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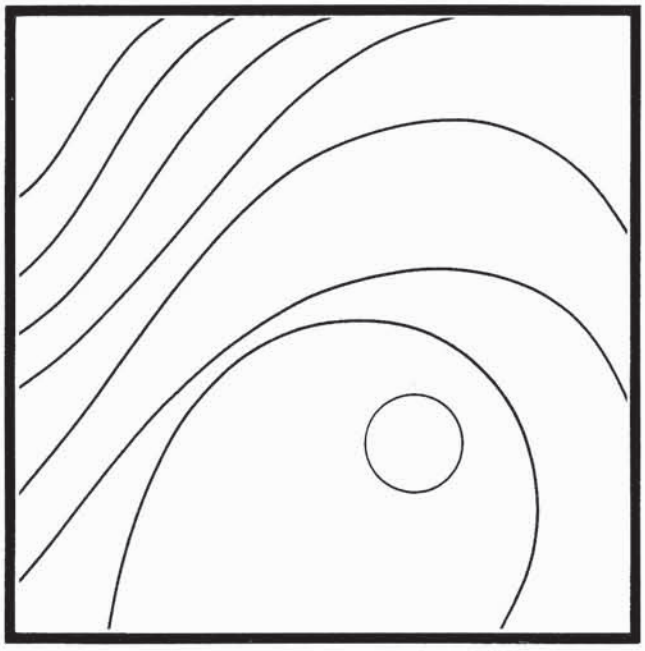

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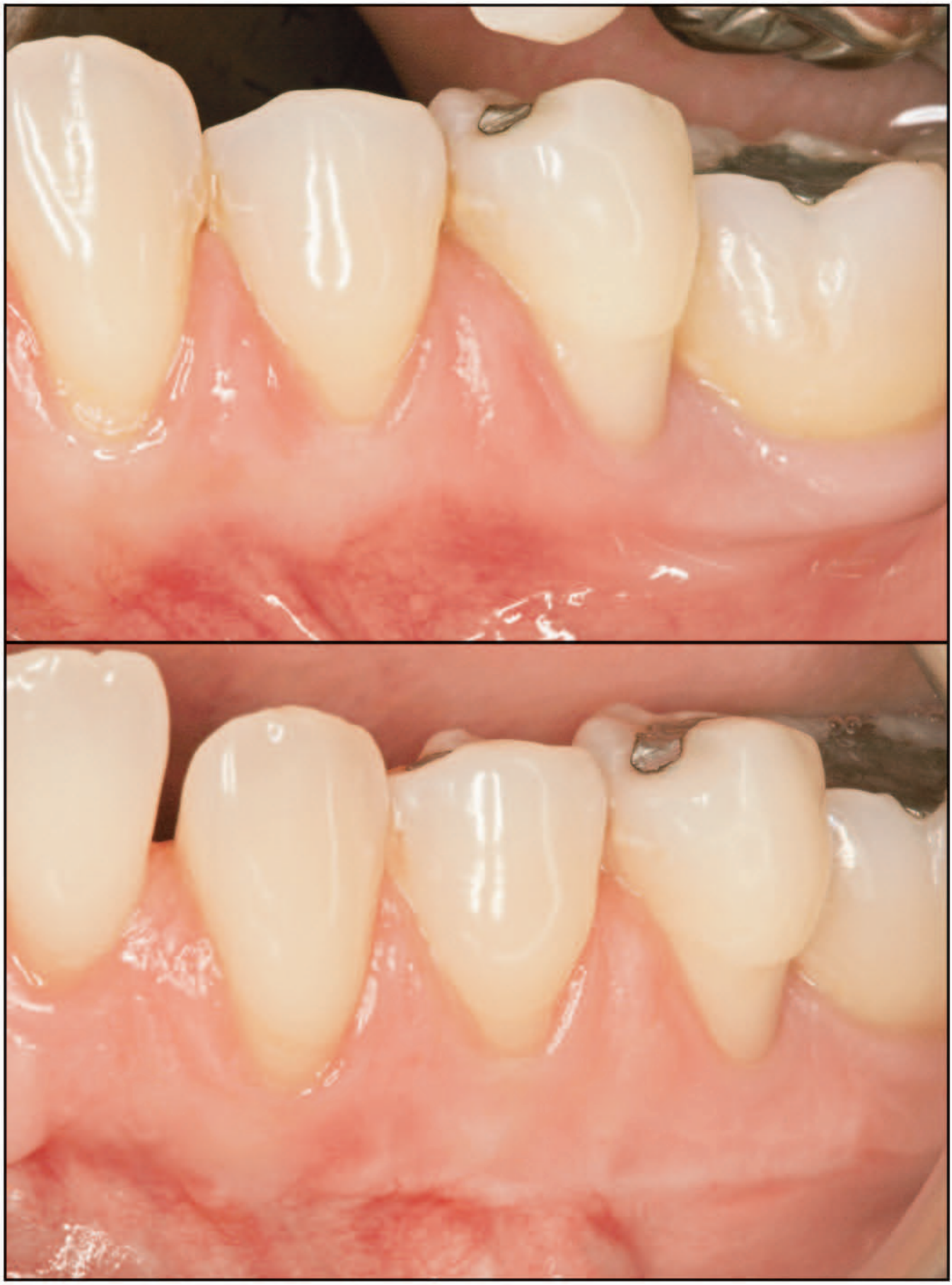

The Clinical Efficacy of DynaMatrix Extracellular Membrane in Augmenting Keratinized Tissue

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This study was conducted to compare the efficacy and feasibility of an extracellular matrix membrane (DynaMatrix) with that of an autogenous gingival graft in increasing the width of attached keratinized tissue. Six patients with an inadequate amount of attached keratinized gingiva on the bilateral facial aspect of the mandibular posterior teeth were recruited for this study. The defect sites were randomly subjected to receive either test (DynaMatrix membrane) or control (autogenous gingival graft) treatment. Both test and control sites achieved a clinically significant increase in the amount of keratinized gingiva, and the DynaMatrix membrane–treated sites blended well with the surrounding tissue, with a better appearance when compared to the autogenous gingival grafted sites. The biopsy specimens of both test and control sites appeared to be similar histologically, with mature connective tissue covered by keratinized epithelium. The results of both clinical and histologic evaluations have suggested a potential application of an extracellular matrix membrane in achieving gingival augmentation. (Int J Periodontics Restorative Dent 2010;30:151–161.)

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Attached keratinized gingiva is an integral part of the periodontium that is tightly bound to the underlying periosteum of alveolar bone or to the root surface, and it serves as an effective barrier in helping to resist damage from physical, chemical, and thermal trauma.[1] The rationale for increasing the zone of keratinized tissue for both teeth and dental implants is to enhance esthetics, to facilitate plaque control, and to prevent further gingival recession after restorative and orthodontic procedures.[2] Some have tried to defend the position that attached gingiva is unnecessary, but most investigators have demonstrated its clinical value.[3–11]

Clinicians have used autogenous gingival autografts and connective tissue grafts in addition to freeze-dried skin allografts and acellular dermal matrix to increase the zone of attached gingiva with a variety of results.[12–17] Autografts perform excellently but require a secondary harvest site that frequently adds to patient discomfort and postoperative complications and offers a limited quantity of donor tissue. Tissue-engineered soft tissue graft substitutes are limited by high production

costs, a small window of utilization, and the complex nature of obtaining tissue-engineered products.[18–22] Clearly, a gingival augmentation procedure that may be performed with only one surgical site (the recipient) is preferable over a procedure requiring two surgical sites when treatment outcomes are comparable.

The purpose of this randomized, controlled split-mouth study was to evaluate the safety, feasibility, and efficacy of an extracellular matrix membrane (DynaMatrix, Keystone Dental) to provide a predictable user-friendly technique for gingival augmentation. This split-mouth study compared the clinical and histologic results when using a DynaMatrix membrane to those obtained when using an autogenous gingival graft. DynaMatrix extracellular matrix membrane is obtained from the submucosa of the small intestine of pigs using a process that retains the natural composition of matrix molecules such as collagens (types I, III, IV, and VI), glycosaminoglycans, glycoproteins, proteoglycans, and growth factors.[23,24] They are known to play important roles in tissue repair and remodeling. Thus, the hypothesis was that the DynaMatrix membrane may promote epithelialization over the membrane and integrate with the surrounding oral mucosa.

Method and materials

Six patients (five women, one man) with a mean age of 41 years and no significant medical history were recruited for the study. The patients presented with less than 2 mm of attached keratinized gingiva bilaterally on the facial aspect of the mandibular posterior teeth (Figs 1a, 2a, and 2b). Subjects were enrolled and prepared for a gingival augmentation procedure in accordance with accepted dental practice guidelines, which included an informed consent form that was reviewed and signed prior to treatment. Initial periodontal therapy, including oral hygiene instructions and adult prophylaxis, was performed prior to surgery.

Clinical assessment

Periodontal evaluations including Plaque Index,[25] Gingival Index,[26] probing depth, gingival recession, and keratinized gingiva were performed at the facial aspect of each tooth at baseline and at 13 weeks by a calibrated clinician to ensure examiner reproducibility. The mucogingival junction was determined by rolling the alveolar mucosa coronally with the side of a probe, and all measurements were made to the nearest millimeter using a periodontal probe (UNC 15, Hu-Friedy). In addition, clinical photographs were taken with a digital camera at baseline and subsequent postsurgical follow-up visits. Differences in clinical measurements between baseline and 13 weeks postsurgery within each group were assessed by the Wilcoxon signed rank test. The Mann-Whitney *U* test was used to analyze differences between DynaMatrix-treated and autogenous gingival graft–treated groups.

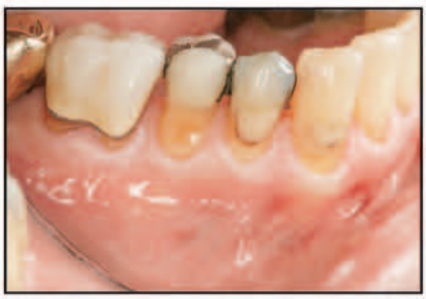
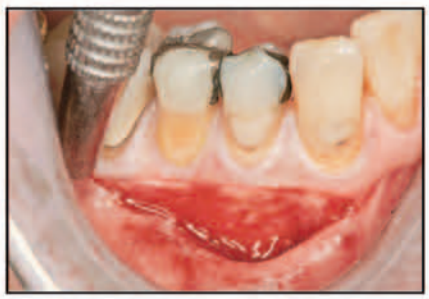


Fig 1a (left) *This patient presented with an inadequate zone of attached keratinized gingiva on the facial aspect of the mandibular right molar and premolars.*

Fig 1b (right) *The initial horizontal incision was made with a no. 15 blade at the mucogingival junction extending along the entire mucogingival defect area, and a partial-thickness flap was raised by a sharp apical dissection to develop the recipient bed.*



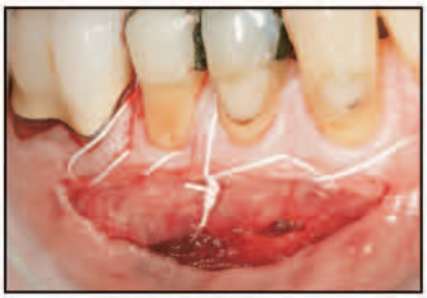


Fig 1c *Simple interrupted and sling suturing techniques were used to achieve close adaptation of the DynaMatrix membrane to the recipient site.*

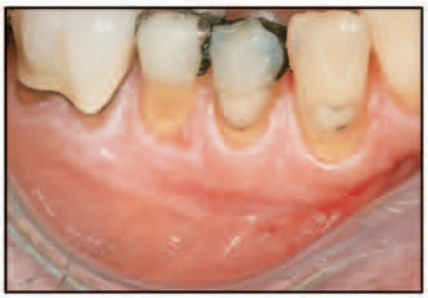


Fig 1d *One-month postsurgical evaluation revealed optimal clinical healing as well as an excellent blend of color and texture.*

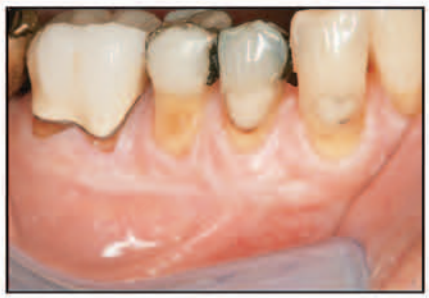
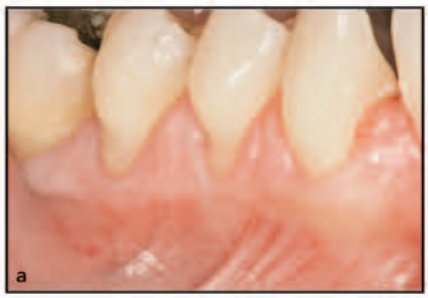
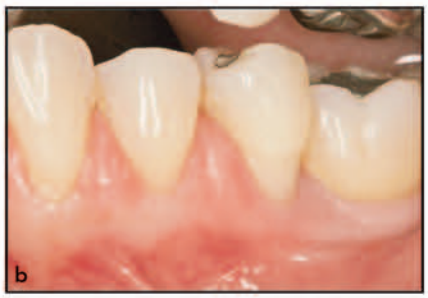


Fig 1e *Eleven-month postsurgical evaluation demonstrated stability of the result that was observed at 1 month.*

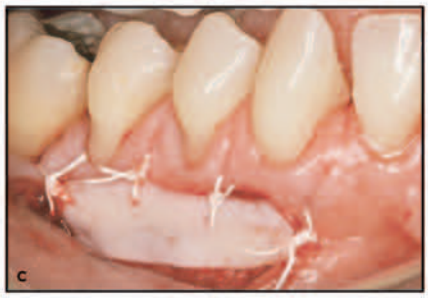
Gingival augmentation procedure

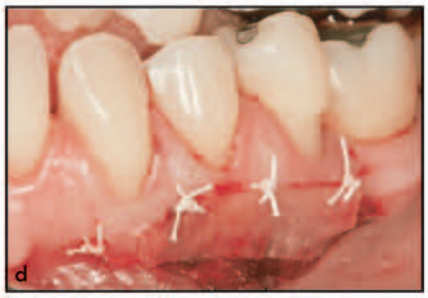
The gingival augmentation procedures were performed on an outpatient basis under local anesthesia (2% lidocaine with 1:100,000 epinephrine). Thorough scaling and root planing were previously performed. The test (DynaMatrix membrane) and control (autogenous gingival graft) treatments were performed at the same surgical appointment. The initial horizontal incision was made with a no. 15 blade at the mucogingival junction and extending along the entire mucogingival defect area, and a partial-thickness flap was raised by a sharp apical dissection to develop the recipient bed (Fig 1b). The recipient sites were randomly subjected to receive either test or control treatment. A gingival graft of uniform thickness was obtained from the hard palate on the same side as the recipient site, and the DynaMatrix was trimmed as necessary. For one of the test sites, a double-layer DynaMatrix membrane was used instead of a single-layer application (specimen 2L). Both grafting materials were stabilized on the firm periosteal bed with simple interrupted expanded polytetrafluoroethylene sutures (CV-5, Gore-Tex, W.L. Gore) at the coronal and lateral borders (Figs 1c, 2c, and 2d). These monofilament sutures were used to prevent bacterial wicking for a period of 2 weeks, and the sites were covered with a periodontal dressing (Coe-Pak, GC America). All patients received oral hygiene instructions and were taught to avoid the treated areas. Appropriate analgesics (ibuprofen, 800 mg three times a day for 5 days) were prescribed and instructions provided. Two weeks after surgery, the periodontal dressing and sutures were removed and the grafted areas were clinically assessed and carefully cleaned with chlorhexidine solution. Patients were seen at 2, 4, 6, 8, and 13 weeks postsurgery to monitor both healing and plaque control.



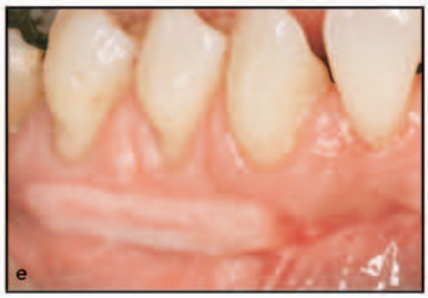


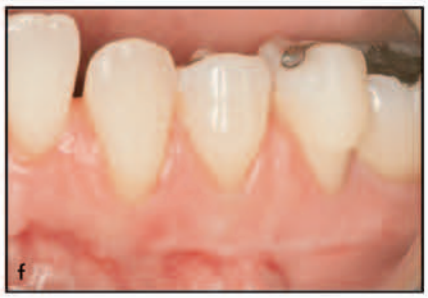
Figs 2a and 2b *This patient presented with less than 2 mm of attached keratinized gingiva bilaterally on the facial aspect of the mandibular premolars.* (a) *Right side, autogenous gingival graft;* (b) *left side, DynaMatrix.*





Figs 2c and 2d *Both grafting materials were stabilized on the firm periosteal bed with simple interrupted expanded polytetrafluoroethylene sutures at the coronal and lateral borders.* (c) *Right side, autogenous gingival graft;* (d) *left side, DynaMatrix.*





Figs 2e and 2f *Both grafted sites appeared to be mature and stable at 13 weeks.* (e) *Right side, autogenous gingival graft;* (f) *left side, DynaMatrix.*

Histologic preparation

A soft tissue biopsy was obtained under local anesthesia from each patient 13 weeks after the gingival augmentation procedure. It was obtained from the healed grafted portion with a 4-mm tissue biopsy punch (Uni-Punch, Premier Medical) from both control and test sites (n = 12 biopsies). The biopsy wound site was packed with a hemostatic agent (Hemostop, Technew) to aid in hemostasis and healing. All specimens were fixed in 10% neutral buffered formalin solution and delivered to a histologist for further descriptive histologic analysis.

Obtained soft tissue punch biopsies were fixed in 4% formalin. Following a wash in 0.185 mol/L sodium cacodylate buffer, the specimens were post-fixed with 1.33% osmium tetroxide in 0.185 mol/L sodium cacodylate buffer. Then, the specimens were washed in the same buffer, dehydrated in ethanol, and embedded in epoxy embedding medium (Fluka). Semithin sections (2 µm) were prepared for light microscopy with a Leica ultracut microtome and stained with methylene blue–Azure II.

Results

All six patients healed without serious adverse events following gingival augmentation surgeries and returned for their regular follow-up visits.

Table 1 Pre- and postsurgical measurements for autogenous gingival graft– and DynaMatrix-treated groups

	PI		GI		Mean PD		GR				KG	
							Vertical		Horizontal			
	AGG	Dyna	AGG	Dyna	AGG	Dyna	AGG	Dyna	AGG	Dyna	AGG	Dyna
Presurgery												
Mean	0.3 ± 0.5	0.3 ± 0.5	0.0 ± 0.0	0.0 ± 0.0	1.9 ± 0.6	2.0 ± 0.5	3.2 ± 2.0	3.4 ± 2.1	3.1 ± 1.0	3.4 ± 0.7	1.1 ± 1.1	0.8 ± 0.7
Range	0.0–1.0	0.0–1.0	0.0–0.0	0.0–0.0	1.0–2.7	1.3–3.0	1.0–6.0	1.0–7.0	2.0–5.0	2.0–4.0	0.0–3.0	0.0–2.0
Median	0	0	0	0	1.7	2.0	3.0	4.0	3.0	4.0	1.0	1.0
Postsurgery												
Mean	0.3 ± 0.5	0.3 ± 0.5	0.0 ± 0.0	0.0 ± 0.0	1.5 ± 0.4	1.6 ± 0.5	2.9 ± 1.7	3.4 ± 2.1	3.5 ± 0.9	3.3 ± 1.6	6.4 ± 0.9	3.4 ± 0.8
Range	0.0–1.0	0.0–1.0	0.0–0.0	0.0–0.0	1.0–2.0	1.0–2.3	0.5–5.0	0.0–6.0	2.0–5.0	0.0–5.0	5.0–8.0	2.5–5.0
Median	0	0	0	0	1.3	1.7	3.0	4.0	3.5	4.0	6.0	3.0
P	> .999	> .999	> .999	> .999	.035*	.049*	.129	> .999	.149	.884	.006*	.007*

PI = Plaque Index; GI = Gingival Index; PD = probing depth; GR = gingival recession; KG = keratinized gingiva; AGG = autogenous gingival graft; Dyna = DynaMatrix.
*Wilcoxon signed rank test ($P < .05$).

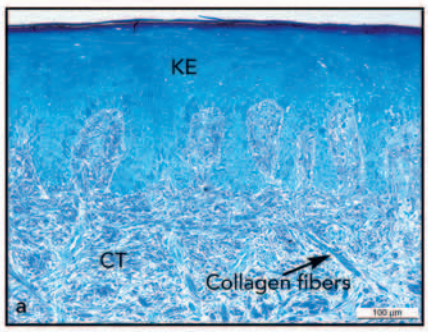
Table 2 Comparison of changes in AGG and Dyna groups

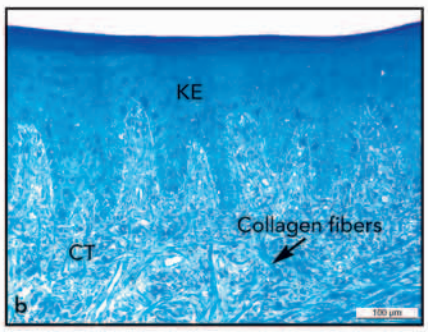
	Change in PD	Change in GRV	Change in GRH	Change in KG
AGG				
Mean	–0.4 ± 0.4	–0.3 ± 0.5	0.4 ± 0.7	5.3 ± 1.3
Range	–1.0–0.3	–1.0–0.5	–1.0–1.0	2.0–6.0
Median	–0.5	0	0.5	6
Dyna				
Mean	–0.4 ± 0.5	0.0 ± 0.9	–0.2 ± 1.7	2.6 ± 1.1
Range	–1.0–0.4	–1.0–1.0	–4.0–1.0	1.0–4.0
Median	–0.5	0	0.5	3
P	.894	.489	.675	.002*

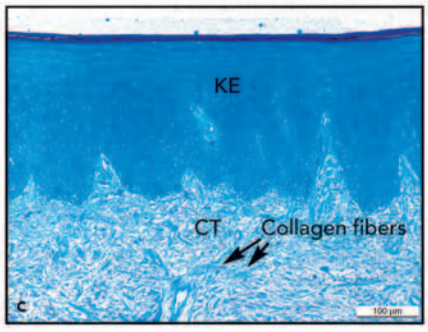
PD = probing depth; GRV = vertical gingival recession dimension; GRH = horizontal gingival recession dimension; KG = keratinized gingiva; AGG = autogenous gingival graft; Dyna = DynaMatrix.
*Mann-Whitney *U* test ($P < .05$).

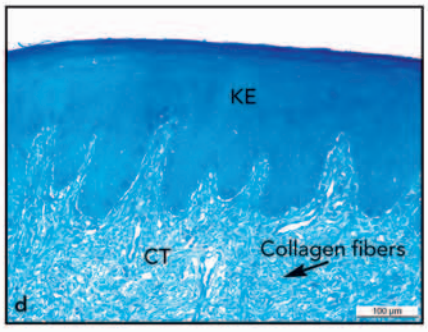
Clinical measurements

The Wilcoxon signed rank test for pre- and postoperative measurements for both control and test sites revealed a significant decrease in probing depth ($P = .035$ for control and $P = .049$ for test) and a significant increase in the amount of keratinized gingiva ($P = .006$ for control and $P = .007$ for test) (Table 1). The Mann-Whitney *U* test, used to compare the values for test and control sites, found no statistically significant differences ($P > .05$) in any of the variables (Plaque Index, Gingival Index, probing depth, or gingival recession) except for the change in the amount of keratinized gingiva ($P = .002$) between test and control groups preoperatively and at 13 weeks postoperative (Table 2). The mean dimensional change of keratinized gingiva postoperatively was 5.3 ± 1.3 mm for autogenous gingival graft sites and 2.6 ± 1.1 mm for DynaMatrix sites. Even though the dimension of keratinized gingiva obtained was less for the DynaMatrix









Figs 3a to 3d *The biopsies of both autogenous gingival graft* (a and c) *and DynaMatrix membrane sites* (b and d) *appear to be similar histologically, with mature connective tissue covered by keratinized epithelium. There was a small band of dense orthokeratinization at the top of the epithelium in all specimens. The size and appearance of the rete pegs were comparable within the individual.* (a) *Specimen 4R,* (b) *specimen 4L,* (c) *specimen 6L,* (d) *specimen 6R. KE = keratinized epithelium; CT = connective tissue.*

site when compared to the autogenous gingival graft site, it appeared that DynaMatrix was effective in increasing the zone of keratinized gingiva in the presence of a deep vestibule.

Clinical observations

When the patients presented for the 2-week postoperative visit, revascularization of the graft was evident since numerous erythematous areas appeared within the healing wound bed at both test and control sites. Both sites demonstrated complete clinical healing, and excellent color and texture blend were noted for DynaMatrix membrane–treated sites at 4 weeks postoperative (Fig 1d). Tissue maturation for the DynaMatrix membrane–treated sites appeared to be similar to that seen for the autogenous gingival grafted sites at 4 weeks. The 8-week postoperative result was maintained and stable up to the 13-week follow-up on both sites. When examined at the time of the biopsy, both grafted sites appeared to be mature and stable at 13 weeks (Figs 2e and 2f).

The mucogingival junction was very distinct for the autogenous gingival grafted sites because of a difference in the quality of the adjacent tissues and its typical "tire-patch" appearance. The DynaMatrix membrane–treated sites blended well with the surrounding tissue, and thus were more esthetically pleasing. The demarcation between the graft and the surrounding tissue was much less noticeable, as the new tissue was similar in color and texture (Fig 1e).

Histologic evaluation

The histologic evaluation was conducted for five pairs of control and test specimens instead of six because one of the control specimens was not embedded in a correct orientation. No membrane remnants were found at the 13-week postoperative visit for the DynaMatrix membrane–treated sites. The biopsies of both test and control sites appeared to be similar histologically, with mature connective tissue covered by keratinized epithelium (Fig 3). DynaMatrix-treated sites clinically appeared to achieve keratinization over the membrane, and the histologic evaluation confirmed that the overlying tissue was keratinized. The thickness of the epithelium was uniform among the collected tissue. The mean thickness of the epithelium is

Table 3 Epithelium thickness for AGG and Dyna groups

	Epithelium thickness (μm)
Dyna	
2L	308
3R	287
4L	296
5L	313
6R	268
AGG	
2R	513
3L	324
4R	254
5R	368
6L	287

Dyna = DynaMatrix; AGG = autogenous gingival graft.

given in Table 3 and was 349 ± 100 μm for the autogenous gingival graft–treated sites and 294 ± 17.9 μm for the DynaMatrix-grafted sites. There was one specimen (2R) in the autogenous gingival group with significantly longer rete ridges, leading to a higher mean in this group. The rete pegs in both groups were not of a consistent morphology, but there was a similarity of the rete pegs between corresponding test and control specimens, ie, long and small rete ridges in pair 2L and 2R, narrow and short in 3L and 3R, long and wide in 4L and 4R, narrow in 5L and 5R, short and narrow in 6L and 6R. The epithelium was of a keratinized type. There was a small band of dense orthokeratinization at the top of the epithelium in all specimens. There was a moderate density of the collagen matrix in all specimens except specimen 2L (double-layer DynaMatrix membrane site), which showed a denser configuration of the collagen matrix. No specimens revealed an inflammatory response.

Discussion

The existence and preservation of attached keratinized gingiva around natural teeth and dental implants seems to play an important role in periodontal and peri-implant health. The width of the attached keratinized gingiva on the facial aspect differs in different areas of the mouth; it is generally greater in the incisor area and becomes less in the posterior dentition.[27] Clinical researchers continue to search for alternative tissue sources to replace autogenous grafting without

the accompanying harvest site morbidity. To date, no optimal material has emerged to replace the autogenous gingival graft.

In an effort to replace the autogenous gingival graft, acellular dermal matrix has been investigated, with conflicting clinical results.[16,17,28–33] Contradictory results demonstrating its limitations and complications, such as an insignificant amount of keratinized gingiva obtained and significant graft shrinkage, have been reported.[17,30–33] Wei et al observed less predictability when compared to the autogenous graft because of the acellular dermal matrix's shrinkage and inflammatory response, which resembled a foreign-body reaction histologically.[30,31]

The current study was conducted to test the feasibility of an extracellular matrix membrane (DynaMatrix) compared to an autogenous gingival graft to increase the width of attached keratinized tissue. The success of the gingival augmentation treatment was evaluated both clinically and histologically. The epithelialization and keratinization of an autogenous gingival graft have been noted to occur by the 28th day.[34] Thus, the authors selected their biopsy time to be 13 weeks after surgery. The DynaMatrix membrane is easily handled when trimmed and placed on the recipient bed. Patients reported less discomfort related to the palatal harvest with the DynaMatrix when compared to the autogenous sites. The results of this study indicate that both procedures were effective and predictable in increasing keratinized gingiva. However, the tissue blended better with the native tissue when DynaMatrix was used. No significant differences in regard to the induced epithelialization and connective tissue outcome were observed.

It has been postulated that only connective tissue from the gingiva and periodontal ligament have the capability to create keratinized epithelium.[35] The authors hypothesize that the epithelium that populated the DynaMatrix membrane migrated from the denuded epithelium that induced secondary epithelialization by "creeping over" the wound bed. This is probably a result of the unique scaffold that allowed repopulation of fibroblasts, blood vessels, and epithelium from the surrounding tissues.[31] It is assumed that the DynaMatrix membrane was most likely incorporated into the recipient bed, and became remodeled because of the essential biologic components of healing that it contains: matrix scaffold (extracellular matrix) and signals (growth factors and extracellular matrix cell receptor–mediated binding sites).[24] Growth factors such as fibroblast growth factor-2, transforming growth factor-β1, and connective tissue growth factor are important stimulators of angiogenesis, capillary ingrowth, and tissue regeneration.[36–38] Preclinical studies have documented that DynaMatrix membrane *(1)* stimulates epidermal cell differentiation and basement formation,[39] *(2)* supports angiogenesis in vitro and in vivo,[40] and *(3)* supports cellular adherence and stimulates differentiation and proliferation.[39,41,42] Thus, these unique properties probably induced keratinization over the membrane similar to autogenous graft healing.

Advantages of using the DynaMatrix membrane included avoiding a

secondary donor site, unlimited graft supply, and a natural esthetic appearance. The risk of a prolonged surgical procedure has been previously demonstrated by Griffin et al,[43] who compared the frequency of postoperative complications among different soft tissue grafting procedures. For each minute of the procedure there was a 4% increase in the probability of developing moderate to severe pain and a 3% increase for moderate or severe swelling.

Further studies, including a larger, multicenter, long-term clinical trial, using the DynaMatrix membrane for gingival augmentation are needed to confirm these results. In addition, the feasibility of the DynaMatrix membrane for patients with recession-type defects should be considered in the future.

Conclusion

Within the limits of this study, the DynaMatrix membrane may present a viable substitute for the autogenous gingival graft when increasing the dimension of keratinized attached gingiva. The use of the DynaMatrix membrane may provide an unlimited source of donor tissue, thus reducing the surgical challenges for the clinician and morbidity for the patient.

Acknowledgment

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