Efficacy of soft tissue augmentation around dental implants and in partially edentulous areas: a systematic review

Thoma, Daniel S; Buranawat, Borvornwut; Hämmerle, Christoph H F; Held, Ulrike; Jung, Ronald E

Abstract: AIM: To review the dental literature in terms of efficacy of soft tissue augmentation procedures around dental implants and in partially edentulous sites. METHODS: A Medline search was performed for human studies augmenting keratinized mucosa (KM) and soft tissue volume around implants and in partially edentulous areas. Due to heterogeneity in between the studies, no meta-analyses could be performed. RESULTS: Nine (KM) and eleven (volume) studies met the inclusion criteria. An apically positioned flap/vestibuloplasty (APF/V) plus a graft material [free gingival graft (FGG)/subepithelial connective tissue graft (SCTG)/collagen matrix (CM)] resulted in an increase of keratinized tissue (1.4-3.3 mm). Statistically significantly better outcomes were obtained for APF/V plus FGG/SCTG compared with controls (APF/V alone; no treatment) ($p < 0.05$). For surgery time and patient morbidity, statistically significantly more favourable outcomes were reported for CM compared to SCTGs ($p < 0.05$) in two randomized controlled clinical trials (RCTs), even though rendering less keratinized tissue. SCTGs were the best-documented method for gain of soft tissue volume at implant sites and partially edentulous sites. Aesthetically at immediate implant sites, better papilla fill and higher marginal mucosal levels were obtained using SCTGs compared to non-grafted sites. CONCLUSIONS: An APF/V plus FGG/SCTG was the best-documented and most successful method to increase the width of KM. APF/V plus CM demonstrated less gain in KM, but also less patient morbidity and surgery time compared to APF/V plus SCTG based on two RCTs. Autogenous grafts (SCTG) rendered an increase in soft tissue thickness and better aesthetics compared to non-grafted sites.

DOI: https://doi.org/10.1111/jcpe.12220

Efficacy of soft tissue augmentation around dental implants and in partially edentulous areas – a systematic review

EWP X

Daniel S. Thoma,[1] Borvornwut Buranawat,[1] Christoph H.F. Hämmerle CHF,[1] Held Ulrike, [2] Ronald E. Jung[1]

Key words:

soft tissue augmentation, keratinized tissue, soft tissue volume, subepithelial connective tissue graft, free gingival graft, allogenic dermal matrix graft, vestibuloplasty, collagen matrix, dental implant

Running title:

Soft tissue grafting – a systematic review

Address for correspondence: Daniel S. Thoma, PD Dr. med. dent.
Clinic of Fixed and Removable Prosthodontics and Dental Material Science
Center for Dental Medicine, University of Zurich
Plattenstrasse 11
CH-8032 Zurich, Switzerland
Phone: +41 44 634 32 57
Fax: +41 44 634 43 05
e-mail: daniel.thoma@zzm.uzh.ch

[1] Clinic for Fixed and Removable Prosthodontics and Dental Material Science, University of Zurich, Zurich, Switzerland
[2] Horten Centre for Patient Oriented Research and Knowledge Transfer. University Hospital Zurich, Zurich, Switzerland

Clinical relevance

Scientific rationale for the study: the aim of this systematic review was to assess the efficacy of soft tissue augmentation procedures to gain keratinized mucosa around dental implants and to increase the soft tissue volume around implants and in partially edentulous areas

Principal findings: An apically positioned flap/vestibuloplasty (APF/V) plus a graft material was considered a successful treatment concept resulting for gain of keratinized mucosa. The amount of keratinized mucosa could statistically significantly be increased combining an APF/V with autogenous tissue (FGG=free gingival graft)/SCTG=subepithelial connective tissue graft) when compared to control groups (no treatment, APF/V alone). The use of collagen matrices (CM) reduced surgery time and patient morbidity, but rendered less gain of keratinized mucosa compared to the use of autogenous tissue (SCTG). Autogenous grafts (SCTG/FGG) rendered a two- and three-dimensional gain of soft tissue thickness at implant sites and partially edentulous sites.

Practical implications: Larger evidence is available for APF/V plus autogenous tissue (FGG/SCTG) and supports these procedures for gain of keratinized mucosa. If surgery time and patient morbidity are considered, APF/V plus CM may be recommended as an alternative treatment modality, even though rendering less gain in keratinized mucosa and being less documented. For soft tissue volume increase, the use of autogenous grafts (SCTG/FGG) has to be considered as gold standard. No soft tissue substitute materials can be recommended for this procedure.

Conflict of interest and source of funding statement

This review was funded by the Clinic of Fixed and Removable Prosthodontics and Dental Material Science, University of Zurich. Dres. Hämmerle, Jung and Thoma have received lecture fees from Geistlich Pharma AG, Wolhusen, Switzerland and are member (Jung, Thoma) of the Osteology Foundation Expert Council or president (Hämmerle) of the Osteology Foundation. Other than mentioned, the authors do not report any conflict of interest for this study.

Abstract

Aim: To review the dental literature in terms of efficacy of soft tissue augmentation procedures around dental implants and in partially edentulous sites.
Methods: A Medline search was performed for human studies augmenting keratinized mucosa and soft tissue volume around implants and in partially edentulous areas. Relevant studies were identified and statistics reported for meta-analyses including weighted mean differences with 95% confidence intervals.
Results: Nine (keratinized mucosa) and eleven (volume) studies met the inclusion criteria. An apically positioned flap/vestibuloplasty (APF/V) plus a graft material (FGG/SCTG/CM) (FGG=free gingival graft/SCTG=subepithelial connective tissue graft/CM=collagen matrix) resulted in an increase of up to 4mm of keratinized mucosa. Based on meta-analysis, statistically significantly better outcomes were obtained for APF/V plus FGG/SCTG compared to controls (APF/V alone; no treatment) ($p<0.05$). For surgery time and patient morbidity, statistically significantly better outcomes were reported for collagen matrices (CM) compared to SCTGs ($p<0.05$), even though rendering less keratinized tissue. SCTGs were the best-documented method for gain of soft tissue volume at implant sites and partially edentulous sites. Esthetically at immediate implant sites, better papilla fill and higher marginal mucosal levels were obtained using SCTGs compared to non-grafted sites.
Conclusions: An APF/V plus FGG/SCTG was the best-documented and most successful method to increase the width of keratinized mucosa. APF/V plus CM demonstrated less gain in keratinized mucosa, but also less patient morbidity and surgery time compared to APF/V plus SCTG based on two randomized controlled clinical trials. Autogenous grafts (SCTG) rendered an increase in soft tissue thickness and better esthetics compared to non-grafted sites.

Introduction

Plastic periodontal procedures to augment keratinized tissue and to increase soft tissue volume are well described (Cairo et al., 2008, Thoma et al., 2009). These procedures are indicated to establish functional and biological stability around teeth and implants, mainly in conjunction with reconstructive therapy. The question whether or not there is a need for keratinized tissue to maintain periodontal health around teeth and peri-implant health around dental implants has been controversially discussed in the literature citing a number of parameters to be considered: i) establishment and maintenance of biological health, ii) prevention of recession, iii) esthetics and, iv) cleansibility of the reconstruction (Hoelscher and Simons, 1994, Marquez, 2004, Mehta and Lim, 2010, Wennstrom and Derks, 2012). For dental implants, clinical evidence suggests that a lack of keratinized mucosa (KM) may not be crucial in maintaining the health of peri-implant soft tissues (Wennstrom et al., 1994), may not be associated with more bone loss (Chung et al., 2006) or that despite the presence of KM, peri-implantitis may occur (Roos-Jansaker et al., 2006). In contrast, more recent clinical studies concluded that a wider zone of KM may better preserve soft and hard tissue stability (Bouri et al., 2008), may be more favorable for the long-term maintenance of dental implants (Kim et al., 2009) and that a lack of KM may result in poorer oral hygiene and greater soft tissue recession (Schrott et al., 2009). This resulted in a clinical recommendation of 2mm for the width of keratinized mucosa (Adibrad et al., 2009, Bengazi et al., 1996), a dimension similar to the zone of keratinized gingiva recommended to be adequate around teeth (Lang and Loe, 1972). Treatment-wise, plastic procedures to augment keratinized tissue include an apically positioned flap or a vestibuloplasty procedure (Thoma et al., 2009, Palacci and Nowzari, 2008). This can be performed prior to implant placement, simultaneously with second stage surgery or post insertion of the final reconstruction. Moreover, in order to compensate for hard and soft tissue deficits in localized defects, soft tissue volume augmentation is mainly indicated for esthetic reasons and to facilitate oral hygiene in pontic areas (Seibert, 1983a, Pini-Prato et al., 2004). In these sites, the classic procedures include the use of free gingival grafts (FGG), subepithelial connective grafts (SCTG) and various types of roll and pedicle flaps (Seibert, 1983b, Studer et al., 2000, Batista et al., 2001, Cho, 1998, Breault et al., 2004). In conjunction with dental implants, plastic augmentative procedures were recommended to enhance the thickness of the soft tissues simultaneously with implant placement or during the healing phase of the implants (Speroni et al., 2010, Grunder, 2000, Schneider et al., 2011). Clinical studies demonstrated various techniques to be successful, resulting in greater flexibility for the choice of the reconstruction material, better esthetic outcomes with respect to the color of the peri-implant tissues, maintenance or even improvement of the marginal mucosal height and higher papillae

scores (Jung et al., 2008, Speroni et al., 2010, Cornelini et al., 2008, Kan et al., 2009). From a functional point of view however, there is still a lack of scientific evidence whether or not thicker peri-implant soft tissues result in better long-term success and survival rates of dental implants.

Since controversy still exists with respect to the efficacy of soft tissue augmentation and new materials were evaluated more recently, there is a strong need to critically assess the dental literature for optimized procedures and graft materials in terms of soft tissue augmentation.

Therefore, the aim of the present systematic review was to assess dental literature focusing on the efficacy of soft tissue augmentation procedures to increase the width of the keratinized mucosa around dental implants and to increase the soft tissue volume around implants and in partially edentulous areas.

Materials and Methods

Protocol development and eligibility criteria

A detailed protocol was developed and followed according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) statement (Liberati et al., 2009, Moher et al., 2009).

Focused question

What is the efficacy of different soft tissue augmentation methods in terms of i) increasing the width of keratinized mucosa, and ii) gain in soft tissue volume around implants and in partially edentulous areas?

Search strategy

A Medline (PubMed) search was performed for human studies, including articles published from January 1, 1966 up to May 15, 2013 in the dental literature. The search was limited to the English and German language. The search was complemented by manual searches of the reference list of all selected full-text articles. Additionally, full text articles of reviews published in the same time period were obtained. An additional hand search was performed searching for relevant studies by screening these reviews.

Search Terms

The following search terms were selected: "acellular dermal matrix" OR "dermal matrix allograft" OR "alloderm" OR "keratinized gingiva" OR "keratinized tissue" OR "soft tissue graft" OR "subepithelial connective tissue graft" OR "connective tissue" OR "free gingival graft" OR "human fibroblast-derived dermal substitute" OR "dermagraft" OR "apligraf" OR "collagen matrix" OR "extracellular membrane" OR "gingival autograft" OR "attached gingiva" OR "attached mucosa" OR "keratinized mucosa" OR "soft tissue augmentation" OR "soft tissue transplantation" OR "vestibuloplasty" OR "ridge augmentation" OR "soft tissue correction" OR "apically positioned flap" AND "dental implants" OR "Jaw, Edentulous, Partially" OR "pontic" (all MeSH terms)

The search was limited to language (english, german), „human trial" (MeSH term, clinical studies), and "Dental Journals". Additionally, the MeSH terms: "case reports", "clinical trial", "comparative study", "controlled clinical trial", "randomized controlled trial", "meta-analysis", "review" and "systematic reviews" were used.

Inclusion criteria

The applied inclusion criteria were different for studies dealing with gain of keratinized mucosa or gain of soft tissue volume.

Increase in width of keratinized mucosa

Any case series, cohort study, controlled clinical trial and randomized controlled clinical trial with at least 5 patients was included. A follow-up period of at least 3 months was required for the primary outcome "gain in keratinized mucosa". The reported treatment outcomes had to include either clinical and/or histological measures of the width of keratinized mucosa. The primary outcome of the studies had to be localized gain in width of keratinized mucosa.

augmentation of soft tissue volume around dental implant and in partially edentulous areas

For studies focusing on soft tissue volume gain, any prospective case series, cohort study, controlled clinical trial and randomized controlled clinical trial with at least 5 patients was included. The minimal follow-up time was 3 months for the primary outcome "gain in soft tissue volume". The reported treatment outcomes had to include either clinical and/or histological measures of the soft tissue volume.

The minimal follow-up time (3 months) for the primary outcome variables chosen in this systematic review is based on a lack of a scientific data with long-term results and in line with a previously published systematic review (Thoma et al., 2009).

Exclusion criteria

Studies not meeting all inclusion criteria were excluded from the review. Publications dealing with the following topics were also excluded: *in vitro* studies, preclinical (animal) studies, studies dealing with the treatment of recession defects, studies augmenting keratinized tissue around teeth only, studies augmenting soft tissue in fully edentulous patients, studies where the effect of soft tissue augmentation surgery could not be extracted from the data (e.g. combination of guided bone regeneration and soft tissue augmentation).

Selection of studies

Titles derived from this broad search were independently screened by 2 authors (DT, BB) based on the inclusion criteria. Disagreements were resolved by discussion. Cohen's Kappa-coefficient was used as a measure of agreement between the 2 readers. Following this, abstracts of all titles agreed on by both authors were obtained, and screened for meeting the inclusion criteria. If no abstract was available in the database, the abstract of the printed article was used. The selected articles were then obtained in

full text. If title and abstract did not provide sufficient information regarding the inclusion criteria, the full report was obtained as well. Again, disagreements were resolved by discussion.

Finally, the selection based on inclusion/exclusion criteria was made for the full text articles. For this purpose Material and Methods, and Results of these studies were screened. This step was again carried out independently by 2 readers. Disagreements were resolved by discussion.

Data extraction

Two reviewers independently extracted the data using data extraction tables. Any disagreements were resolved by discussion aiming for consensus.

Quality assessment

A quality assessment of the included randomized controlled clinical trials and controlled clinical studies was performed independently by two reviewers (BB, DTH) according to the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011) (Higgins and Green, 2011). Three main quality criteria were assessed: allocation concealment, blinding treatment outcomes to outcome examiners and completeness of follow-up. The studies were then rated to have a low risk of bias (all 3 criteria met) or a high risk of bias (one or more criteria not met).

Statistical Analysis

A test of heterogeneity was calculated to determine whether fixed or random effects models should be used for pooling of studies. Studies were pooled with inverse-variance weighting, and between study heterogeneity was estimated with the DerSimonian-Laird estimator. Meta-analyses were performed to compare treatment vs. no treatment, treatment a vs. treatment b and treatment a vs. treatment b vs. treatment c.

Results

Study characteristics

The electronic search identified a total of 2396 titles (for details, refer to Fig. 1). From assessing the titles, 2283 were excluded (inter-reader agreement k = 0.98 ± 0.48). The resulting number of abstracts obtained was 113, out of which 83 were excluded (inter-reader agreement k= 0.98 ± 0.25). Thirty full-text articles were obtained, 7 articles were further excluded after reading full text. Finally, including studies found through hand searching, 9 studies of keratinized tissue and 11 studies of soft tissue volume articles met the inclusion criteria.

Exclusion of studies

The reasons for excluding studies (7) after full text was obtained were: no reported or insufficient clinical details (n=3), an insufficient number of patients (n=1), only hard tissue augmentation (n=2) and soft tissue augmentation in combination with implant placement and guided bone regeneration (n=1). Details are provided in Table 1.

Included studies

The 20 studies that met the inclusion criteria are presented in Table 2 - 5. Table 2 and 4 represent data for "keratinized tissue augmentation studies" (9 studies) and Table 3 and 5 refer to clinical studies regarding "soft tissue volume" (11 studies).

Increase in width of keratinized mucosa

Patient-based treatment outcomes for the width of keratinized tissue retrieved from 9 studies are presented in Table 2 and 4. Three studies were designed as randomized controlled trials (RCT), two as controlled clinical trials (CCT) and the rest of four studies were case series reports. 198 patients were treated for gain of keratinized tissue around the implants. The methods and techniques used for gain of keratinized tissue included no treatment, vestibuloplasty, APF/V (apically positioned flap/vestibuloplasty) in combination with autogenous tissues (FGG=free gingival graft), SCTG=subepithelial connective tissue graft) and APF/V in combination with allogenic grafts (ADMG) or collagen matrices (CM). The mean follow up period was 16.2 months (6-48). The main reason for treating the patients encompassed a lack of or an inadequate with of attached gingival/keratinized tissue. In summary, three studies were eligible for comparison using meta-analyses. The hypothesis of the heterogeneity test could not be rejected (p=0.43), therefore a fixed effects model was chosen.

Quality assessment

The quality assessment of the included studies revealed a high risk of bias for all included studies except for the three RCTs (Sanz et al., 2009, Basegmez et al., 2012, Lorenzo et al., 2012).

Treatment outcomes

Width of keratinized tissue

A total of 7 studies (3 RCTs, 2 CCTs, 2 case series) reported on the width of augmented keratinized tissue; three studies could be compared for mean gain in keratinized tissue using meta-analyses. Four studies investigated the efficacy of collagen matrices (Mucograft®, Geistlich, Switzerland and Collatape®, Zimmer Dental, USA) or an acellular dermal matrix graft (SureDerm™, Hans Biomed Corp, Korea) compared to autogenous grafts (FGG, SCTG) for augmenting the band of keratinized tissue. In two RCTs, the application of a CM demonstrated a gain of keratinized tissue as effective and predictable as the gold standard, an autogenous SCTG (Sanz et al., 2009, Lorenzo et al., 2012). One study evaluated the changes in width of keratinized tissue following APF/V, APF/V plus CM and APF/V plus FGG. After 3-4 weeks, the FGG cases showed a greater increase in keratinized tissue, while the APF/V plus CM demonstrated a more physiologic and a more favorable morphology than the APF/V only cases (Lee et al., 2010). In addition, one study reported on the effects of different time-points for performing FGGs (Stimmelmayr et al., 2011). In this study no statistical significance (p=0.562) in width of keratinized tissue between FGGs performed at the time of implant placement or at the time of uncovering the implants (Stimmelmayr et al., 2011). Three studies were eligible for meta-analyses (Sanz et al., 2009, Lorenzo et al., 2012, Lee et al., 2010). The I-square value of 0% demonstrated homogeneity between the two studies (p=0.4252). The overall estimate for mean difference in width of keratinized tissue was -0.32mm (95% CI -0.67mm; 0.03mm) in favor of the control groups (control sites using autogenous tissue compared to APF/V plus CM). The resulting forest plot diagram is displayed in Figure 2.

Percent shrinkage or contraction of keratinized tissue

Two RCTs (Sanz et al., 2009, Basegmez et al., 2012) and one case series (Park, 2006) reported postoperative shrinkage or contraction of augmented tissue. All studies found shrinkage of the augmented grafts (SCTG, CM, ADMG, FGG). Only one study reported on % mean graft contraction, revealing more favorable results for the autogenous control group (SCTG; 59.7%) compared to a CM group (67.2%) at 30 days (Sanz et al., 2009).

Width of attached mucosa

One RCT study (Basegmez et al., 2012) reported on the efficacy of two techniques (APF/V+FGG or APF/V alone) for increasing the amount of keratinized tissue around the implants. Sixty-four patients with 64 implants with a minimal keratinized tissue (<1.5 mm) and signs of peri-implant mucositis were randomly assigned and treated. The result demonstrated that the width of the attached mucosa and the final gains in the FGG group were significantly greater than in the APF/V group (Basegmez et al., 2012).

Immobilized mucosa

In order to extend the immobilized mucosa, a case series (Lauer et al., 1996) reported on an APF/V procedure in combination with implant placement using transalveolar sutures to increase the stability of the lingual peri-implant soft tissue. More immobilized mucosa was obtained lingually compared to a control group of six patients with no APF/V (Lauer et al., 1996).

Surgery time

Two RCT studies reported on total surgery time spent to increase the width of keratinized tissue (Sanz et al., 2009, Lorenzo et al., 2012). Surgery time spent in both studies was less in the CM group compared to the SCTG group. These differences were statistically significantly different in both studies. The results of the two studies could be pooled, again with a fixed effects model (test for heterogeneity: I-square value=0% p-value 0.591). The resulting mean difference in surgery time (minutes) was -14.78 (95% CI -19.4842; -10.0682) in favor of the test groups (CM) compared to the control groups (autogenous tissue). The corresponding forest plot is shown in Figure 3.

Patient-reported outcomes

Two RCT studies assessed the postoperative pain (Sanz et al., 2009, Lorenzo et al., 2012). In both studies, patient morbidity was evaluated using a visual analogue scale (VAS, with a grading of 0-10) through a questionnaire whilst the perception of pain was measured based on the utilization of the intake of a postoperative analgesic. Comparable results with less morbidity in the CM groups were observed in both studies. At 10 days, patients in the SCTG group had higher mean pain scores compared to the CM group. These differences were statistically significant. In addition, the amount of anti-inflammatory medication (ibuprofen) needed by patients during postoperative was statistically significantly higher in the SCTG group compared to CM group (Sanz et al., 2009).

Augmentation of soft tissue volume

Eleven studies met the inclusion criteria as they report on soft tissue volume (Table 3 and 5). Two studies were designed as randomized control trials (RCT), three as controlled clinical trials (CCT) and the remaining six studies were case series reports. In total, 295 patients with 320 sites were treated to enhance the soft tissue volume around implants and in partially edentulous areas. The mean follow-up period was 14.5 months (range 1-108 months). In four of the studies grafting procedures were performed to augment localized alveolar ridge defects (Allen et al., 1985, Studer et al., 2000, Batista et al., 2001, Akcali et al., 2013), while in the remaining studies, soft tissue was grafted at the day of implant placement (Bianchi and Sanfilippo, 2004, Cornelini et al., 2008, Kan

et al., 2009, Wiesner et al., 2010, Simion et al., 2012) and/or during the healing period of the implant (Speroni et al., 2010, Schneider et al., 2011, Simion et al., 2012). The methods and surgical techniques used for increasing soft tissue volume included: immediate implant placement with SCTG, hydroxylapatite graft, a collagen matrix in combination with a growth factor (platelet-derived growth factor-BB=PDGF-BB), allogenic dermal matrix graft (ADMG), a SCTG (alone) and a palatal vascularized interpositional periosteal-connective tissue graft (VIPCG). No meta-analysis could be performed due to heterogeneity in the study design and treatment modalities.

Quality assessment

The quality assessment of the included studies revealed a high risk of bias for all included studies except for one RCT (Wiesner et al., 2010).

Treatment outcomes

Volume increase measured by two-dimensional methods

Four studies reported horizontal and/or vertical changes in soft tissue volume following soft tissue grafting procedures using stents and periodontal probes or endodontic instruments to measure the changes over time. In a case series, localized alveolar defects in eight patients with 18 sites were treated with ADMG. A gain in vertical ridge width of 0.61mm (SD 0.77) and in horizontal ridge width of 1.72mm (SD 0.59) was reported during the course of 6 months (Batista et al., 2001). A newly developed collagen matrix was evaluated in a prospective case series, using the matrix in combination with a growth factor (PDGF-BB) at the day of implant placement or at second stage surgery (Simion et al., 2012). The obtained gains in ridge width ranged between 0.35mm and 2.14mm with standard deviations of up to 3.27mm at 4 months depending on the level where the measurements were taken using a stent and an endodontic instrument. Since no other treatment modalities were tested, neither the effect of the collagen matrix alone nor the effect of the growth factor can be estimated (Simion et al., 2012). Three years after grafting with SCTGs at the day of implant uncovering, 14 sites in 14 patients demonstrated a mean gain of 1.4mm in mucosal thickness in a subsequent case series (Speroni et al., 2010). The only RCT reporting on soft tissue volume increase following grafting at implant placement, tested the effect of SCTGs vs. no treatment in 10 patients in a split-mouth design (Wiesner et al., 2010). Statistically significant more favorable outcomes were obtained using SCTGs (mean thickness of 3.2mm±0.42mm) compared to sites not receiving soft tissue grafting (1.9mm±0.32mm).

Volume increase measured by three-dimensional methods

Only three studies reported truly three-dimensional changes of the soft tissue volume following grafting. In the first one, the Moiré method was used to calculate the volume changes following grafting with two types of autogenous tissue grafts in localized alveolar defects (Studer et al., 2000). The study demonstrated a volume gain between 159 mm3 (SCTG; SD = 80) and 104 mm3 (FGG; SD = 31). The differences between the two treatment modalities were statistically significant in favor of the SCTG group, while untreated defects showed a slight increase in volume of 6mm3 (SD = 5.4), which was statistically significantly different compared to the two test groups using autogenous tissue (Studer et al., 2000). In a more recent RCT, SCTGs were compared to VIPCGs (interpositional connective tissue grafts) for augmentation of localized alveolar defects (Akcali et al., 2013). A more advanced technique was used to calculate the volume changes and revealed statistically significant more volume for VIPCG-treated sites (1.18mm; range 0.16mm to 1.75mm) compared to free SCTGs (0.63mm; 0.28mm-1.22mm). In a case series, SCTGs were used during the healing phase of implants in 16 sites and patients (Schneider et al., 2011). The mean increase due to grafting was 0.55mm with a standard deviation of 0.53mm after 4 weeks of healing (Schneider et al., 2011).

Shrinkage

In a case series, 21 patients with 26 localized alveolar defects were treated either with a SCTG or hydroxylapatite implants. All sites with SCTG demonstrated some shrinkage within the first 4-6 weeks, but the augmented sites remained stable for three years. In all but 2 sites (out of 12) treated with hydroxylapatite implants, no shrinkage was observed (Allen et al., 1985). The shrinkage of the horizontal ridge width amounted to 41.4% over 6 months when localized alveolar defects were augmented with ADMGs in a case series (Batista et al., 2001). This is in line with results from a RCT comparing SCTGs (shrinkage 47% after 6 months) with similar defects to VIPCG= Interpositional connective tissue grafts (shrinkage of 6.4% only) (Akcali et al., 2013).

Esthetic outcomes

The Jemt score (Jemt, 1997) was used to evaluate the esthetic outcomes in two studies (Cornelini et al., 2008, Kan et al., 2009). Both studies demonstrated favorable results for soft tissue grafting with higher papilla scores during the course of the study (2.15 years; (Kan et al., 2009) and significantly better outcomes (higher papilla scores) compared to sites without grafting for immediate implants combined with SCTGs (Cornelini et al., 2008). The same two studies also evaluated the position of the mucosal margin compared to neighboring teeth. Similar to the Jemt scores, a more favorable outcome with a higher mean facial line was observed after 2.15 years (Kan et al., 2009), while

grafted sites revealed significantly higher mucosal margin levels for grafted sites after 12 months (Cornelini et al., 2008).

Additional outcome parameters

Additional outcome measures included the amount of keratinized mucosa, the stability of the emergence profile, the patient satisfaction (all in (Bianchi and Sanfilippo, 2004) and the tissue biotype changes (Kan et al., 2009).

Discussion

The present systematic review focused on the question whether there is superiority of one method over others for soft tissue grafting around implants and in partially edentulous spaces. For keratinized tissue, nine studies were included and three of them could be compared using meta-analyses. For the augmentation of soft tissue volume, a final number of 11 studies met the inclusion criteria. Due to heterogeneity between the studies, no meta-analysis could be performed.

Increase in width of keratinized tissue

Gain of keratinized tissue

Seven studies specifically reported on various techniques and materials to augment keratinized tissue around dental implants. In all studies, the width of keratinized tissue could be successfully augmented. Due to a large heterogeneity between the studies, with some studies missing control groups and different time-points applying the soft tissue grafting (simultaneous with implant placement, during the healing phase of the implants and after the insertion of the final reconstruction), it is difficult to recommend a specific technique. The selection of the included studies also demonstrates advances and trends in clinical research. In older studies, either an APF/V alone or in combination with autogenous tissue harvested from the patient's palate was the treatment of choice (Lauer et al., 1996, ten Bruggenkate et al., 1991). The main disadvantage of using autogenous tissue results from the morbidity associated with the harvesting procedure and the subsequent healing. Research has therefore focused on alternative materials and techniques. In one of the studies, a human-derived ADMG was applied (Park, 2006). This material has been documented extensively in dentistry in various fields, such as for gain of keratinized tissue around teeth, for recession coverage, for gain of keratinized mucosa around dental implants and for volume increase (Wei et al., 2000, Aichelmann-Reidy et al., 2001, Batista et al., 2001, Carney et al., 2012). The advantage of using alternative materials is documented with less patient morbidity compared to autogenous tissue for gain of keratinized gingiva (Griffin et al., 2006). Around dental implants, the combination of an APF/V and ADMG was successful to augment keratinized tissue (Park, 2006). However, due to the lack of a control group, any comparison to the gold standard (autogenous tissue) is missing. No further included studies were using this material. In contrast, a number of human studies used ADMG for gain of keratinized tissue. High shrinkage rates were reported during healing around teeth (Wei et al., 2000) and the tissue, histologically resembled scar tissue (Wei et al., 2002). More recently, collagen matrices were developed and extensively evaluated in preclinical and clinical studies (Rocchietta et al., 2012, Jung et al., 2011, Thoma et al., 2012a, Vignoletti et al., 2011, Jung et al., 2013, Jepsen et al., 2013). Three of the included studies reported on the use of two types of collagen matrices (Sanz et al., 2009, Lee et al., 2010, Lorenzo et al.,

2012). In all three studies, autogenous tissue served as a control group. The increase in width of keratinized tissue with a range of 1.8mm to 2.3mm indicates a successful use of both CM types. Still, the meta-analysis revealed inferiority of the collagen matrices in all three studies compared to control groups with autogenous tissue. Clinically, the WMD of -0.32mm only may be negligible. This may even more serve as part of the discussion, since alternative devices (e.g. CM) can significantly reduce patient morbidity, reduce the overall treatment time and slightly improve esthetics compared to control groups (Griffin et al., 2006, Sanz et al., 2009, Lorenzo et al., 2012, Thoma et al., 2012a). In one study, the width of keratinized mucosa was reported as gain in width of attached mucosa (Basegmez et al., 2012). While at teeth, the keratinized tissue (i.e. the gingiva) consist of two parts, the attached gingiva and the free gingiva, at implant sites, no such terms exist. The dimension of the keratinized tissue appears to be similar at teeth and implant sites, but a clear soft tissue attachment to implants has yet to be reported (Berglundh and Lindhe, 1996). It may therefore be speculated that the reported attached mucosa represents the keratinized mucosa found in other studies.

Percent shrinkage and contraction of keratinized tissue

The changes in width over time following the initial augmentation procedure is of great importance and serves as a reliable mean to estimate the predictability of the applied technique. Therefore, the overall contraction or shrinkage over time needs to be evaluated. Three studies reported on these outcomes and revealed that independently of the applied surgical technique or material used to augment, a certain loss of the initially augmented width has to be accepted. This ranged quite extensively in the present systematic review, with one study reporting only 2% of shrinkage over 12 months (Basegmez et al., 2012), while the remaining two studies reported shrinkage rates higher than 50% at one or six months (Park, 2006, Sanz et al., 2009). The variability may be due to the use of different techniques (vestibuloplasty according to Edlan & Mejchar, APF/V), different observation time-points (1, 6 and 12 months), differences in graft materials (CM, FGG, SCTG) and different indications (inadequate width of keratinized mucosa, inadequate width of attached mucosa, peri-implant mucositis). Other influences such as the thickness of the graft, which appears to be important when augmenting keratinized tissue around teeth (Mormann et al., 1981) and the lack of a prevascularization (for CM compared to autogenous tissue) could not be evaluated due to a low number of include studies reporting these outcomes.

Surgery time

As reported above, the gain in width of keratinized mucosa is not the only outcome parameter that may favor one over the other technique. In two RCTs, the overall treatment time was calculated and clearly demonstrated that by avoiding the use of

autogenous tissue and the associated harvesting procedure, the surgery time can be significantly reduced (Sanz et al., 2009, Lorenzo et al., 2012). The meta-analysis revealed a mean difference of roughly 15 minutes in favor of the CM groups. This has to be considered as a major advantage for the use of alternative devices and may be directly correlated with the postoperative healing and the patient morbidity.

Patient-reported outcomes

The postoperative complications of soft tissue grafting procedure include bleeding, swelling as major contributors (Wessel and Tatakis, 2008, Dordick et al., 1976b, Dordick et al., 1976a, Griffin et al., 2006, Farnoush, 1978, Del Pizzo et al., 2002). Several studies evaluated the patient morbidity following gingival augmentation. The data are not conclusive, but predominantly demonstrate less morbidity associated with soft tissue substitutes compared to autogenous tissue (McGuire et al., 2008, Griffin et al., 2006, McGuire and Nunn, 2005). Only two included studies provided data of postoperative pain in the present review. The information derived from the two RCTs clearly demonstrates superiority with less morbidity for soft tissue substitutes compared to autogenous tissue (Sanz et al., 2009, Lorenzo et al., 2012). Data were provided by questionnaires and the intake of pain killer medication in the follow-up. Since both studies were not designed as split-mouth studies, the data are conclusive and more relevant than data obtained in previous studies. In older studies, split-mouth designs appeared to confuse patients, making it difficult to differentiate between two sites (McGuire and Nunn, 2005, McGuire et al., 2008). Therefore, in a previous systematic review on soft tissue grafting procedures, no benefit was shown for soft tissue substitutes (Thoma et al., 2009). The outcomes on patient morbidity are of major relevance and might help to thrive the choice for a grafting material towards soft tissue substitutes in the future.

Augmentation of soft tissue volume

Compared to a previous systematic review (Thoma et al., 2009), the number of included studies increased with 11 studies finally meeting the inclusion criteria. The difference is due to broader inclusion criteria (implant sites, partially edentulous sites), a number of very recent studies applying new materials and techniques (growth factors, soft tissue substitutes) and the development of new techniques to assess soft tissue volume changes (non-invasive three-dimensional analyses). Still, due to heterogeneity between the studies, no meta-analysis could be performed.

Volume increase measured by two-dimensional methods

Four studies reported two-dimensional changes of soft tissue volume applying autogenous tissue (SCTG) and soft tissue substitutes (CM, ADMG) (Batista et al., 2001, Simion et al., 2012, Speroni et al., 2010, Wiesner et al., 2010). The measurements were

performed using endodontic instruments or periodontal probes, mostly with the aid of a standardized stent. The outcomes provided variability with respect to the increase in soft tissue thickness over time with a range of 0.35mm to 3.2mm depending on the location (buccal at different levels, occlusal) and the follow-up time-point (4 months to 3 years). In all studies, a volume increase was obtained independent of the technique and material, but it was also demonstrated that some shrinkage might occur over time. Similar to studies for gain of keratinized tissue, autogenous tissue appears to be the gold standard as it was used most often, but new soft tissue substitutes are being evaluated. Research has strongly focused on the development and testing of alternative devices with collagen matrices being the most promising ones (Thoma et al., 2013). Unlike for gain of keratinized tissue where preclinical and clinical data are published (Jung et al., 2011, Sanz et al., 2009, Lorenzo et al., 2012), collagen matrices for gain of soft tissue volume are scare and mostly documented in vitro and in preclinical studies (Mathes et al., 2010, Thoma et al., 2010, Thoma et al., 2011, Thoma et al., 2012b). Only one clinical study used a collagen matrix (Simion et al., 2012), which was originally designed to serve as a matrix for gain of keratinized tissue and showed only a minimal increase in thickness based on preclinical data (Jung et al., 2011). Therefore, this matrix was combined with a growth factor to enhance the vascularization and the connective tissue formation (Simion et al., 2012). The outcomes of the study demonstrated a short-term increase in soft tissue volume at all levels. Some more data at just one buccal level over 3.5 years, however, revealed that the obtained soft tissue thickness decreased by more than 50% to roughly 0.9mm (Simion et al., 2012). This demonstrates that a soft tissue substitute for soft tissue volume increase may have additional requirements for long-term stability and a successful outcome. In order to overcome these issues and to meet the demands and requirements for soft tissue substitutes, a new modified collagen matrix with cross-linking has been tested over the course of the past years. In vitro and preclinical data are favorable and a direct comparison with the gold standard, the autogenous graft, demonstrated non-inferiority in a canine model (Mathes et al., 2010, Thoma et al., 2010, Thoma et al., 2011, Thoma et al., 2012b). Clinical data however are still lacking.

Volume increase measured by three-dimensional methods

Recent development not only focused on new devices but also on the evaluation of non-invasive methods to assess volumetric changes (Windisch et al., 2007, Fickl et al., 2009, Strebel et al., 2009). Three studies used casts to evaluate the soft tissue volume over time. In all three studies, autogenous tissue was used for volume increase, in two studies for partially edentulous sites (Studer et al., 2000, Akcali et al., 2013), in one for volume increase at implant sites (Schneider et al., 2011). Again, due to heterogeneity, the outcomes could not be compared, but data provide clinically more relevant data since the measurements capture the entire augmented area. The mean augmented thickness

ranged between 0.55mm and 1.18mm, while the remaining study provided an increase of 104mm3 to 159mm3 (Studer et al., 2000). The outcomes at partially edentulous sites are difficult to put into context unless esthetic, functional and/or long-term data are provided. At implant sites, a soft tissue thickness of 2mm appears to be the threshold thickness at the buccal aspect for more esthetic outcomes (Jung et al., 2007, Jung et al., 2008, van Brakel et al., 2011). Unfortunately, the entire soft tissue thickness and suitable esthetic outcome parameters were not provided by the included study (Schneider et al., 2011). Conclusions on whether or not the treatment was successful are difficult to draw.

Shrinkage

Similar to keratinized tissue, the overall shrinkage rate provides data on the reliability of the applied technique and material. Autogenous tissue was reported to shrink by more than 40% in two studies, while a pedicle flap (VIPCG) appears to be more reliable resulting in less shrinkage over time (6.4% at 6 months) (Akcali et al., 2013). Data on soft tissue substitutes were not reported in the included studies.

Esthetic outcomes

There is a huge variety of esthetic factors reported in the literature (Benic et al., 2012). For maximal esthetics, the soft tissue thickness at the buccal aspect of the implant sites and the height of the papillae appears to be the key factors (Thoma et al., 2013). The Jemt score (Jemt, 1997) is considered an easily applicable method to assess the esthetic outcome in the papilla area and provides relevant clinical information on the esthetic outcome at implant sites. Two included studies demonstrated that the use of autogenous tissue combined with immediate placement results in favorable clinical esthetics at one and 2.15 years (Kan et al., 2009, Cornelini et al., 2008). Since one of the studies was designed as a CCT, data on non-grafted sites are included. The outcomes clearly demonstrate that necessity and the superiority of grafted sites resulting in better esthetics over the course of one year (Cornelini et al., 2008).

Conclusion

The present systematic review revealed that for gain of keratinized mucosa at implant sites, various methods and various materials could be used successfully. All applied techniques were based on an APF/V in combination with autogenous tissue (SCTG/FGG) or a soft tissue substitute (ADMG/CM) and rendered a gain in keratinized tissue for an observation period of up to 48 months. In contrast to gingival augmentation, only one study reported on APF/V alone, which might indicate that most studies were commercially funded. However, some shrinkage may occur with all applied grafting materials and may result in a decrease in width of keratinized tissue of more than 50% within a couple of months. For soft tissue volume augmentation, autogenous tissue (SCTG) has to be considered as treatment of choice resulting in an increase in soft tissue thickness at implant sites and in partially edentulous sites. Soft tissue substitute lack clinical data and can currently not be recommended. Again, some shrinkage of the augmented sites has to be considered. From an esthetic point of view, soft tissue volume grafting concomitant with immediate implant placement may result in superior outcomes with respect to papilla height and the level of the marginal mucosa compared to natural teeth and control groups.

Future direction of research

The present systematic identified a relatively low number of studies to be included for gain of keratinized tissue around dental implants and for gain of soft tissue volume around dental implants and in partially edentulous sites. Moreover, there was a lack of randomized controlled clinical trials (RCTs), specifically for gain of soft tissue volume. For gain of keratinized tissue, some RCTs were available, but appeared to be fully sponsored by companies, thereby including a greater risk of bias. In order to provide the clinicians with data on optimal techniques and materials, more self-funded studies or studies funded by independent organizations and foundations are needed. Such RCTs would have a great impact for the benefit of patients and clinicians.

Figure legends

Figure 1: Search strategy

Figure 2:
Meta-analyses for gain in width of keratinized tissue. Mean difference (mm) for test minus control. APF = apically positioned flap; SCTG = subepithelial connective tissue graft; FGG = free gingival graft; CM=Collagen matrix; I squared (percentage variation attributable to heterogeneity) = 0%, P =0.4254; CI = confidence interval)

Figure 3:
Meta-analyses for surgery time. Mean difference shorter surgery time (min) for test minus control. APF = apically positioned flap; SCTG = subepithelial connective tissue graft; CM=Collagen matrix; I squared (percentage variation attributable to heterogeneity) = 0%, P =0.591; CI = confidence interval)

References

Adibrad, M., Shahabuei, M. & Sahabi, M. (2009) Significance of the width of keratinized mucosa on the health status of the supporting tissue around implants supporting overdentures. *Journal of Oral Implantology* **35,** 232-237.

Aichelmann-Reidy, M. E., Yukna, R. A., Evans, G. H., Nasr, H. F. & Mayer, E. T. (2001) Clinical evaluation of acellular allograft dermis for the treatment of human gingival recession. *Journal of Periodontology* **72,** 998-1005.

Akcali, A., Schneider, D., Ünlü, F., Bicakci, N., Köse, T. & Hämmerle, C. H. F. (2013) Soft tissue augmentation of ridge defects using two different methods: a randomized controlled clinical trial.

Allen, E. P., Gainza, C. S., Farthing, G. G. & Newbold, D. A. (1985) Improved technique for localized ridge augmentation. A report of 21 cases. *Journal of Periodontology* **56,** 195-199.

Alpert, A. (1994) A rationale for attached gingiva at the soft-tissue/implant interface: esthetic and functional dictates. *Compendium* **15,** 356, 358, 360-352 passim; quiz 368.

Basegmez, C., Ersanli, S., Demirel, K., Bolukbasi, N. & Yalcin, S. (2012) The comparison of two techniques to increase the amount of peri-implant attached mucosa: free gingival grafts versus vestibuloplasty. One-year results from a randomised controlled trial. *European Journal of Oral Implantology* **5,** 139-145.

Batista, E. L., Jr., Batista, F. C. & Novaes, A. B., Jr. (2001) Management of soft tissue ridge deformities with acellular dermal matrix. Clinical approach and outcome after 6 months of treatment. *Journal of Periodontology* **72,** 265-273.

Becker, W. (2001) Esthetic soft-tissue augmentation adjacent to dental implants. *Compendium of Continuing Education in Dentistry* **22,** 250-252, 254, 256 passim.

Bengazi, F., Wennstrom, J. L. & Lekholm, U. (1996) Recession of the soft tissue margin at oral implants. A 2-year longitudinal prospective study. *Clinical Oral Implants Research* **7,** 303-310.

Benic, G. I., Wolleb, K., Sancho-Puchades, M. & Hammerle, C. H. (2012) Systematic review of parameters and methods for the professional assessment of aesthetics in dental implant research. *Journal of Clinical Periodontology* **39 Suppl 12,** 160-192.

Berglundh, T. & Lindhe, J. (1996) Dimension of the periimplant mucosa. Biological width revisited. *Journal of Clinical Periodontology* **23,** 971-973.

Bianchi, A. E. & Sanfilippo, F. (2004) Single-tooth replacement by immediate implant and connective tissue graft: a 1-9-year clinical evaluation. *Clinical Oral Implants Research* **15,** 269-277.

Bidra, A. S. & Rungruanganunt, P. (2011) Omega-shaped (Omega) incision design to enhance gingival esthetics for adjacent implant placement in the anterior region. *Journal of Oral and Maxillofacial Surgery* **69,** 2144-2151.

Bouri, A., Jr., Bissada, N., Al-Zahrani, M. S., Faddoul, F. & Nouneh, I. (2008) Width of keratinized gingiva and the health status of the supporting tissues around dental implants. *International Journal of Oral and Maxillofacial Implants* **23,** 323-326.

Breault, L. G., Lee, S. Y. & Mitchell, N. E. (2004) Fixed prosthetics with a connective tissue and alloplastic bone graft ridge augmentation: a case report. *J Contemp Dent Pract* **5,** 111-121.

Bruschi, G. B., Crespi, R., Cappare, P. & Gherlone, E. (2012) Clinical Study of Flap Design to Increase the Keratinized Gingiva around Implants. 4-Year Follow-Up. *Journal of Oral Implantology*.

Cairo, F., Pagliaro, U. & Nieri, M. (2008) Soft tissue management at implant sites. *Journal of Clinical Periodontology* **35,** 163-167.

Carney, C. M., Rossmann, J. A., Kerns, D. G., Cipher, D. J., Rees, T. D., Solomon, E. S., Rivera-Hidalgo, F. & Beach, M. M. (2012) A comparative study of root defect coverage using an acellular dermal matrix with and without a recombinant human platelet-derived growth factor. *Journal of Periodontology* **83,** 893-901.

Cho, J. Y. (1998) The periodontist and the edentulous area--localised ridge augmentation. *International Dental Journal* **48,** 326-329.

Chung, D. M., Oh, T. J., Shotwell, J. L., Misch, C. E. & Wang, H. L. (2006) Significance of keratinized mucosa in maintenance of dental implants with different surfaces. *Journal of Periodontology* **77,** 1410-1420.

Collins, T. A. & Nunn, W. (1994) Autogenous veneer grafting for improved esthetics with dental implants. *Compendium* **15,** 370, 372-374, 376.

Cornelini, R., Barone, A. & Covani, U. (2008) Connective tissue grafts in postextraction implants with immediate restoration: a prospective controlled clinical study. *Pract Proced Aesthet Dent* **20,** 337-343.

Del Pizzo, M., Modica, F., Bethaz, N., Priotto, P. & Romagnoli, R. (2002) The connective tissue graft: a comparative clinical evaluation of wound healing at the palatal donor site. A preliminary study. *Journal of Clinical Periodontology* **29,** 848-854.

Dordick, B., Coslet, J. G. & Seibert, J. S. (1976a) Clinical evaluation of free autogenous gengival grafts placed on alveolar bone. Part I. Clinical predictability. *Journal of Periodontology* **47,** 559-567.

Dordick, B., Coslet, J. G. & Seibert, J. S. (1976b) Clinical evaluation of free autogenous gingival grafts placed on alveolar bone. Part II. Coverage of nonpathologic dehiscences and fenestrations. *Journal of Periodontology* **47,** 568-573.

Fagan, M. C., Owens, H., Smaha, J. & Kao, R. T. (2008) Simultaneous hard and soft tissue augmentation for implants in the esthetic zone: report of 37 consecutive cases. *Journal of Periodontology* **79,** 1782-1788.

Farnoush, A. (1978) Techniques for the protection and coverage of the donor sites in free soft tissue grafts. *Journal of Periodontology* **49,** 403-405.

Fickl, S., Schneider, D., Zuhr, O., Hinze, M., Ender, A., Jung, R. E. & Hurzeler, M. B. (2009) Dimensional changes of the ridge contour after socket preservation and buccal overbuilding: an animal study. *Journal of Clinical Periodontology* **36,** 442-448.

Griffin, T. J., Cheung, W. S., Zavras, A. I. & Damoulis, P. D. (2006) Postoperative complications following gingival augmentation procedures. *Journal of Periodontology* **77,** 2070-2079.

Grunder, U. (2000) Stability of the mucosal topography around single-tooth implants and adjacent teeth: 1-year results. *International Journal of Periodontics and Restorative Dentistry* **20,** 11-17.

Higgins, J. & Green, S. (2011) Higgins JPT, Altmann DG (editors) Chapter 8: Assessing risk of bias in included studies. *Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.1 [updated September 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.*

Hoelscher, D. C. & Simons, A. M. (1994) The rationale for soft-tissue grafting and vestibuloplasty in association with endosseous implants: a literature review. *Journal of Oral Implantology* **20,** 282-291.

Jemt, T. (1997) Regeneration of gingival papillae after single-implant treatment. *International Journal of Periodontics and Restorative Dentistry* **17,** 326-333.

Jepsen, K., Jepsen, S., Zucchelli, G., Stefanini, M., de Sanctis, M., Baldini, N., Greven, B., Heinz, B., Wennstrom, J., Cassel, B., Vignoletti, F. & Sanz, M. (2013) Treatment of gingival recession defects with a coronally advanced flap and a xenogeneic collagen matrix: a multicenter randomized clinical trial. *Journal of Clinical Periodontology* **40,** 82-89.

Jung, R. E., Holderegger, C., Sailer, I., Khraisat, A., Suter, A. & Hammerle, C. H. (2008) The effect of all-ceramic and porcelain-fused-to-metal restorations on marginal peri-implant soft tissue color: a randomized controlled clinical trial. *International Journal of Periodontics and Restorative Dentistry* **28,** 357-365.

Jung, R. E., Hurzeler, M. B., Thoma, D. S., Khraisat, A. & Hammerle, C. H. (2011) Local tolerance and efficiency of two prototype collagen matrices to increase the width of keratinized tissue. *Journal of Clinical Periodontology* **38,** 173-179.

Jung, R. E., Philipp, A., Annen, B. M., Signorelli, L., Thoma, D. S., Hammerle, C. H., Attin, T. & Schmidlin, P. (2013) Radiographic evaluation of different techniques for ridge preservation after tooth extraction: a randomized controlled clinical trial. *Journal of Clinical Periodontology* **40,** 90-98.

Jung, R. E., Sailer, I., Hammerle, C. H., Attin, T. & Schmidlin, P. (2007) In vitro color changes of soft tissues caused by restorative materials. *International Journal of Periodontics and Restorative Dentistry* **27,** 251-257.

Kan, J. Y., Rungcharassaeng, K., Morimoto, T. & Lozada, J. (2009) Facial gingival tissue stability after connective tissue graft with single immediate tooth replacement in the esthetic zone: consecutive case report. *Journal of Oral and Maxillofacial Surgery* **67,** 40-48.

Kim, B. S., Kim, Y. K., Yun, P. Y., Yi, Y. J., Lee, H. J., Kim, S. G. & Son, J. S. (2009) Evaluation of peri-implant tissue response according to the presence of keratinized mucosa. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics* **107,** e24-28.

Kwakman, J. M., Voorsmit, R. A. & Freihofer, H. P. (1998) Treatment of the edentulous mandible with a vestibuloplasty combined with Intramobil Zylinder implants: a 5-year follow-up. *British Journal of Oral and Maxillofacial Surgery* **36,** 296-300.

Lang, N. P. & Loe, H. (1972) The relationship between the width of keratinized gingiva and gingival health. *Journal of Periodontology* **43,** 623-627.

Lauer, G., Schwarz, U. & Schilli, W. (1996) Transalveolar fixation of the peri-implant soft tissue in the mandible: surgical method and clinical follow-up. *Journal of Oral and Maxillofacial Surgery* **54,** 690-697.

Lee, K. H., Kim, B. O. & Jang, H. S. (2010) Clinical evaluation of a collagen matrix to enhance the width of keratinized gingiva around dental implants. *J Periodontal Implant Sci* **40,** 96-101.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gotzsche, P. C., Ioannidis, J. P., Clarke, M., Devereaux, P. J., Kleijnen, J. & Moher, D. (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Annals of Internal Medicine* **151,** W65-94.

Liu, C. L. & Weisgold, A. S. (2002) Connective tissue graft: a classification for incision design from the palatal site and clinical case reports. *International Journal of Periodontics and Restorative Dentistry* **22,** 373-379.

Lorenzo, R., Garcia, V., Orsini, M., Martin, C. & Sanz, M. (2012) Clinical efficacy of a xenogeneic collagen matrix in augmenting keratinized mucosa around implants: a randomized controlled prospective clinical trial. *Clinical Oral Implants Research* **23,** 316-324.

Marquez, I. C. (2004) The role of keratinized tissue and attached gingiva in maintaining periodontal/peri-implant health. *General Dentistry* **52,** 74-78; quiz 79.

Mathes, S. H., Wohlwend, L., Uebersax, L., von Mentlen, R., Thoma, D. S., Jung, R. E., Gorlach, C. & Graf-Hausner, U. (2010) A bioreactor test system to mimic the biological and mechanical environment of oral soft tissues and to evaluate substitutes for connective tissue grafts. *Biotechnology and Bioengineering* **107,** 1029-1039.

McGuire, M. K. & Nunn, M. E. (2005) Evaluation of the safety and efficacy of periodontal applications of a living tissue-engineered human fibroblast-derived dermal substitute. I. Comparison to the gingival autograft: a randomized controlled pilot study. *Journal of Periodontology* **76,** 867-880.

McGuire, M. K., Scheyer, E. T., Nunn, M. E. & Lavin, P. T. (2008) A pilot study to evaluate a tissue-engineered bilayered cell therapy as an alternative to tissue from the palate. *Journal of Periodontology* **79,** 1847-1856.

Mehta, P. & Lim, L. P. (2010) The width of the attached gingiva--much ado about nothing? *Journal of Dentistry* **38,** 517-525.

Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Journal of Clinical Epidemiology* **62,** 1006-1012.

Mormann, W., Schaer, F. & Firestone, A. R. (1981) The relationship between success of free gingival grafts and transplant thickness. Revascularization and shrinkage--a one year clinical study. *Journal of Periodontology* **52,** 74-80.

Palacci, P. & Nowzari, H. (2008) Soft tissue enhancement around dental implants. *Periodontology 2000* **47,** 113-132.

Park, J. B. (2006) Increasing the width of keratinized mucosa around endosseous implant using acellular dermal matrix allograft. *Implant Dentistry* **15,** 275-281.

Pini-Prato, G. P., Cairo, F., Tinti, C., Cortellini, P., Muzzi, L. & Mancini, E. A. (2004) Prevention of alveolar ridge deformities and reconstruction of lost anatomy: a review of surgical approaches. *International Journal of Periodontics and Restorative Dentistry* **24,** 434-445.

Rocchietta, I., Schupbach, P., Ghezzi, C., Maschera, E. & Simion, M. (2012) Soft tissue integration of a porcine collagen membrane: an experimental study in pigs. *International Journal of Periodontics and Restorative Dentistry* **32,** e34-40.

Roos-Jansaker, A. M., Renvert, H., Lindahl, C. & Renvert, S. (2006) Nine- to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. *Journal of Clinical Periodontology* **33,** 296-301.

Sanz, M., Lorenzo, R., Aranda, J. J., Martin, C. & Orsini, M. (2009) 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* **36,** 868-876.

Schneider, D., Grunder, U., Ender, A., Hammerle, C. H. & Jung, R. E. (2011) Volume gain and stability of peri-implant tissue following bone and soft tissue augmentation: 1-year results from a prospective cohort study. *Clinical Oral Implants Research* **22,** 28-37.

Schrott, A. R., Jimenez, M., Hwang, J. W., Fiorellini, J. & Weber, H. P. (2009) Five-year evaluation of the influence of keratinized mucosa on peri-implant soft-tissue health

and stability around implants supporting full-arch mandibular fixed prostheses. *Clinical Oral Implants Research* **20,** 1170-1177.

Seibert, J. S. (1983a) Reconstruction of deformed, partially edentulous ridges, using full thickness onlay grafts. Part I. Technique and wound healing. *Compendium of Continuing Education in Dentistry* **4,** 437-453.

Seibert, J. S. (1983b) Reconstruction of deformed, partially edentulous ridges, using full thickness onlay grafts. Part II. Prosthetic/periodontal interrelationships. *Compendium of Continuing Education in Dentistry* **4,** 549-562.

Simion, M., Rocchietta, I., Fontana, F. & Dellavia, C. (2012) 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. *International Journal of Periodontics and Restorative Dentistry* **32,** 273-282.

Speroni, S., Cicciu, M., Maridati, P., Grossi, G. B. & Maiorana, C. (2010) Clinical investigation of mucosal thickness stability after soft tissue grafting around implants: a 3-year retrospective study. *Indian Journal of Dental Research* **21,** 474-479.

Stimmelmayr, M., Stangl, M., Edelhoff, D. & Beuer, F. (2011) Clinical prospective study of a modified technique to extend the keratinized gingiva around implants in combination with ridge augmentation: one-year results. *International Journal of Oral and Maxillofacial Implants* **26,** 1094-1101.

Strebel, J., Ender, A., Paque, F., Krahenmann, M., Attin, T. & Schmidlin, P. R. (2009) In vivo validation of a three-dimensional optical method to document volumetric soft tissue changes of the interdental papilla. *Journal of Periodontology* **80,** 56-61.

Studer, S. P., Lehner, C., Bucher, A. & Scharer, P. (2000) Soft tissue correction of a single-tooth pontic space: a comparative quantitative volume assessment. *Journal of Prosthetic Dentistry* **83,** 402-411.

ten Bruggenkate, C. M., Krekeler, G., van der Kwast, W. A. & Oosterbeek, H. S. (1991) Palatal mucosa grafts for oral implant devices. *Oral Surgery, Oral Medicine, Oral Pathology* **72,** 154-158.

Thoma, D. S., Benic, G. I., Zwahlen, M., Hammerle, C. H. & Jung, R. E. (2009) A systematic review assessing soft tissue augmentation techniques. *Clinical Oral Implants Research* **20 Suppl 4,** 146-165.

Thoma, D. S., Hammerle, C. H., Cochran, D. L., Jones, A. A., Gorlach, C., Uebersax, L., Mathes, S., Graf-Hausner, U. & Jung, R. E. (2011) Soft tissue volume augmentation by the use of collagen-based matrices in the dog mandible -- a histological analysis. *Journal of Clinical Periodontology* **38,** 1063-1070.

Thoma, D. S., Jung, R. E., Schneider, D., Cochran, D. L., Ender, A., Jones, A. A., Gorlach, C., Uebersax, L., Graf-Hausner, U. & Hammerle, C. H. (2010) Soft tissue volume augmentation by the use of collagen-based matrices: a volumetric analysis. *Journal of Clinical Periodontology* **37,** 659-666.

Thoma, D. S., Mühlemann, S. & Jung, R. E. (2013) Critical soft tissue dimensions along dental implants and treatment concepts. *Periodontology 2000* **in press**.

Thoma, D. S., Sancho-Puchades, M., Ettlin, D. A., Hammerle, C. H. & Jung, R. E. (2012a) Impact of a collagen matrix on early healing, aesthetics and patient morbidity in oral mucosal wounds - a randomized study in humans. *Journal of Clinical Periodontology* **39,** 157-165.

Thoma, D. S., Villar, C. C., Cochran, D. L., Hammerle, C. H. & Jung, R. E. (2012b) Tissue integration of collagen-based matrices: an experimental study in mice. *Clinical Oral Implants Research* **23,** 1333-1339.

van Brakel, R., Noordmans, H. J., Frenken, J., de Roode, R., de Wit, G. C. & Cune, M. S. (2011) The effect of zirconia and titanium implant abutments on light reflection of the supporting soft tissues. *Clinical Oral Implants Research* **22,** 1172-1178.

Vignoletti, F., Nunez, J., Discepoli, N., De Sanctis, F., Caffesse, R., Munoz, F., Lopez, M. & Sanz, M. (2011) Clinical and histological healing of a new collagen matrix in combination with the coronally advanced flap for the treatment of Miller class-I recession defects: an experimental study in the minipig. *Journal of Clinical Periodontology* **38,** 847-855.

Wei, P. C., Laurell, L., Geivelis, M., Lingen, M. W. & Maddalozzo, D. (2000) Acellular dermal matrix allografts to achieve increased attached gingiva. Part 1. A clinical study. *Journal of Periodontology* **71,** 1297-1305.

Wei, P. C., Laurell, L., Lingen, M. W. & Geivelis, M. (2002) Acellular dermal matrix allografts to achieve increased attached gingiva. Part 2. A histological comparative study. *Journal of Periodontology* **73,** 257-265.

Wennstrom, J. L., Bengazi, F. & Lekholm, U. (1994) The influence of the masticatory mucosa on the peri-implant soft tissue condition. *Clinical Oral Implants Research* **5,** 1-8.

Wennstrom, J. L. & Derks, J. (2012) Is there a need for keratinized mucosa around implants to maintain health and tissue stability? *Clinical Oral Implants Research* **23 Suppl 6,** 136-146.

Wessel, J. R. & Tatakis, D. N. (2008) Patient outcomes following subepithelial connective tissue graft and free gingival graft procedures. *Journal of Periodontology* **79,** 425-430.

Wiesner, G., Esposito, M., Worthington, H. & Schlee, M. (2010) Connective tissue grafts for thickening peri-implant tissues at implant placement. One-year results from an explanatory split-mouth randomised controlled clinical trial. *European Journal of Oral Implantology* **3,** 27-35.

Windisch, S. I., Jung, R. E., Sailer, I., Studer, S. P., Ender, A. & Hammerle, C. H. (2007) A new optical method to evaluate three-dimensional volume changes of alveolar contours: a methodological in vitro study. *Clinical Oral Implants Research* **18,** 545-551.

Table 1. Excluded studies with reason for exclusion

author	**reason for exclusion**
(Alpert, 1994)	only descriptive, no data
(Becker, 2001)	hard tissue only
(Bidra and Rungruanganunt, 2011)	2 cases only
(Collins and Nunn, 1994)	hard tissue augmentation only
(Fagan et al., 2008)	no data, immediate implant placement and soft tissue augmentation at the same time
(Kwakman et al., 1998)	no detailed information about procedures
(Liu and Weisgold, 2002)	no data, only classifications

Table 2. Included studies: augmentation of keratinized mucosa

Author	Year of publication	Study design	Indication for treatment	Test treatment	Control 1 treatment	control 2 treatment	Follow-up period (months)
(ten Bruggenkate et al., 1991)	1991	Case series	Inadequate width of keratinized mucosa <2 mm	APF/V plus FGG	NA	NA	6-32
(Lauer et al., 1996)	1996	Case series	Inadequate width of attached gingiva	APF/V in combination with implant placement	No treatment	NA	18
(Park, 2006)	2006	Case series	Inadequate width of attached gingival ≤ 2 mm	APF/V plus ADMG	NA	NA	6
(Sanz et al., 2009)	2009	RCT	Inadequate width of keratinized mucosa <2 mm	APF/V plus CM (Mucograft)	APF/V plus SCTG	NA	6
(Lee et al., 2010)	2010	CCT	If keratinized mucosa > 3 mm ; APF/V 2-3 mm ; APF/V plus CM minimal ; APF/V plus FGG	APF/V plus CM (Collatape)	APF/V	APF/V plus FGG	6
(Lorenzo et al., 2012)	2012	RCT	Inadequate width of keratinized mucosa <1 mm	APF/V plus CM (Mucograft)	APF/V plus CTG	NA	6
(Stimmelmayr et al., 2011)	2011	CCT	Inadequate width of keratinized tissue, from buccal to lingual had to be 3.5 mm or more	Single stage implant placement and ridge augmentation with later FGG	Two stage ridge augmentation and later implant placement and FGG	NA	12
(Basegmez et al., 2012)	2012	RCT	Inadequate width of attached mucosa <1.5 mm, perimplant mucositis	APF/V plus FGG	vestibuloplasty according to Edlan & Mejchar)	NA	12
(Bruschi et al., 2012)	2012	Case series	Inadequate width of attached gingiva	APF/V in combination with implant placement	NA	NA	48

(CCT = controlled clinical trial; RCT = randomized controlled clinical trial; APF/V = apically positioned flap/vestibuloplasty procedure; SCTG = subepithelial connective tissue graft;
FGG = free gingival graft; ADMG = acellular dermal matrix graft; CM=collagen matrix)

Table 3. Included studies: augmentation of soft tissue volume

Author	Year of publication	Study design	Indication for treatment	Test treatment	Control 1 treatment	control 2 treatment	Follow-up period (months)
(Allen et al., 1985)	1985	Case series	Localized alveolar ridge defect	SCTG	Hydroxylapatite	NA	36 for SCTG and 18 for HA
(Studer et al., 2000)	2000	RCT	Localized alveolar ridge defect	SCTG	FGG	No treatment	3.5
(Batista et al., 2001)	2001	Case series	Localized alveolar ridge defect	ADMG	NA	NA	6
(Bianchi and Sanfilippo, 2004)	2004	CCT	Immediate implant placement	Immediate implant +SCTG	Immediate implant	NA	12-108
(Cornelini et al., 2008)	2008	CCT	Extraction socket and immediate implant placement	Immediate implant +SCTG	Immediate implant	NA	12
(Kan et al., 2009)	2009	Case series	Immediate implant placement	Immediate implant +SCTG	NA	NA	25.8
(Wiesner et al., 2010)	2010	RCT	At implant placement	SCTG at implant placement	No SCTG	NA	12
(Speroni et al., 2010)	2010	retrospective case series	At second stage surgery	SCTG at 2nd stage surgery	NA	NA	36
(Schneider et al., 2011)	2011	Case series	During healing period of implant placement	SCTG at healing period of implant	NA	NA	4

(Simion et al., 2012)	2012	Case series	Localized ridge augmentation at implant placement or after implant placement	CM+PDGF-BB	NA	NA	4
(Akcali et al., 2013)	2013	RCT	Localized alveolar defect	Interpositional connective tissue graft (VIPCG)	SCTG	NA	6

CCT = controlled clinical trial; RCT = randomized controlled clinical trial; SCTG = subepithelial connective tissue graft; FGG = free gingival graft; ADMG = acellular dermal matrix graft; CM=Collagen matrix; PDGF = platelet derived growth factor; VIPCG= Interpositional connective tissue graft.

Table 4. Characteristics of included studies: width of keratinized mucosa

author	year of publication	study design	total number of patients	total number of sites	number of patients test	number of sites test	number of patients control 1	number of sites contol 1	number of patients control 2	number of sites control2	follow-up period (months)	test treatment	control 1 treatment	control 2 treatment
(ten Bruggenkate et al., 1991)	1991	Case series	30			30		30			6-32	APF/V plus FGG		
(Lauer et al., 1996)	1996	Case series	12	12	6	6	6	6			18	APF/V in combination with implant placement	No treatment	
(Park, 2006)	2006	Case series	10	10	10	10					6	APF/V plus ADMG		
(Sanz et al., 2009)	2009	RCT	20	20	10	10	10	10			6	APF/V plus CM (Mucograft)	APF/V plus SCTG	
(Lee et al., 2010)	2010	CCT	9	14	3	3	3	3	3	8	6	APF/V plus CM (Collatape)	APF/V	APF/V plus FGG
(Lorenzo et al., 2012)	2012	RCT	24	24	12	12	12	12			6	APF/V plus CM (Mucograft)	APF/V plus CTG	
(Stimmelmayr et al., 2011)	2011	CCT	29	70	19	46	10	24			12	Single stage implant placement and ridge augmentation with later FGG	Two stage ridge augmentation and later implant placement and FGG	

(Basegmez et al., 2012)	2012	RCT	64	64	32	32	32	32		12	APF/V plus FGG	vestibuloplasty according to Edlan & Mejchar)
(Bruschi et al., 2012)	2012	CCT	85	131	85	131				48	APF/V in combination with implant placement	

Table 4 (continue)

author	outcome measure	baseline test	SD	post-surgery test	SD	change test	change test SD	baseline control 1	SD	post-surgery control 1	SD	change control 1	change control SD
(ten Bruggenkate et al., 1991)	Width of keratinized tissue (mm)	NR	NR	5 (3-8)	NR	NR	NR	NR	NR	NR	NR	NR	NR
(Lauer et al., 1996)	Immobile mucosa (mm) Attached gingiva (mm)	NR	NR	L4.2,B2.2 L2.9,B0.7	NR	NR	NR	NR	NR	L2.5,B2.6 L0.8.B0.8	NR	NR	NR
(Park, 2006)	Width of keratinized tissue (mm)	1.62	0.09	6.24	0.19	NR	NR	1.59	0.07	1.66	0.1	NR	NR
(Sanz et al., 2009)	Width of keratinized tissue (mm)	2.13	1.2	6.3	1.67	NR	NR	1.76	1.27	5.08	1.49	NR	NR
(Lee et al., 2010)	Width of keratinized tissue (mm)	1.3	0.5	3.1	1	1.8	0.75	3	0	4.6	0.5	1.6	0.25
(Lorenzo et al., 2012)	Width of keratinized tissue (mm)	0.5	0.52	2.8	0.42	NR	NR	0.42	0.51	2.75	1.55	NR	NR
(Stimmelmayr et al., 2011)	keratinized tissue (mm)	3	NR	B3.7,L2.6	NR	B+3.3,L-0,05	NR	2.75	NR	B3.3,L2.65	NR	NR	NR
(Basegmez et al., 2012)	Width of attached mucosa (mm)	0.75	0.36	3.11	0.58	2.36	0.49	0.67	0.32	1.83	0.72	1.15	0.81

(Bruschi et al., 2012)	keratinized tissue (mm)	2.3	0.25	7.37	2.12	NR	NR	NR	NR	NR	NR	NR	NR

Table 4 (continue)

author	baseline control 2	SD	post-surgery control 2	SD	change control 2	SD	effect of test vs. control 1	effect of test vs. control 2	effect of control 1 vs. control 2
(ten Bruggenkate et al., 1991)	NR	NR	NR	NR	NR	NR	NR	NR	NR
(Lauer et al., 1996)	NR	NR	NR	NR	NR	NR	significant	NR	NR
(Park, 2006)	NR	NR	NR	NR	NR	NR	NR	NR	NR
(Sanz et al., 2009)	NR	NR	NR	NR	NR	NR	Not significant	NR	NR
(Lee et al., 2010)	0.5	0	3	1.6	2.5	0.55	NR	NR	NR
(Lorenzo et al., 2012)	NR	NR	NR	NR	NR	NR	Not significant	NR	NR
(Stimmelmayr et al., 2011)	NR	NR	NR	NR	NR	NR	Not significant	NR	NR

(Basegmez et al., 2012)	NR	NR	NR	NR	NR	NR	significant	NR	NR
(Bruschi et al., 2012)	NR	NR	NR	NR	NR	NR	NR	NR	NR

Table 5: Table 5: Characteristics of included studies: augmentation of soft tissue volume

author	year of publication	study design	total number of patients	total number of sites	number of patients test	number of sites test	number of patients control 1	number of sites control 1	number of patients control 2
(Allen et al., 1985)	1984	Case series	21	26	NA	14	NA	12	NA
(Studer et al., 2000)	2000	RCT	30	30	12	12	12	12	6
(Batista et al., 2001)	2001	Case series	8	18	8	18	NA	NA	NA
(Bianchi and Sanfilippo, 2004)	2004	CCT	116	116	96	96	20	20	NA
(Cornelini et al., 2008)	2008	CCT	34	34	17	17	17	17	NA
(Kan et al., 2009)	2009	Case series	20	20	20	20	NA	NA	NA
(Wiesner et al., 2010)	2010	RCT	10	20	10	10	10	10	NA
(Speroni et al., 2010)	2010	retrospective case series	14	14	14	14	NA	NA	NA
(Schneider et al., 2011)	2011	Case series	16	16	15	15	NA	NA	NA
(Simion et al., 2012)	2012	Case series	6	6	6	6	NA	NA	NA
(Akcali et al., 2013)	2013	RCT	20	20	10	10	NA	NA	NA

Table 5 continue

number of sites control 2	follow-up period (month)	test treatment	control 1 treatment	control 2 treatment	outcome measure	outcome test	SD
NA	1.5	SCTG	Hydroxylapatite	NA	shrinkage (descriptive)	14 of 14 sites: shrinkage within first 4-6 weeks, then stable for 3 years	NR
6	3.5	SCTG	FGG	untreated defect	soft tissue volume gain in horizontal ridge width (mm)	159 mm3	80 mm3
NA	6	ADMG	NA	NA	keratinized mucosa	1.72	0.59
NA	48	immediate implants + SCTG	immediate implants	NA	papilla Index (Jemt)	NR	NR
NA	12	immediate implants + SCTG	immediate implants	NA	biotype	19 papillae (score 2); 15 papillae (score 3)	NR
NA	26	immediate implants + SCTG	NA	NA	pink esthetic score	thick biotype at latest follow-up in all sites	NR
NA	12	SCTG	no SCTG	NA	mucosal thickness (stent)	11.32	1.63
NA	36	SCTG	NA	NA	3D volume measurements based on casts	1.4mm	NR
NA	4	SCTG	NA	NA	2D volume measurements using stents	0.55mm	0.53mm
NA	4	collagen matrix + rhPDGF-BB	NA	NA	3D volume measurements based on casts	0.87mm (apical); 2.14mm (central); 0.35mm (occlusal)	2.13mm (apical); 3.27mm (central); 3.20mm (occlusal)
NA	6	VIPCG	SCTG			1.18mm	0.16mm-1.75mm

Table 5 continue

outcome control 1	SD control 1	outcome control 2	SD control 2	effect of test vs. control 1	effect of test vs. control 2	effect of control 1 vs. control 2
10 of 12 sites: no shrinkage						
104mm3	31mm3	6mm3	5.4mm3	significant	significant	significant
NR	NR	NA	NA	higher values for test group	NA	NA
22 papillae (score 2); 12 papillae (score 3)	NA	NA	NA	in favor of test group	NA	NA
8.45	1.46	NA	NA	statistically significant in favor of test group	NA	NA
0.63mm	0.28mm-1.22mm	NA	NA	statistically significant in favor of test group	NA	NA

(CCT = controlled clinical trial; RCT = randomized controlled clinical trial; SCTG = subepithelial connective tissue graft; FGG = free gingival graft; ADMG = acellular dermal matrix graft; VIPCG=palatal vascularized interpositional periosteal-connective tissue graft; SD=standard deviation

.

Figure 1

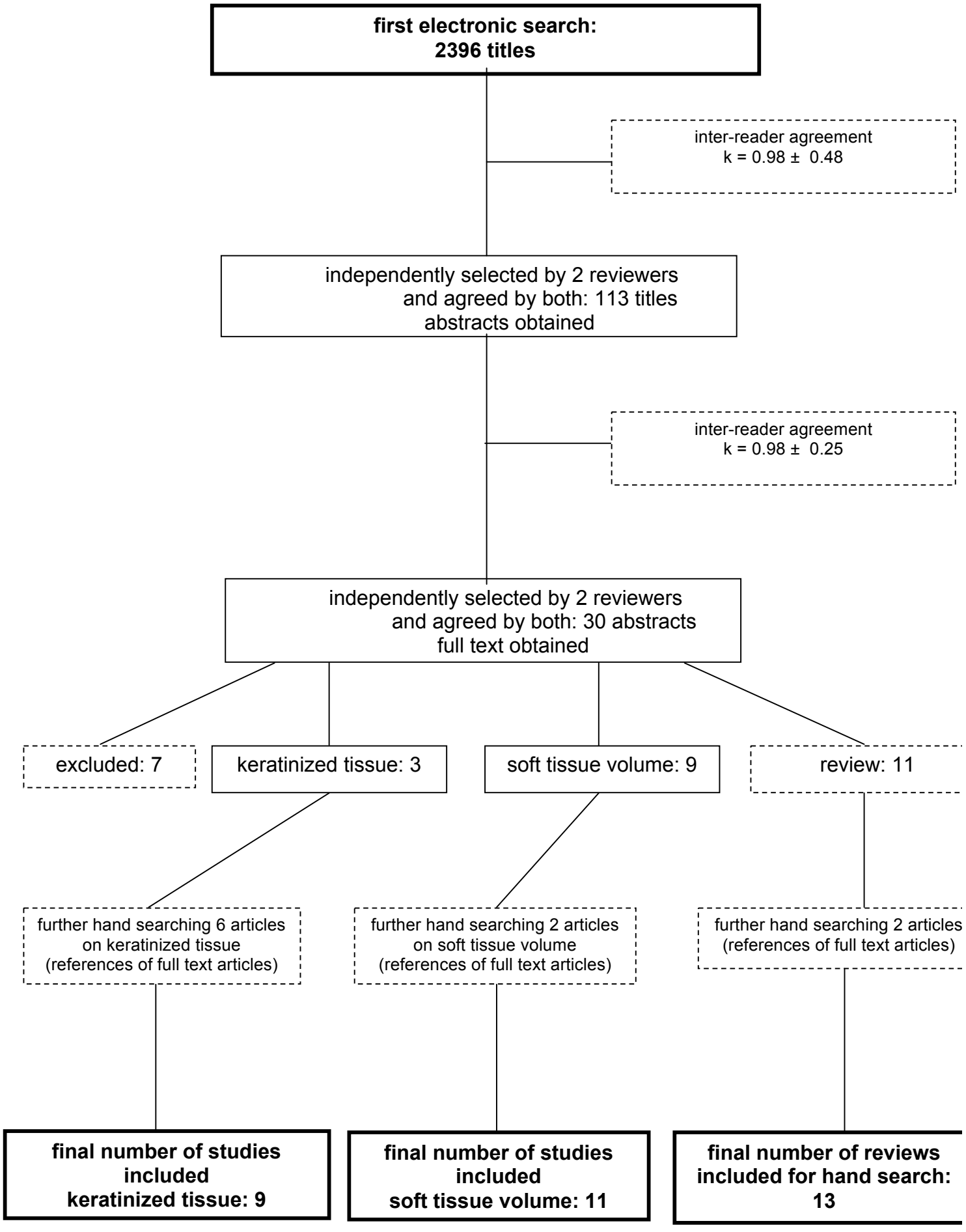

first electronic search:
2396 titles
inter-reader agreement
k = 0.98 ± 0.48
independently selected by 2 reviewers
and agreed by both: 113 titles
abstracts obtained
inter-reader agreement
k = 0.98 ± 0.25
independently selected by 2 reviewers
and agreed by both: 30 abstracts
full text obtained
excluded: 7
keratinized tissue: 3
soft tissue volume: 9
review: 11
further hand searching 6 articles
on keratinized tissue
(references of full text articles)
further hand searching 2 articles
on soft tissue volume
(references of full text articles)
further hand searching 2 articles
(references of full text articles)
final number of studies
included
keratinized tissue: 9
final number of studies
included
soft tissue volume: 11
final number of reviews
included for hand search:
13

Figure 2

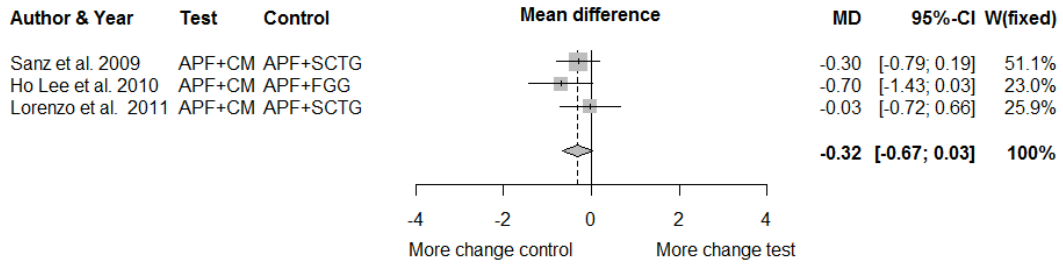
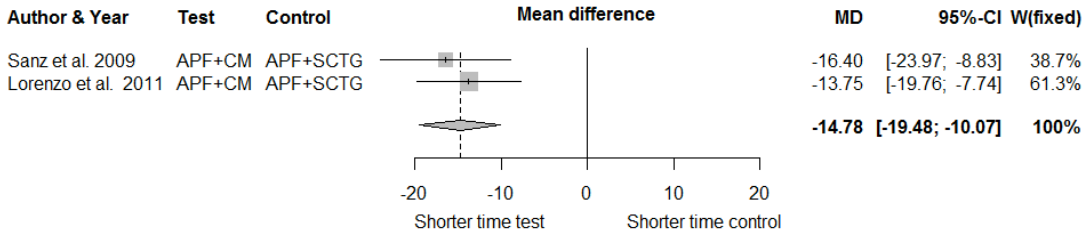

Author & Year
Test
Control
Mean difference
MD
95%-CI
W(fixed)
Sanz et al. 2009 APF+CM APF+SCTG -0.30 [-0.79; 0.19] 51.1%
Ho Lee et al. 2010 APF+CM APF+FGG -0.70 [-1.43; 0.03] 23.0%
Lorenzo et al. 2011 APF+CM APF+SCTG -0.03 [-0.72; 0.66] 25.9%
-0.32 [-0.67; 0.03] 100%
-4
-2
0
2
4
More change control
More change test

Figure 3


Author & Year
Test
Control
Mean difference
MD
95%-CI
W(fixed)
Sanz et al. 2009
APF+CM
APF+SCTG
-16.40
[-23.97; -8.83]
38.7%
Lorenzo et al. 2011
APF+CM
APF+SCTG
-13.75
[-19.76; -7.74]
61.3%
-14.78
[-19.48; -10.07]
100%
-20
-10
0
10
20
Shorter time test
Shorter time control