Xenogeneic Collagen Matrix With Coronally Advanced Flap Compared to Connective Tissue With Coronally Advanced Flap for the Treatment of Dehiscence-Type Recession Defects

Michael K. McGuire* and E. Todd Scheyer*

Background: For root coverage therapy, the connective tissue graft (CTG) plus coronally advanced flap (CAF) is considered the gold standard therapy against which alternative therapies are generally compared. When evaluating these therapies, in addition to traditional measures of root coverage, subject-reported, qualitative measures of esthetics, pain, and overall preferences for alternative procedures should also be considered. This study determines if a xenogeneic collagen matrix (CM) with CAF might be as effective as CTG+CAF in the treatment of recession defects.

Methods: This study was a single-masked, randomized, controlled, split-mouth study of dehiscence-type recession defects in contralateral sites; one defect received CTG+CAF and the other defect received CM+CAF. A total of 25 subjects (8 male, 17 female; mean age: 43.7 ± 12.2 years) were evaluated at 6 months and 1 year. The primary efficacy endpoint was recession depth at 6 months. Secondary endpoints included traditional periodontal measures, such as width of keratinized tissue and percentage of root coverage. Subject-reported values of pain, discomfort, and esthetic satisfaction were also recorded.

Results: At 6 months, recession depth was on average 0.52 mm for test sites and 0.10 mm for control sites. Recession depth change from baseline was statistically significant between test and control, with an average of 2.62 mm gained at test sites and 3.10 mm gained at control sites for a difference of 0.4 mm ($P = 0.0062$). At 1 year, test percentage of root coverage averaged 88.5%, and controls averaged 99.3% ($P = 0.0313$). Keratinized tissue width gains were equivalent for both therapies and averaged 1.34 mm for test sites and 1.26 mm for control sites ($P = 0.9061$). There were no statistically significant differences between subject-reported values for esthetic satisfaction, and subjects' assessments of pain and discomfort were also equivalent.

Conclusion: When balanced with subject-reported esthetic values and compared to historical root coverage outcomes reported by other investigators, CM+CAF presents a viable alternative to CTG+CAF, without the morbidity of soft tissue graft harvest. *J Periodontol 2010;81:1108-1117.*

KEY WORDS

Collagen; connective tissue; gingival recession; tissue regeneration; transplantation.

Currently in the United States, the connective tissue graft plus coronally advanced flap (CTG+CAF) is considered the gold standard for root coverage therapy. Alternative root coverage techniques are generally compared to CTG+CAF and evaluated according to their ability to reduce recession and achieve root coverage.[1-3] In such comparisons, clinical parameters of clinical attachment level (CAL) and keratinized tissue (KT) gain, pocket reduction, and tissue color and texture match are also considered. The impetus for examining these alternative therapies is the morbidity and time associated with soft tissue graft harvest and the limited supply of donor tissue.[4,5] Accordingly, healing modifiers, barrier membranes, and graft substitutes have been investigated.[6-11] To date, some alternative therapies have matched the effectiveness of CTG+CAF in regards to select clinical parameters (e.g., enamel matrix derivative [EMD] plus CAF has matched CTC+CAF in

* Private practice, Houston, TX.

doi: 10.1902/jop.2010.090698

terms of complete root coverage); however, none have matched the effectiveness of CTG+CAF in regards to all clinical efficacy measures.[12]

Besides traditional clinical efficacy measures, researchers have begun to consider subject-reported, qualitative measures, which may better reflect the inherent value of alternative root coverage techniques. Subject assessments of esthetics, subject evaluations of pain, and overall preferences for alternative procedures are now being reported.[4,5,13,14]

Recently, a new two-layer, xenogeneic collagen matrix (CM)† has been cleared by the US Food and Drug Administration for regenerative therapy involving teeth and implants, including treatment of dehiscence defects around teeth (510[K] number K073711). Because CM seems to be a promising soft tissue graft substitute, we decided to test whether its placement under a CAF in subjects with recession defects might be as effective as the CTG+CAF gold standard. Considering subject assessment criteria, a root coverage procedure using CM could be a suitable alternative to CTG+CAF because it would be less invasive and time consuming and provide unlimited "off-the-shelf" supply of grafting material.

MATERIALS AND METHODS

Study Design

We designed and implemented a single-masked, randomized, controlled, split-mouth study of dehiscence-type recession defects in two sites with comparable disease involvement in contralateral quadrants of the upper or lower jaw. The study sample was derived from the population of subjects who presented at our practice between February and August 2007 and met predetermined selection criteria. In eligible subjects, one defect received CM+CAF (test site), whereas the other defect received a subepithelial CTG+CAF (control site). Twenty-five subjects (8 male, 17 female; mean age: 43.7 ± 12.2 years) received both treatments and were evaluated over 6 months, with a 1-year follow-up to assess continuity of the 6-month findings. The study protocol and written informed consent were approved by the Essex Institutional Review Board, Lebanon, NJ. All subjects had to read, understand, and sign the informed consent and be willing to follow study procedures and instructions.

Parameters

The primary efficacy parameter for the study was recession depth at 6 months. Secondary efficacy parameters included: 1) clinical attachment level, 2) probing depth reduction, 3) width of keratinized tissue, 4) percentage of root coverage, 5) recession width, 6) color and texture of treatment sites, 7) subject esthetic satisfaction, and 8) subject pain or discomfort.

Calibrated UNC 15-mm probes‡ were used, and measurements were rounded up to the nearest 0.5 mm. Vertical probing measures were made at the mid-buccal aspect of treated teeth measured from the cemento-enamel junction (CEJ) to the free gingival margin. All measures were recorded at baseline, except treatment-dependent measures of percentage of root coverage (%RC), color and texture, esthetic satisfaction, and pain or discomfort. Probing measures were again recorded at 6 months and 1 year.

A masked, calibrated examiner (Rebecca Garcia, Perio Health Clinical Research Center, PHCRC, Houston, TX) assigned color and texture binary ratings of "equal or not equal to surrounding native tissue" through visual observation and palpation at 1, 2, 3, and 6 months. Examinations were made in the clinic, not by comparing photographs. Subjects recorded esthetic satisfaction ("unsatisfied" to "very satisfied") on a five-point scale at 6 months and pain or discomfort assessments ("no pain" to "extreme pain") on 10-cm visual analog scales at 1 week, 1 month, and 6 months. At the same time intervals, subjects also indicated whether test, control, or donor sites presented the greatest discomfort, or whether all sites were equivalent. Photographs of treatment sites were made at baseline, at surgery, and at all follow-up time points.

Sample Size, Identification, and Selection

Given data reported by Roccuzzo et al.,[15] the sample size was calculated based on the null hypothesis that the test (CM+CAF) and control (CTG+CAF) were not equivalent and that test site recession would differ from the control by 0.5 mm (or about 15%) at a two-sided test alpha level of 0.05% and 80% power. Using these calculations, 20 evaluable subjects were required to detect a difference of 1-mm change in recession depth, with 95% power and assuming a within-subject variation (standard deviation, estimated from previous studies with similar inclusion-exclusion criteria) of 1 mm. A total sample of 25 subjects was therefore enrolled to achieve at least 20 evaluable subjects. No subjects were lost to follow-up at 6 months, and two were lost at 1 year because of personal circumstances.

Potential study subjects with a self-reported history of smoking (within the previous 6 months), pregnant or lactating, exhibiting poor plaque control, or with systemic healing disorders (e.g., uncontrolled diabetes or bone metabolic diseases) were excluded. Molar, mobile, full restoration, or prominent root surface teeth were also excluded. Included subjects were 18 to 70 years of age with similar recession defects, ≥3 mm deep by ≥3 mm wide, located in contralateral

† Mucograft collagen matrix, Geistlich Pharma, Wolhusen, Switzerland.
‡ 15 UNC Novatech Color-Coded Probe, Hu-Friedy, Chicago, IL.

quadrants of the same jaw, and with some keratinized tissue present.

In cases of adjacent teeth with recession defects, only one tooth acted as test or control; no adjacent teeth were grafted. Subjects with parafunctional habits were fitted with occlusal bite guards.

Study Test Material

The CM test material was a 510(K) cleared device (Food and Drug Administration) fabricated as a matrix and composed of pure porcine collagen obtained by standardized, controlled manufacturing processes. The collagen was extracted from veterinary-certified pigs and purified to avoid antigenic reactions. The matrix was made of collagen type I and type III without further cross-linking or chemical treatment. CM was sterilized in double blisters by gamma irradiation.

CM has two layers and is approximately 2.5 mm thick (Fig. 1). The first layer is a compact layer, facing the oral cavity, consisting of a denser collagen that protects the wound but allows tissue adherence for favorable wound healing. This layer has a smooth texture with appropriate properties to accommodate suturing to the host mucosal margins. The second layer is a thicker, porous collagen that encourages tissue integration. This porous surface is placed adjacent to the host tissue to facilitate organization of the blood clot and promote neoangiogenesis.

Surgical Procedure

Subjects were randomized at baseline, with test or control treatment assigned to right or left sides according to a computer-generated randomization schedule. Immediately before surgery, the treating surgeons (MKM and ETS) opened an envelope dictating treatment assignment.

The surgical technique used to achieve soft tissue coverage was CAF. Following administration of local anesthesia, the exposed portion of the root was prepared using chisels, curets, and finishing burs as needed. Following root preparation, an intracrevicular incision was made with a 15-blade at the treatment site to mobilize a partial-thickness mucosal flap. The incision was extended to involve the papilla region on each side of the tooth to be treated. Vertical releasing incisions, extending from the papilla out into the lining mucosa, were placed at each side of the tooth to facilitate the planned coronal repositioning of the flap tissue over the exposed root surface. The partial-thickness flap was elevated in an apical direction until the mucogingival line had been passed. The periosteum was then cut, and a blunt dissection into the vestibular lining mucosa was carried out to eliminate muscle tension so that the mucosal flap could be passively positioned at or slightly above the level of CEJ on the tooth.[16]

The facial portion of the interdental papilla was deepithelialized to create a connective tissue bed to which CAF could later be sutured. Further instrumentation of the previously exposed root surface was carried out as necessary. Root surface not exposed to the oral environment was left intact.

The exposed root surface was conditioned with 24% EDTA for 2 minutes to remove the smear layer, then thoroughly rinsed with sterile saline.[17] CM test material was cut to the exact size of the defect, hydrated (although hydration is not a requirement), and placed over the dehisced defect, sutured to the interdental papillae and subsequently covered with CAF. The tissue flap was secured at or coronal to the level of CEJ by suturing the flap to the deepithelialized papilla regions, using 5-0 and 6-0 plain gut sutures in an interrupted fashion. The vertical incisions were also closed by resorbable sutures. At all times caution was maintained to avoid overcompression of the test material (Fig. 2).

The control site surgical procedure was identical to the test site, with the exception that in the place of CM, a subepithelial CTG was used. An attempt was made to harvest mainly connective tissue with very little adipose tissue. The donor area was the palate in the bicuspid region. The graft was sutured to the papilla region on either side of the denuded root. In addition, a suspensory suture was placed, if needed, in the periosteum apical to the graft and looped around the neck of the tooth to make certain that the graft was tightly adapted to the root surface. CAF was then advanced over the graft as previously described.

Post-Surgical Care

Use of antiseptics and analgesics was noted. Subjects were prescribed doxycycline, 100 mg, antibiotic therapy twice a day for 10 days post-surgery. Subjects with allergies to cycline derivatives were prescribed

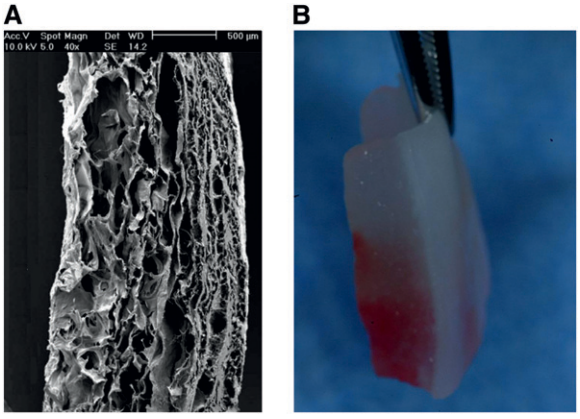


Figure 1.
A) *Collagen matrix compact and porous layers in cross-section under scanning electron microscope.* ***B)*** *Collagen matrix trimmed prior to suturing.*

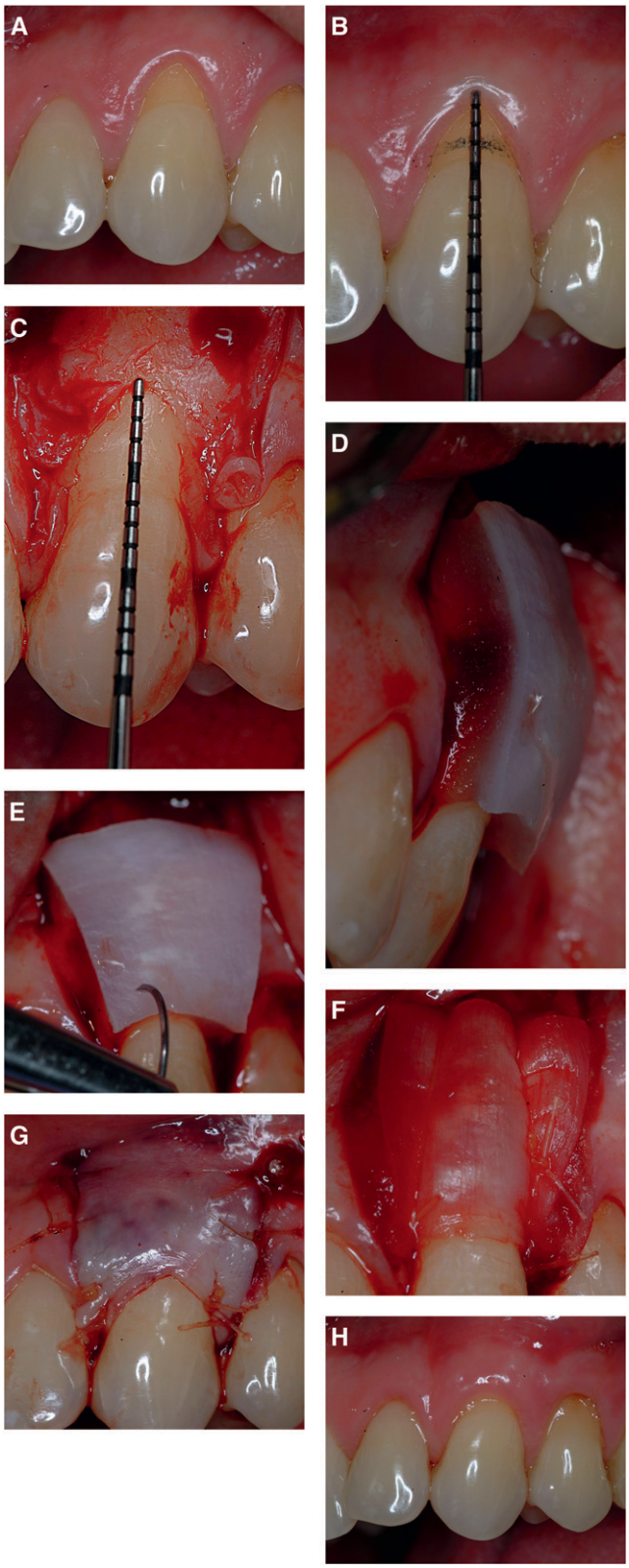


Figure 2.
*Recession defect test site **(A)** measured at baseline (pencil mark indicates cemento-enamel junction) **(B)**. Partial-thickness flap **(C)**; collagen matrix sutured in place **(D**, **E**, and **F)**; coronally advanced flap completely covering the matrix **(G)**; and 6 months following surgery **(H)**.*

amoxicillin (500 mg; 3x daily for 7 days). Analgesics (ibuprofen, 800 mg, or hydrocodone, 7.5 mg) were prescribed as needed for pain.

Subjects were instructed to avoid excessive muscle tractioning or trauma to the treated areas for the first 3 weeks and told not to brush study teeth but to use chlorhexidine (0.2%) mouth rinse for 1 minute twice a day for the first 2 weeks. During weeks 2 to 4, subjects were instructed to apply chlorhexidine rinse with a cotton swab. After this period, subjects were instructed in the Bass technique with an ultrasoft toothbrush.[18] All subjects were recalled for professional cleanings at weeks 4, 12, and 24. There was no subgingival instrumentation at postoperative weeks 4 and 12.

Data Analyses

For continuous or quasicontinuous variables, the summary statistics recorded and calculated were number available, mean, standard deviation, median, 95% confidence interval, and range. To account for the split-mouth design of the study, paired Wilcoxon signed-rank tests were used to test for unadjusted treatment differences at individual time points and for unadjusted treatment differences of change across time points.

For categorical variables, all categories were summarized with counts and percentages. To account for the split-mouth design of the study, McNemar test (for two category variables) and Bowker test of symmetry (for ≥3 category variables) were used to test for unadjusted treatment differences at individual time points and for unadjusted treatment differences of change across time points.

The primary and secondary variables were also analyzed using analysis of covariance (ANCOVA). The ANCOVA models tested for treatment differences, adjusting for variation because of subject, site (left or right), and baseline value (with the exception of the color and texture rating and pain or discomfort, which were only recorded post-treatment).

A statistical software program was used[§] and statistical tests were two-tailed, with P values <0.05 considered statistically significant. Plus–minus figures cited are standard deviations.

RESULTS

Twenty-five subjects (mean age: 43.7 ± 12.2 years) were treated at baseline. Approximately two-thirds of the subjects (17 of 25) were female. Twelve subjects self-reported to have never smoked, whereas 13 were former smokers. Randomly assigned contralateral test and control sites proved statistically equivalent in terms of CAL, probing depth (PD), KT width, and the primary parameter of interest, recession

§ SAS, version 9.1.3, Cary, NC.

depth (Table 1). On average, subjects presented with recession defects just over 3-mm deep and KT widths ranging from 0.5 to 5 mm and averaging 2.6 mm. Average recession width was slightly larger (by 0.24 mm) for control defects. For each of the primary and secondary measures, ANCOVA models accounted for baseline covariates before assessing treatment differences. In each of these models, the baseline covariates were not statistically significant, implying that baseline levels did not significantly impact the evaluation of endpoints.

Surgery and postoperative sequelae were uneventful with normal healing observed at both test and control sites (Fig. 2). One subject had trauma at a test site (a seizure) at 1 week, and one subject had trauma at a test site (subject could not recall a specific injury) at 3 weeks, adversely affecting the outcome. A third subject underwent mastectomy and radiation therapy, and a fourth subject began methotrexate therapy during the course of the investigation.

At 6 months, the primary endpoint of recession depth was on average 0.52 mm for test sites and 0.10 mm for control sites (Table 2). Recession depth change from baseline to 6 months was statistically significant between test and control, with an average of 2.62 mm gained at test sites and 3.10 mm gained at control sites, for a difference of 0.48 mm ($P = 0.0062$). Likewise, average change in recession width was also significant between test and control, and average %RC was greater for control sites (97% ± 10.6%) versus test sites (83.5% ± 23%), which proved more variable ($P = 0.0059$). At 1 year 23 of 25 subjects remained in the study, and %RC either remained stable or improved in all but one test subject (parafunctional habit and extreme bruxism). Control %RC was 99.3% ± 3.5%, and test %RC was 88.5% ± 21.2% ($P = 0.0313$).

Test and control clinical parameters of average CAL, PD, and KT width proved to be equivalent between test and control sites at 6 months and 1 year, although CAL was slightly greater (by 0.5 mm) for control sites at 1 year. On average, CAL improved by approximately 2.5 mm for both test and control, and KT width gains for test sites (1.34 mm) and control sites (1.26 mm) were also equivalent ($P = 0.9061$) (Fig. 3).

Note that for all parameters tested, *P* values for differences between treatment groups were also calculated using ANCOVA, adjusting for subject and treated side. The results from the ANCOVA tests were found to be substantially similar to the paired Wilcoxon signed-rank test values (i.e., no statistically significant differences between treatments were found in terms of CAL, PD, or KT).

At 6 months no statistically significant test or control treatment difference could be discerned in terms of color or texture match to surrounding tissue. In both test and control treatments, approximately two-thirds of sites were "equally red," whereas the remaining sites were deemed "redder" by the examiner. Likewise, no statistically significant treatment difference could be discerned in texture match to surrounding tissue, although both test and control sites appeared "thicker," particularly when viewed along the margins (former vertical incision lines) of the treatment sites, as is expected for CTG+CAF treatment.

When comparing test and control treatments at 6 months, subjects' assessments of pain or discomfort and esthetics were also equivalent. No statistically significant treatment differences could be discerned in visual analog scale pain scores at 1 week, 4 weeks, or 6 months. When considering the site of greatest discomfort (Table 3), there was no statistical difference between sites; however, test sites did seem to diminish in pain beginning at 4 weeks, and obviously there were no donor soft-tissue graft sites involved with test treatments. For both test and control treatments, >90% of subjects recorded improvement, as measured by at least one gain in satisfaction level; about two-thirds of subjects recorded improvement by at least two satisfaction levels, generally from an "unsatisfied" to "satisfied" or "very satisfied" level. When subjects evaluated the two treatments, there were no statistically significant differences between the esthetic changes from baseline to 6 months.

DISCUSSION

To our knowledge, this study is the first clinical trial designed to test whether the xenogeneic CM could be useful for recession defect coverage compared to the gold standard subepithelial CTG+CAF. The study assesses traditional clinical measurement parameters of root coverage along with PD and CAL, but also assesses criteria of color and texture match and subject-reported considerations of pain or discomfort and esthetics. In terms of traditional measures of root coverage, at 6 months CM+CAF achieved an average %RC of 83.5% compared to 97% for CTG+CAF, and at 1 year, 88.5% versus 99.3%, respectively. Evaluated statistically, these measures are different, but balanced with subject-reported outcomes, CM+CAF presents an intriguing comparison to the traditional CTG gold standard.

CM has been investigated as a substitute for palatal grafts in the following studies.[19,20] CM was tested as a substitute for free mucosal and skin grafts in baboon vestibuloplasties, where CM healed uneventfully, was rapidly populated by native tissue, and was found to generate a normal-appearing mucosa.[19] In this open-healing, wound-bed grafting model, CM was still apparent at 3 weeks, but by 6 weeks it had been completely replaced by epithelialized tissue. When tested clinically over prepared wound beds around dental implants, at 6

Table 1.

Baseline Measures

Baseline Clinical Parameters (mm)	SD	95% Confidence Interval	*P* Value*
Recession depth			
Test	3.14 ± 0.23	(3.05 to 3.23)	0.4326
Control	3.20 ± 0.35	(3.06 to 3.34)	
Clinical attachment level			
Test	4.40 ± 0.61	(4.16 to 4.64)	0.5806
Control	4.50 ± 0.61	(4.26 to 4.74)	
Probing depth			
Test	1.26 ± 0.52	(1.06 to 1.46)	0.5942
Control	1.38 ± 0.71	(1.10 to 1.66)	
Width of keratinized tissue			
Test	2.44 ± 1.02	(2.04 to 2.84)	0.1963
Control	2.78 ± 1.35	(2.25 to 3.31)	
Recession width			
Test	4.06 ± 0.49	(3.87 to 4.25)	0.0410
Control	4.30 ± 0.60	(4.07 to 4.53)	
		N (%)	*P* Value†
Plaque B, presence (buccal and lingual presence or lack thereof)			
Test		7 (28)	0.7389
Control		6 (24)	
Bleeding following angulated probing (midline treatment site)			
Test		13 (52)	0.4142
Control		15 (60)	

* *P* values testing differences between treatment groups were calculated using paired Wilcoxon signed-rank tests.
† *P* values testing differences between treatment groups were calculated using McNemar tests.

months CM was as effective as a palatal graft in the generation of KT and provided significantly lower subject morbidity, while also reducing surgery time by approximately one-third.[20] The savings in time and discomfort is weighed against the cost of the matrix.

Cairo et al.[12] recently published a systematic review of the root coverage literature including CAF alone or in combination with CTG, barrier membranes, EMD, and graft substitute materials. Only randomized controlled clinical trials of ≥6 months duration that included a split-mouth model were considered. A total of 794 Miller Class I and II gingival recessions in 530 subjects from 25 randomized controlled clinical trials were evaluated. The addition of CTG or EMD was found to enhance the clinical outcomes of CAF in terms of complete root coverage, whereas barrier membranes did not. No treatment except EMD+CAF matched the effectiveness of CTG+CAF in terms of complete root coverage. The Cairo et al.[12] meta-analysis confirms and expands findings in other recent root coverage reviews performed in both the United States and Europe.[2,3,15] Mean %RC for CTG+CAF in the Cairo et al.[12] meta-analysis ranged from 64% to 96%, so the mean %RC reported in our study (97% for CTG+CAF and 83.5% for CM+CAF) compares favorably.

Like the CM investigated in our study, acellular dermal matrix (ADM) was introduced as a connective tissue graft alternative to reduce subject graft-site discomfort. The Cairo et al.[12] meta-analyses reports no statistically significant difference between ADM+CAF and CAF alone in terms of complete root coverage, recession, or KT gain, suggesting ADM+CAF provides no additional benefit over CAF alone, a treatment already inferior to the gold standard CAF+CTG. Moreover, when directly comparing ADM+CAF to CTG+CAF, statistically significant differences for KT gain favoring CTG+CAF were detected (mean difference of 0.90 mm; $P = 0.004$). In our study, the test treatment CM+CAF was able to produce an equivalent amount of KT gain (1.34 mm) compared to CTG+CAF (1.26 mm), an agreeable outcome considering the

Table 2.

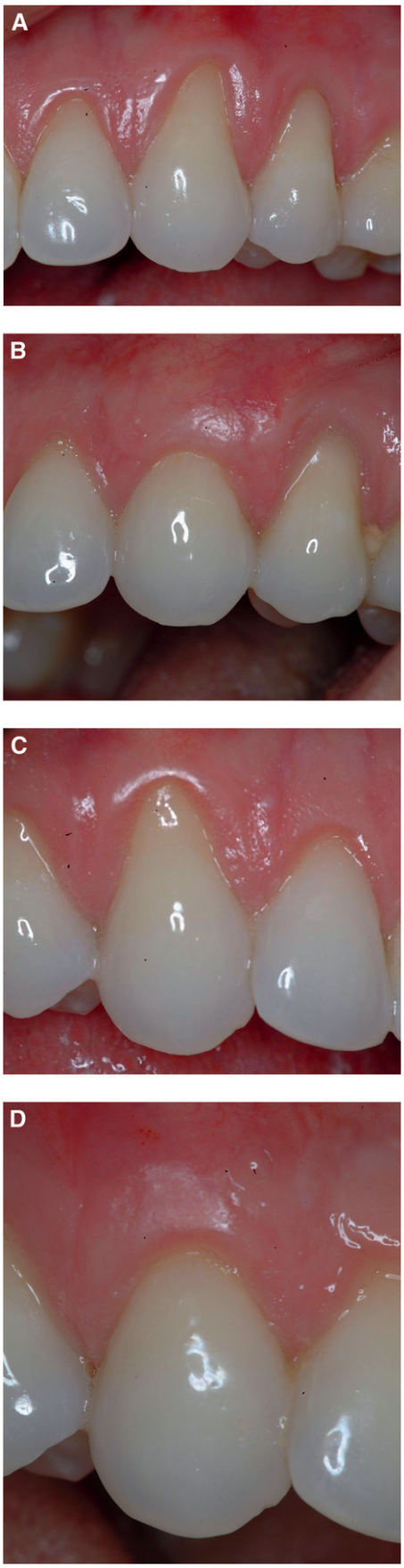
Measures at 6 and 12 Months

Clinical Parameters	Test (95% CI)	Control (95% CI)	*P* Value*
Recession depth (mm)			
Baseline	3.14 (3.05 to 3.23)	3.20 (3.06 to 3.34)	
6 months	0.52 (0.23 to 0.81)	0.10 (–0.04 to 0.24)	0.0078
12 months	0.37 (0.09 to 0.65)	0.02 (–0.02 to 0.06)	0.0313
Change from baseline to 6 months	–2.62 (–2.91 to –2.33)	–3.10 (–3.29 to –2.91)	0.0062
Change from baseline to 12 months	–2.78 (–3.06 to –2.51)	–3.17 (–3.33 to –3.02)	0.0172
Recession width (mm)			
Baseline	4.06 (3.87 to 4.25)	4.30 (4.07 to 4.53)	
6 months	1.34 (0.67 to 2.01)	0.26 (–0.10 to 0.62)	0.0059
12 months	0.85 (0.23 to 1.46)	0.11 (–0.10 to 0.32)	0.0313
Change from baseline to 6 months	–2.72 (–3.45 to –1.99)	–4.04 (–4.50 to –3.58)	0.0024
Change from baseline to 12 months	–3.22 (–3.90 to –2.54)	–4.22 (–4.62 to –3.82)	0.0024
Root coverage (%)			
Baseline	NA	NA	
6 months	83.5 (74.5 to 92.6)	97.0 (92.8 to 100.0)	0.0059
12 months	88.5 (79.8 to 97.2)	99.3 (97.9 to 100.0)	0.0313
Clinical attachment level (mm)			
Baseline	4.40 (4.16 to 4.64)	4.50 (4.26 to 4.74)	
6 months	2.12 (1.79 to 2.45)	1.80 (1.50 to 2.10)	0.1488
12 months	2.13 (1.78 to 2.49)	1.63 (1.42 to 1.85)	0.0381
Change from baseline to 6 months	–2.28 (–2.71 to –1.95)	–2.70 (–2.98 to –2.42)	0.0731
Change from baseline to 12 months	–2.26 (–2.76 to –1.76)	–2.85 (–3.11 to –2.59)	0.0193
Probing depth (mm)			
Baseline	1.26 (1.06 to 1.46)	1.38 (1.10 to 1.66)	
6 months	1.60 (1.37 to 1.83)	1.70 (1.50 to 1.90)	0.4463
12 months	1.74 (1.56 to 1.92)	1.61 (1.40 to 1.81)	0.5078
Change from baseline to 6 months	0.34 (0.01 to 0.67)	0.32 (0.06 to 0.58)	0.8623
Change from baseline to 12 months	0.50 (0.16 to 0.84)	0.24 (–0.07 to 0.55)	0.2303
Width of keratinized tissue (mm)			
Baseline	2.44 (2.04 to 2.84)	2.78 (2.25 to 3.31)	
6 months	3.78 (3.31 to 4.25)	4.04 (3.53 to 4.55)	0.3180
12 months	3.59 (3.18 to 4.00)	3.98 (3.53 to 4.42)	0.1838
Change from baseline to 6 months	1.34 (0.92 to 1.76)	1.26 (0.63 to 1.89)	0.9061
Change from baseline to 12 months	1.11 (0.77 to 1.45)	1.09 (0.43 to 1.75)	0.9668

* *P* values testing differences between treatment groups were calculated using paired Wilcoxon signed-rank tests.
CI = confidence interval; NA = not applicable.

value of KT in promoting and maintaining a healthy periodontium.[21-24]

In regards to postoperative pain, the Cairo et al.[12] meta-analysis indicated, "CTG+CAF was frequently associated with swelling and pain at the donor site." The Cairo et al.[12] analysis also reported a concern with root coverage procedures, even when achieving complete root coverage, was that "poor color match, inadequate integration with adjacent tissues or a flat gingival contour may affect the aesthetic perception



of treatment." The CM+CAF alternative reported in our study avoids the morbidity of donor graft harvest, and color texture match scores were equivalent to CTG+CAF control. Although not measured definitively, our observation was that CM, like CTG, provided a tissue substrate or scaffold capable of thickening tissues, which may be a desirable attribute when treating thin tissue biotypes or managing contour deformities.

Vascular supply, muscle pull, and access can make surgery and healing in the mandible more difficult than the maxilla and could, accordingly, influence root coverage outcomes.[25] In our study, if only maxillary cases are considered (n = 20), test and control results are more nearly matched and become statistically indistinguishable at 1 year: 91.1% ± 19.6% %RC for test and 99.2% ± 3.6% %RC for control ($P = 0.125$). Similarly, when four problematic subjects are excluded from the overall study results (two graft trauma subjects, one methotrexate prescribed subject, and one oncology radiation subject) overall root coverage results draw even closer together (93.3% ± 14.7% for test and 99.2% ± 3.7% for control; $P = 0.125$) and are, again, statistically indistinguishable at 1 year.

Kokich et al.[26] compared dentist and lay perceptions of dental esthetics. At times, professionally evaluated outcomes were found to be more stringent than subject-evaluated outcomes. Scientists and clinicians may struggle with less than perfect results, but subjects do not seem to be as critical, and the professional "ideal" may not always be necessary. In private practice, improved subject-reported outcomes are the goal; although scientists may argue the relative statistical value of one root coverage technique over another, treatment success relates more to subject satisfaction than it does to "fractional" root coverage measures. It is presumptuous to assume complete root coverage is a surrogate for subject satisfaction.

A recent Cochrane review of root coverage procedures stressed that "limited data exist on aesthetic condition change related to subjects' opinion and subjects' preference for a specific procedure."[1] The purpose of our study is to evaluate CM to see if its placement under CAF would be as effective or nearly as effective as CTG+CAF. "Nearly as effective" is an important qualifier if it takes into consideration subject-reported outcomes of pain or discomfort and esthetics and consequent treatment preferences. Despite any root coverage differences detected by the masked examiner in our study, >90% of subjects cited

Figure 3.
*Control CTG+CAF at baseline **(A)** and 6 months post-surgery **(B)**. Test CM+CAF at baseline **(C)** and 6 months post-surgery **(D)**.*

Table 3.

Site of Greatest Discomfort*

Time	N (sites)	Control (CTG+CAF)	Control Donor Site	Test (CM+CAF)	Test Donor Site	All Sites Equivalent†
1 Week	25	9 (36%)	3 (12%)	8 (32%)	NA	6 (24%)
4 Weeks	25	7 (28%)	5 (20%)	3 (12%)	NA	10 (40%)
6 Months	25	7 (28%)	3 (12%)	2 (8%)	NA	14 (56%)

* Subjects could select multiple sites; all selected choices are presented.
† Indistinguishable pain or discomfort between control, test, and donor sites.

improvement, designated as a change from "unsatisfied" to "satisfied" or "very satisfied"; and overall satisfaction with both test and control treatments was equivalent (Fig. 3).

Our study demonstrates that CM+CAF is an appealing alternative to CTG+CAF, particularly when subject-valued outcomes are considered. CM seems to be an acceptable alternative to CTG that avoids the morbidity and time of palatal harvest and is available in unlimited, off-the-shelf supply. We found CM to possess good handling characteristics, and its thickness compared to other membranes was unique. In the future, a study that specifically measures subject-reported treatment preferences would be helpful. In addition, a longer-term study, histologic evaluations, and an examination that quantifies gingival "thickening" would be beneficial. Also, the performance of CM with multiple teeth and implants should be examined.

In terms of development, CM might be an ideal substrate for the delivery of growth factors, cytokines, and live cell therapies. Studies are confirming the importance of these "biologics" therapies in improving periodontal repair and regeneration.[27,28] Further studies are necessary to determine binding and release kinetics of biologic factors to CM as a carrier device for such factors. There is little doubt that biologics will play a growing role in clinical periodontics, but it is equally clear that there are times when biologics are not necessary or desirable, and a cost-effective soft tissue graft substitute would provide a clinically effective option.

CONCLUSIONS

Within the limits of the study, CM+CAF achieved an average %RC of 83.5% at 6 months and 88.5% at 1 year. Although %RC was statistically slightly less than CTG+CAF control, when problematic subjects were excluded and when maxillary sites only were compared, root coverage results for CM+CAF were statistically indistinguishable from CTG+CAF. CM+CAF produced an equivalent amount of KT gain (1.34 mm) compared to CTG+CAF (1.26 mm), which is an intriguing outcome considering previous KT analyses with other root coverage therapy alternatives and considering the value of KT in promoting and maintaining a healthy periodontium.

Evaluating subject-reported outcomes of pain or discomfort, esthetics, and consequent treatment preference, the CM+CAF alternative not only avoided the morbidity of donor graft harvest but also presented color and texture scores equivalent to the CTG+CAF control. Overall subject-reported esthetic satisfaction with both test and control treatments was equivalent. When balanced with subject-reported outcomes for esthetics and compared to historical root coverage reported by other investigators, CM+CAF seems to present a viable alternative to the traditional CTG+CAF gold standard, without the morbidity of graft harvest.

ACKNOWLEDGMENTS

This study was supported in part by an educational grant from Geistlich Pharma (10812-008). Drs. Scheyer and McGuire have received financial support for research from Geistlich Pharma, and Dr. McGuire has received lecture fees from Geistlich Pharma. The authors thank Rebecca Garcia, RDH, Director of Clinical Research, Perio Health Clinical Research Center (PHCRC), Houston, Texas, for recording outcome measures and coordinating data, and Cindy Wainscott, CDA, PHCRC, for study administration.

REFERENCES

1. Chambrone L, Sukekava F, Araújo MG, Pustiglioni FE, Chambrone LA, Lima LA. Root coverage procedures for the treatment of localized recession-type defects. *Cochrane Database Syst Rev* 2009;(Issue 2): CD007161.
2. Oates TW, Robinson M, Gunsolley JC. Surgical therapies for the treatment of gingival recession. A systematic review. *Ann Periodontol* 2003;8:303-320.
3. Academy Report. Oral reconstructive and corrective considerations in periodontal therapy. *J Periodontol* 2005;76:1588-1600.
4. Wessel JR, Tatakis DM. Patient outcomes following subepithelial connective tissue graft and free gingival graft procedures. *J Periodontol* 2008;79:425-430.

5. Griffin TJ, Cheung WS, Zavras AI, Damoulis PD. Postoperative complications following gingival augmentation procedures. *J Periodontol* 2006;77:2070-2079.
6. da Silva RC, Joly JC, de Lima AF, Tatakis DN. Root coverage using the coronally positioned flap with or without a subepithelial connective tissue graft. *J Periodontol* 2004;75:413-419.
7. Zucchelli G, Clauser C, De Sanctis M, Calandriello M. Mucogingival versus guided tissue regeneration procedures in the treatment of deep recession type defects. *J Periodontol* 1998;69:138-145.
8. McGuire MK, Nunn M. Evaluation of human recession defects treated with coronally advanced flaps and either enamel matrix derivative or connective tissue. Part 1: Comparison of clinical parameters. *J Periodontol* 2003;74:1110-1125.
9. Wilson TG Jr., McGuire MK, Nunn ME. Evaluation of the safety and efficacy of periodontal applications of a living tissue-engineered human fibroblast-derived dermal substitute. II. Comparison to the subepithelial connective tissue graft: A randomized controlled feasibility study. *J Periodontol* 2005;76:881-889.
10. Aichelmann-Reidy ME, Yukna RA, Evans GH, Nasr HF, Mayer ET. Clinical evaluation of acellular allograft dermis for the treatment of human gingival recession. *J Periodontol* 2001;72:998-1005.
11. McGuire MK, Scheyer ET, Schupbac P. Growth factor–mediated treatment of recession defects: A randomized controlled trial and histologic and microcomputed tomography examination. *J Periodontol* 2009;80:550-564.
12. Cairo F, Pagliaro U, Nieri M. Treatment of gingival recession with coronally advanced flap procedures: A systematic review. *J Clin Periodontol* 2008;35 (Suppl. 8):136-162.
13. McGuire MK, Scheyer ET, Nunn ME, Lavin PT. A pilot study to evaluate a tissue-engineered bilayered cell therapy as an alternative to tissue from the palate. *J Periodontol* 2008;79:1847-1856.
14. Zucchelli G, Mele M, Mazzotti C, Marzadori M, Montebugnoli L, De Sanctis M. Coronally advanced flap with and without vertical releasing incisions for the treatment of multiple gingival recessions: A comparative controlled randomized clinical trial. *J Periodontol* 2009;80:1083-1094.
15. 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.
16. Langer B, Langer L. Subepithelial connective tissue graft technique for root coverage. *J Periodontol* 1985; 56:715-720.
17. Polson AM, Proye MP. Effect of root surface alterations on periodontal healing. II. Citric acid treatment of the denuded root. *J Clin Periodontol* 1982;9:441-454.
18. Gibson JA, Wade AB. Plaque removal by the Bass and roll brushing techniques. *J Periodontol* 1977;48:456-459.
19. Boyne PJ, Herford AS. Evaluation of a special collagen implant material as a substitute for free mucosal or skin grafts in oral soft tissue surgery. *Proc Am Institute Oral Biol* 2002;103-109.
20. Sanz M, Lorenzo R, Aranda JJ, Martin C, Orsini M. Clinical evaluation of a new collagen matrix (Mucograft-R prototype) to enhance the width of keratinized tissue in patients with fixed prosthetic restorations: A randomized prospective clinical trial. *J Clin Periodontol* 2009;36:868-876.
21. Lang NP, Löe H. The relationship between the width of keratinized gingiva and gingival health. *J Periodontol* 1972;43:623-627.
22. Wennström J, Lindhe J, Nyman S. Role of keratinized gingiva: Gingival health. Clinical and histological study of normal and regenerated gingival tissues in dogs. *J Clin Periodontol* 1981;8:311-328.
23. Wennström JL. Mucogingival therapy. *Ann Periodontol* 1996;1:671-706.
24. Wilson R. Marginal tissue recession in general dental practice: A preliminary study. *Int J Periodontics Restorative Dent* 1983;3:40-53.
25. Periodontal Literature Reviews. Surgical therapy. *J Periodontol* 1996;(Chapter 9):145-203.
26. Kokich VO Jr., Kiyak HA, Shapiro PA. Comparing the perception of dentists and lay people to altered dental esthetics. *J Esthet Dent* 1999;11:311-324.
27. Giannobile WV, Somerman MJ. Growth and amelogenin-like factors in periodontal wound healing. A systematic review. *Ann Periodontol* 2003;8:193-204.
28. 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.

Correspondence: Dr. Michael K. McGuire, 3400 S. Gessner St., #102, Houston, TX 77063. E-mail: mkmperio@swbell.net.

Submitted December 10, 2009; accepted for publication March 4, 2010.