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Running Title: Autogenous grafts for periodontal and peri-implant plastic surgery

One Sentence Summary: The latest evidence and current status of autogenous soft tissue grafting for gingival tissue augmentation and recession coverage at teeth and dental implant sites

Abstract

This state-of-the-art review presents the latest evidence and the current status of autogenous soft tissue grafting for soft tissue augmentation and recession coverage at teeth and dental implant sites. The indications and predictability of the free gingival graft (FGG) and connective tissue graft (CTG) techniques are highlighted, together with their expected clinical and esthetic outcomes. CTG can be harvested from the maxillary tuberosity or from palate with different approaches that can have an impact on graft quality and patient morbidity. The influence of CTG on soft tissue thickness and keratinized tissue width are also discussed.

Keywords: autogenous grafts, autografts, dental implants, gingival recession, periodontal, soft palate, soft tissue grafting

Periodontal and peri-implant plastic augmentation using autogenous soft tissue grafts

Since its early introduction over 50 years ago¹, soft tissue grafting has been increasingly utilized in clinical practice for augmenting tissue thickness, re-establishing an adequate width of keratinized tissue, correcting mucogingival deformities, and improving esthetics, at teeth and dental implant sites²⁻⁴. The present manuscript provides the latest evidence in periodontal plastic procedures since the 2015 AAP Regeneration Workshop^{5,6}, while presenting insights on the emerging field of peri-implant soft tissue plastic surgery.

The Free Gingival Graft

A soft tissue graft harvested from the palate with the overlying epithelium is defined as the free gingival graft (FGG), and it was first introduced for increasing keratinized tissue developmentally missing or lost¹. The healing events and the principles affecting the outcomes of a FGG that have been extensively investigated^{7,8}, may have contributed to the high predictability of this procedure. Several features were suggested as risk factors for the outcomes of FGG, these include but are not limited to: improper preparation of the recipient site, inadequate graft size and thickness, poor adaptation to the recipient bed and failure to stabilize the graft⁸. As it has been shown that FGG undergoes a significant shrinkage (around 30%) during the healing process^{9,10}, a graft wider than the site needing soft tissue augmentation has to be harvested, and this may account for the post-operative discomfort and complications reported at the donor site^{11,12}. More recently, several authors have focused on the shrinkage of FGG compared to apically positioned flap alone or graft substitutes, such as collagen matrix or acellular dermal matrix (ADM)^{10,13}. These studies confirmed a significant shrinkage of all the graft materials, with FGG showing a greater capacity of increasing the keratinized tissue width (KTW), however with a higher patient morbidity, increased surgical time and poor color match with the surrounding tissue^{10,13}. It has been also reported that FGG stabilization

with cyanoacrylate may decrease not only the shrinkage of the graft, but also pain discomfort compared to the conventional stabilization by suturing¹⁴. One of the main indications of FGG is to re-establish an adequate KTW and gingival thickness in presence of mucogingival defects² (Figures 1A through 1E). The long-term efficacy of an FGG compared to contralateral untreated sites has been assessed by Agudio et al. that observed the stability (or coronal migration) of the gingival margin and the prevention (or worsening) of gingival recessions (GRs) following the FGG; however, untreated contralateral sites were associated with increased recession depth or development of GRs¹⁵. Regarding its use in root coverage, Cortellini et al. introduced a modification of the conventional approach (“partially epithelialized FGG”) in the lower anterior area to overcome the esthetic deficiencies that have been reported and to increase the percentage of mean root coverage, facilitating at the same time an ideal repositioning of the alveolar mucosa¹⁶.

The importance of possessing an adequate width and thickness of keratinized tissue seems to be crucial both for natural teeth and dental implants^{17,18}. Indeed, similarly to teeth lacking KTW that were found to be more prone to further attachment loss¹⁸, a deficiency of (or minimal) keratinized mucosa around implants has shown to hinder patient oral hygiene, leading to higher soft tissue inflammation, mucosal recession and attachment loss¹⁹. Although the role of KTW in maintaining peri-implant health is not uniformly accepted²⁰, several trials showed that soft tissue augmentation using FGG was effective in reducing mucosal inflammation, patient discomfort and facilitating optimal plaque control around implants lacking KT^{21,22}. Moreover, it has been reported that peri-implant soft tissue thickness can also affect marginal bone loss¹⁷. A recent meta-analysis by Thoma et al., concluded that soft tissue augmentation by autogenous grafts is the most predictable technique for maintaining peri-implant health by increasing KT width and thickness (Figures 1F through 1K)²³. Indeed, having at least 2 mm of KT was found to demonstrate a protective effect on peri-implant health²⁴ and implants with < 2 mm of KT were more prone to develop peri-implant biological complications in erratic compliers²⁵. Lastly, it should be recognized that the FGG is also used for increasing vestibular depth and KT width prior to implant reconstruction.

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The Connective Tissue Graft

According to Zuhr et al., the introduction of connective tissue grafts (CTG) ²⁶ and the increasing changeover from the FGG to the CTG presents the transition from traditional mucogingival surgery to periodontal plastic surgery ³. While traditional mucogingival approaches were aimed primarily at increasing the KTW, the principal goal of modern periodontics should embrace the ultimate esthetic outcomes ^{3,27}. There is extensive evidence that a CTG is the technique of choice in treating gingival/mucosal recessions at teeth and implant sites ²⁸⁻³⁰ (Figure 2), for increasing soft tissue thickness ³¹, masking discolored roots or visible implant components ³, as well as interdental papilla reconstruction ³² (Table 1).

Several techniques either with a CTG or other graft substitutes have been proposed for the treatment of gingival recessions, such as the coronally advanced flap (CAF), lateral rotational flap, semilunar flap, tunnel technique or the VISTA technique ^{27,33,34}. Among them, CTG-based approaches demonstrate the strongest potential of achieving complete root coverage, together with the highest esthetic results ^{27,28,35}. It has been speculated that the CTG acts as a biologic filler, improving the adaptation and the stability of the flap to the root during early wound repair ³⁶. As a result, the gingival phenotype becomes thicker and the chances of achieving complete root coverage higher ³⁷. In presence of an increased soft tissue thickness, the coronal migration of the gingival margin over time, a phenomenon defined “creeping attachment”, can also occur ²⁹. This may explain the trend towards stability of the gingival margin over time of recession defects treated with CTG ³⁸⁻

While the FGG retains its original appearance of the palatal soft tissue at the recipient site ⁴¹ and may result in poor esthetic integration and a scar tissue-like texture ³, the CTG is able to increase soft tissue volume and quality, as well as provide a harmonious gingival margin ^{3,27}. Nevertheless,

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during the last decade, the improvement of the techniques and the introduction of the microsurgical approach, consisting of magnification, illumination, micro-instruments and new suture materials, has contributed to the greater predictability of root coverage procedures⁴². This led Chambrone and Pini Prato to speculate that flap preparation and management are the more crucial elements in root coverage⁴².

In addition, it was demonstrated that CAF + CTG provides superior outcomes as compared to CAF alone only when the gingival thickness is ≤ 0.8 mm (i.e., thin gingival phenotype)³⁶. Therefore, it has been suggestive the selective use of CTG for sites presenting with gingival thickness < 1 mm and KTW ≤ 1 mm^{43, 44}.

Contrastingly, when treating peri-implant soft tissue dehiscences, the use of CTG is highly recommended, regardless of keratinized mucosa width or thickness^{45, 46}, while autogenous graft substitutes are often used for increasing tissue thickness and minimizing the post-operative mucosal recession during immediate implant placement⁴⁷ or at the time of implant uncovering^{48, 49}.

Several harvesting approaches, such as the trap-door, the single incision and parallel incisions technique have been proposed for obtaining a CTG from the palate^{3, 50}. These methods were mainly aimed at achieving a healing by primary intention by preserving a primary palatal flap that is then sutured to the donor site after the harvesting. These approaches were initially considered the gold standard as they accompanied less post-operative morbidity than the FGG that comprises of a secondary intension healing^{11, 12}.

However, it has been demonstrated that a CTG can be obtained by harvesting and de-epithelializing a FGG, with similar patient discomfort compared to the traditional trap door technique, if the FGG donor site is protected⁵⁰. More recently, several approaches claiming to minimize patient morbidity and enhancing palatal wound healing following FGG harvesting were proposed^{51, 52} (Table 2).

It has been speculated that the harvesting technique may also affect the quality of the graft, being a CTG derived from de-epithelialization of an FGG mainly composed of lamina propria, while a CTG from conventional harvesting approaches (i.e., deep palate) is more rich in glandular and adipose tissue^{2, 3, 50, 53}. This dissimilar nature of the graft renders a CTG distinctively different from the FGG by being firmer, more stable, and easier to manage than a CTG that is harvested from a deep palate^{50, 53}. Furthermore, since a CTG can promote the keratinization of the overlying epithelia⁵⁴, it has been suggested that the adipose and glandular tissue of the graft may act as barriers to the plasmatic diffusion and vascularization during the first phase of healing, and also impair their ability to induce epithelial keratinization^{55, 56}.

The maxillary tuberosity presents a promising alternative donor site to the palate for soft tissue harvesting, providing lower patient morbidity⁵⁷, while containing more lamina propria and less submucosa than a CTG harvested from the deep lateral palate⁵⁸. However, it is still unclear to which extent the composition of the graft influences the outcomes of a mucogingival surgery. The limited evidence available from the literature suggests that the nature of a CTG can play a role in determining the soft tissue thickness and KT width^{57, 59}, but does not directly affect the amount of root coverage^{50, 57}. Molecular analyses also confirmed different cellular and tissue behaviors of CTGs harvested from the maxillary tuberosity as compared to the palate⁶⁰. Given its tendency for a hyperplastic response, it may be suggested that CTG from the tuberosity may be used for increasing soft tissue volume and KTW, when esthetic is not the primary goal⁵⁶.

Limitations, complications and patient perspective related to palatal harvesting

Patient morbidity has been reported as one of the major shortcomings of an autologous soft tissue graft harvesting procedure^{61, 62}. In addition, further post-operative complications have been described, including hemorrhage at the donor site, palatal sensory dysfunction, infection, and/or

increased surgical time^{11,63}. In particular, prolonged intra- and post-operative bleeding from the palate is not a rare event regardless of the technique performed¹¹. Several cadaver studies have been conducted to investigate the course of the greater palatine artery and its branches^{64,65}.

However, the anatomy of the palatal vault, age, gender, population and the variability of these vessels prevent making a definitive conclusion and providing universal guidelines for a “safe” palatal harvesting⁶⁶. On the other hand, it is generally accepted that a soft tissue harvesting should be limited from the region of the canine to the palatal root of the first molar³ (or even to the second molar/ tuberosity area), and therefore, the availability of the autologous graft may be inadequate when treating multiple augmentation sites. In addition, the thickness of the palatal mucosa is another potential limiting factor for palatal harvesting, as minimal residual soft tissue thickness over the bone has been related to a greater analgesic consumption⁵⁰. A thin palatal mucosa may also enhance the risk of over-thinning the primary flap (when performing the trap-door, envelope or parallel incisions techniques) which has been associated with wound sloughing and increased patient morbidity⁵⁰. Lastly, autogenous soft tissue grafting requires a second surgical site and increases surgery duration, which has been related to higher post-operative pain and swelling^{11,67}. In this scenario, it is not surprising that studies utilizing subjective-reported qualitative measures have shown patient preference towards approaches avoiding the harvesting of tissue from a second surgical site^{61,68}. Similarly, clinicians have demonstrated increased interest in graft substitutes, such as ADM^{69,70} or collagen matrix^{62,71}.

Concluding remarks

Significant evidence supports the use of autologous soft tissue grafting for periodontal and peri-implant plastic surgical reconstruction for soft tissue health and esthetics. While the free gingival graft technique is still considered the approach of choice for increasing soft tissue thickness and keratinized tissue/mucosa at teeth and dental implant sites, connective tissue graft-based

techniques provide the greatest predictability for achieving complete root coverage (or soft tissue dehiscence coverage), together with high esthetic results. Adequate tissue thickness and keratinized tissue width seem to be crucial factors for peri-implant health. Autogenous graft-based techniques can be considered the most effective in achieving peri-implant soft tissue augmentation.

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Figure Legend

Figure 1. A-E) Free Gingival Graft at lower central incisors; **A)** Baseline; **B)** Immediately post-op; **C)** 5-months post-op; **D)** Coronally advanced flap; **E)** 6-months post-op showing the complete root coverage of the recession defects together with increased keratinized gingiva. F-K) Free gingival graft around a posterior implant with minimal keratinized mucosa on the buccal aspect; **F)** Baseline; **G-H)** Flap preparation and suturing to the periosteum; **I-J)** Free gingival graft sutured to the periosteum and to the adjacent soft tissue; **K)** 6-month healing

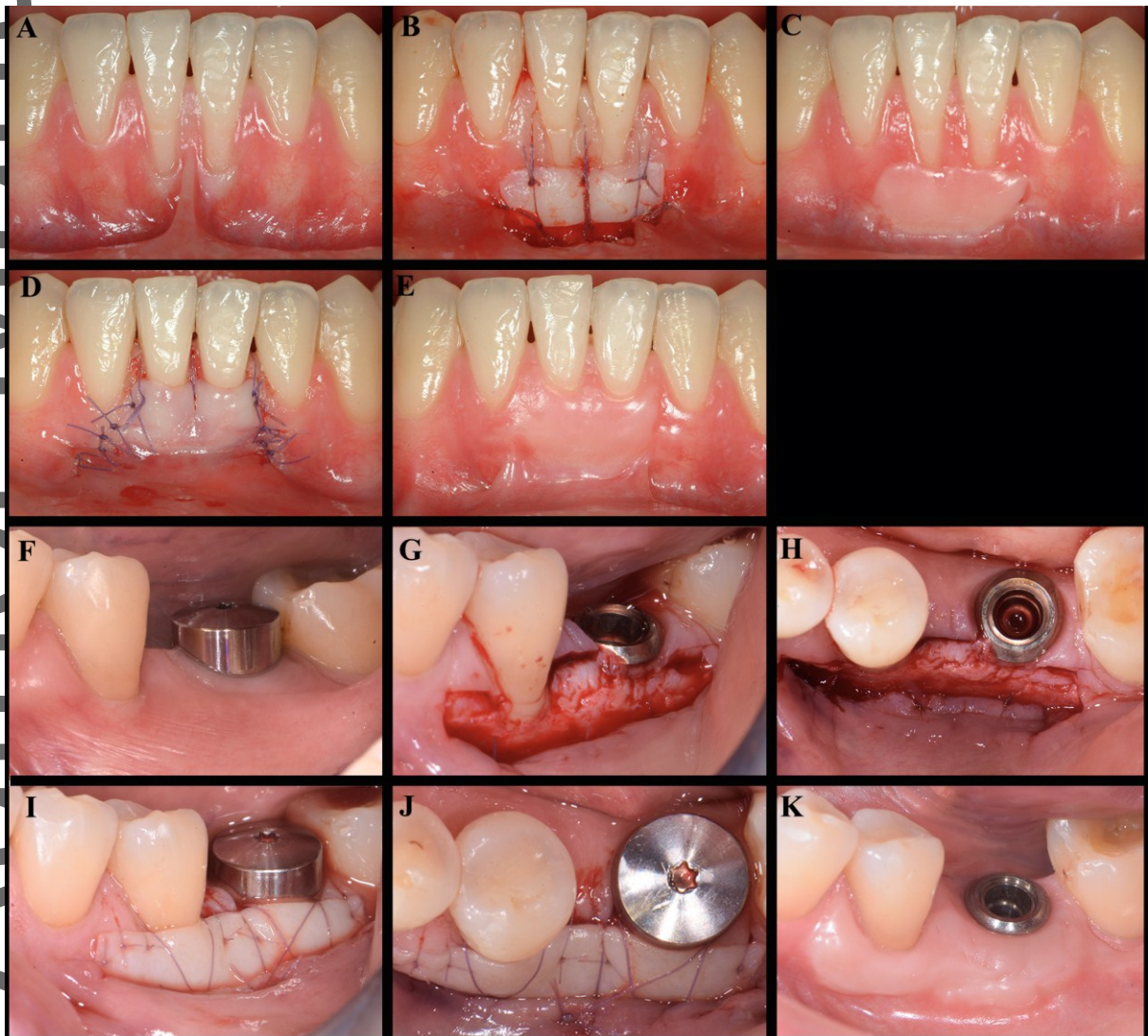


Figure 2. A-E) Coronally advanced flap and connective Tissue Graft for the treatment of an isolated gingival recession in a lower canine; **A)** Baseline; **B)** Split-full-split flap preparation; **C)** A connective tissue graft harvested from the palate was sutured over the root surface. Note the de-epithelialization of the anatomical papillae; **D)** Flap coronally advanced and sutured; **E)** 6-month healing with complete root coverage. **F-K)** Soft tissue dehiscence at an implant site treated with a surgical-prosthetic approach and a connective tissue graft. **F)** Baseline; **G)** The crown was removed and the thinner abutment was placed for facilitating the growth of the interdental soft tissue; **H)** 1-month after the abutment replacement, a split-thickness flap was elevated at the implant site; **I)** a connective tissue graft harvested from the palate was sutured to the de-epithelialized papillae; **J)** Flap closure; **K)** 6-month healing showing the complete resolution of the soft tissue dehiscence (Adapted with Permission from Periodontology 2000)⁴⁵



Tables

Table 1. Indications for autogenous soft tissue grafts

Autogenous Graft	Indications	References	
Free Gingival Graft	KT augmentation around teeth	Agudio et al. 2009 ⁷²	
	Primary	Peri-implant KT augmentation	Roccuzzo et al. 2016 ²¹ , Oh et al. 2017 ²²
		Increasing vestibulum depth	Yadav et al. 2014 ⁷³
	Secondary	Root coverage	Cortellini et al. 2012 ¹⁶ , Zucchelli & De Sanctis ⁷⁴
		Ridge augmentation	Urban et al. 2019 ⁷⁵
Connective Tissue Graft	Root coverage	Zucchelli et al. 2010 ⁵⁰ , Stefanini et al. 2018 ⁴⁴	
	Primary	Peri-implant soft tissue thickness augmentation	Cairo et al. 2017 ⁶² , Zeltner et al. 2017 ⁴⁹
		Immediate implant placement	Frizzera et al. 2018 ⁷⁶ , Zuiderveld et al. 2018 ⁴⁷
		Peri-implant soft tissue dehiscence	Mazzotti et al. 2018 ⁴⁵ , Zucchelli et al. 2018 ²⁹
	Secondary	Ridge augmentation	Akcali et al. 2015 ⁷⁷

Legend. KT: Keratinized Tissue. FGG: Free Gingival Graft. CAF: Coronally Advanced Flap

Table 2. Factors affecting patient morbidity and wound healing of the palatal donor site following free gingival graft harvesting

<p>Factors that may reduce the post-operative morbidity</p>	<p>Graft dimension (height \leq 4 mm, width $<$ 14 mm and thickness $<$ 2 mm) ^{50, 51, 78, 79}</p> <p>Thickness of the palatal mucosa $>$ 4 mm ⁷⁸</p> <p>Use of diode laser for the harvesting and for wound irradiation ⁸⁰</p> <p>Protective material on the donor site:</p> <ul style="list-style-type: none"> • Collagen sponge and cyanoacrylate ^{50, 51, 79}, • Biologics: Platelet-rich plasma ⁸¹ and Platelet-rich fibrin ^{82,83} • Ozone therapy ⁸⁴ • Hyaluronic acid ⁵²
<p>Factors that may increase the post-operative morbidity</p>	<p>Graft dimension (height $>$ 4 mm, width \geq 14 mm and thickness $>$ 2 mm) ^{50, 51, 78, 79}</p> <p>Thickness of the palatal mucosa \leq 4 mm ⁷⁸</p>
<p>Factors that may accelerate wound healing</p>	<p>Use of biologic agents (Platelet-rich plasma ⁸¹, Platelet-rich fibrin ^{82,83} and Topical erythropoietin ⁸⁵)</p> <p>Hyaluronic acid ⁵²</p> <p>Ozone therapy ⁸⁴</p> <p>Advanced glycation end-products ^{86*}</p>

*based on preclinical animal models