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Case Report

## **COLLAGEN MATRIX FOR SOFT TISSUE REGENERATION: BASIC PRINCIPLES AND CASE REPORT**

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### **ABSTRACT**

Currently, the first-choice surgical technique for the regeneration of periodontal tissues is the execution of a free flap harvest from the palate. Starting from the 1990s, the use of collagen matrices of heterologous origin was introduced to replace the palatal graft with the main purpose of obtaining comparable results but reducing morbidity. In the following case study, a graft with a collagen matrix is reported. Resorbable matrix intended to provide support to soft tissue avoiding localized gingival recessions.

**KEYWORDS:** *collagen matrix, soft tissue regeneration, soft tissue augmentation, soft tissue defect*

### **INTRODUCTION**

Currently, the first-choice surgical technique for regeneration of periodontal tissues is the execution of a free flap harvest from the palate and then repositioned at the receiving site. The graft can be composed of connective tissue or by both epithelium and connective tissue. This technique gives appreciable and stable results over time (1).

Starting from the 1990s, the use of collagen matrices of heterologous origin was introduced to replace the palatal graft with the main purpose of obtaining comparable results but reducing the risk of postoperative complications. In fact, the literature highlights the frequent and various complications related to collecting tissue from the palate: edema, bleeding, tissue necrosis, intense pain, patient discomfort, and greater operating times (2, 3).

The most recent literature shows that collagen matrices are useful in increasing the volume of soft tissues and can lead to similar qualitative clinical results compared to the surrounding tissues in terms of texture, volume, and color (4). This new technique, therefore, appears promising for the regeneration of periodontal and peri-implant soft tissues; it can be

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Received: 16 June, 2021  
Accepted: 04 September, 2021

ISSN: 2038-4106

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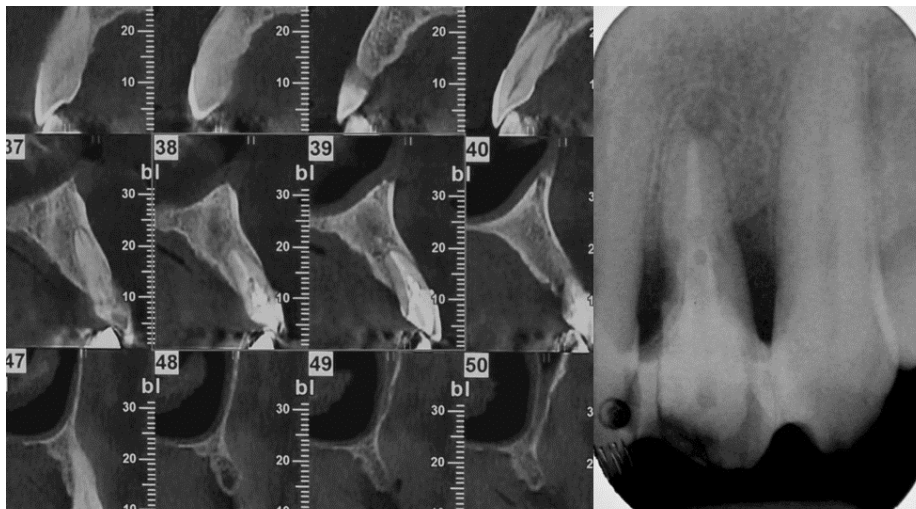
potentially the first-choice technique. To better investigate the procedure, a case grafted with collagen matrix is reported and pertinent literature is discussed.

### Case report

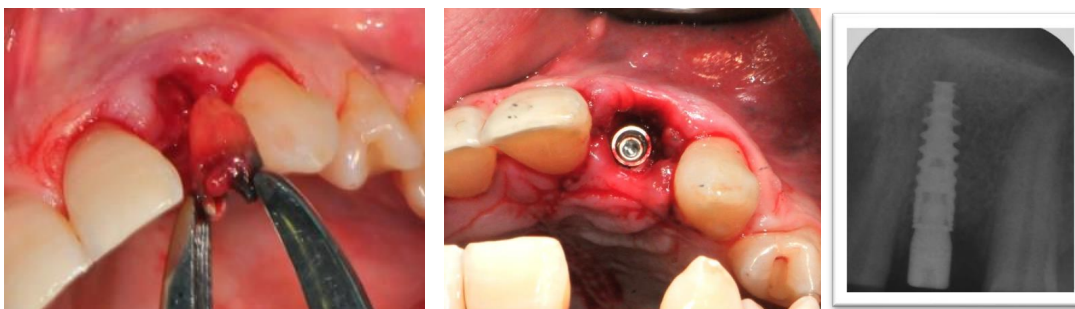
A male patient came to the Dental Clinic of Borgo Roma Hospital (Verona) asking a rehabilitation for the upper left lateral incisor. He was in good health, and, at oral examination, had good periodontal health, not presenting inflammatory conditions. Radiographic exams were performed on tooth revealing caries and root fractures. The following surgical



**Fig.1** Initial clinical situation: the anesthetically critical situation is evident on element upper left lateral incisor, with dark pigmentation on the root, compromising the smile of the patient.



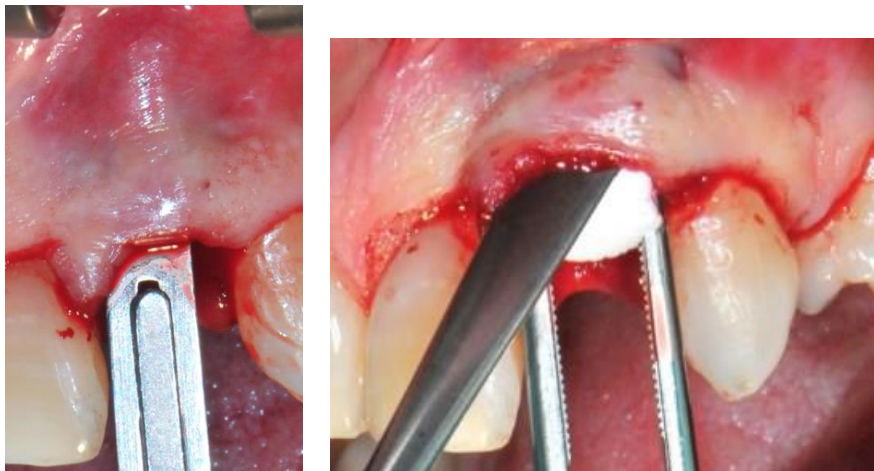
**Fig. 2** TC and Intraoral radiography: a periapical radiolucency is evident on the element upper left lateral incisor which presents root caries and root fracture. A moderate bone loss is also evident.



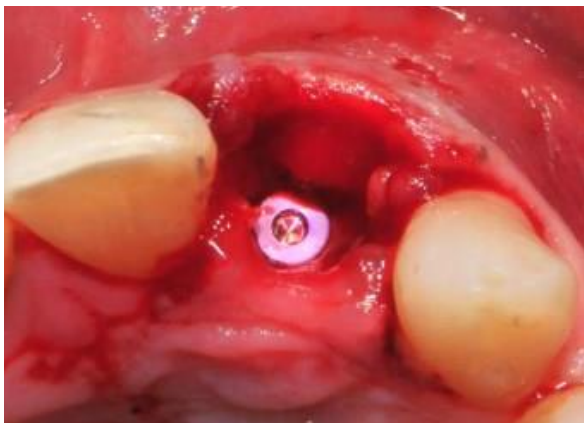
**Fig. 3** Atraumatic extraction of the tooth is performed, and then a post-extractive implant is inserted without immediate loading.



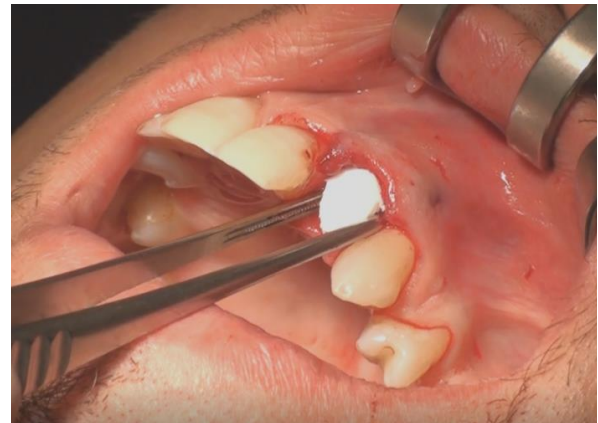
**Fig.4.** Insertion of collagen matrix to fill the bone defect



**Fig.5** Preparation of the envelope flap and insertion of collagen matrix inside the envelope



**Fig. 6** Collagen matrix inside the pocket formed by two folds of the gingiva.



**Fig.7.** Collagen matrix covering the post-extractive alveolus on the occlusal surface.

approach was performed: extraction plus guided bone regeneration (GBR) insertion of collagen matrix (CM) to obtain soft tissue augmentation and coronally advanced flap (CAF). In this case, socket preservation and a post-extractive implant without immediate loading were performed. The surgery took place on May 2015, and a 4-year follow-up is reported (Fig. 1-7).

#### *Envelope technique and box technique*

The insertion of the collagen matrix (Creos™ mucogain, Nobelbiocare) inside an envelope flap requires a partial thickness flap on the buccal side, without therefore involving the periosteum. The flap must go beyond the mucogingival line to be able to create a tension-free envelope. At this point, the collagen matrix can be easily inserted into the created space and the flap is coronally advanced (CAF) (Fig. 8).

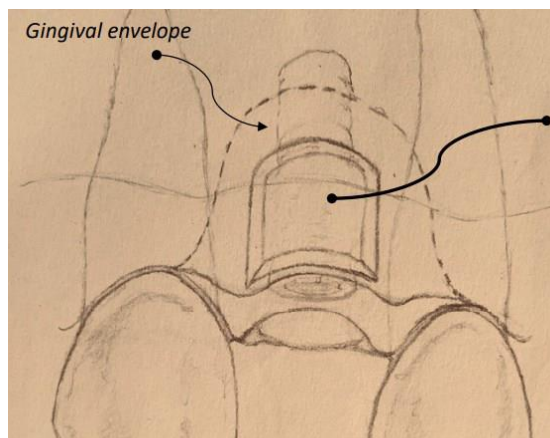
By carrying out an extension of the envelope technique, the box technique is introduced, which involves the use of two portions of collagen matrix: one, cut in a triangular shape (a), is placed in a vestibular envelope flap, and the other, rectangular (b), covers the post-extraction socket in the occlusal area. The box technique is therefore used when it is necessary to preserve the soft tissues at the same time as the alveolus volume (Fig. 9, 10).

After 4 years of follow-up, a good convexity of the buccal side of the alveolar ridge is obtained, which reproduces the curvature physiologically given by the presence of the root. This characteristic was maintained over time, with the tissues that undergo maturation and recession in a more evident way at the level of upper left central incisor. The color of the regenerated soft tissues is well camouflaged compared to that of the surrounding gums (Fig. 11, 12).

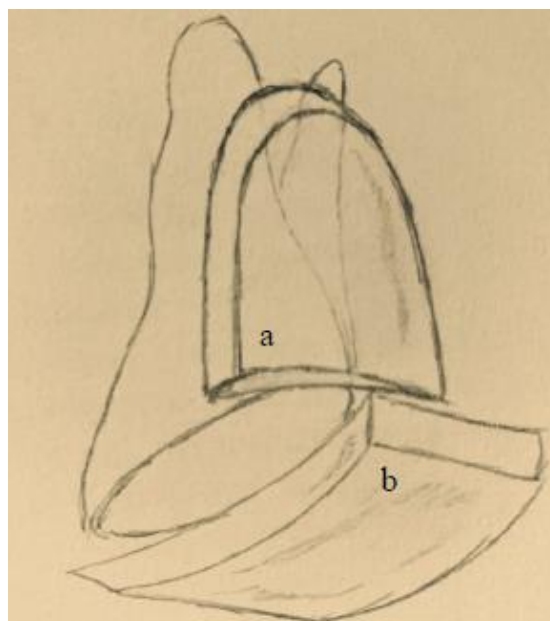
## DISCUSSION

Periodontal soft tissue treatment is considered in relation to two types of needs:

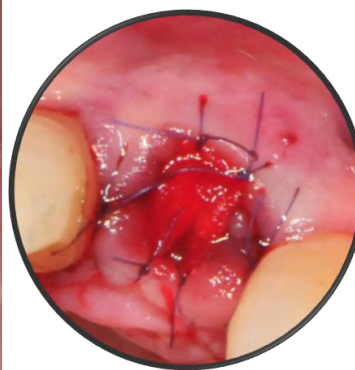
- Aesthetic needs: promoting a natural appearance of soft tissues to obtain the integration of prosthetic elements with adjacent teeth, increasing the volume of soft tissues in patients



**Fig. 8.** Explanatory drawing of the envelope technique.



**Fig. 9.** Explanatory drawing of the box technique: two portions of collagen matrix are placed (a and b).



**Fig. 10.** Suture of the wound

with thin gingival biotype, correcting the mucogingival line when the smile line is high (5, 6).

- Functional needs: preventing soft tissue recession and volume loss is essential to reduce dental sensitivity and root caries, allow effective oral hygiene, protect post-extraction sites that have received grafts, and avoid exposure of the dental root or implant with consequent periodontitis and peri-implantitis. In case of the presence of subgingival restorative margins, modest plaque and inflammation control, specific orthodontic movements, and removable prosthesis hooks, a minimum thickness of 2 mm of keratinized tissue is required to maintain periodontal and peri-implant health (5).

The current approach to periodontal soft tissues is performed by using autologous palatal grafts in 75 - 80% of cases.

To preserve soft tissues, protect grafted sites, and increase the volume of soft tissues, connective tissue graft (CTG) is the first choice; for augmenting peri-implant soft tissues the most used methods are free gingiva grafting (FGG) and CTG; to augment connective tissue the most effective approach is a coronally advanced flap (CAF) associated with CTG / FGG (7); finally, to correct recessions around teeth and implants, the procedure of first choice is the association of a CAF plus CTG (8).

Autologous gingival grafts (FGG and CTG) are therefore now considered the “gold standard” procedures when an increase in soft tissues is necessary: in fact, they offer success rates and clinical results unmatched by other solutions, especially in long-term evaluation. However, heterologous grafting materials, such as collagen matrices, could represent a valid option for mucogingival surgery as they can provide an augmentation of keratinized tissue without the need for a palate harvest (5).

Collagen is the main component of the matrix used in mucogingival surgery. It has numerous properties, including those offering support to cells, being resorbable, biocompatible, and easily manipulated. Collagen also has hemostatic activity and represents a chemotactic factor for the cells responsible for tissue regeneration (4).

Collagen material has the following advantages: biodegradable, bioabsorbable, non-toxic, and biocompatible; hemostatic, not antigenic, widely available and readily obtainable in pure form from living organisms (constitutes more than 30% of vertebrate tissues), synergic with other bioactive components, formulated in many different forms, plasticity due to high tensile strength, easily modifiable via functional groups to obtain desired materials (i.e., long-lasting depolymerization)

Collagen material has the following critical issues: hydrophilicity leading to too rapid degradation, high cost of purifying type I collagen, and possible trojan for infection.

In 1979, Green et al. (9) showed that it was possible to obtain growth of epithelial cells in vitro; in the same study, it was seen that fibroblasts also easily undergo proliferation. For a long time, therefore, the possibility of using epithelium and connective tissue obtained “in the laboratory” as grafts to resolve wounds or improve their healing has been under study.

Then, the Verona School published three studies, two in vivo and one in vitro, which demonstrate the favorable biological effects that these collagen membranes have on soft tissue healing (10, 11, 12).

The in vitro results demonstrated that a collagen matrix of porcine origin could have favorable biological effects on the proliferation and adhesion of gingival keratinocytes: an increase in the production of IL-6, a factor favoring cell proliferation, was observed if the collagen matrix was present. The keratinocytes adhered in a short time and in a fixed manner to the membrane and were able to interconnect with each other: they formed an epithelium with an architecture



**Fig. 11.** Clinical situation after 6 months of follow up



**Fig. 12.** Clinical situation after 4 years of follow up

that could be superimposed on the “in vivo” one (10).

Promising results for tissue regeneration with collagen membranes have also been obtained in vivo, both in patients (11) and animal cavies (12).

The study published by De Santis et al. in 2019 showed that the collagen matrix can integrate into connective and epithelial tissues within 10 days and be reabsorbed in 20 days. It is able to reduce the inflammatory infiltrate and stimulate the proliferation of fibroblasts and keratinocytes, as well as induce a process of neo-angiogenesis; acts as a scaffold for tissue regeneration, thus allowing a process called mucus - neo – genesis (11).

Tissue healing via allogeneic collagen matrix was also evaluated by Thoma et al. (13) in a randomized controlled clinical trial on twenty patients: each patient underwent two palatal biopsies, one group was then left to heal spontaneously, and the other group received the insertion of the collagen membrane. Biopsies of the treated sites were then performed at variable intervals to histologically evaluate the healing process. It was observed how, in the sites treated with the collagen membrane, keratinization was higher than in the control sites as early as the fourth and eighth-day post-surgery. So, the membrane, maintaining the space and causing less granulation tissue formation, was beneficial during the early stages of healing.

The formation of new connective tissue within the matrix develops with collagen degradation. The breakdown of the membrane into oligopeptides and amino acids is accomplished by collagenase, gelatinase and protease (14, 15).

## CONCLUSIONS

Collagen matrix instead of the palatal graft is a promising device to be grafted in a proper periodontal bed; it has the potential to be the preferred in the future if more studies confirm a clinical good and stable results over time.

### *Funding*

This research received no external funding.

### *Conflict of Interest*

The authors declare no conflict of interest.

## REFERENCES

1. Lindhe J, Karring T, Araujo M. Mucogingival Therapy: Periodontal Plastic Surgery. In: *Clinical Periodontology and Implant Dentistry*. John Wiley & Sons Ltd; 2015:995-1071.
2. Griffin TJ, Cheung WS, Zavras AI, Damoulis PD. Postoperative complications following gingival augmentation procedures. *Journal of Periodontology*. 2006;77(12):2070-2079. doi:10.1902/jop.2006.050296
3. Aguirre-Zorzano L, Garcia-De La Fuente A, Estefania-Fresco R, Marichalar-Mendia X. Complications of harvesting a connective tissue graft from the palate. A retrospective study and description of a new technique. *Journal of Clinical and Experimental Dentistry*. 2017;9(12). doi:10.4317/jced.54337
4. Mahesh L, Kurtzman GM, Shukla S. Regeneration in Periodontics: Collagen-A Review of Its Properties and Applications in Dentistry. *Compendium of Continuing Education in Dentistry (Jamesburg, NJ: 1995)*. 2015;36(5):358-363.
5. Kim DM, Neiva R. Periodontal Soft Tissue Non-Root Coverage Procedures: A Systematic Review From the AAP Regeneration Workshop. *Journal of Periodontology*. 2015;86(2-s):S56-S72. doi:10.1902/jop.2015.130684
6. Zucchelli G, Tavelli L, McGuire MK, et al. Autogenous soft tissue grafting for periodontal and peri-implant plastic surgical reconstruction. *Journal of Periodontology*. 2019;91(1):9-16. doi:10.1002/jper.19-0350
7. Schmitt CM, Moest T, Lutz R, Wehrhan F, Neukam FW, Schlegel KA. Long-term outcomes after vestibuloplasty with a porcine collagen matrix (Mucograft®) versus the free gingival graft: a comparative prospective clinical trial. *Clinical Oral Implants Research*. 2015;27(11):e125-e133. doi:10.1111/clr.12575
8. Chambrone L, Salinas Ortega MA, Sukekava F, et al. Root coverage procedures for treating localised and multiple recession-type defects. *The Cochrane database of systematic reviews*. 2018;10(10):CD007161. doi:10.1002/14651858.CD007161.pub3

9. Green H, Kehinde O, Thomas J. Growth of cultured human epidermal cells into multiple epithelia suitable for grafting. *Proceedings of the National Academy of Sciences*. 1979;76(11):5665-5668. doi:10.1073/pnas.76.11.5665
10. Nocini PF, Zanotti G, Castellani R, Grasso S, Cristofaro MG, De Santis D. Bi-layered collagen nano-structured membrane prototype (collagen matrix 10826®) for oral soft tissue regeneration: an “in vitro” study. *Clinical Oral Implants Research*. 2012;24(6):612-617. doi:10.1111/j.1600-0501.2012.02427.x
11. De Santis D, Gelpi F, Castellani R, et al. Bi-layered collagen nano-structured membrane prototype collagen matrix CM-10826 for oral soft tissue regeneration: an in vivo ultrastructural study on 13 patients. *Journal of Biological Regulators and Homeostatic Agents*. 2019;33(1 Suppl. 1):29-41.
12. De Santis D, Menchini Fabris GB, Lotti J, et al. Bi-layered collagen nano-structured membrane prototype collagen matrix 10826® for soft tissue regeneration in rabbits: an in vivo ultra-structural study of the early healing phase. *Journal of Biological Regulators and Homeostatic Agents*. 2017;31(2 Suppl. 2):91-97.
13. Thoma DS, Hilbe M, Bienz SP, Sancho-Puchades M, Hämmerle CHF, Jung RE. Palatal wound healing using a xenogeneic collagen matrix - histological outcomes of a randomized controlled clinical trial. *Journal of Clinical Periodontology*. 2016;43(12):1124-1131. doi:10.1111/jcpe.12624
14. Wei PC, Laurell L, Lingen MW, Geivelis M. Acellular Dermal Matrix Allografts to Achieve Increased Attached Gingiva. Part 2. A Histological Comparative Study. *Journal of Periodontology*. 2002;73(3):257-265. doi:10.1902/jop.2002.73.3.257
15. Sanz M, Lorenzo R, Aranda JJ, Martin C, Orsini M. Clinical evaluation of a new collagen matrix (Mucograft®prototype) to enhance the width of keratinized tissue in patients with fixed prosthetic restorations: a randomized prospective clinical trial. *Journal of Clinical Periodontology*. 2009;36(10):868-876. doi:10.1111/j.1600-051x.2009.01460.x