



## Alternatives to the Autologous Connective Tissue Graft: Challenging the Gold Standard

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### Introduction

The sub-epithelial connective tissue graft (SECTG) is a periodontal surgical modality utilizing autologous connective tissue to correct mucogingival deformities around teeth and implants. First described by Langer<sup>1</sup> in the 1980's, the SECTG revolutionized periodontal surgery as an improvement over the free gingival graft (FGG) – achieving more predictable root coverage, with greater esthetic results and less post-operative discomfort.<sup>2</sup> Classically, the outcome measures when treating recession defects have included percent root coverage (%RC), the percent of the recession defect that becomes covered by gingiva, and complete root coverage (CRC), the frequency in which complete root coverage is obtained. The SECTG is considered to be the gold standard for the treatment of gingival recession (GR) with reported mean %RC of up to 98% and CRC up to 89%<sup>2</sup> and remain stable long term.<sup>3</sup> Unlike the FGG, only the connective tissue layer is harvested, leaving the epithelium and a supportive layer of connective tissue to aid in primary closure at the donor site (fig 1). While the literature supports reduced post operative sequelae when compared to a FGG,<sup>4</sup> reports exist of donor site morbidity associated with the SECTG, such as post-operative pain, bleeding, flap necrosis, infection and paresthesia.<sup>5,6</sup> These complications may cause hesitation in a patient or practitioner to proceed with a SECTG. Alternatives exist that spare the patient the donor site morbidity associated with SECTG harvest, yet produce acceptable root coverage outcomes. The purpose of this clinical update is to review the currently available “off-the-shelf” SECTG alternatives that preclude the need for a second surgical site to obtain the donor tissue; specifically acellular dermal matrix, xenogeneic collagen matrix, enamel matrix proteins and guided tissue regeneration.

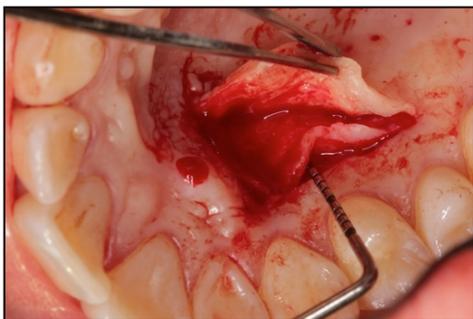


Figure 1: Harvesting of an SECTG

### Acellular Dermal Matrix

Aseptically processed to remove immunogenic cells, acellular dermal matrix (ADM) is a human dermis allograft that provides a biologic scaffold of connective tissue, proteins and vascular channels.<sup>7</sup> The structure of the dermal matrix remains intact after processing and allows new fibroblasts, vascular elements and collagen from the host to become incorporated with the allograft.<sup>7</sup> Indications include root coverage, gingival augmentation and soft tissue augmentation on edentulous ridges and around implants.<sup>7</sup> While the initial clinical studies showed promise with GR correction comparable to the SECTG (93.4% vs. 96.6%), long-term

results revealed that the mean root coverage at 5 years is a disappointing 65.8%.<sup>3</sup> The advantages to the use of ADM include similar histologic results compared to SECTG<sup>8</sup> and the availability of multiple sizes that have a 2-year shelf life.<sup>7</sup> The disadvantages include decreased long-term results<sup>3</sup>, the necessity to be completely covered and a peri-operative rehydration process<sup>7</sup> that may hamper surgical efficiency.

### Xenogeneic Collagen Matrix

Xenogeneic collagen matrix (XCM) is a bilayered three-dimensional collagen matrix that provides a scaffold for regenerating gingiva, allowing surrounding tissue of the recipient site to grow through the matrix rather than beneath it.<sup>9</sup> Obtained from a porcine source, this bilayer design incorporates pure type I and III collagen originating from peritoneal tissue in a dense layer, adding rigidity; and a spongy matrix derived from dermal tissue, promoting the ingrowth of host cells.<sup>9</sup> XCM is sterilized by gamma irradiation and carefully purified to avoid antigenic reactions.<sup>9,10</sup> XCM is indicated in the treatment of insufficient keratinized tissue, deepening shallow vestibules, and achieving primary closure over immediate implants, as well as the correction of GR.<sup>10</sup> XCM has been reported to be a suitable replacement in terms of percent root coverage when compared to connective tissue grafts<sup>11</sup>, achieving 88.5% RC at one year.<sup>11</sup> XCM has a long shelf life of 36 months, is available in unlimited quantities and has been shown to be successful in situations where full graft coverage may not be possible.<sup>9</sup> While XCM has several purported benefits, data are not yet available showing long term surgical results comparable to autologous connective tissue.

### Enamel Matrix Derivative Proteins

Enamel matrix derivatives (EMD) are a collection of proteins secreted by Hertwig's epithelial root sheath during tooth development.<sup>12</sup> This extract is derived from developing tooth buds of 6-month old piglets, 90% of which is amelogenin – a protein strongly linked to cementogenesis in humans.<sup>12</sup> The remaining organic components are ameloblastin, enamelin, tuftelin, enamelysin (a matrix metalloproteinase) and enamel matrix serum proteinase.<sup>13</sup> In 2000, several case reports<sup>14,15</sup> introduced using EMD as a stand-alone option with a coronally advanced flap (CAF) or adjunctively with a SECTG in the treatment of GR. In 2003, McGuire compared both the SECTG and EMD under a CAF for GR treatment, publishing both clinical and histologic results.<sup>16,17</sup> The performance of EMD was comparable to that of the control, with 95.1% average %RC and CRC obtained 89.5% of the time. In a follow-up study with 10 year results, the same author found that both EMD and SECTG treated sites remained stable.<sup>18</sup> A potential advantage of EMD is its availability in 3 sizes (0.7ml, 0.3ml and 0.15ml) depending on the extent of the surgical site to be treated; possibly eliminating the waste of unused portions. Disadvantages include the added cost (approximately \$105-172 per site), the need for refrigeration of the product at 2-8°C and the technically demanding nature of the product as it is critical to keep the site free of saliva and blood during application of EMD.

## Guided Tissue Regeneration

Guided tissue regeneration (GTR) is a procedure typically employed with the goal of regenerating lost periodontal attachment (bone, cementum and PDL) of intrabony and furcation defects by excluding epithelial invasion to the root surface while promoting mesenchymal cell proliferation and differentiation.<sup>19</sup> The results from a meta-analysis and a review suggest that when used to correct gingival recession, GTR with a barrier membrane can achieve up to 42% CRC and an average RC of 74%.<sup>2,20</sup> Recently, Nickels et al found that after 10 years, the long-term stability of root coverage with GTR matched that of the SECTG.<sup>21</sup> Benefits of GTR for recession can be surmised from a histologic study that showed that a new periodontal attachment including newly formed cementum might be achieved.<sup>22</sup> However, in a larger case series involving four teeth, Harris showed that a long junctional epithelial attachment dominated.<sup>23</sup> When compared to the SECTG, which has been demonstrated to achieve a new attachment termed a connective tissue adhesion<sup>24</sup> that does not include the formation of new cementum,<sup>24</sup> the advantage of GTR becomes less clear. Similar to the XCM, compared to the SECTG there is the added cost of a barrier membrane.

## Conclusion

While the SECTG still remains the gold standard for the treatment for GR, many alternatives exist that alleviate the need for a second surgical site to harvest donor tissue. These alternatives – acellular dermal matrix, xenogeneic collagen matrix, enamel matrix proteins, and guided tissue regeneration – all offer the benefit of off-the-shelf availability, but none match the clinical results when attempting to achieve complete root coverage. However, in the case of a patient who either refuses to undergo SECTG harvesting or is not a candidate due to medical concerns, these products may offer an attractive substitute. As with all periodontal surgeries, patient selection is critical as is patient education to all the risks and benefits.

## References

1. Langer B, Langer L. Subepithelial Connective Tissue Graft Technique for Root Coverage. *J Periodontol* 1985;56:715-720.
2. Wennström, J. Mucogingival Therapy. *Ann Periodontol*. 1996. 1; 1671-701.
3. Harris RJ. A Short-Term and Long-Term Comparison of Root Coverage With an Acellular Dermal Matrix and a Subepithelial Graft. *J Periodontol* 2004;75:734-743
4. Wessel JR, Tatakis DN. Patient Outcomes Following Subepithelial Connective Tissue Graft and Free Gingival Graft Procedures. *J Periodontol* 2008;79(3):425-430.
5. Griffin, TJ. Postoperative Complications Following Gingival Augmentation Procedures. *J Periodontol* 1996; 77:2070-2079.
6. Harris RJ, Miller R, Miller, LH, Harris C. Complications with Surgical Procedures Utilizing Connective Tissue Grafts: A Follow-up of 500 Consecutively Treated Cases. *Int J Periodontics Restorative Dent* 2005;25:449-459.
7. Alloderm®–Manufacturer IFU (Download 4/22/14) <http://www.biohorizons.com/documents/LD101.pdf>
8. Cummings LC, Kahldahl WB, Allen EP. Histologic Evaluation of Autogenous Connective Tissue and Acellular Dermal Matrix Grafts in Humans. *J Periodontol* 2005;76:178-186
9. Herford SA, et al. Use of a Porcine Collagen Matrix as an Alternative to Autogenous Tissue for Grafting Oral Soft Tissue Defects. *J Oral Maxillofac Surg* 2010. 68:1463-1470
10. Geistlich. Section 510(k) premarket notification. Reference # K073711. FDA document W02 EAST:9EJJ1\200052247.1

11. McGuire, M. Xenogeneic Collagen Matrix With Coronally Advanced Flap Compared to Connective Tissue with Coronally Advanced Flap for the Treatment of Dehiscence-Type Recession Defects. *J Periodontol* 2010;81:1108-1117.
12. Hammarstrom L. Enamel Matrix, Cementum Development and Regeneration. *J Clin Periodontol* 1997;24(9) :658-68.
13. Stout BM, Alent BJ, Pedalino P, Holbrook R, Gluhak-Heinrich J, Cui Y, Harris MA, Gemperli AC, Cochran DL, Deas DE, Harris SE. Enamel matrix derivative: protein components and osteoinductive properties. *J Periodontol* 2014; 85(2):e9-e17.
14. Rasperini G, Silvestri M, Schenk RK, Nevins ML. Clinical and histologic evaluation of human gingival recession treated with a subepithelial connective tissue graft and enamel matrix derivative (Emdogain): a case report. *Int J Periodontics Restorative Dent* 2000;20:269-75.
15. Modica F, Del Pizzo M, Rocuzzo M, Romagnoli R. Coronally Advanced Flap for the Treatment of Buccal Gingival Recessions With and Without Enamel Matrix Derivative. A Split-mouth Study. *J Periodontol* 2000;71:1693-8.
16. 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(8):1110-25.
17. McGuire MK, Cochran DL. Evaluation of human recession defects treated with coronally advanced flaps and either enamel matrix derivative or connective tissue. Part 2: Histological evaluation. *J Periodontol* 2003;74(8):1126-35
18. McGuire MK, Scheyer ET, Nunn M. Evaluation of human recession defects treated with coronally advanced flaps and either enamel matrix derivative or connective tissue: comparison of clinical parameters at 10 years. *J Periodontol* 2012;83(11):1153-62.
19. AAP Position Paper: Periodontal Regeneration. *J Periodontol*. 2005; 9: 1601-1622.
20. Khalid, A. Guided Tissue Regeneration-Based Root Coverage: Meta-Analysis. *J Periodontol*. 2003; 10: 1520-1533.
21. Nickles K, Ratka-Krüger P, Neukranz E, Raetzke P, Eickholz P. Ten-year results after connective tissue grafts and guided tissue regeneration for root coverage. *J Periodontol*. 2010; 81(6): 827-36
22. Cortellini P, Clauser C, Pini Prato G. Histologic Assessment Of New Attachment Following The Treatment Of A Human Buccal Recession By Means Of A Guided Tissue Regeneration Procedure. *J Periodontol* 1993, 64:387-391.
23. Harris RJ. Histologic Evaluation of Root Coverage Obtained with GTR in Humans: a Case Report. *Int J Periodontics Restorative Dent* 2001;21(3):240-251.
24. Bruno JF, Bowers GM. Histology Of A Human Biopsy Section Following The Placement Of A Subepithelial Connective Tissue Graft. *Int J Periodontics Restorative Dent* 2000; 20(3):225-231.

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