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

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Background: The subepithelial connective tissue graft, traditionally harvested from the patient's palate, is commonly used for root coverage in periodontal recession defects. This study evaluates the safety and effectiveness of a living human fibroblast-derived dermal substitute (HF-DDS) compared to a connective tissue graft (CTG) for root coverage in these situations.

Methods: Thirteen patients were selected for this study. Each patient had Miller Class I or II bilateral facial recession defects ≥3 mm on two non-adjacent teeth. The test tooth received an HF-DDS graft, while a CTG was placed on the control site. The 10 test surgeries were performed by one operator and three pilot surgeries were performed by another surgeon. Eight of the HF-DDS sites received a single thickness of material; five received a double thickness. Clinical measurements were taken at baseline; 1 week; and 1, 3, and 6 months following surgery. Parameters measured were plaque index, recession depth, clinical attachment levels, recession width, probing depth, and width of keratinized tissue. All clinical readings were taken by a masked, calibrated examiner.

Results: There were no statistically significant differences between the test and control groups. The amount of root coverage was slightly greater for the control group than for the test group, but statistically the difference was insignificant. The width of the recession defect measured at the cemento-enamel junction (CEJ) for the test group was slightly smaller than that of the control group at the conclusion of the study. The amount of keratinized tissue was the same in both groups at 6 months. The probing depth was slightly greater in the control group as was the gain in clinical attachment, but neither was statistically significant. The amount of root coverage obtained when one layer of HF-DDS was used compared to the amount of coverage obtained when two layers were used approached statistical significance, but the small sample size may have been responsible for the difference.

Conclusion: Within the limits of this study, the human fibroblast-derived dermal substitute may offer potential as a substitute to the connective tissue graft for covering areas of facial Miller Class I or Class II gingival recession in humans. *J Periodontol 2005;76:881-889.*

KEY WORDS

Comparison studies; fibroblasts; gingival recession/surgery; gingival recession/therapy; grafts, connective tissue; grafts, dermal replacement; tissue engineering.

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Gingival recession is a common clinical finding and when therapy is deemed necessary, numerous corrective measures have been proposed for these defects.[1-13] Treatment is generally focused on resolving patient-centered concerns including, but not limited to, root sensitivity, increased potential for root caries, difficulty in plaque control, and esthetics. A number of papers suggest that the subepithelial connective tissue graft (CTG) has not only the highest percentage of mean root coverage, but also the least variability.[2-4] A recent systematic review of the literature[5] which included a meta-analysis reinforced the experience of many clinicians by confirming that the connective tissue graft is the most predictable technique for root coverage in most situations, although the analysis did not find the connective tissue graft to be significantly better than the coronally advanced flap in attaining complete coverage. A limiting factor of this technique is the requirement of a remote surgical site to harvest the connective tissue. Often the donor site has more morbidity than the graft site and is associated with surgical challenges for the clinician. In addition, the amount of donor tissue is limited for any single surgical procedure.

Tissue engineering may provide the solution to this dilemma by providing an unlimited source of donor tissue. Part I of this series evaluated the safety and efficacy of a living tissue-engineered human fibroblast-derived substitute (HF-DDS) compared to a gingival autograft.[6]

The aim of the current randomized, controlled, split-mouth design pilot study was to compare the feasibility of HF-DDS placed under a coronally advanced flap (test group) to subepithelial connective tissue graft (CTG) placed under a coronally advanced flap (control group) in patients with recession type defects. Patients were followed for 6 months.

MATERIALS AND METHODS

Study Population

Thirteen patients with Miller Class I or II[14] buccal gingival recession ≥3 mm on two teeth in different quadrants of the same jaw who met the inclusion criteria were selected from patients seeking treatment in the authors' private practices. Non-adjacent test and control teeth had the same Miller classification with recession depth measurements within ≤2 mm of each other. Root coverage was indicated at the time of grafting. Patients had sufficient palatal donor tissue available for the indicated connective tissue graft, and the graft could be taken from either side of the palate. If a patient was capable of bearing children, she was using a medically accepted means of birth control and tested negative on a urine pregnancy test. The patient population, ranging in age from 38 to 60 years (mean age 47.7 years), included two men and 11 women. A written Institutional Review Board approved consent form regarding the study was obtained from each patient. All patients were able and willing to participate in the study and gave their informed consent. No patients were participating in another clinical study involving a therapeutic intervention (either medical or dental) nor had they participated in such a study within 30 days of the day 0 visit. Twelve of the patients (92.3%) were of Caucasian descent, and one was Hispanic (7.7%). All patients were non-smokers with no history of diabetes. Occlusal interferences were identified and eliminated through occlusal adjustment, and hard acrylic bite guards were constructed for those patients with parafunctional habits. No patient had: 1) teeth with extremely prominent root surfaces (more than one-half the diameter of the root facial to the cortical plate); 2) one or more medical condition(s), including severe renal, hepatic, hematologic, neurologic, or immune disease that, in the opinion of the investigator, would make the patient an inappropriate candidate for the study; 3) a malignant disease not in remission for 5 years or more. No patient had taken any medications known to affect tissue repair/wound healing within 2 weeks of the day 0 visit, nor was any patient taking warfarin sodium or heparin or had a clinically significant infection in the area(s) intended for surgery. No prior grafting procedure had been performed on one or both of the study teeth. No patient received greater than 20% on the O'Leary plaque index.[13] No molar teeth or any tooth with a mobility ≥2 (scale 0 to 3) was included. No patients had known allergies to medications used during therapy and follow-up. Because of the study design, each patient served as his or her own control, so that extraneous factors such as oral hygiene, compliance, etc., would be controlled within each subject. The first three patients were used to determine surgical and material handling techniques and were not included in the statistical analysis.

Clinical Assessment

At baseline and post-surgical follow-ups, the treated sites were clinically examined, defect measurements recorded, and clinical photographs taken. Radiographs were taken at baseline. The primary study objective was the reduction of recession depth. The secondary feasibility parameters included change in tooth mobility, recession width, amount of keratinized tissue, probing depth reduction, clinical attachment level, color and texture, and patient discomfort and satisfaction. A medical history, a complete dental history, and periodontal evaluation were performed at the screening visit. Baseline parameters included: 1) recession depth measured from the CEJ to the free gingival margin (FGM) on the mid-facial of the tooth; 2) clinical attachment level cal-

culated by adding the recession depth and the probing depth; 3) recession width at the CEJ; 4) amount of keratinized tissue measured from the mucogingival junction (MGJ) to the FGM; 5) probing depth at the point of the gingival defect measured from the FGM to the location of the tip of the periodontal probe inserted into the sulcus; and 6) width of attached gingiva calculated by subtracting the probing depth measurement from the amount of keratinized tissue. Measurements were made to the nearest millimeter with standardized UNC periodontal probes with 1.5 mm graded tip. Patient discomfort and satisfaction were evaluated by questionnaire. Baseline measurements were repeated at 3 (with the exception of probing) and 6 months. All assessments were performed by a masked calibrated examiner. Training and calibration was conducted prior to the start of the study to ensure intra- and extra-examiner reproducibility.

Test Material

The test material is a tissue-engineered human dermal replacement graft (HF-DDS)§ manufactured through a 3-dimensional cultivation of human diploid fibroblast cells on a polymer scaffold. The fibroblasts secrete a mixture of growth factors and the dermal implant contains matrix proteins and glycosaminoglycans. A detailed description of the test material can be found in Part I of this study.[6]

Surgical Procedure

Following the screening examination, all subjects received oral hygiene instructions and patients were not appointed for surgery until they achieved a modified O'Leary plaque index score of less than 80%.[13] The test and control treatments were performed at the same surgical appointment. A predetermined randomization scheme was contained in a sealed envelope and labeled by the patient identification number. The randomization scheme assigned the study site designation for each tooth, a donor site, and the treatment modality. Patients were not informed as to which treatment either study tooth would be receiving. However, if the patient became aware of which treatment a study tooth received, they were not disqualified from the study. Within group 1, patients had one layer of HF-DDS placed under a coronally advanced flap in one of the deficient zones. Within group 2, patients had two layers of HF-DDS placed under a coronally advanced flap in one of the deficient zones. In both groups, the tooth randomized to the control regimen had an autogenous subepithelial connective tissue graft placed under the coronally advanced flap in the other deficient zone.

To avoid potential bias from mechanical stress secondary to preferential chewing on the side of the mouth opposite the control donor graft site, patients were stratified such that 50% of the patients had the donor palatal graft placed on the same side of the mouth from which it was taken and 50% had the donor palatal graft placed on the opposite side.

The following prescriptions were provided: five non-steroidal anti-inflammatory tablets to be taken once daily following the procedure, 30 amoxicillin (250 mg) tablets taken 3 times daily for 10 days beginning the day prior to the procedure or azithromycin if allergic to amoxicillin, three bottles of 0.12% chlorhexidine to rinse with twice daily for 1 month beginning the day prior to the procedure, and 20 hydrocodone tablets one or two to be taken every 4 to 6 hours as needed for any pain following the procedure.

Surgical Protocol

Following the onset of local anesthesia, the exposed root surface was planed and scaled using (as needed) chisels, curets, and finishing burs to remove plaque and other accretions, as well as root surface irregularities, and to reduce root prominence (Figs. 1 through 3). Following the protocol originally outlined by Langer and Langer,[15] a sulcular incision was made at the site of recession and the incision was extended horizontally into the adjacent interdental areas slightly coronal to the tooth's CEJ. The horizontal incisions were connected to vertical releasing incisions both mesially and distally. A partial thickness flap was elevated in an apical direction until the mucogingival junction had been passed. The incision was then extended with blunt dissection into the vestibular lining mucosa to eliminate muscle tension. This tension-free flap would be positioned coronally at the level of the CEJ following placement of the graft. The exposed root surface was then conditioned with a neutrally buffered EDTA‖ for 2 minutes following the manufacturer's instructions, and then the area was thoroughly rinsed with saline.

Following the manufacturer's instructions, the bioreactor containing the frozen HF-DDS was taken through the rinse and thaw process. The amount of HF-DDS needed to cover the denuded root and the adjacent periosteal bed was measured with a periodontal probe and the appropriate size piece of HF-DDS was cut with scissors from the sheet of HF-DDS in the bioreactor.

The exposed root surface and the adjacent periosteal bed in the test site were covered with either a single layer or double layer of HF-DDS. The HF-DDS was sutured at each interproximal area. The test material was then covered by coronally advancing the flap and securing it at the level of the CEJ with 5-0 chromic gut sutures secured to the papilla. Both vertical incisions were closed with chromic gut sutures. Slight pressure was

§ Dermagraft, Advanced Tissue Sciences, Inc., La Jolla, CA.
‖ PrefGel, Straumann Biologics Division, Waltham, MA.

applied to the flap after suturing. All surgical procedures were the same for the control site except that a CTG, which had been harvested from the palate, was placed.

All patients received instruction in proper oral hygiene measures. Patients were instructed not to brush the teeth in the treated areas, but to use 0.12% chlorhexidine gluconate mouthrinse for 1 minute twice daily for the first month following surgery. Patients were instructed to avoid excessive muscle tractioning or trauma to the treated areas for the first 3 weeks. After this period, patients were instructed in a brushing technique that minimized apically directed trauma to the soft tissue of the treated teeth. After 4 weeks, the patients were instructed in normal toothbrushing. All patients were seen 1 week after surgery and at months 1, 3, and 6. At these visits any adverse events as well as adverse device effects were recorded; clinical data were taken and recorded, including medication taken. The patients responded to a discomfort and satisfaction questionnaire and completed a pain scale. In addition to the preceding measurements, an assessment of color and texture of each

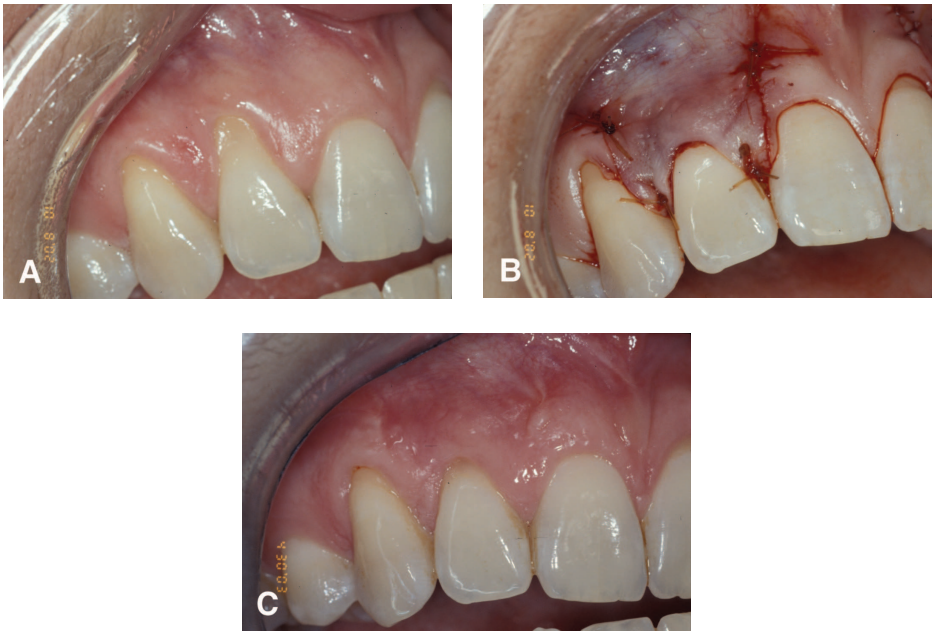

Figure 1.
Maxillary right lateral incisor, test. ***A)*** *Preoperative view.* ***B)*** *Right side sutured after HF-DDS was placed.* ***C)*** *The right side 6 months after surgery.*

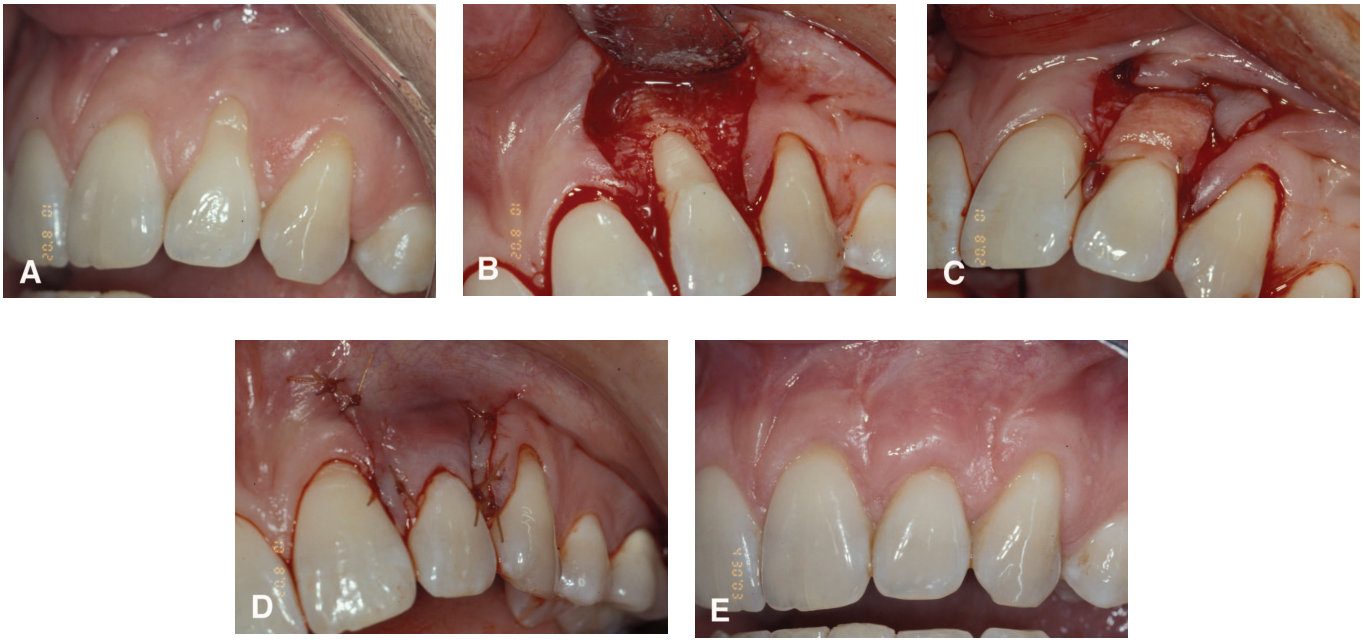

Figure 2.
Maxillary left lateral incisor, control. ***A)*** *Preoperative view.* ***B)*** *and* ***C)*** *The connective tissue graft, taken from the palate, is positioned.* ***D)*** *Left side sutured.* ***E)*** *The left side 6 months after surgery.*

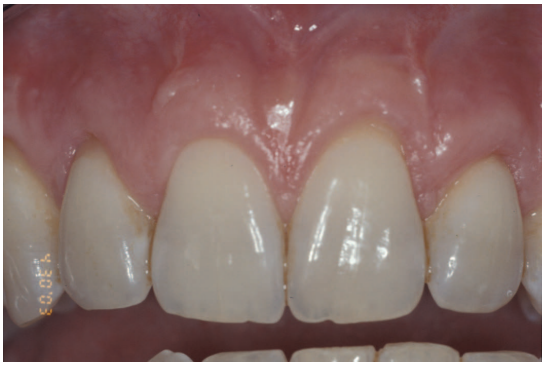

Figure 3.
A frontal view of the case shown in Figures 1 and 2 seen 6 months after surgery.

Table 1.

Baseline Clinical Parameters Summary Statistics

	Mean (Median)	SD	Range	*P**
Recession depth				
Control	3.9 (4.0)	0.88	(3-5)	
Test	3.7 (3.9)	0.82	(3-5)	NS†
Recession width				
Control	3.9 (4.0)	0.88	(3-5)	
Test	4.2 (4.0)	0.92	(3-6)	NS
Keratinized tissue				
Control	1.9 (2.0)	0.88	(1-3)	
Test	1.9 (2.0)	0.88	(1-4)	NS
Probing depth				
Control	0.8 (1.0)	0.42	(0-1)	
Test	0.9 (1.0)	0.32	(0-1)	NS
Clinical attachment				
Control	4.7 (4.5)	0.82	(4-6)	
Test	4.6 (4.5)	0.97	(3-6)	NS

* Based on Wilcoxon signed-rank test.
† Not significant.

study site and a mobility assessment of each study tooth were recorded at months 3 and 6. Probing depth was recorded at 6 months. Photographs were taken at each visit.

RESULTS

The mean recession depths for the two groups at baseline were 3.9 mm (CTG) and 3.7 mm (HF-DDS). There was a mean recession width of 3.9 mm (CTG) versus 4.2 mm (HF-DDS). The coronoapical dimension of the keratinized tissue before surgery was 1.9 mm in both groups, while the mean probing depths were 0.8 mm (CTG) and 0.9 mm (HF-DDS) and attachment levels were 4.7 mm (CTG) and 4.6 mm (HF-DDS) (Table 1).

The average amount of root coverage at 6 months was +2.25 mm for the CTG group and +2.13 mm for the HF-DDS group (data not shown). The primary efficacy parameter was the change in depth of the recession defect. A gain of 64.4% (control) and 56.7% (test) of root coverage was seen at 6 months (Table 2).

Following surgery, the control sites had less residual recession (0.7 versus 1.4 mm) but test and control sites were essentially the same (1.4 versus 1.6 mm) at 6 months. The width of keratinized tissue found at 6 months was the same for both groups (2.1 mm), while probing depths were essentially the same, 1.1 mm (CTG) and 1.0 mm (HF-DDS), as were clinical attachment levels, 2.5 mm versus 2.8 mm (Table 3).

Table 2.

Summary Statistics of Root Coverage (%) (N = 10)

	Mean (Median)	SD	Range	*P**
1 month				
Control	83.7 (80.0)	15.3	(60-100)	
Test	62.8 (63.3)	17.6	(33.3-100)	0.018
3 months				
Control	64.2 (70.8)	23.8	(25-100)	
Test	47.0 (50.0)	20.3	(0-66.7)	NS†
6 months				
Control	64.4 (58.3)	31.9	(25-100)	
Test	56.7 (60.0)	27.8	(0-100)	NS
Last visit‡				
Control	67.5 (73.3)	28.9	(25-100)	
Test	53.7 (55.0)	25.6	(0-100)	NS

* Based on Wilcoxon signed-rank test.
† Not significant.
‡ Last visit that patient was examined; this includes the eight subjects who completed the study and data for two subjects at the 3-month follow-up.

Statistical Analysis

Three patients (1, 2, and 3) were used to determine surgical and material handling techniques and were not included in the statistical analysis. Eight patients were available for all follow-ups and two patients did not return for the 6-month evaluation for unknown reasons.

Summary statistics were computed for clinical parameters at baseline for test and control sites and are shown in Table 1. The Wilcoxon signed-rank test was used to compare baseline clinical parameters. No statistically significant differences were detected, although the dif-

Table 3.

Summary Statistics of Clinical Parameters

	Mean (Median)	SD	Range	P*
Recession depth				
1 month				
Control	0.7 (1.0)	0.68	(0-2)	
Test	1.4 (1.5)	0.70	(0-2)	0.035
3 months				
Control	1.4 (1.0)	0.97	(0-3)	
Test	1.9 (2.0)	0.57	(1-3)	NS†
6 months				
Control	1.4 (1.5)	1.30	(0-3)	
Test	1.6 (2.0)	0.92	(0-3)	NS
Recession width 6 months				
Control	2.4 (3.0)	2.07	(0-5)	
Test	3.4 (3.5)	1.77	(0-5)	NS
Keratinized tissue 6 months				
Control	2.1 (2.0)	0.84	(1-3)	
Test	2.1 (2.0)	0.64	(1-3)	NS
Probing depth 6 months				
Control	1.1 (1.0)	0.35	(1-2)	
Test	1.0 (1.0)	0.54	(0-2)	NS
Clinical attachment 6 months				
Control	2.5 (2.5)	1.20	(1-4)	
Test	2.8 (3.0)	0.46	(2-3)	NS

* Based on Wilcoxon signed-rank test.
† Not significant.

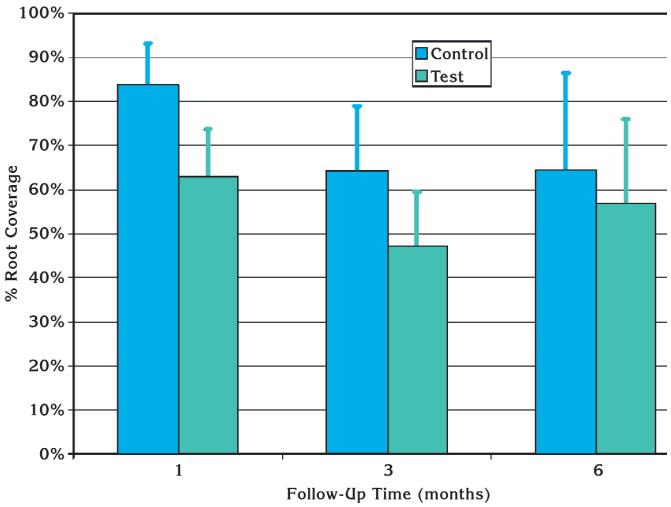

Figure 4.
Percent root coverage over time.

ference in recession width at baseline approached statistical significance ($P = 0.083$) with the test sites being somewhat wider than the control sites.

Summary statistics were calculated for clinical parameters over time by treatment group and compared using Wilcoxon signed-rank tests (Table 3). The only statistically significant difference detected was for recession depth at 1 month with control sites demonstrating half the recession depth of test sites ($P = 0.035$).

Percent of root coverage was calculated for test and control sites at 1, 3, and 6 months and for the last time seen (Table 2; Fig. 4). Comparisons between test and control sites for percent root coverage were conducted using Wilcoxon signed-rank tests. Control sites demonstrated significantly greater root coverage after 1 month compared to test sites and approached statistical significance at 3 months with control sites demonstrating somewhat greater root coverage. No statistically significant differences were noted for either 6 months or for the last time period examined. The percent root coverage at 3 months for the two patients lost to follow up was used in the comparison for the last time period examined.

This study was designed by one of the authors (MKM) in conjunction with the sponsor. It was originally designed as a multi-center investigation to test the feasibility of the HF-DDS as an alternative to the CTG. The results reported in this paper represent only one center and are therefore, underpowered, so little inference can be drawn from the lack of statistical significance at 3 months, 6 months, and for the last period of follow-up. At 3 months, we had 41% power to detect a 15% difference in root coverage between test and control groups, and at 6 months, we had 30% power to detect a 15% difference in root coverage between test and control groups. The drop-off in root coverage after 1 month did not appear to be as great for the test sites as for the control sites. Furthermore, after 6 months, three subjects demonstrated greater root coverage in test sites compared to control sites, four subjects demonstrated greater root coverage in control sites compared to test sites, and one subject demonstrated 100% root coverage in both the test site and control site.

DISCUSSION

The purpose of this randomized, controlled, split-mouth design study was to test the feasibility of human fibroblast-derived dermal substitute placed under a coronally advanced flap (CAF) (test) as a potential substitute for subepithelial connective tissue graft (CTG) placed under a coronally advanced flap (control) in patients with recession type defects. The summary of evidence indicates that both procedures are effective in covering recession defects. It is because of its predictability that the CTG was used for comparison in this study.[1,5] Based on the information generated in Part I[6] of this series on the clinical

effect of various layers of HF-DDS, a decision was made to subdivide the test group evaluating one layer versus two layers of HF-DDS under the CAF. Significantly more root coverage was achieved with one layer of HF-DDS (2.5 mm versus 1.75 mm with the two layer subset). Even though the difference between the two subgroups was significant, the fact that there were only five sites in each category makes strong comparisons difficult.

This study demonstrated that there was no statistically significant difference in probing depth at baseline and between the two procedures at 6 months. Probing depths did increase by 0.1 mm in the HF-DDS group and by 0.3 mm in the CTG at 6 months compared to baseline (Table 2). Both procedures resulted in easily maintainable probing depths of less than 2 mm. A well-recognized benefit of the CTG is the corono-apical amount of keratinized tissue consistently produced. This study found that keratinized tissue increased at both test and control sites by an identical +0.2 mm at 6 months, resulting in a 2.1 mm zone of keratinized tissue (Table 2).

Many root coverage grafts are performed at the request of the patient because of esthetic concerns, root sensitivity, and to facilitate home care. Tissue contours and color match are important patient-related outcomes. Patient satisfaction was similar at all times regardless of the graft material used and the patients perceived no difference between test and control sites in terms of bleeding, appearance, or color match.

The clinical handling characteristics of the HF-DDS are favorable compared to a CTG. The membrane is easy to trim and place on the bed. Because it is very thin, the CAF is easier to advance over the HF-DDS than the CTG. A technique series using HF-DDS to cover a denuded root series can be seen in Figure 5. Because this was one of the initial three patients from the pilot study reported in Part I[6] of this series, the patient was followed for 12 months. As mentioned earlier, three patients, in the study described in Part I of this series, were used to determine surgical and material handling techniques and were not included in the statistical analysis.

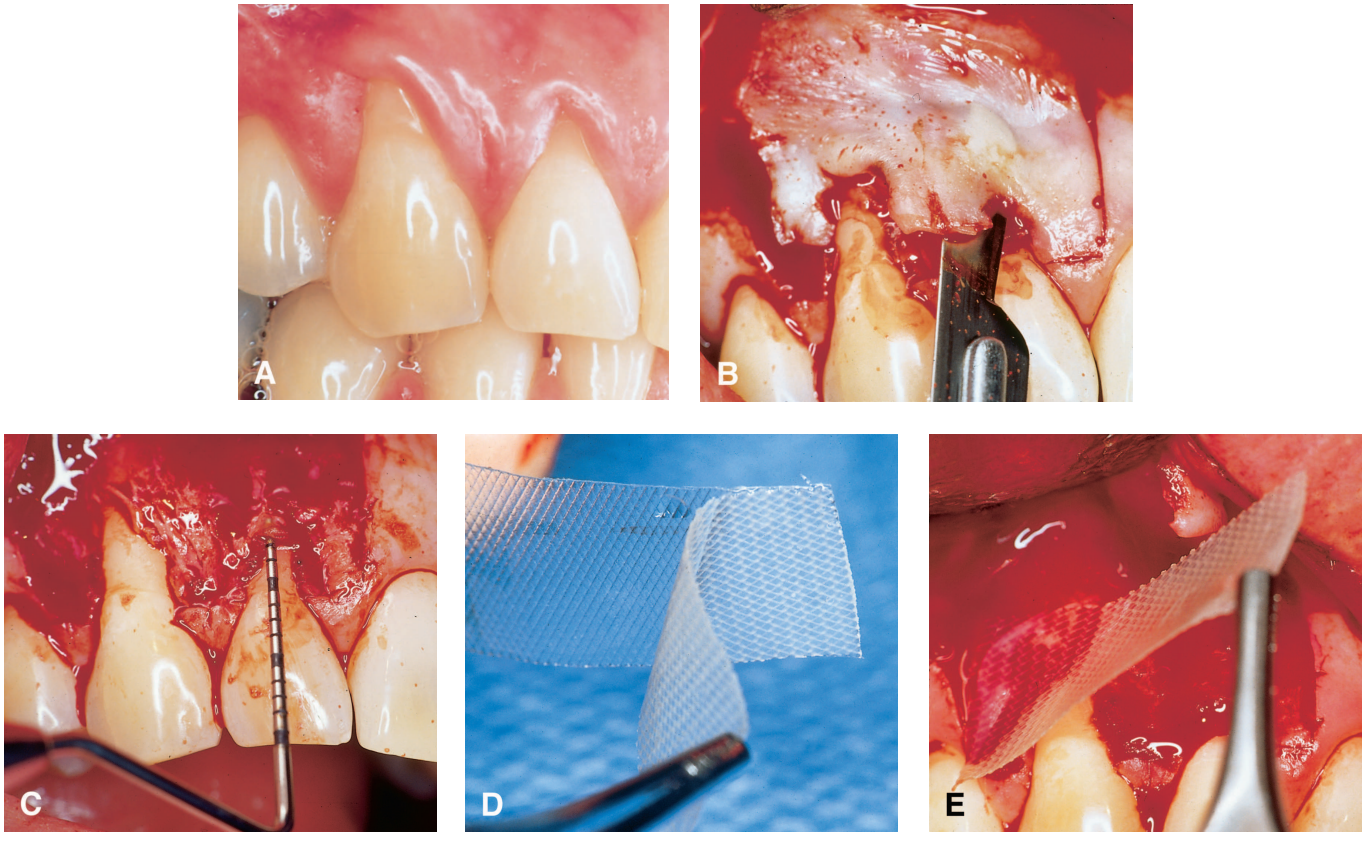

Figure 5.
Maxillary right lateral incisor and cuspid, test. ***A)*** *Preoperative view.* ***B)*** *The incision design for the flap.* ***C)*** *A partial-thickness flap was elevated and intraoperative measurements were obtained.* ***D)*** *The appropriate amount of HF-DDS was removed from the bioreactor.* ***E)*** *The HF-DDS was placed over the denuded root surfaces and recipient bed.*

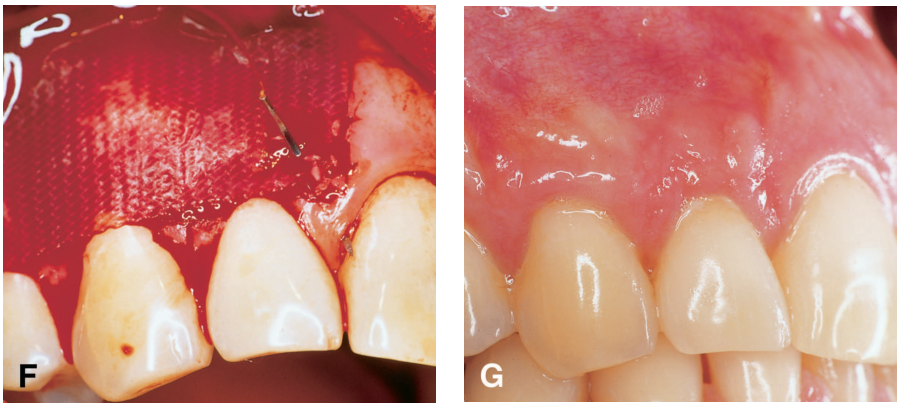

Figure 5. (continued)
F) *The graft was sutured at each interproximal area.* ***G)*** *Postoperative view at 6 months demonstrating complete root coverage and good tissue tone and texture.*

In the past, regardless of the type of graft placed over the avascular root surface, success depended on an adequate blood supply obtained by the placement over the graft of a coronally advanced flap. Though the bed upon which the graft is placed also provides blood supply, it has been shown to be inadequate, by itself, to support grafts over avascular root surfaces.[12] To the authors' knowledge, this study represented the first time that a living, metabolically active graft had been used to attempt root coverage. Because of the vitality of this graft, it was thought that perhaps complete coverage of the test material by a CAF might not be necessary. Based on that hypothesis, in patients 1, 2, and 3 root coverage was attempted by completely covering the HF-DDS with a CAF, by covering only the apical half of the test material by a CAF, or by placing the HF-DDS over the denuded roots and adjacent graft bed without covering any portion of it with a CAF. In all cases, root coverage grafts using the HF-DDS were successful only when all of the material was covered with a CAF. Even though the test material is a living, metabolically active graft with inherent angiogenic activity, it was not by itself robust enough to maintain viability over avascular root surfaces.

The positive results in the test sites of this pilot study may represent the effects of the living fibroblasts, the polymer matrix that carried the cells, or both of these elements. A case report describing the use of polyglactin 910 membranes for root coverage combined with collagen-hydroxyapatite graft material has been published,[11] but no papers describing the use of polyglactin 910 alone were found in electronic data base searches on the topic. As mentioned earlier, CTGs have produced superior root coverage results when compared to membranes. Thus, one would expect to have seen superior clinical results with CTGs, which did not occur in this study. A future study is warranted comparing the carrier matrix alone with one containing fibroblasts. A larger, multicenter, clinical trial using the approach outlined in this pilot study is a future possibility. Many questions remain, but if the results of a multicenter trial are found to be similar to this pilot study, the use of human fibroblast-derived dermal substitute may provide an unlimited source of donor tissue, thus reducing surgical challenges for the clinician and morbidity for the patient. Clearly, these results do not completely answer the question of the effectiveness of human fibroblast-derived dermal substitute in treating gingival defects. Further studies should be conducted to fully explore the potential of HF-DDS in treating gingival defects.

CONCLUSION

Within the limits of this study, the human fibroblast-derived dermal substitute may present an acceptable substitute to the connective tissue graft for covering recession defects. The coronally advanced flap with HF-DDS represents a simpler technique for the clinician and a less invasive surgery for the patient.

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REFERENCES

1. Clauser C, Nieri M, Franceschi D, Pagliaro U, Pini-Prato G. Evidence-based mucogingival therapy. *J Periodontol* 2003;74:741-756.
2. Raetzke PB. Covering localized areas of root exposure employing the "envelope" technique. *J Periodontol* 1985; 56:397-402.
3. Nelson SW. The subepithelial connective tissue graft. A bilaminar reconstructive procedure for the coverage of denuded root surfaces. *J Periodontol* 1987;58:95-102.
4. Harris RJ. A comparative study of root coverage obtained with guided tissue regeneration utilizing a bioabsorbable membrane versus the connective tissue with partial-thickness double pedicle graft. *J Periodontol* 1997;68:779-790.
5. Roccuzzo M, Bunno 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.
6. McGuire MK, Nunn ME. Evaluation of the safety and efficacy of periodontal applications of a living tissue-engineered human fibroblast-derived dermal substitute. I. Comparison to the gingival autograft: A randomized controlled pilot study. *J Periodontol* 2005;76:867-880.

7. Tatakis DW, Trombelli L. Gingival recession treatment: Guided tissue regeneration with bioabsorbable membranes versus connective tissue graft. *J Periodontol* 2000;71:299-307.
8. Aichelman-Reidy ME, Yukna RA, Evans GH, Nasr HF, Mayer ET. Clinical evaluation of acellular allograft dermis for the treatment of human recession. *J Periodontol* 2001;72:998-1005.
9. Wang H, Bunyaratavej P, Labadie M, MacNeil R. Comparison of 2 clinical techniques for treatment of gingival recession. *J Periodontol* 2001;72:1301-1311.
10. Wennström JL, Zucchelli G. Increased gingival dimensions. A significant factor for successful outcome of root coverage procedures? A 2-year prospective clinical study. *J Clin Periodontol* 1996;12:770-777.
11. De Sanctis M, Zucchelli G. Guided tissue regeneration with a resorbable barrier membrane (Vicryl) for the management of buccal recession: A case report. *Int J Periodontics Restorative Dent* 1996;16:435-441.
12. Paolantonio M, di Murro C, Cattabriga A, Cattabriga M. Subpedicle connective tissue graft versus free gingival graft in the coverage of exposed root surfaces. A 5-year clinical study. *J Clin Periodontol* 1997;24:51-56.
13. O'Leary T, Drake R, Naylor J. The plaque control record. *J Periodontol* 1972;43:38.
14. Miller PD. A classification of marginal tissue recession. *Int J Periodontics Restorative Dent* 1985;5(2):8-13.
15. Langer P, Langer L. Subepithelial connective tissue graft for root coverage. *J Periodontol* 1985;56:715-720.

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