Evidence-Based Alternatives for Autogenous Grafts Around Teeth: Outcomes, Attachment, and Stability

Michael K. McGuire, DDS

ABSTRACT
Although the use of autogenous harvested tissues has proven to be the gold standard for soft tissue augmentation procedures involving root coverage or generation of keratinized tissue, harvest site morbidity and limited supply have prompted clinicians to seek graft alternatives. Using a hierarchy of evidence, the author reviews both clinical and patient-reported results for harvest graft substitutes and, considering his own research experience, reviews autogenous graft substitute outcomes, attachment, and stability over time. Overall, when the goal is keratinized-tissue generation, living cellular constructs and xenogeneic collagen matrices have provided acceptable clinical results, but with better esthetics and patient preference than autogenous free gingival grafts. For root coverage therapy, enamel matrix derivatives, platelet-derived growth factors, and xenogeneic collagen matrices have provided acceptable results with equivalent esthetics to autogenous connective tissue grafts, while also being preferred by patients. Long-term results for enamel matrix derivatives, platelet-derived growth factors, and xenogeneic collagen matrices indicate root coverage can be maintained over time. In the author’s hands, xenogeneic collagen matrices have been the only harvest graft alternatives that can be used either covered or uncovered by soft tissue.

LEARNING OBJECTIVES
After reading this article, the reader should be able to:

- Understand and list the goals of soft tissue augmentation therapies around teeth.
- List both “gold standard” autogenous graft and harvest graft alternative therapies.
- Describe and compare, using evidence-based methodology, the short- and long-term clinical and patient-reported outcome results for autogenous graft and harvest graft alternative therapies.
ALTENATIVE APPROACHES FOR AUTOGENOUS GRAFTS

esthetics and satisfaction. In a recent study, the investigators examined an alternative to FGG for generating KT. As with most of their studies, this research was a prospective, randomized, within-subject, controlled (split-mouth), non-inferiority comparison trial. They studied 30 patients for 6 months. The primary outcome measure was a change in KT, and the secondary outcomes included traditional clinical measures such as AT and bleeding on probing, but also PRO measures of texture and color match and satisfaction with these therapies.

The investigators studied a xenogeneic collagen matrix (XCM) (Mucograft®, Geistlich Pharma, wwwgeistlich-na.com (Figure 3), which is comprised of porcine type I and III collagen. The outer layer of XCM contains compact collagen and is designed for tissue adherence and wound protection. The inner matrix layer is a clot-stabilizing macrostructure with a cell-signaling microstructure. Animal studies have shown rapid and organized healing with early vascularization (2 weeks). Historical collagen research suggests that the combination of intact and fragmented collagen fibrils found in XCM-activated endothelial progenitor cells for angiogenesis and mesenchymal stem cells with anti-inflammatory properties to divert healing away from inflammatory and fibrotic repair toward a more organized, vascularized, and regenerative healing (Figure 4).

As depicted in Figure 5, randomized contralateral teeth with insufficient KT were treated with either control FGG+APF or test XCM+APF therapies. The primary outcome average KT width at 6 months for the two therapies was 2.92 mm ± 0.88 mm for the test XCM+APF and 4.42 mm ± 0.64 mm for the control FGG+APF. Of the 30 test teeth, 29 achieved at least 2 mm of KT. Most importantly, XCM+APF’s color and texture match was superior (Figure 6), and patients preferred the XCM+APF esthetics, while an extensive evaluation of PROs indicated that overall discomfort was reduced by the use of XCM+APF therapy.

The author and his co-investigator have also examined LCCs (Gintuit™, Organogenesis, Inc., www.organogenesis.com (at the present time this device is no longer available in dentistry) for KT generation. In a pivotal multicenter trial, a live sheet of allogeneic fibroblasts and keratinocytes was used to cover the wound beds of apically positioned flaps and acted not as a graft but as a bioadhesive “stimulant” for wound healing. A total of 96 patients was examined for 6 months, and again, a suitable, though statistically inferior, amount of KT width was generated (3.21 mm ± 1.14 mm for LCC and 4.57 mm ± 1.00 mm for FGG). However, color and texture matches were superior with LCC, and, given donor-site morbidity with the control FGG therapy, patients preferred it.

In both the XCM+APF and LCC studies, the harvest graft alternatives generated suitable KT attachment and biopsies showed normal mucoperiosteum with keratinized epithelium (Figure 6).

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**Fig 1.** Soft tissue augmentation procedures are designed to maintain health, prevent recession, and provide comfort and esthetics. In this illustration, KT and non-keratinized tissue (alveolar mucosa) are delineated by the mucogingival junction. Note that attached gingiva is the difference of KT and free gingiva (the gingival sulcus or periodontal pocket).

**Fig 2.** Evidence Hierarchy. (Adapted from Navigating the Maze, University of Virginia, Health Sciences Library.)
The remaining question is whether these soft tissue augmentation therapies endure for the long term. To answer this, at least 5 years of data is preferable. The good news is that preliminary analysis of LCC and XCM+APF at 3 years have indicated stable results; however, the investigators will follow these patients for 5 years and will publish the results at that time.

To address root coverage therapy, it is necessary to refer to the literature, which has several reviews and meta-analyses. The 1994 European Workshop on Periodontology and the 1996 World Workshop in Periodontics Mucogingival Therapy, along with systematic reviews from Rocuzzo et al and Oates et al provide a wide range of results for mean root (43%-96%) and complete root coverage (0%-96%), suggesting once again that not only grafting materials but patient/tooth selection and techniques influence results. Interestingly, the review by Oates et al is the first to note that recession treatment has “mainly been justified by the patient’s wish to improve the esthetic appearance when there is an exposed root.” Surgical technique, especially flap tension (best if 0 g-4 g), flap thickness (best if >0.8 mm), and maintenance of a gingival margin coronal to the cementoenamel junction (CEJ), as well as surgical experience, all contributed to success.

Acellular dermal matrix (ADM) (AlloDerm, BioHorizons, Inc., www.biohorizons.com) was one of the first harvest graft alternatives tested for root coverage. However, Gapski et al in a 2005 meta-analysis found it “difficult to draw anything other than tentative conclusions...primarily because of the weakness in the design and reporting of existing trials.” Harris found that, compared with connective tissue graft (CTG), mean root coverage for ADM did not hold up over time. In 2008, when reviewing ADM and guided tissue regeneration with resorbable membranes for root coverage, Chambrone et al concluded that, compared with these alternative therapies, CTG+coronally advanced flap (CAF) provided a statistically significant increase in root coverage. Overall comparisons showed CTG+CAF to be the “gold standard” procedure for the treatment of recession defects.

Also in 2008, a root coverage review by Cairo et al concluded that only CTG+CAF or enamel matrix derivative (EMD)+CAF could improve outcomes over CAF alone.

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Fig 3. Free gingival graft and xenogeneic collagen matrix.

Fig 4. The combination of intact and fragmented collagen fibrils is designed to divert healing away from inflammatory and fibrotic repair pathways toward organized regenerative healing.
In each case, CTG and EMD improved KT compared with CAF alone. Most recently, Chambrone et al\textsuperscript{20} in a 2012 meta-analysis concluded that CTG+CAF, EMD+CAF, and XCM+CAF therapies were superior in achieving complete root coverage compared with CAF alone. A Bayesian network meta-analysis\textsuperscript{21}—in some regard, a meta-analysis of meta-analyses—confirmed that CTG+CAF, EMD+CAF, and XCM+CAF therapies could all “be considered very effective combination techniques for treating gingival recessions” (Figure 7).

The author’s own studies\textsuperscript{22,23} with EMD+CAF and platelet-derived growth factor (PDGF)+CAF have shown good root coverage and patient satisfaction, when compared with CTG+CAF. As with all harvest graft substitutes tested, the learning curve has been less than that required for harvest grafts. With these alternative therapies, the author and his team also have histologic evidence of true regeneration (new cementum and periodontal ligament with inserting collagen fibers and bone)—all without using the palate to harvest grafts.

In the author’s study of XCM+CAF for root coverage,\textsuperscript{24} the team followed 25 patients for 12 months, again using contralateral, within-subject, matched defects to compare the test therapy against the gold standard CTG+CAF (Figure 8). While recession depth (and hence, root coverage) was the primary efficacy endpoint, the author and his co-investigator also followed traditional clinical parameters such as KT width, along with PROs such as color/texture esthetics, satisfaction, and pain/discomfort.

At 6 months (and 12 months), results looked esthetically similar to surrounding native tissue, and XCM+CAF yielded an acceptable 88.5% root coverage compared with CTG+CAF (99.3%). Though not equivalent, the XCM+CAF result was more than adequate, particularly when compared with the range of root coverage measures reported in the literature for both the gold standard CTG+CAF and other harvest graft alternatives. Remarkably, no significant difference was observed between KT width generation for the test XCM+CAF or control CTG+CAF (mean change in KT for XCM+CAF was +1.34 mm, and for CTG+CAF +1.26 mm, \( P = .906 \)). KT width is important not only for long-term health prognosis but also as a predictor for the success of root coverage.\textsuperscript{25}

For comparisons of soft tissue augmentation therapy effectiveness over time, the literature remains the guide. Longer-term data show the success of CAF alone in maintaining complete root coverage is somewhat disappointing at approximately 35%, compared with CTG+CAF at approximately 52%.\textsuperscript{26} Similarly, ADM+CAF is approximately 35% and apparently no better than CAF alone.\textsuperscript{27} In the author’s own work (Table 1), complete root coverage for CTG+CAF tends to be 75% to 90% at 10 years. EDM+CAF is maintained at approximately 56% at 10 years, with 83% mean coverage, while PDGF+CAF (data to be published) remains similarly stable at 5 years. XCM+CAF complete root coverage is 71% at 6 months and remains stable at 5 years (data collected and analyzed for journal submission), with no significant change detected over the 5-year interval. Patients were pleased with and preferred this alternative therapy.

In summary, when considering alternative therapies for soft tissue augmentation, clinicians should evaluate outcomes, attachment, and stability and should use the hierarchy of evidence-based studies—always looking for long-term results of at least 5 years. For therapies designed to increase KT around teeth, the clinical outcomes with FGG+APF are the gold standard; however, in the author’s studies, LCC and XCM have provided acceptable clinical
results with better PROs for esthetics and patient preference; however, the author must follow these alternative treatments for at least 5 years to confirm their long-term effectiveness. For root coverage therapy, the clinical outcomes with CTG+CAF remain the gold standard; however, EMD+CAF, PDGF+CAF, and XCM+CAF therapies provide more than acceptable results, with equivalent esthetics, and they are patient preferred. EMD+CAF and PDGF+CAF have produced true regeneration, and EMD+CAF, PDGF+CAF, and XCM+CAF have yielded long-term (>5 years) results showing that root coverage can be maintained over time. Notably, in the author’s hands, XCM has proven to be the only harvest graft alternative that can be used successfully either covered (XCM+CAF) or uncovered (XCM+APF).

Fig 6. Normal mucoperiosteum with no inflammatory cells seen at both FGG (left) and XCM (right) treatment biopsy sites. At baseline, contralateral matched pairs of root coverage defects are identified.

Fig 7. A Bayesian network meta-analysis. (Adapted from Buti et al J Clin Perio 2013.)
Finally, regardless of the results reviewed and presented here, clinicians should remember that patient, site selection, and surgical technique can influence soft tissue augmentation outcomes, and, as helpful as they might be, literature reviews are no substitute for experience.

About the Author
Michael K. McGuire, DDS
Perio Health Clinical Research Center
Houston, Texas
Queries to the author regarding this course may be submitted to authorqueries@aegiscomm.com.

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Conflicts of Interest
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