Title:

Efficacy of a Harvest Graft Substitute for Recession Coverage and Soft Tissue Volume Augmentation: A Randomized Controlled Trial

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**Summary:**

Using a randomized, controlled and blinded contralateral comparison of matched-pair, within patient recession defects, a volume-stable, harvest graft alternative collagen matrix (VCMX) plus coronally advanced flap (CAF) is compared with autogenous connective tissue graft (CTG) plus CAF in Class I & II recession defects.

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**Authors' Contributions:**

Drs McGuire, Scheyer, Janakievski and Velásquez were investigators (performed surgeries). Dr Heard was the blinded evaluator. Dr Morellis performed intraoral scanner soft tissue volume analyses, and Dr Gunsolley was the biostatistician.

**Conflicts of Interest:**

This study was supported by a grant from the Geistlich Pharma AG, Wolhussen, Switzerland. Drs. McGuire, Scheyer, Janakievski and Velasquez have provided lectures sponsored by the

company (and other companies), and Dr Gunsolley's statistical and Dr Morelli's digital scan analyses were supported by Geistlich. The authors declare no conflicts of interest.



**Abstract:**

**Background:**

The autogenous connective tissue graft with coronally advanced flap (CTG+CAF) is the "gold standard" for recession defect coverage; however, researchers continue to pursue lower morbidity, more convenient and unlimited supply harvest graft substitutes, including those that could provide soft tissue volume augmentation.

**Methods:**

A randomized, controlled, double-blinded comparison of a volume-stable collagen matrix (VCMX) versus CTG was conducted at 4 clinical investigation sites. Single, contralateral, within patient matched-pair, RT1 recession defects were treated with VCMX+CAF (test) and CTG+CAF (control). The primary efficacy endpoint was percent root coverage at 6-months. Secondary efficacy endpoints included clinical measures such as soft tissue volume, attachment level and keratinized tissue width. Patient reported outcomes (PROs) included measures such as discomfort, esthetics and overall satisfaction. 6-month endpoint results were followed to 1-year.

**Results:**

30 patients received control and test therapies, and all patients were available for follow-up measures. Average percent root coverage for CTG+CAF was 90.5±14.87% vs 70.7±28.26% for VCMX+CAF, $p < 0.0001$. Both therapies produced significant soft tissue volume increases (84.8±47.43 $mm^2$ control vs 48.90±35.58 $mm^2$ test, $p = 0.0006$). The test, harvest graft substitute produced less post-operative pain and was preferred by patients at the 6-month endpoint. All other endpoint measures were not significantly different.

**Conclusions:**

VCMX+CAF root coverage was inferior to CTG+CAF but produced less morbidity and was preferred by patients. Case/ patient selection and surgical technique appear key to achieving successful results with the harvest graft alternative.

**Key Words:**

Gingival Recession; Collagen; Connective Tissue; Personal Satisfaction; Esthetics, Dental



## Introduction:

The subepithelial connective tissue graft (CTG) combined with a coronally advanced flap (CAF) has been advanced as the "gold standard" for recession coverage around teeth[1,2] But in the quest for easier to use, unlimited supply alternatives to painful harvest grafts, researchers continue to test harvest graft substitutes. Recently, a volume stable, fully resorbable, porous, collagen matrix of porcine origin and spongious consistency (volume stable collagen matrix - VCMX*) has become available for soft tissue augmentation. The collagen is extracted from veterinary certified pigs and is purified to avoid antigenic reactions. Its scaffold is chemically cross-linked weakly and sterilized in double packaging using Gamma-irradiation. The biomaterial is indicated for insufficient tissue volume in the alveolar ridge and tissue recessions. It was designed to include mechanical properties appropriate to withstand the mechanical stresses that occur after wound closure in soft tissue augmentation procedures, i.e., it provides volume stability and withstands early resorption, while encouraging formation of new soft tissue.[3,4] Due to its wettability, suture-ability and biological properties, the device has been reported to become well integrated with surrounding soft tissue.[5,6]

Given these characteristics, the authors conducted a study to examine non-inferiority in the efficacy of VCMX+CAF compared to CTG+CAF with respect to percent root coverage (%RC) at 6 months (24 weeks) in the treatment of recession defects.

## Materials and Methods:

Study Design

The study was a prospective, randomized, controlled, split-mouth, double-blind (patients and calibrated examiners), multi-center evaluation assessing non-inferiority of VCMX (test) in comparison with CTG (control). The target population was patients aged 18-75, inclusive, with recession defects (RT1 – 2018 World Workshop), with 2 qualifying, matched-pair, contralateral defects. Qualifying defects had recessions > 3 mm in both width and depth and occurred in either the maxilla or mandible, excluding the molar regions. Patients with esthetic concerns and hypersensitivity at qualifying recession sites were eligible for enrollment (for a full list of patient inclusion and exclusion criteria, please see Table 1, supplemental online). Matched-pair defects were randomized 1:1 to receive test or control therapies.

The study was performed in accordance with the Declaration of Helsinki, Good Clinical Practices and ICH Guidelines and was registered with ClinicalTrials.gov, identifier NCT04260152. The protocol and patient informed consent process were approved by an Institutional Review Board† and complied with federal (21 CFR 56) and HIPAA requirements.

Treatment

Pre-surgery, patients received full mouth cleanings, and if diagnosed with parafunctional habits, bite guards. Indexing measurement stents were also fabricated. Patients provided their pre-operative anxiety and esthetics satisfaction assessments and were instructed in the use of post-operative, PROs daily-diaries. Study teeth were scaled, root planed and prepared using appropriate instrumentation. Exposed root surfaces were conditioned with EDTA‡, and surgery was initiated. (See Figure 1.)

Preparation of the recipient sites was the same for both test and control sites. Treatment site, randomized assignments to test or control were not revealed to investigators until immediately prior to surgery, and the right side of the mouth was treated first. Sites were prepared using a facial sulcular incision to join two vertical incisions. The mucoperiosteal flap – combined partial, full thickness - was elevated and released. VCMX was thinned to approximately 3.0 mm after hydration (hydration increases the volume of VCMX by approximately 25%) and cut to size for the defect, rounding and sloping the matrix edges so they were thinner around the perimeter (see Figure 1). For the CTG control therapy, the donor area for the subepithelial harvest graft was the bicuspid region of the palate on the side of the mouth receiving CTG+CAF therapy. The harvest site was sutured, but no surgical dressings or protective stents were employed. VCMX and CTG were sutured in place to the papillary area using braided, resorbable (polyglycolic acid) 6-0/ 7-0 sutures. CTGs and VCMXs were positioned over the dehiscence defect approximately 2-3 mm apical to the CEJ, and VCMX was also placed 2-3 mm away from vertical releasing incisions. Flaps were advanced using light pressure so as not to crush VCMX and were secured by suturing to the papillary area with monofilament polypropylene 6-0/7-0, with interrupted sutures to close the vertical releasing incisions. For both VCMX and CTG therapies, matrix

and graft dimensions were recorded using manual and digital scan measures. Surgery times for test and control therapies were also recorded - from first incision to final suture.

Patients were prescribed Amoxicillin 500 mg, one-tab TID beginning the day prior to surgery and for 10-days post-surgery (with Azithromycin employed for allergies) and instructed to take 400 mg ibuprofen with 500 mg acetaminophen TID for the first three-days following surgery. Patients recorded all medications in their daily-diaries, were instructed to avoid muscle traction or trauma at the treatment sites and told not to brush the surgical sites but to use chlorhexidine (0.2%) mouth rinse for one-minute BID for the first two-weeks following surgery. During weeks 3 and 4, patients were instructed to apply chlorhexidine to the treatment sites using a cotton swab, and starting week 4, patients were taught a soft brush technique to avoid apically directed trauma. Patients were recalled for professional cleanings at weeks 4, 7 (optional), 12 and 24.

Assessments

The primary evaluation endpoint was percent recession coverage (%RC), measured by blinded and calibrated examiners as recession depth, using UNC-15 probes[§] and rounding down to the nearest half millimeter. Secondary measures included clinical measures such as soft tissue dimensions, pocket depth, plaque and gingival inflammation indices, along with patient reported outcome (PRO) measures for pain, esthetics and overall treatment preference. Soft tissue dimensions were measured using both indexing stents and an intraoral scanner[**]. Following previously published methodology, the scans were converted to stereolithography (.STL) files of tissue contour and analyzed using non-contact reverse engineering software[††] and indexed over time against subsequent visits to track volume changes. [7] For 7-days following surgery, patients completed daily diaries for pain/ discomfort and analgesics and/ or anti-inflammatories consumed, with additional PROs recorded at subsequent office visits by staff not

involved in the patients' therapy and reading scripted questions. All assessments are listed in Table 2 - supplemental online. Results were evaluated at the 6-month endpoint, with follow-up at 1-year.



Statistics

As a randomized, controlled, multi-center study, each subject contributed paired defects to the study, and randomization was 1:1 for the paired defects within each subject. There was no need for blocking by center and/ or stratification by any other variable. Patients were not allocated but rather treated at each investigation site as they appeared and met study criteria. The primary endpoint hypothesis was that %RC at 6-months for VCMX+CAF (test) was non-inferior to CTG+CAF (control). The power analysis was based on 80% power and past McGuire/ Scheyer matched-pair defect recession coverage studies.[8-13] A one-sided confidence interval of 0.025 indicated that, in order to detect a 12% difference in root coverage with ± 15% standard deviation, a sample of 25-patients would be required. (Past McGuire/ Scheyer studies, as cited above, also used 25-patients.) Given the multi-center nature of the study and the intention to follow patients long-term, with normal attrition, 30 subjects were estimated as needed to ensure long-term follow-up and provide a "power buffer" for any outcome differences that might be seen between investigation centers.

Given within patient, defect pairing, patient related variables were the same for both defects, so descriptive statistics only were used to describe patients treated, with no hypothesis testing. Baseline defect characteristics were used to ensure paired test and control defects were similar. Continuous variables were evaluated with one sample t-tests, categorical variables with chi squared analysis and dichotomous variables with McNemar's test for paired observations. The primary outcome variable (%RC) was tested for non-inferiority by paired t-test. If significant, the primary outcome was further verified by repeated measures of variance with both subject and center as random effects. The

secondary and exploratory measures were described by descriptive statistics (mean, standard error) and, where appropriate, tested for group differences by paired t-tests. If significant, they were also verified by repeated measures of variance, with subject and center as random effects. Safety endpoints, including adverse events, if any, were tested to determine occurrence differences using McNemar's test for paired observations. 1-year follow-up analyses was done in a similar fashion to that done at the 6-months endpoint; however, time as a random effect was added to the overall ANOVA model.

## Results:

30-patients, mean age 50.7±11.4 years and meeting inclusions and exclusion criteria, were entered into the study between September 2018 and June 2019. All 30-patients were evaluated at the 6-month endpoint and 1-year follow-up. Patients were treated at three investigation centers by four investigators/ surgeons (the authors), with blinded and calibrated examiners at each center. All examiners were calibrated for inter- and intra-agreement of PPD, CAL and recession probing measures, and agreement was 94.9% within 1 mm, which compares favorably with the measures reported in other, published calibration reports.[14-16] Patient populations treated and results per center are reported in online, Supplemental Table 3. Overall patient population descriptive statistics are provided in Table 1. Clinical results and PROs are provided in Table 2.

The mean difference at 6-months for the primary outcome variable of %RC favored the control, CTG+CAF therapy by 19.81%, with a 95% confidence interval upper limit of 10.28% and lower limit of 29.34%. Given the non-inferiority limit of 12%, mean VCMX+CAF %RC did not meet the non-inferiority threshold. It should be noted that the standard deviation of this difference between therapies was 25.52%, indicating result variability. Remaining analyses of recession coverage, i.e., linear horizontal

and vertical recession measures, also demonstrated inferiority for VCMX, $p < 0.0002$. When center was added to the model it was not significant, nor was there an interaction between center and treatment type.

Figure 2 depicts paired defect comparisons of %RC results. 100% RC was achieved in ten (33%) VCMX+CAF and twenty (66%) CTG+CAF defects, with an additional 2-defects (7%) for each therapy within 0.5 mm of 100% coverage. (Please refer to case photos in Figure 1.) Using a blinded evaluator (RH), an *ad hoc* assessment of pre-operative, paired defects in which VCMX+CAF achieved ≤ 50 %RC and ≥ 33% less recession coverage than CTG+CAF (5 patients/ 17% of cases) was conducted. In all cases (100%), the blinded evaluator chose the randomized CTG+CAF, control sites as likely to achieve better %RC. Reasons cited included root prominence, narrow interdental space, more severe recession on adjacent teeth and more inflammation at the test site (this site from a patient who did not follow home care instructions and brushed surgical sites post-operatively). Regardless, analysis of the entire population of defects indicated the test therapy, on average, was inferior.

In regard to the remaining, secondary and exploratory endpoints, only baseline graft dimensions, overall volume of soft tissue augmentation gained, and PROs results were significantly different between the two therapies. Both therapies added significant soft tissue volume. At implantation VCMX+CAF, trimmed to be larger than traditional CTGs, produced more soft tissue volume than CTG+CAF, but volume at 6-months and 1-year, as measured by intraoral scanner, was less for VCMX+CAF, though not significantly less at 6-months according to direct, mechanical measures using indexing stents. Wound closure and soft tissue dehiscence measures indicated two test (VCMX+CAF) therapy sites were not closed and remained dehisced out to 2-weeks, with all sites closed at 4-weeks; however, there was no significant difference in inflammation between the two therapies, and healing progressed

uneventfully for all sites at all time point. Gingival phenotype at baseline was roughly split between "thick" and "thin" for both therapies, with all (30) of the control sites exhibiting thick phenotype at 6-months and 1-year, and with 27 and 24 test sites, respectively, exhibiting thick phenotype at 6-months and 1-year. There was a significant ($p < 0.0001$) KTw increase for both control and test therapies from 2.3±0.9 and 2.5±1.2 mm pre-operative at baseline to 3.6±1.3 mm and 3.2±1.3 mm at 6-months, respectively, producing no statistical difference for KTw between therapies. Likewise, and also significantly ($p < 0.0001$), over the course of the investigation CAL improved by 2-3 mm, and inflammation decreased significantly for both therapies, with no significant differences between therapies. Surgery time for the test therapy was, on average, 3-minutes faster than the control therapy, though this difference was not statistically significant. Regarding tissue texture and color, there were no differences between therapies at any time points.

Over the first 7-days post-surgery, patients reported significantly more pain for the control therapy, at both the gumline treatment site and the palatal harvest site (see Figure 3 for combined gumline and harvest site discomfort). Also, over the first week following surgery, from days 4 through 7, all patients avoided chewing on the CTG+CAF/ harvest graft side of their mouths. At baseline, pre-surgery root dentinal sensitivity (patient response to 3-second air blast) was reported for 5 control sites and 4 test sites, with no control and 3 test sites reporting sensitivity at 1-year. PRO appearance preference was roughly split between test and control at 6-months but favored GTC+CAF at 1-year. At 6-months, considering the therapies overall, twenty patients (two-thirds) preferred VCMX+CAF, but their opinions changed at 1-year so that preference was roughly split between the two therapies.

## Discussion:

This multi-center, double-blind (patients and study site examiners), split-mouth recession coverage evaluation compared the effectiveness of a volume stable, harvest graft substitute (VCMX) with subepithelial connective tissue graft (CTG) for coverage of single-tooth recessions. Increased root coverage and decreased CAL for both therapies suggest that the %RC achieved was due to new, attached tissue - a result further reinforced by the lack of any clinically significant changes in probing pocket depth at 1-year. While mean %RC was inferior for the test therapy, the most disparate results between test and control therapies occurred in a small subset (17%) of patients.

Though CTG+CAF has been considered the recession coverage gold standard, harvest graft substitutes that provide similar, though not necessarily equivalent, root coverage have been advanced as acceptable alternatives.[1,2,12] Clinicians appear interested in less time consuming and unlimited supply harvest graft alternatives, and patients tend to prefer less painful and reduced post-operative morbidity procedures. Also, patients do not appear to discriminate between 0.5-1.0 mm (10-20 %RC) defect coverage differences in RT1 recession defects.[12,17] The authors' (MM's & ES's) experience with harvest graft alternatives in similar matched-pair defect comparisons, including experiences with a non-cross-linked collagen matrix[‡‡] and an amelogenins biologic[§§], indicate harvest graft alternatives can produce acceptable %RC that can be maintained long-term, while being preferred by patients overall.[10,13] In this regard, and as proposed by Chambrone *et al* in 2016, clinical rather than statistical significance may be important, and PROs might be the key differentiators between treatment alternatives.[18]

Depending on patient and defect selection, VCMX appears to provide patient and clinical benefits. It is available in unlimited supply; and, if indicated and desired, increases soft tissue volume, though not to

the extent that CTG did within the recession defects studied herein. Digital, intraoral scanning measures revealed volume differences not detected by the more variable and error prone indexing stent/ manual probe measures. Likewise, others have reported good root coverage and esthetics outcomes, but gingival thickness increases without statistical significance.[19] VCMX may also provide procedure time saving, as shown in previous studies with the biomaterial, but these savings could depend on clinician experience.[20,21] VCMX was not as "forgiving" as CTG in the range of defect anatomies tested, with more soft tissue dehiscences reported – 2 out of 30, or 6% - and providing root coverage results more similar to CTG and the harvest graft substitutes noted above in selected patients and defect anatomies. Better and more predictable results might be expected in patients compliant with post-operative healing instructions and in defects favoring roots within the arch (non-prominent), with suitable interproximal space and limited recession of adjacent teeth. The harvest graft substitute appears best indicated for patients concerned about harvest graft morbidity and/ or with limited harvest graft potential, with more predictable results expected in patients compliant with post-operative healing instructions and in defects favoring roots within the arch (non-prominent), with suitable interproximal space and limited recession of adjacent teeth.[22]

Patients experienced less pain with VCMX, not only because of the additional harvest site required for CTG+CAF therapy but also because CTG treatment sites themselves proved to be more painful. Anti-inflammatories and analgesics diminish pain measures overall and, therefore, modulate reported pain differences,[23,24] so the differences reported here may have also been modulated. Additional PRO esthetic and overall satisfaction ratings, though equivalent or favoring VCMX at 6-months, favored CTG (esthetics) or were more evenly matched (overall preference) at 1-year. Perhaps, over time, patients' memories of oral surgery pain, which might initially outweigh esthetic concerns, also fade, so that their overall preferences for and their ability to discriminate between harvest and non-harvest graft therapies diminish. However, such conjecture could only be addressed through further PRO investigations.

Additional studies suggested by this investigation could include a test of the preferred patient and case selection criteria proposed by this investigation, i.e., patients compliant with postoperative care instructions and recession defects that avoid root prominences and provide suitable interproximal/ papillary spaces for the matrix to engage surrounding tissues. Considering surgical technique, rather than the extended, coronally advanced flap technique used to accommodate VCMX, a tunneling approach might improve results by preventing exposure of the biomaterial and favoring earlier vascularization of and tissue integration with the collagen matrix.[25] Angiogenic and soft tissue proliferative growth factors might also aid in early integration of VCMX with surrounding tissues and, in effect, more closely mimicking "live" harvest CTGs.[26]

## Conclusion:

VCMX+CAF was inferior to CTG+CAF in providing root coverage, but it may be a suitable substitute for harvest graft therapy where additional soft tissue volume is desired and in selected patients and recession defects. VCMX+CAF created significantly less post-operative pain and produced similar %RC in the majority of RT1 defects treated.

**Endnotes**

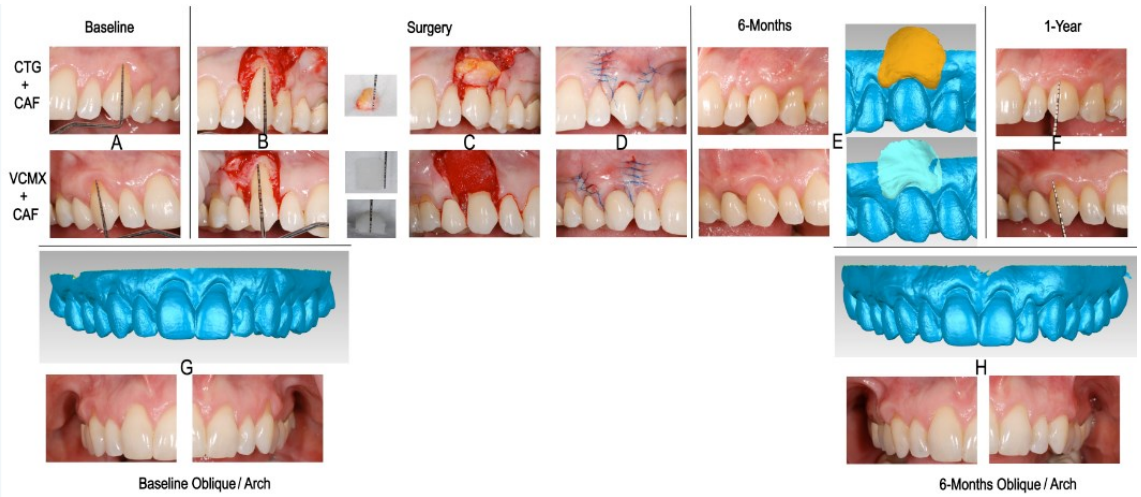


**Figure 1 – Case Series.** (A) Baseline, matched-pair defects, (B) CTG harvest and VCMX preparation, (C) placement of control and test materials and (D) suturing of sites, (E) 6-month endpoint including intraoral scan soft tissue augmentation volumes, (F) 1-year follow-up, and (G) baseline and (H) 6-month full-mouth intraoral scans and oblique views.

**Figure 2**

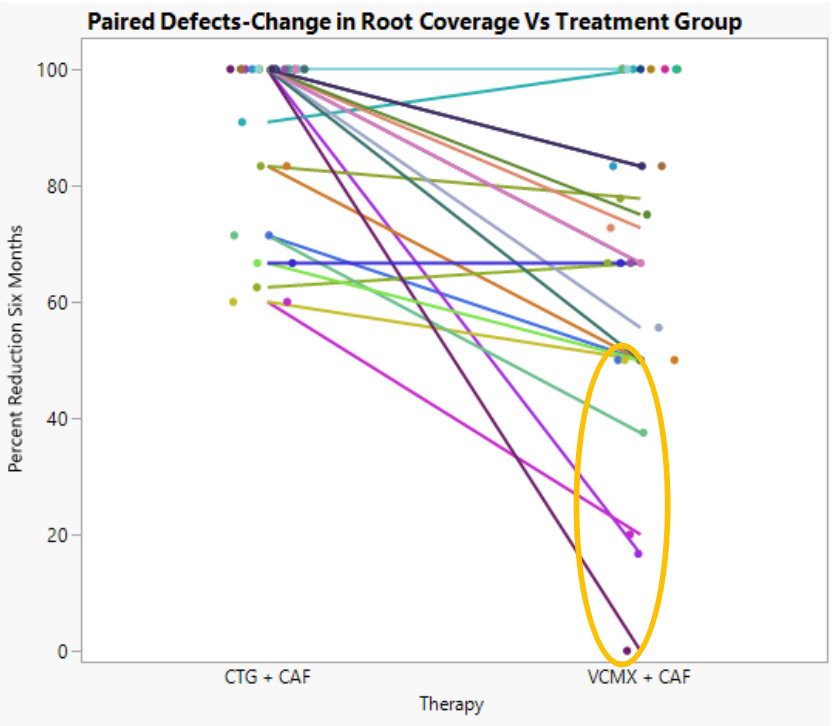

**Figure 2 – Paired Defect Change in %RC by Treatment**. Note: Dots indicate the number of sites/ teeth for each recorded result. Orange oval indicates paired teeth used for *ad hoc* evaluation (5 patients/ 17% of cases).

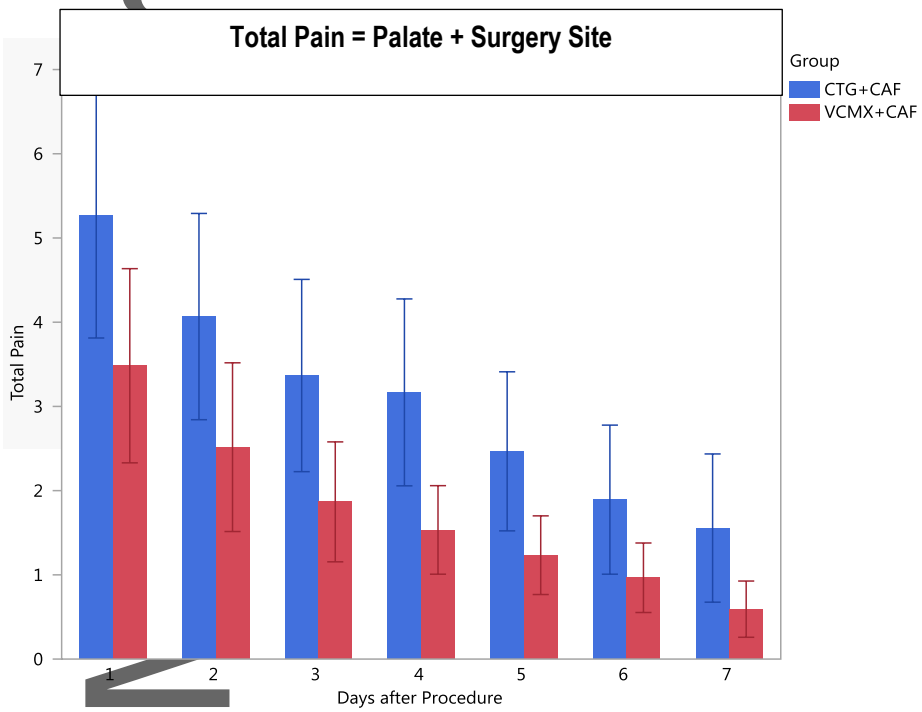


**Figure 3 – Combined Surgery Site/ Palatal Roof Pain by Procedure**. Note: Differences are significant, and error bars were constructed using the 95% confidence interval for each mean.

[*] Geistlich Fibro-Gide®, Geistlich Pharma AG, Wolhusen, Switzerland.
[†] Advarra, Columbia, MD.
[‡] PrefGel® Straumann Holding AG, Basel, Switzerland.
[§] 15 UNC Novatech® Color Coded Probe, Hu-Friedy, Chicago, IL.
[**] TRIOS® 3 Scanner with Pen grip Pod, 3Shape, Inc., Copenhagen, Denmark.
[††] Geomagic Control®, 3D Systems, Inc., Santa Clarita, CA.
[‡‡] Geistlich Mucograft®, Geistlich Pharma AG, Wolhusen, Switzerland.

[§§] Straumann Emdogain®, Straumann Holding AG, Basel, Switzerland.

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**Conflicts of Interest:**
This study was supported by a grant from the Geistlich Pharma AG, Wolhussen, Switzerland. Drs. McGuire, Scheyer, Janakievski and Velasquez have provided lectures sponsored by the company (and other companies), and Dr Gunsolley's statistical and Dr Morelli's digital scan analyses were supported by Geistlich. The authors declare no conflicts of interest.

**References:**

1. Chambrone L, Tatakis DN. Periodontal soft tissue coverage procedures: A systemic review from AAP Regeneration Workshop. *J Periodontal* 2015;86(Suppl.):S8-S51.
2. Buti J, Baccini M, Nieri M, La Marca M, Pini-Prato GP. Bayesian network meta-analysis of root coverage procedures: ranking efficacy and identification of best treatment. *J Clin Periodontol* 2013;40:372-86.
3. Mathes SH, Wohlwend L, Uebersax L, et al. A bioreactor test system to mimic the biological and mechanical environment of oral soft tissues and to evaluate substitutes for connective tissue grafts. *Biotechnol Bioeng* 2010;107:1029-1039.
4. Thoma DS, Villar CC, Cochran DL, Hämmerle CH, Jung RE. Tissue integration of collagen-based matrices: an experimental study in mice. *Clin Oral Implants Res* 2012;23:1333-1339.
5. Ferrantino L, Bosshardt D, Nevins M, Simion M. Tissue integration of a volume-stable collagen matrix in an experimental soft tissue augmentation model. *Int J Periodontics Restorative Dent* 2016;36:807-816.
6. Thoma DS, Zeltner M, Hilbe M, Hämmerle CH, Hüsler J, Jung RE. Randomized controlled clinical study evaluating effectiveness and safety of a volume-stable collagen matrix compared to autogenous connective tissue grafts for soft tissue augmentation at implant sites. *J Clin Periodontol* 2016;43:874-85.
7. Morelli T, Zhang S, Monaghan E, Moss KL, Lopez B, Marchesan J. Three-Dimensional Volumetric Changes After Socket Augmentation with Deproteinized Bovine Bone and Collagen Matrix. *Int J Oral Maxillofac Implants* 2020;35:566-575.
8. Wilson TG, 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 Periodontal* 2005;76:881-889.
9. 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 Periodontal* 2008;79:1847-1856.
10. 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;83:1353-1362.
11. McGuire MK, Scheyer ET, Snyder MB. Evaluation of recession defects treated with coronally advanced flaps and either recombinant human Platelet-Derived Growth Factor-BB plus Œ≤-

Tricalcium phosphate or connective tissue: Comparison of clinical parameters at 5 years. *J Periodontal* 2014;85:1361-1370.
12. McGuire MK, Scheyer ET. Xenogeneic collagen matrix with coronally advanced flap compared to connective tissue with coronally advanced flap for the treatment of dehiscence-type recession defects. *J Periodontal* 2010;81:1108-1117.
13. McGuire MK, Scheyer ET. Long-term results comparing xenogeneic collagen matrix and autogenous connective tissue grafts with coronally advanced flaps for treatment of dehiscence-type recession defects. *J Periodontal* 2016;87:221-227.
14. Goodson JM. Clinical measurements of periodontitis. *J Clin Periodontol* 1986;13:446-60.
15. Aeppli DM, Boen JR, Bandt CL. Measuring and interpreting increases in probing depth and attachment loss. *J Periodontol* 1985;56:262-4.
16. Badersten A, Nilvéus R, Egelberg J. Reproducibility of probing attachment level measurements. *J Clin Periodontol* 1984;11:475-85.
17. 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.
18. Chambrone L, Armitage GC. Commentary: Statistical significance versus clinical relevance in periodontal research: implications for clinical practice. *J Periodontol* 2016;87:613-6.
19. Stefanini M., Mounssif I., Barootchi S, et al. An exploratory clinical study evaluating safety and performance of a volume-stable collagen matrix with coronally advanced flap for single gingival recession treatment. *Clin Oral Invest* 2020;24:3181–3191.
20. Thoma DS, Buranawat B, Hämmerle CH, Held U, Jung RE. Efficacy of soft tissue augmentation around dental implants and in partially edentulous areas: a systematic review. *J Clin Periodontol* 2014;41 Suppl 15:S77-91.
21. Gargallo-Albiol J, Barootchi S, Tavelli L, Wang HL. Efficacy of xenogeneic collagen matrix to augment peri-implant soft tissue thickness compared to autogenous connective tissue graft: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants* 2019;34:1059–1069.
22. Zucchelli G, Tavelli L, Barootchi S, Stefanini M, Wang HL, Cortellini P. Clinical remarks on the significance of tooth malposition and papillae dimension on the prediction of root coverage. *Int J Periodontics Restorative Dent* 2020;40:795-803.
23. Grøvle L, Hasvik Ei, Haugen AJ. Rescue and concomitant analgesics in placebo-controlled trials of pharmacotherapy for neuropathic pain and low back pain. *PAIN* 2020;161: 3-10.
24. Katz N. Methodological issues in clinical trials of opioids for chronic pain. *Neurology* 2005;65:S32-S49.
25. Schulze-Späte U, Lee CT. modified vestibular incision subperiosteal tunnel access procedure with volume-stable collagen matrix for root coverage: report of three cases. *Int J Periodontics Restorative Dent* 2019;39:e181-e187.
26. Sculean A, Nikolidakis D, Nikou G, Ivanovic A, Chapple IL, Stavropoulos A. Biomaterials for promoting periodontal regeneration in human intrabony defects: a systematic review. *Periodontol 2000* 2015;68:182-216.

**Table 1 - Gender, History of Tobacco Use, Race/ Ethnicity and Baseline Recession Depth (mm ± SD)**

| Gender | Count | Prior Tobacco Use | Count | Race | Count | Recession Depth |
|---|---|---|---|---|---|---|
| F | 19 | N | 20 | Cauc' | 27 | 3.73±0.95 |
| M | 11 | Y | 10 | Asian | 1 | 3.63±0.79 |
| | | | | Asian+Cauc' | 1 | |
| | | | | Other/ Hisp' or Non-Hisp' | 1 | |
| Total | 30 | | 30 | | 30 | p = 0.66 |

**Table 2 - Baseline, 6-Month and 1-Year Results**

| | Baseline | | | 6-Months | | 1-Year | |
|---|---|---|---|---|---|---|---|
| Group | N | Mean | Std Dev | Mean | Std Dev | Mean | Std Dev |
| | Percent Recession Coverage (%RC) | | | | | | |
| CTG+CAF | 30 | 0 | na | 90.5 | 14.87 | 84.49 | 19.98 |
| VCMX+CAF | 30 | 0 | na | 70.7 | 28.26 | 63.2 | 31.56 |
| p value | | | na | | <.0001 | | <.0001 |
| | Recession Depth (mm) | | | | | | |
| CTG+CAF | 30 | 3.73 | 0.95 | 0.38 | 0.63 | 0.62 | 0.82 |
| VCMX+CAF | 30 | 3.63 | 0.79 | 1.08 | 1.08 | 1.37 | 1.22 |
| p value | | 0.5214 | | | <.0001 | | <.0001 |
| | Recession Width (mm) | | | | | | |
| CTG+CAF | 30 | 3.7 | 0.48 | 0.6 | 0.99 | 0.7 | 0.93 |
| VCMX+CAF | 30 | 3.7 | 0.64 | 1.4 | 1.25 | 1.5 | 1.27 |
| p value | | | 0.91 | | <.0001 | | <.0001 |
| | Probing Pocket Depth Mid Buccal (mm) | | | | | | |
| CTG+CAF | 30 | 1.5 | 0.57 | 2.1 | 0.48 | 2.3 | 0.48 |
| VCMX+CAF | 30 | 1.4 | 0.50 | 2.0 | 0.41 | 2.3 | 0.47 |
| | No clinically significant differences, thus no hypothesis testing | | | | | | |
| | Clinical Attachment Level (CAL in mm) | | | | | | |
| CTG+CAF | 30 | 4.90 | 1.40 | 1.80 | 0.66 | 2.20 | 0.89 |
| VCMX+CAF | 30 | 4.70 | 1.51 | 2.23 | 1.17 | 2.60 | 1.16 |
| | No clinically significant differences, thus no hypothesis testing | | | | | | |
| | Keratinized Tissue Width (KTw in mm) | | | | | | |
| CTG+CAF | 30 | 2.3 | 0.88 | 3.6 | 1.32 | 3.6 | 1.31 |
| VCMX+CAF | 30 | 2.5 | 1.25 | 3.2 | 1.50 | 3.3 | 1.30 |
| p value | 0.4051 | | | | | | |
| | Digital Scan Soft Tissue Volume ($mm^2$) | | | | | | |
| CTG+CAF | 30 | 158.37* | 72.89 | 84.80 | 47.43 | 72.35 | 38.40 |
| VCMX+CAF | 30 | 189.40* | 73.87 | 48.90 | 35.58 | 39.23 | 30.92 |
| p value | 0.0006 | | | | | | |
| *Baseline immediately post-surgery as compared with pre-surgery | | | | | | | |
| | Linear Soft Tissue Dimensions at Margin using Stent (mm) | | | | | | |
| CTG+CAF | 30 | 5.7 | 1.69 | 4.3 | 1.49 | na | na |
| VCMX+CAF | 30 | 5.5 | 1.66 | 4.5 | 1.63 | na | na |
| | No clinically significant differences, thus no hypothesis testing | | | | | | |

| | **Measure** | **Count** | **Count** | **Count** |
|---|---|---|---|---|
| | Bleeding on Probing (Yes/ No) | | | |
| CTG+CAF | N | 24 | 30 | 29 |
| | Y | 6 | 0 | 1 |
| VCMX+CAF | N | 24 | 28 | 29 |
| | Y | 6 | 2 | 1 |

| | | | | |
|---|---|---|---|---|
| | No clinically significant differences, thus no hypothesis testing | | | |
| | Root Dentinal Hypersensitivity (Yes/ No) | | | |
| CTG+CAF | N | 25 | 30 | 29 |
| | Y | 5 | 0 | 1 |
| VCMX+CAF | N | 26 | 28 | 29 |
| | Y | 4 | 2 | 1 |
| | No clinically significant differences, thus no hypothesis testing | | | |
| | Gingival Index/ Inflammation (0 = absent , 1 = mild/ partial gingiva or papillary, 2 = mild/ all gingiva or papillary, 3 = moderate, 4 = severe) | | | |
| CTG+CAF | 0 | 27 | 25 | 24 |
| | 1 | 3 | 3 | 5 |
| | 2 | 0 | 2 | 1 |
| | 3 | 0 | 0 | 0 |
| VCMX+CAF | 0 | 25 | 25 | 24 |
| | 1 | 5 | 5 | 3 |
| | 2 | 0 | 0 | 2 |
| | 3 | 0 | 0 | 1 |
| | No clinically significant differences, thus no hypothesis testing | | | |
| | Tissue Biotype (1 = thin, 2 = thick) | | | |
| CTG+CAF | 1 | 15 | 0 | 0 |
| | 2 | 15 | 30 | 30 |
| VCMX+CAF | 1 | 17 | 3 | 6 |
| | 2 | 13 | 27 | 24 |
| | No clinically significant differences, thus no hypothesis testing | | | |
| | Soft Tissue Texture (1=firmer, 2=less firm, 3=equally firm) | | | |
| CTG+CAF | 1 | 0 | 1 | 2 |
| | 2 | 3 | 13 | 12 |
| | 3 | 27 | 16 | 16 |
| VCMX+CAF | 1 | 1 | 0 | 1 |
| | 2 | 2 | 16 | 10 |
| | 3 | 27 | 14 | 19 |
| | No clinically significant differences, thus no hypothesis testing | | | |
| | Soft Tissue Color (1=redder, 2=less red, 3=equally red) | | | |
| CTG+CAF | 1 | 4 | 7 | 7 |
| | 2 | 0 | 0 | 0 |
| | 3 | 26 | 23 | 23 |
| VCMX+CAF | 1 | 8 | 10 | 5 |
| | 2 | 1 | 0 | 1 |
| | 3 | 21 | 20 | 24 |
| | No clinically significant differences, thus no hypothesis testing | | | |

| | | | |
|---|---|---|---|
| | PRO Appearance Preference (Count/ %) | | |
| CTG+CAF | na | 17 (59%)* | 22 (73%) |
| VCMX+CAF | na | 12 (41%)* | 8 (27%) |
| | * 29 of 30 patients reporting | | |
| | PRO Treatment Preference (Count/ %) | | |
| CTG+CAF | na | 10 (33%) | 16 (53%) |
| VCMX+CAF | na | 20 (67%) | 14 (47%) |