-derived growth factor and beta-tricalcium phosphate for the treatment of periodontal intraosseous defects. Int J Periodontics Restorative Dent 2008;28:171–179.

24. McGuire MK, Scheyer ET. Comparison of recombinant human platelet-derived growth factor-BB plus beta tricalcium phosphate and a collagen membrane to subepithelial connective tissue grafting for the treatment of recession defects: A case series. Int J Periodontics Restorative Dent 2006;26:127–133.

25. Malizos KN, Papatheodorou LK. The healing potential of the periosteum molecular aspects. Injury 2005;36 Suppl 3:S13–19.

26. Emans PJ, Surtel DA, Frings EJ, Bulstra SK, Kuijer R. In vivo generation of cartilage from periosteum. Tissue Eng 2005;11: 369–377.

27. Stevens MM, Marini RP, Schaefer D, Aronson J, Langer R, Shastri VP. In vivo engineering of organs: The bone bioreactor. Proc Natl Acad Sci USA 2005;102: 11450–11455.

28. Carnio J, Camargo PM, Kenney EB. Root resorption associated with a subepithelial connective tissue graft for root coverage: Clinical and histologic report of a case. Int J Periodontics Restorative Dent 2003 ;23:391–398.

29. Hokett SD, Peacock ME, Burns WT, Swiec GD, Cuenin MF. External root resorption following partial-thickness connective tissue graft placement: A case report. J Periodontol 2002;73:334–339.