Review Article

The use of a xenogenic collagen matrix (Mucograft®) in the treatment of the implant site: a literature review

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Abstract: Lack of adequate amount of keratinized gingiva around dental or implants is generally treated with coronally advanced flap in combination with connective tissue graft. The procedures of harvesting the soft tissue grafting are usually associated with a certain degree of morbidity; for this reason xenogenic collagen matrix was proposed to be used as an option to reduce morbidity. This collagen matrix quickly stabilizes the blood clot and promotes rapid vascularization. Moreover, this product promotes root coverage, reduction of recession and regeneration of keratinized gingiva both in width and thickness. Recently, xenogenic collagen matrix was also proposed as a biological material able to regenerate keratinized gingiva around implants. In this review, the role of xenogenic collagen matrix (Mucograft®) has been critically analyzed to evaluate its effectiveness and predictability in keratinized tissue augmentation around implants supporting prosthetic restorations. Most of the studies showed that xenogenic collagen matrix was effective in increasing the thickness of the peri-implant mucosa and in the gaining of keratinized gingiva with comparable or slightly lower results than autologous connective tissue grafts. From the aesthetics point of view, the gold standard appeared to be the autologous connective tissue graft. Histologic analysis showed a good integration of the collagen membrane that matures into a healthy tissue. Mucograft® seems an effective alternative to the autologous connective tissue graft with regard to the gain of keratinized tissue and the increase in thickness of peri-implant soft tissues, with less post-operative morbidity and reduced operative times.

Keywords: Xenogenic collagen matrix; implant; perimplantitis; soft tissue augmentation; recession

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Introduction

In 1957, the term of mucogingival surgery is introduced by Friedman in order to indicate "*the surgical procedures aimed to preserve keratinized gingival tissue, remove aberrant frenulum or muscle attachments, and increase vestibular depth*" (1). During the following years the promotion of periodontal health and the improvement of patient's aesthetic become mucogingival surgery's targets together with the preservation or creation of keratinized gingival tissue (2). However, only in 2012 Zucchelli introduced a more complete definition, including among the objectives of mucogingival surgery also the increased gingival height and thickness around prosthetic elements or implants (3). In general there were two schools of thought: the first, subsequently denied, believed the presence of a sufficient keratinized gingiva is necessary for the periodontal health

(3,4) and the second one claimed that periodontal health is possible even if the amount of keratinized gingiva is poor or absent (3,5). However, the presence of keratinized gingiva is very important when dental implants are concerned. In fact, in 2009 Linkevicius *et al.* showed that the thickness of peri-implant mucosa was a critical factor for marginal bone stability, documenting the correlation between a thin mucosa and greater marginal bone loss (6). More recently the consensus report from the Osteology Foundation concluded that a sufficient peri-implant mucosa width is useful to guarantee a greater plaque control and a higher marginal bone stability when compared to sites lacking (or with minimal) mucosal thickness and keratinized mucosa (7). The aesthetic factor must also be considered; marginal tissue recession around dental implants is a functional but also an aesthetic problem. At least 2 mm of mucosal thickness is necessary to obtain better aesthetic outcomes (8). The peri-implant mucosa anatomically differs from periodontal soft tissue around teeth for the following characteristics: a longer junctional epithelium, parallel orientation of the connective tissue fibers, lower number of fibroblasts, and reduced vascularity (9). That's why the soft tissue seal around dental implant is weaker than the natural teeth, thus making important having enough keratinized mucosa to maintaining peri-implant health (10). First of all, to successfully treat a recession defect, it's important to identify the etiology and remove it. There are anatomical factors (inadequate keratinized attached mucosa, buccally positioned implant platform, osseous dehiscence or fenestration, muscle pull, thin gingival biotype) and pathological factors (recurrent inflammation and iatrogenic factors such as vigorous toothbrushing or overcontoured prosthesis) which can cause gingival recession around dental implants (2). The conventional periodontal plastic surgical techniques commonly used to manage marginal tissue recession around dental implants can be divided into pedicle soft tissue grafts (rotational flap procedures and advanced flap procedures) and free soft tissue grafts (epithelialized and non-epithelialized grafts) or a combination of both (2). The success of the chosen surgical technique is influenced by patient-related factors, such as bad habits (smoking), systemic diseases and inadequate plaque control, or by defect-related factors, such as the presence of interproximal bone or the defect width and depth or by procedural-related factors (flap thickness) (2,11). Soft tissue grafts in particular, useful in increasing the thickness of the peri-implant mucosa, can be harvested from retromolar pad or from edentulous site, but the preferred site is the palate with free gingival grafts or sub-epithelial connective tissue grafts (12). Many limitations and complications are reported in association with soft tissue grafts harvested from the palate, including the need of a second surgical site with the donor site morbidity (bleeding, pain, infections, sensitivity disorders) (2,12,13). Alternative techniques have been explored to avoid these difficulties: allogenic grafts (acellular dermal matrix harvested from human dermis and processed to remove all the cellular and epidermal components), xenogeneic grafts (pure porcine collagen type I and III extracted and purified), guided tissue regeneration (a barrier membrane is used to exclude undesirable cells, such as epithelial cells), a tissue-engineered skin or gingival graft (living cellular construct that consists of purified type I bovine collagen and vial allogeneic neonatal keratinocytes and fibroblasts extracted from human foreskin) and growth factors (2). Among the soft tissue graft substitutes, recent studies have suggested that xenogeneic collagen matrix may provide outcomes comparable to the connective tissue graft (14,15), with the advantages of unlimited supply, less invasiveness, no donor site morbidity and less surgical time needed (16). Various options of xenogeneic grafts are available: MucoMatrixX, Alloderm®, Mucoderm®, Platelet rich fibrin, Puros® Dermis and Mucograft®. Mucograft® is a 3D pure porcine collagen matrix obtained by standardized, controlled manufacturing processes, consisting of a double functional layer: a compact layer and a spongy layer (17). The aim of this literature review is to investigate whether the use of xenogeneic collagen matrix, Mucograft® in particular, is an effective method for increasing soft tissue in patients with insufficient peri-implant mucosal width and thickness.

Methods

An electronic search is performed on the MEDLINE database, through PubMed (www.ncbi.nlm.nih.gov/pubmed), SCOPUS (www.scopus.com), Cochrane Library (www.thecochranelibrary.com) and Web of Science (www.webofknowledge.com) using the following key words connected by the boolean operators OR, AND: "xenogeneic collagen matrix", "mucograft", "dental implants", "soft tissue augmentation" and "mucosal recession". The last electronic search was carried out on 17 September 2019. No time restrictions and no restrictions regarding the classification of the studies were applied; both literature reviews, clinical trials and observational studies were considered. Only articles in English were considered.

Table 1 Outcomes of reviews published following use of a xenogenic collagen matrix

Author/year	Study type	Sample size	Follow-up	Outcomes
Esposito *et al.*, 2012	Systematic Review and Meta-Analysis	6 randomized controlled trials	≥6 months	Palatal autografts or the use of a xenogeneic collagen matrix are both effective in increasing the height of peri-implant keratinised mucosa. Recommendations on the soft tissue augmentation technique to be preferred (flap design, materials, incision, suture...) are not possible due to insufficient evidence
Gargallo-Albiol *et al.*, 2019	Systematic Review and Meta-Analysis	7 radomized clinical trials with a total number of 218 implant sites (108 in the connective tissue graft group, 110 in the collagen matrix group)	≥3 months and <1 year	Xenogeneic collagen matrix is equally effective when compared to connective tissue graft in increasing peri-implant mucosal thickness and keratinized mucosa width, but with significantly lower patient morbidity
Bassetti *et al.*, 2017	Systematic Review	4 randomized controlled trials and 5 prospective studies	≥3 months	Apically positioned partial thickness flap + free gingival graft or subepithelial connective tissue graft or Mucograft® are equivalent regarding the gain of peri-implant keratinised tissue. Split thickness flap + subepithelial connective tissue graft and coronally advanced flap + subepithelial connective tissue graft are equivalent regarding recession coverage. Split thickness flap + Mucograft® and coronally advanced flap + allogenic graft materials did not reach significant coverage
Fu *et al.*, 2012	Review	26 studies: 3 about soft tissue augmentation around dental implants (1 case-series, 1 randomized clinical trial and 1 systematic review)	≥6 months	Subepithelial connective tissue graft > xenogeneic collagen matrix in mean amount of KT gain, in tissue thickness gain and in esthetic outcome
Ramachandra *et al.*, 2014	Review	Not specified	Not specified	MucoMatrixX, platelet rich fibrin, Alloderm®, Puros® Dermis and Mucograft® are valid alternatives to avoid the second surgical site
Vignoletti *et al.*, 2014	Review	14 studies: only one with xenogeneic soft tissue substitute in animal model	3 months	No histological data are currently available regarding peri-implant soft tissue augmentation

In vitro and animal studies were excluded. The selected articles were classified according to the study type and divided in three different tables (literature reviews, clinical trials, observational studies). The following data were extracted from each article: names of the authors, year of publication, study type, description of the sample size, follow-up period and outcomes.

Results

The electronic search provided a total of 88 articles. After examining the titles and abstracts, the articles that did not meet the inclusion criteria were excluded and 22 articles were selected, 21 from Pubmed and 1 from the Cochrane Library (2,9,10,12,14,15,18-33). Six literature reviews were selected (including two meta-analyzes), eight clinical trials (six randomized, one non-randomized, and one with unspecified randomization) and eight observational studies. The articles were divided according to the study type in *Table 1*, *Table 2* and *Table 3*. The subjects considered in the various studies are mostly female. Age range of the subjects considered in the various studies is ≥18 and <88 years. Only one study considers the presence of differences in prognostic terms related to sex, age and gingival biotype of

Table 2 Outcomes of clinical trials published following use of a xenogenic collagen matrix

Author/year	Study type	Treatment	Sample size	Follow-up	Outcomes
Schmitt *et al.*, 2015	Non randomized controlled clinical trial	Mucograft® *vs.* free gingival grafts from palate	176 implants on 48 patients (26 women and 22 men) >18 years (32–75 years), healthy periodontally and systemically, with ≤2 mm of keratinized mucosa + shallow vestibule after dental implant surgery and/or bone grafting in the anterior region (lower jaw) and prior implant uncovering	5 years	Both free gingival grafts and Mucograft® are effective in regenerating peri-implant keratinized mucosa. The total loss of width of keratinized mucosa after 5 years was significant between the two groups: the free gingival grafts group had minor loss of width in the keratinized mucosa. The Mucograft® group had significantly shorter operation time
Lorenzo *et al.*2012	Randomized controlled clinical trial	Mucograft® *vs.* connective tissue autogratf from palate	24 patients >18 years (mainly female), healthy periodontally and systemically, with dental implants and at least one location with minimal keratinized tissue (1 mm). Selected anterior/posterior sites were in lower jaw, except 1, with more posterior sites in experimental group	6 months	At 6 months the differences between the groups are not statistically significant. Mucograft® was as effective and predictable as the connective tissue autogratf for the gain of keratinized tissue
Froum *et al.*, 2015	Randomized controlled clinical trial	Mucograft® *vs.* no soft tissue augmentation	31 implants (21 mandibular molar sites, 6 maxillary premolar and 4 mandibular premolar) on 31 patients between the ages of 18 and 70 years, healthy periodontally and systemically, that require one posterior implant in an edentulous area with thin or deficient keratinized tissue (≤ 2 mm buccally) for at least 8 weeks postextraction	3 months	Statistically significant differences are not found between the two groups (placement of Mucograft® at the time of implant placement or not) for the soft tissue change in height or thickness at 3 months post-surgery. The measure of pre-surgically keratinized tissue thickness against the one present at 3 months post-surgery is statistically significant in favor of Mucograft®
Cairo *et al.*, 2017	Randomized controlled clinical trial	Mucograft® *vs.* connective tissue autogratf: 29 from palate and 1 from maxillary tuberosity	60 implants on 60 patients (44 women and 16 men) ≥18 years, periodontally and systemically healthy, that need to increase buccal soft tissue thickness at implant site at time of implant uncovering for aesthetic purpose and/or functional reasons on a single-tooth gap at upper and lower jaw	6 months	Connective tissue autogratf is more effective than Mucograft® for improving horizontal peri-implant soft tissue thickness. At 6 months post-surgery, in the two groups a similar amount of apico-coronal keratinized tissue was obtained. Mucograft® is associated with lower patient morbidity and shorter surgical time
Puzio *et al.*, 2017	Randomized controlled clinical trial	Connective tissue graft from palate *vs.* Mucograft®	75 implants in healthy patients (34 women, 23 men) between 18 to 60 years, with gingival augmentation before or after implants insertion in both jaws (aesthetic area)	1 year	Mucograft® is an alternative method in gingival augmentation, yet with a lower value of soft tissue increase. Soft tissue augmentation before implant placement + connective tissue graft is the most efficient method for the maximum aesthetic results in the frontal part of jaws
Sanz *et al.*, 2009	Randomized controlled clinical trial	Mucograft® Prototype *vs.* connective tissue graft from palate	20 patients >18 years, periodontally and systemically healthy, with at least one location with minimal keratinized tissue (≤1 mm). The selected tooth/ implant must be part of a fixed partial restoration	6 months	Mucograft® is as effective and predictable as the connective tissue graft from palate in attaining a band of keratinized tissue, but with a significantly lower patient morbidity

Table 2 (*continued*)

Table 2 (*continued*)

Author/year	Study type	Treatment	Sample size	Follow-up	Outcomes
Vellis *et al.*, 2019	Controlled clinical trial (randomization not specified)	Collagen matrix grafts *vs.* free gingival grafts from palate	60 implants on 30 patients, 22–78 years, healthy periodontally and systemically, treated with 2 contralateral implants, with less than 1 mm of KT at the facial site	6 months	Collagen matrix grafts are an alternative to free gingival grafts for peri-implant soft tissue augmentation, with comparable results. Collagen matrix grafts potentially decrease postoperative morbidity and offer a more esthetic final result compared to free gingival grafts from palate
Zuiderveld *et al.*, 2018	Randomized controlled clinical trial	Connective tissue graft from palate *vs.* Mucograft®	60 patients ≥18 years, healthy periodontally and systemically, with a maxillary single failing tooth (incisor, canine, first premolar). All patients presented with a vertical buccal bone wall defect of >5 mm of the extraction socket. All extraction sockets were augmented prior to implant insertion and closed with a mucosa graft	1 year	The soft tissue graft combined with the placement of a single implant in a preserved alveolar ridge in the esthetic area does not give in a more favorable esthetic outcome compared to no soft tissue graft application. No significant differences between the groups were noticed with regard to sex, age, gingival biotype, implant site location, implant length and implant diameter.

Table 3 Outcomes of observational studies published following use of a xenogenic collagen matrix

Author/year	Study type	Treatment	Sample size	Follow-up	Outcomes
Schallhorn *et al.*, 2015	Multicenter pilot study/ case-series	Mucograft®	35 implant sites on 30 patients between the ages of 18 and 75 years, healthy periodontally and systemically, with peri-implant soft tissue deficiencies (gray show-through or facial soft tissue contour deficiency or keratinized tissue width <2 mm)	6 months	Statistically significant increases were noticed in mean tissue thickness and keratinized tissue width. Relevant reduction in probing depths was found. There was no significant change in mean recession and in gray show-through
Simion *et al.*, 2012	Case-series	Mucograft® infused with rhPDGF-BB	6 healthy patients with dental implants placed with GBR in the maxillary anterior region. Mucograft® was applied during stage-two surgery, when titanium-reinforced membrane was removed	3.5 years	In peri-implant sites, when applying the collagen matrix infused with rhPDGF-BB, the soft tissue volume increased moderately
Stankovic *et al.*, 2018	Pilot study/ case-series	Mucograft® used to cover bone substitute and barrier membrane in GBR	3 healthy patients with very shallow vestibulum and shortly attached gingiva in need of alveolar ridge augmentation for implants placement. GBR was selected with the use of Bio-Oss + Bio-Gide + Mucograft® after teeth removal	3 years	Soft tissue appeared matured with a gain in attached mucosa at 8 mo, 2 y and 3 y after surgery

Table 3 (*continued*)

Table 3 (*continued*)

Author/year	Study type	Treatment	Sample size	Follow-up	Outcomes
Lorenz *et al.*, 2017	Prospective cohort study	Mucograft®	51 implants on 8 (3 women, 5 men) patients aged between 60 to 71 years, with head and neck cancer with oral manifestation. At implant rehabilitation, patients were free of any tumor recurrence for at least 1 years, with edentulous jaw, a width of the attached gingiva <2 mm and adequate oral hygiene. After 4–8 months: implant exposure + vestibuloplasty	6 months	Mucograft® is indicated to increase the peri-implant attached gingiva in head and neck cancer patients without adverse reactions or a multinucleated giant cell- triggered tissue reaction
Sanz-Martin *et al.*, 2019	Prospective case-series	Resorbable collagen matrix (Mucomaix)	12 patients >18 years, periodontally and systemically healthy, that had one non-maintainable tooth in the anterior region of the maxilla or first premolar area with adjacent natural teeth, with an intact buccal plate at the time of extraction	1 year	High aesthetic scores and patient satisfaction resulted immediately after implants in conjunction with xenogeneic hard and soft tissue grafting together with immediate provisionalization. There was no significant increase in soft tissue thickness
Maiorana *et al.*, 2016	Clinical prospective study/case-series	Mucograft®	15 patients >18 years, periodontally and systemically healthy, presenting edentulous areas of deficient attached and unattached mucosa and/or deficient vestibular depth. Patients, prepared for implant supported reconstruction, underwent vestibuloplasty and grafting, both in the mandible and the maxilla, with a collagen matrix	1 year	Mucograft® provided a very good integration with the surrounding tissues and it was more suitable in the patients who needed a greater aesthetic outcome and for those who could bear a moderate pain. However, a sample of 15 patients cannot be considered statistically significant
Maiorana *et al.*, 2018	Prospective clinical study/ case-series	Mucograft®	15 patients (12 women, 3 men), 43–72 years, periodontally and systemically healthy, underwent a vestibuloplasty and keratinized tissue reconstruction around dental implants: 11 received surgery in the mandible and 4 in the maxilla	5 years	Mucograft® was effective in keratinized tissue augmentation and gave the possibility to use a soft tissue substitute with less morbidity and bigger areas treated in a single surgery
Thoma *et al.*, 2018	Split-mouth pilot study/ case series	Apically positioned flap *vs.* apically positioned flap + Mucograft® and apically positioned flap + free gingival graft	36 sites on 9 patients, 46–88 years, periodontally and systemically healthy, fully edentulous and in need of implant therapy in the mandible and with the ability to be placed with dental implants in the two canine and the two first molar positions, with a reduced width of keratinized tissue (<2 mm)	3 months	Mucograft® was more effective in terms of gaining keratinized tissue than apically positioned flap alone. Apically positioned flap + free gingival graft in anterior sites resulted in a gain similar to apically positioned flap + Mucograft® in the posterior region. Postoperative bleeding was frequent in all treatment modalities. Absence of pain was more frequent in apically positioned flap group and in apically positioned flap + Mucograft®

the patients. According to the study of Zuiderveld *et al.* no significant differences emerged (27). Where specified, only healthy patients from a systemic and periodontal point of view appear to have been considered, with optimal plaque control. The observational study of Lorenz *et al.* (24) selects patients suffering from head-neck cancer, but who have been cured for at least 1 year at the time of implant rehabilitation and with adequate oral hygiene. None of the analyzed studies, apart from one, takes into account the possible presence of differences related to the adopted type of implant. In the study of Zuiderveld *et al.* no significant differences were noted related to the length and diameter of the used implants (27). None of the studies analyzed consider the possible presence of differences linked to the site of intervention (mandible/maxilla, anterior sectors/posterior sectors). In the study of Zuiderveld *et al.* there are no significant differences related to the site of intervention (27). With regard to the gain of keratinized tissue in the apico-coronal sense, according to two studies the autologous connective tissue graft provides superior results to the collagen matrix (2,21). Eight studies support the superiority of the xenogenic matrix over collagen grafting (10,15,18,25,26,29,30,33). Five studies support the usefulness of the xenogenic matrix in the gain of peri-implant keratinized tissue (19,20,22,24,28). According to the review of Gargallo *et al.*, the autologous connective tissue graft and the xenogenic collagen matrix are comparable in terms of increased thickness of peri-implant soft tissues (10). According to three studies the connective graft gives superior results compared to the collagen matrix (2,15,23). Two studies conclude by supporting the usefulness of the xenogenic matrix in increasing the thickness of peri-implant soft tissues (20,32). First (23) or contextually (19) implant insertion seems to be the most correct time to perform the graft, which gives better results in terms of keratinized tissue gain when combined with an apical limb with partial thickness (29,30). According to the Maiorana's study a perfect integration of Mucograft® with the surrounding tissue was obtained (31). However, according to the majority of studies that take into consideration the aesthetic factor in terms of recession coverage and gray show-through (2,20,27,30), no significant improvements are obtained with Mucograft®. Almost all of the studies agree that the advantages of using Mucograft® include having less post-operative morbidity and complications, since the second surgical site is avoided altogether. In the observational study of Thoma *et al.*, the frequent post-operative bleeding is found to be independent of the treatment used (29). Surgical chair time, if xenogenic collagen matrix is used, is reduced according to two clinical trials (15,21). The review of Gargallo *et al.* estimates a time reduction of 15.46 minutes when the collagen matrix is used instead of the autologous connective tissue graft (10). Only 4 studies (*Table 4*) consider the histological aspect (22,24,29,32) for a total of 21 samples analyzed. These studies conclude that 2 months after surgery the collagen membrane is well integrated and covered with epithelium; 4 months after surgery there is complete resorption of the collagen membrane and the tissue architecture is similar to that of a healthy gum.

Discussion

A well-represented band of keratinized gingiva (at least 2 mm) has a positive influence on peri-implant health by establishing a seal around the implant which leads the reduction in tissue inflammation and plaque accumulation and, consequently, the reduction of development of perimplantitis. Having an adequate thickness of peri-implant mucosa is important not only to guarantee marginal bone stability over time, but also to mask the gray show-through. Adequate peri-implant mucosal thicknesses are therefore important both from the functional and aesthetic point of view. Most of the studies analyzed show that the xenogenic collagen matrix is effective in increasing the thickness of the peri-implant mucosa and in the gain of keratinized gingiva with comparable or slightly lower results than the autologous connective tissue graft. This difference could be attributed to the different years in which the studies were conducted; the most recent studies report more comforting results regarding the use of xenogenic collagen matrix (Mucograft®) and this could be due to the improvement of the matrix application technique and to the collection of more clinical cases to be compared. However, almost all studies conclude that the collagen matrix is a valid substitute for autologous connective tissue grafting in increasing the volume of peri-implant soft tissues, especially when the main concern is to reduce patient morbidity and operative surgical time. Despite the possible protocols to minimize post-operative pain after palatal collection, there is no doubt that the use of a non-autogenous graft, by avoiding a second surgical site, is less invasive, faster and more tolerable for the patient. From the aesthetics point of view, on the other hand, according to the studies analyzed, the preferred standard appears to be the autologous connective tissue graft, while the Mucograft® would not significantly

Table 4 Histological outcomes following use of a xenogeneic collagen matrix

Author/year	Study type	Treatment	Sample size	Follow-up	Histologic outcomes
Simion *et al.*, 2012	Case-series	Mucograft® collagen matrix infused with rhPDGF-BB	6 healthy patients with dental implants placed with GBR in the maxillary anterior region. Mucograft® was applied during stage-two surgery, when titanium-reinforced membrane was removed	3.5 years	There was a complete resorption of Mucograft® at 4 months follow-up, with no areas of necrosis or inflammatory infiltrate. Regenerated soft tissue appeared similar to the healthy gingival mucosa
Stankovic *et al.*, 2018	Pilot study/ case-series	Mucograft® used to cover bone substitute and barrier membrane in GBR	3 healthy patients with very shallow vestibulum and shortly attached gingiva in need of alveolar ridge augmentation for implants placement. GBR was selected with the use of Bio-Oss + Bio-Gide + Mucograft® after teeth removal	3 years	Histological observations of patient 2 taken 4 months after surgery revealed stratified squamous epithelium and lamina propria beneath the basement membrane. Epithelial layer showed orthokeratosis and parakerstosis and low-grade acanthosis. In lamina propria there were mild peri-vascular mononuclear infiltrations
Lorenz *et al.*, 2017	Prospective cohort study	Mucograft®	51 implants on 8 (3 women, 5 men) patients between 60 to 71 years, with head and neck cancer with oral manifestation. At implant rehabilitation, patients were free of any tumor recurrence for at least 1 years, with edentulous jaw, a width of the attached gingiva <2 mm and adequate oral hygiene. After 4–8 months: implant exposure + vestibuloplasty	6 months	A well-integrated collagen matrix covered with epithelium resulted 8 weeks postsurgery
Thoma *et al.*, 2018	Split-mouth pilot study/ case series	Apically positioned flap *vs.* apically positioned flap + Mucograft® and Apically positioned flap + free gingival graft	36 sites on 9 patients, 46–88 years, periodontally and systemically healthy, fully edentulous in need of implant therapy in the mandible and the ability to be placed with dental implants in the two canine and the two first molar positions, with a reduced width of keratinized tissue (<2 mm)	3 months	A soft tissue similar to native gingiva, mature and stable, results from all 3 treatments at 3 months postsurgery (24 biopsies: 5 Apically positioned flap sites, 5 Mucograft® sites, 7 free gingival graft sites, and 7 control sites)

improve the aesthetics in terms of recession coverage and gray show-through. Which procedure proves the most effective in terms of gaining keratinized gingiva and for the thickness of the soft tissues around the implants is one of the points investigated in the studies of Thoma *et al.* (29) and of Bassetti *et al.* (30), which conclude by suggesting the combination of graft (connective or Mucograft®) and partial thickness flap apically positioned. None of the selected studies, except for the one by Zuiderveld *et al.* (27), which find no statistically significant difference, considers the presence of differences in prognostic terms related to sex, age and gingival biotype of the patients, the type of implants used and the site of intervention. Almost all studies consider healthy patients from both a systemic and periodontal point of view, and a worsening of mucogingival treatment in prognostic terms can otherwise be easily hypothesized. We

could as well hypothesize the possible indication of adopting collagen matrix instead of the autologous connective tissue graft in those patients who present pathologies compromising tolerance and pain threshold. Histological evaluation is performed only in 4 of the 22 studies considered, for a total of 21 analyzed samples. Within the limits of the reduced samples' population, the histology shows a good integration of the collagen membrane that matures into a healthy tissue, similar to the native gingiva. Limitations to the present revision are to be attributed to the still relatively scarce available literature, in reason of which a broader range of study types were included, among which reviews, clinical trials and observational studies. This necessarily leads to an increased heterogeneity of results and the potential development of evaluation errors. Finally, the different surgical approaches chosen in the various studies and the different timing of the grafts (increase of soft tissues before, during or after implantology) cause heterogeneity of results as well. However, the revision of these articles seems to suggest the grafting of soft tissues using Mucograft®, before or at the same time as implant insertion, to counter post-surgical bone remodeling in the absence of adequate thickness.

Conclusions

The present systematic review of the literature, based on the analysis of six reviews, eight clinical trials and eight observational studies, suggests that Mucograft® is an effective alternative to the autologous connective tissue graft with regard to the gain of keratinized tissue and the increase in thickness of peri-implant soft tissues, and with less post-operative morbidity and less operating time required. However, new randomized clinical trials with an adequate follow-up period would be desirable for a histological evaluation of the collagen matrix graft samples, expanding the samples currently available.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/fomm-20-25). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Friedman N. Mucogingival surgery. Texas Dental Journal 1957;75:358-62.
2. Fu JH, Su CY, Wang HL. Esthetic soft tissue management for teeth and implants. J Evid Based Dent Pract 2012;12:129-42.
3. Zucchelli G. Chirurgia Estetica Mucogengivale. Rho (MI): Quintessenza Edizioni; 2012, 2.
4. Lang NP, Loe H. The relationship between the width of keratinized gingiva and gingival health. J Periodontol 1972;43:623-7.
5. Kennedy JE, Bird WC, Palcanis KG, et al. A longitudinal evaluation of varying widths of attached gingiva. J Clin Periodontol 1985;12:667-75.
6. Linkevicius T, Apse P, Grybauskas S, et al. The influence of soft tissue thickness on crestal bone changes around implants: a 1-year prospective controlled clinical trial. Int J Oral Maxillofac Implants 2009; 24:712-9.
7. Giannobile WV, Jung RE, Schwarz F, et al. Evidence-based knowledge on the aesthetics and maintenance of peri-implant soft tissues: Osteology Foundation Consensus Report Part 1-Effects of soft tissue augmentation procedures on the maintenance of peri-implant soft tissue health. Clin Oral Implants Res 2018;29:7-10.
8. Jung RE, Sailer I, Hammerle CH, et al. In vitro color changes of soft tissues caused by restorative materials. Int J Periodontics Restorative Dent 2007; 27:251-7.
9. Sculean A, Gruber R, Bosshardt DD. Soft tissue wound healing around teeth and dental implants. J Clin

Periodontol 2014;41:S6-S22.
10. Gargallo-Albiol J, Barootchi S, Tavelli L, et al. 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;34:1059-69.
11. Chambrone L, Pannuti CM, Tu YK, et al. Evidence-based periodontal plastic surgery. II. An individual data meta-analysis for evaluating factors in achieving complete root coverage. J Periodontol 2012;83:477-90.
12. Ramachandra SS, Rana R, Reetika S, et al. Options to avoid the second surgical site: a review of literature. Cell Tissue Bank 2014;15:297-305.
13. Griffin TJ, Cheung WS, Zavras AI, et al. Post-operative complications following gingival augmentation procedures. J Periodontol 2006;77:2070-9.
14. Cairo F, Barbato L, Tonelli P, et al. Xenogeneic collagen matrix versus connective tissue graft for buccal soft tissue augmentation at implant site. A randomized, controlled clinical trial. J Clin Periodontol 2017;44:769-76.
15. Thoma DS, Naenni N, Figuero E, et al. Effects of soft tissue augmentation procedures on peri-implant health or disease: A systematic review and meta-analysis. Clin Oral Implants Res 2018;29:32-49.
16. Sanz M, Lorenzo R, Aranda JJ, et al. 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. J Clin Periodontol 2009;36:868-76.
17. Available online: www.geistlich-mucograft.com
18. Lorenzo R, Garcia V, Orsini M, et al. Clinical efficacy of a xenogeneic collagen matrix in augmenting keratinized mucosa around implants: a randomized controlled prospective clinical trial. Clin Oral Implants Res 2012;23:316-24.
19. Froum SJ, Khouly I, Tarnow DP, et al. The Use of a Xenogeneic Collagen Matrix at the Time of Implant Placement to Increase the Volume of Buccal Soft Tissue. Int J Periodontics Restorative Dent 2015;35:179-89.
20. Schallhorn RA, McClain PK, Charles A, et al. Evaluation of a porcine collagen matrix used to augment keratinized tissue and increase soft tissue thickness around existing dental implants. Int J Periodontics Restorative Dent 2015;35:99-103.
21. Schmitt CM, Moest T, Lutz R, et al. Long-term outcomes after vestibuloplasty with a porcine collagen matrix (Mucograft®) versus the free gingival graft: a comparative prospective clinical trial. Clin Oral Implants Res 2016;27:e125-33.
22. Stankovic D, Labudovic-Borovic M, Radosavljevic R, et al. Use of acellular collagen matrix for the closure of the open oral wound in bone regeneration. J Stomatol Oral Maxillofac Surg 2018;119:446-9.
23. Puzio M, Błaszczyszyn A, Hadzik J, et al. Ultrasound assessment of soft tissue augmentation around implants in the aesthetic zoneusing a connective tissue graft and xenogeneic collagen matrix - 1-year randomised follow-up. Ann Anat 2018;217:129-41.
24. Lorenz J, Blume M, Barbeck M, et al. Expansion of the peri-implant attached gingiva with a three dimensional collagen matrix in head and neck cancer patients-results from a prospective clinical and histological study. Clin Oral Investig 2017;21:1103-11.
25. Sanz-Martín I, Encalada C, Sanz-Sánchez I, et al. Soft tissue augmentation at immediate implants using a novel xenogeneic collagen matrix in conjunction with immediate provisional restorations: A prospective case series. Clin Implant Dent Relat Res 2019;21:145-53.
26. Vellis J, Kutkut A, Al-Sabbagh M. Comparison of Xenogeneic Collagen Matrix vs. Free Gingival Grafts to Increase the Zone of Keratinized Mucosa Around Functioning Implants. Implant Dent 2019;28:20-7.
27. Zuiderveld EG, Meijer HJA, Vissink A, et al. The influence of different soft-tissue grafting procedures at single implant placement on esthetics: A randomized controlled trial. J Periodontol 2018;89:903-14.
28. Maiorana C, Pivetti L, Signorino F, et al. The efficacy of a porcine collagen matrix in keratinized tissue augmentation: a 5-year follow-up study. Int J Implant Dent 2018;4:1.
29. Thoma DS, Alshihri A, Fontolliet A, et al. Clinical and histologic evaluation of different approaches to gain keratinized tissue prior to implant placement in fully edentulous patients. Clin Oral Investig 2018;22:2111-9.
30. Bassetti RG, Stähli A, Bassetti MA, et al. Soft tissue augmentation around osseointegrated and uncovered dental implants: a systematic review. Clin Oral Investig 2017;21:53-70.
31. Maiorana C, Beretta M, Pivetti L, et al. Use of a Collagen Matrix as a Substitute for Free Mucosal Grafts in Pre-Prosthetic Surgery: 1 Year Results From a Clinical Prospective Study on 15 Patients. Open Dent J 2016;10:395-410.
32. Simion M, Rocchietta I, Fontana F, et al. Evaluation of a Resorbable Collagen Matrix Infused with rhPDGF-BB in

Peri- implant Soft Tissue Augmentation: A Preliminary Report with 3.5 Years of Observation. Int J Periodontics Restorative Dent 2012;32:273-82.
33. Esposito M, Maghaireh H, Grusovin MG, et al. Interventions for replacing missing teeth: management of soft tissues for dental implants (Review). Cochrane Database Syst Rev 2012;(2):CD006697.

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