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Treatment of gingival recession defects with a coronally advanced flap and a xenogeneic collagen matrix: a multicenter randomized clinical trial

Karin Jepsen[1], Søren Jepsen[1], Giovanni Zucchelli[2], Martina Stefanini[2], Massimo de Sanctis[3], Nicola Baldini[3], Björn Greven[4], Bernd Heinz[4], Jan Wennström[5], Björn Cassel[5], Fabio Vignoletti[6] and Mariano Sanz[6]

[1]Department of Periodontology, University of Bonn, Bonn, Germany; [2]Department of Stomatology, Bologna University, Bologna, Italy; [3]Department of Periodontology, Siena University, Siena, Italy; [4]Private Practice, Hamburg, Germany; [5]Department of Periodontology, University of Göteborg, Göteborg, Sweden; [6]Department of Periodontology, University of Madrid, Madrid, Spain

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Abstract

Aim: To evaluate the clinical outcomes of the use of a xenogeneic collagen matrix (CM) in combination with the coronally advanced flap (CAF) in the treatment of localized recession defects.

Material & Methods: In a multicentre single-blinded, randomized, controlled, split-mouth trial, 90 recessions (Miller I, II) in 45 patients received either CAF + CM or CAF alone.

Results: At 6 months, root coverage (primary outcome) was 75.29% for test and 72.66% for control defects ($p = 0.169$), with 36% of test and 31% of control defects exhibiting complete coverage. The increase in mean width of keratinized tissue (KT) was higher in test (from 1.97 to 2.90 mm) than in control defects (from 2.00 to 2.57 mm) ($p = 0.036$). Likewise, test sites had more gain in gingival thickness (GT) (0.59 mm) than control sites (0.34 mm) ($p = 0.003$). Larger (≥ 3 mm) recessions ($n = 35$ patients) treated with CM showed higher root coverage (72.03% *versus* 66.16%, $p = 0.043$), as well as more gain in KT and GT.

Conclusions: CAF + CM was not superior with regard to root coverage, but enhanced gingival thickness and width of keratinized tissue when compared with CAF alone. For the coverage of larger defects, CAF + CM was more effective.

Key words: collagen (matrix); gingival recession; keratinized tissue; root coverage; tissue regeneration; xenograft

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Conflict of interest and source of funding statement

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Several surgical techniques and flap designs have been utilized to correct gingival recession defects by augmenting gingival tissue dimensions and hence, covering the exposed root surfaces (Pini-Prato et al. 1995). Procedures using pedicle flaps, free soft tissue grafts, combination of pedicle flaps with grafts, barrier membranes or enamel matrix derivative are all effective for this purpose as attested by many studies (Cairo et al. 2008). More specifically, it was demonstrated that localized gingival recessions can be successfully treated with a coronally advanced flap (CAF),

although the additional use of a connective tissue graft (CTG) or other biomaterials has shown to improve mean root coverage and the predictability of complete root coverage, when compared with CAF alone (Cairo et al. 2008, Cortellini et al. 2009). A recent Cochrane systematic review (Chambrone et al. 2010) concluded that the subepithelial CTG procedure, the CAFs alone or associated with other biomaterials may render good results, although in cases where root coverage and gain in keratinized tissue are expected, the use of CTG seems to be more adequate. However, the wound at the palatal donor site for harvesting the CTG is frequently associated with discomfort for the patient (Cairo et al. 2008, Chambrone et al. 2010).

To reduce patient discomfort, swelling and sometimes pain associated with the wound at the palatal donor site when harvesting the CTG, alternatives are needed. A newly developed xenogeneic collagen matrix (CM) has been shown to promote regeneration of keratinized gingiva around teeth and implants in association with tissue augmentation procedures (Sanz et al. 2009) and to improve early mucosal wound healing (Thoma et al. 2012). McGuire & Scheyer (2010) studied the safety and efficacy of this CM + CAF for recession therapy in 25 patients with bilateral Miller I and II recessions in a mono-centre, randomized, single-blind, split-mouth designed trial. Although values of root coverage for CAF + CTG (99.3%) were higher than for CAF + CM (88.5%), they found the procedure to be less invasive and time consuming with unlimited "off-the-shelf" supply of grafting material, and concluded that it presents a viable alternative to the CTG procedure.

There are, however, no data available on the possible added benefit of the use of this CM in combination with CAF when compared to the standard CAF procedure for the treatment of localized gingival recessions. It was, therefore, the primary objective of this randomized clinical trial to evaluate the effect of CM in combination with CAF treatment compared to CAF alone with respect to root coverage. As secondary objectives, the amount of soft tissue augmentation and patient-centred outcomes were evaluated.

Material and methods

Study design and patients

This investigation was designed as a multicentre multinational, single-blind, split-mouth randomized clinical trial (Fig. 1). The study protocol was registered with ClinicalTrials.gov, Registration number: NCT00902876. A total of 45 patients were consecutively selected to participate in the study from six different clinics in Germany, Italy, Sweden and Spain and were treated with both experimental and control surgical procedures by expert periodontists. These patients were selected according to the following inclusion criteria:

- Presence of at least one localized gingival recession in each side of the maxilla and/or mandible.
- The cemento–enamel junction (CEJ) was visible in the teeth for root coverage procedures.
- All recessions were Class I or II defects (Miller 1985).
- The two defects within one patient did not deviate more than 2 mm in recession depth.
- All patients demonstrated adequate plaque control with a full-mouth plaque score $\leq 20\%$ and with no clinical signs of active periodontal disease.
- All patients were at least 18 years of age.

The criteria for exclusion were:

- Patients smoking more than 10 cigarettes per day.
- Patients with insulin-dependent diabetes.
- Patients with a history of malignancy, radiotherapy, or chemotherapy for malignancy.
- Patient pregnant or nursing during the past 5 months.
- Patients taking medications or having treatments with an effect on mucosal healing in general (e.g. steroids, large doses of anti-inflammatory drugs).
- Patients with a disease affecting connective tissue metabolism.
- Patients allergic to collagen.
- Patients who participated in a clinical trial within the past 6 months.

After a thorough explanation of the study procedures and their associated risks and benefits, participants signed an informed consent in accordance with the Helsinki Declaration of 1975 as revised in 2000. The study protocol had been previously approved by the respective ethical committees for human subject trials from the centres participating in the study. All female patients confirmed not to be pregnant and agreed for contraception measures for at least 6 months after surgery.

Clinical measurements

The primary endpoint of this trial was the percentage of root coverage (RC) at 6 months. Secondary endpoints were reductions in recession depth (REC), recession width (RW), complete root coverage (CRC), gain in thickness of gingival tissue (GT), gain in clinical attachment and increase in width of keratinized tissue (KT).

At baseline, 3-month and 6-month visits, one single-blinded examiner per study site, different from the surgical operator, recorded all the clinical outcome variables.

The following parameters were assessed in millimetres with the use of a University of North Carolina periodontal probe (Hu-Friedy, Chicago, IL, USA):

- REC from the free gingival margin to the cemento–enamel junction.
- RW at the cemento–enamel junction.
- KT from the free gingival margin to the mucogingival junction.
- GT with an injection needle (Sopira Carpule 0.3×16 mm, Heraeus Kulzer) and a silicon marker, 1 mm below the gingival margin.

Pre-operative (Fig. 2) and follow-up photographs were taken at each visit. For patient-related factors, a questionnaire as well as a visual analogue scale (VAS) were given to the patients to assess pain and discomfort during the initial healing phase.

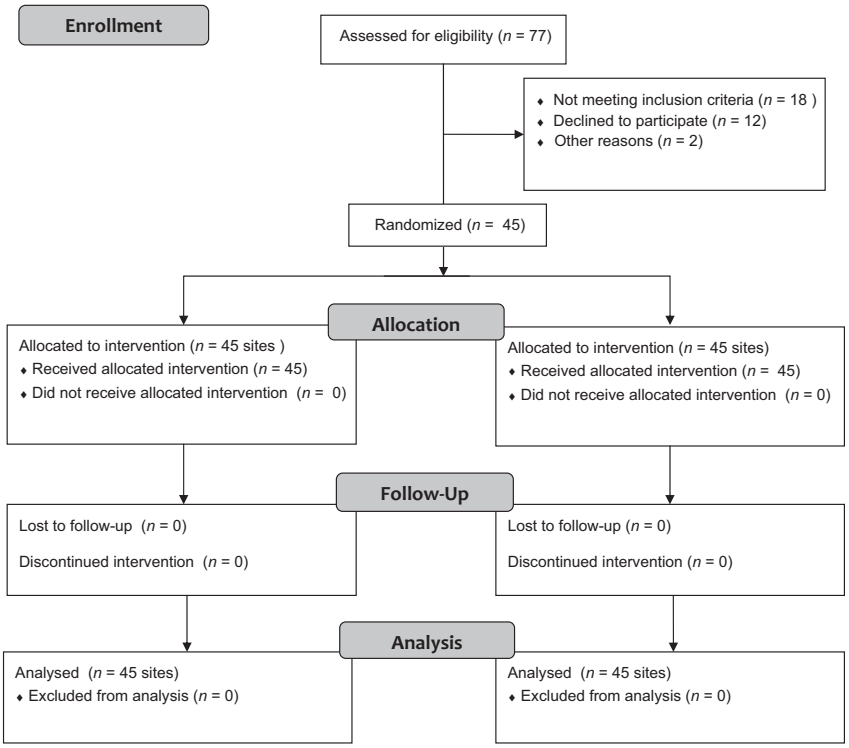

Fig. 1. Consort flow diagram of the study.

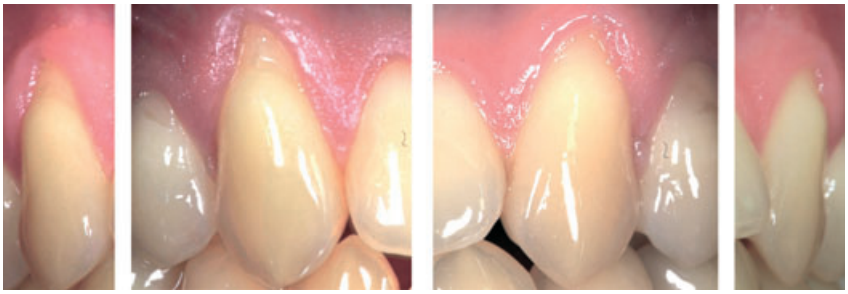

Fig. 2. Baseline. Gingival recessions on right and left canine scheduled to undergo coronally advanced flap procedures.

Selection of clinical centres and training of investigators

Twelve expert periodontists in different clinical centres who were experienced operators in mucogingival surgery were selected to participate in the study. All participating investigators were required to attend training and calibration meetings to review the objectives of the study and the protocol. Organizational strategies were discussed to optimize patient accrual and retention and data management. Preliminary clinical cases were discussed to standardize case selection, the measurement techniques and the surgical procedures. Prior to starting the study, each operator was video trained on the surgical procedure in detail.

An external monitor frequently reassured on-site rules for the compilation of the data collection sheets for appropriate oversight to ensure the validity of the data.

Treatment

Pre-surgical phase

As part of the screening phase for inclusion, all patients had a full-mouth periodontal examination with registration of probing pocket depths (PD) and full-mouth bleeding scores (FMBS), Once the selected patients agreed to participate in the study, they were provided with customized oral hygiene instructions, including control of traumatic tooth brushing techniques as well as a dental prophylaxis and polishing.

Randomization, allocation concealment and blinding

Selected patients were randomly assigned to treatment by a central registrar using a computer-generated randomization list with random permuted blocks (Fig. 1). The treatment allocation was concealed to the therapist by opaque envelopes that were opened upon completion of the common part of the surgical treatment (flap elevation and root conditioning). The clinical examiners remained blinded to the treatment assignment. Blinding was broken after completion of the statistical analysis.

Surgical procedures

The coronally advanced procedure (CAF) as described by De Sanctis & Zucchelli (2007) was used in this investigation for both experimental and control sites (see Data S1), only the order of sutures was reversed.

The exposed root surfaces were conditioned with 24% EDTA for 2 min. to remove the smear layer

from the dentine tubules (Blomlöf et al. 1997) and thus improve coagulum adhesion to the root surface (Gamal 2011). After EDTA application, the root surface was rinsed with saline for 60 s.

Following treatment allocation, the test material was applied in the test sites. This material consisted of a three-dimensional collagen matrix (Mucograft®; Geistlich Pharma AG, Wolhusen, Switzerland).

The collagen matrix was cut to the size of the experimental defect, allowing a slight overlap and placed on the prepared recipient bed with the smooth surface facing the oral cavity and the porous surface facing the bone. Sharp edges were removed and the matrix was fixed to the root surface with resorbable sling sutures (Vicryl® 6-0, V492, P-3; Ethicon Inc., Johnsson & Johnsson, NJ, USA). Complete moistening by blood and exudates allowed perfect adhesion of the matrix.

Subsequently, in both treatment sites, the root surface was covered with the coronally advanced flap and secured with sutures slightly coronally of the CEJ by means of a sling suture placed at the adjacent papillae, using non-irritating sutures (Prolene® 6-0, 8697, P-1; Ethicon Inc.). The vertical incisions were then closed by means of interrupted periosteal 6-0 sutures starting at the most apical extension of the vertical release incisions. No periodontal dressing was applied.

Post-surgical protocol

Following surgery, patients were instructed to rinse twice daily with chlorhexidine mouth rinse (0.2%) for 1 month. Patients were instructed to avoid any mechanical trauma and tooth brushing for 4 weeks in the surgical area. Anti-inflammatory therapy and additional analgesics were prescribed according to the individual needs and the patient was instructed to record daily the intensity of pain and the dose of medication in the patient questionnaire.

The lateral sutures were removed after 7 days if possible, and the sling suture was removed after 14 days. Clinical photographs were taken after cleaning and polishing to document the healing process (Fig. 3). Patients were recalled at 3 and 6 months after surgery for professional oral hygiene procedures.

Data analysis

The study was conducted under international quality standards (ISO14155) and the applicable national laws to avoid bias including clinical monitoring, data management, GCP audits and statistical analysis.

The main hypothesis was that CAF combined with the xenogeneic collagen matrix would result in improved outcomes (superiority trial) (Cairo et al. 2012a, Tonetti & Palmer 2012) in terms of percentage of root coverage when compared with CAF alone was tested by one-sided paired Wilcoxon signed rank test at the 5% level of significance (Sackett 2004). This procedure was further used for an exploratory comparison of the treatments with respect to other endpoints. Paired differences were tested using Wilcoxon's signed rank tests for paired samples.

For differences in primary outcomes of maxillary and mandibular defects, a two-sided Mann–Whitney *U*-test was performed.

To determine the association between the primary end point percentage of root coverage and baseline recession depth, Pearson's and Spearman's correlation coefficients were calculated for test and control sites separately.

Possible differences in the primary outcome between study centres were explored by the Kruskal–Wallis test.

The analysis was performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

Sample size calculation

The calculation of patients to be treated was based on the primary objective to detect a true mean difference of at least 10 percentage points between test and control treatment for root coverage after 6 months (McGuire & Scheyer 2010). With a power of 80% and alpha = 0.05, based on superiority considerations, a total of 35 patients were required using a one-sided *t*-test for paired samples. The standard deviation of the differences was assumed to be 23 percentage points. To allow for non-parametric testing and dropouts, 45 patients were recruited.

Results

Forty-five patients (mean age: 39.5 ± 13.8 years, 20–73 years, 17 men, 28 women) were recruited and treated between 2009 (February) and 2010 (December). The number of patients per centre ranged from 3 to 11. All patients were able to complete the follow-up examination after 6 months.

Study teeth were maxillary central incisors (2), canines (40), premolars (24) and first molars (4) as well as mandibular incisors (2), canines (4) and pre-molars (14), yielding 35 pairs of defects in the maxilla and 10 pairs in the mandible. Surgeries and post-operative sequelae were uneventful and no patient in any group developed any significant complication.

Table 1 depicts the descriptive statistics for all clinical parameters. Contra-lateral test and control defects were well balanced at baseline. The results for the primary and secondary clinical outcomes are presented in Table 2. At 6 months, the primary end point percentage of root coverage was on average 75.29% for test sites and 72.66% for control sites ($p = 0.1695$). For the secondary outcomes, the following results were obtained: Mean recession depth at 6 months was decreased to 0.87 mm for test sites and 1.02 mm for control sites. The split-mouth design of the study allowed calculation of intra-patient differences (change for test minus change for control), which translated to a significant mean difference of 0.27 mm in recession depth changes from baseline to 6 months ($p = 0.0175$) in favour of the test treatment. In contrast, for the reductions in recession width, no significant differences between treatments were observed ($p = 0.3925$). At 6 months, 36% of test defects and 31% of control defects showed complete root coverage.

The width of keratinized tissue could be increased on average from 1.97 to 2.90 mm for test sites and from 2.00 to 2.57 mm at control sites. The difference in gain of 0.37 mm was significant ($p = 0.036$). Likewise, for test defects, there was

a significantly higher increase in the thickness of gingival tissue (0.24 mm, $p = 0.0035$).

For the test treatment, no linear relation could be found between baseline recession depth and the primary outcome % recession coverage at 6 months (Fig. 4). This was in contrast to the control treatment, where a negative linear relationship may be claimed (Pearson's correlation coefficient: −0.4193, $p = 0.0041$, Spearman's correlation coefficient: −0.509, $p = 0.0004$) between baseline recession and the primary outcome with 95% confidence (Fig. 5). Following CAF treatment, shallow defects had a higher percentage of recession coverage than deeper defects.

No significant centre effect with regard to the primary outcome could be determined (Kruskall–Wallis, $p = 0.2450$).

In a further analysis, patients with shallow defects (REC < 3 mm) were excluded (Tables 3 and 4). For the remaining 35 patients, at 6 months root coverage was higher for test (72.03%) than for control sites (66.16%) ($p = 0.0430$). More keratinized tissue was gained by test treatment (0.54 mm, $p = 0.0055$). Likewise, for test defects, there was a significantly higher increase in the thickness of gingival tissue (0.31 mm, $p = 0.0030$).

When comparing test and control treatments, patient assessments of pain or discomfort were equivalent (Table. 5). No differences could be observed in visual analogue pain scores at 7 days (2.32 *versus* 2.04) and 14 days (0.68 *versus* 0.59) post surgery (Table. 6). The overall surgical chair time for CAF was 31 ± 14 min. *versus* 39 ± 14 min. for CAF + CM.

Discussion

To the best of our knowledge, this is the first randomized clinical trial designed to evaluate the additional benefit of the use of a xenogeneic collagen matrix in combination with the CAF procedure for the treatment of localized gingival recessions, when compared with CAF alone. As the primary outcome for efficacy, we measured the % of root coverage at 6 months, resulting in the test group (CAF + CM) in a higher % RC of 75.29% *versus* 72.66% in the control group (CAF). This difference, however, was not significant. Hence, the hypothesis of an enhanced outcome by the use of the CM could not be confirmed. However, the use of the CM resulted in significantly more gain in gingival thickness and width of keratinized tissue.

The use of a xenogeneic collagen matrix as an adjunct to the CAF procedure might be relevant for several reasons; first because the CAF surgical procedure has demonstrated very good results in the treatment of localized gingival recessions, both in terms of root coverage as well as in aesthetic outcomes (Pini-Prato et al. 1995). The demonstrated additional effect shown in this RCT, therefore, may improve the predictability of this procedure in the treatment of Class I and II recession defects. When the CAF procedure has been compared with the adjunctive use of an auto graft, recent systematic reviews have clearly shown the advantage of placing a connective tissue graft under the flap (Cairo et al. 2008, Chambrone et al. 2010). In fact, when identifying which were the significant factors, both patient and procedure- related, in the attainment of complete root coverage, an individual patient data meta- analysis of randomized controlled clinical trials showed that the adjunctive use of a subepithelial connective tissue graft achieved superior results than the coronally advanced flap alone (Chambrone et al. 2012). On the other hand, when assessing the incidence of adverse effects, such as discomfort with or without pain, these events were directly related to the donor sites source of the connective tissue grafts and a second wound area (Cairo et al. 2008, 2012b, Chambrone et al. 2010).

Hence, an alternative for the connective tissue graft, which renders better results than the CAF procedure, might be a good therapeutic option in the treatment of Class I and II recession defects.

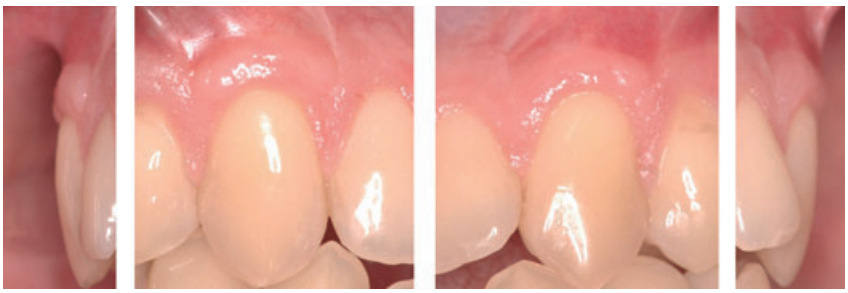

Fig. 3. Six-month follow-up. Coronally advanced flap (CAF) + xenogeneic collagen matrix (CM) and CAF alone were performed and complete root coverage was achieved at treated teeth. Tooth 13 received CAF + CM.

Table 1. Clinical parameters at baseline (BL), 3 and 6 months

Mean (SD)	Control (CAF)			Test (CAF + CM)		
	BL	3M	6M	BL	3M	6M
Recession depth (REC)	3.34 (1.00)	0.89 (1.11)	1.02 (1.08)	3.46 (0.90)	0.84 (0.95)	0.87 (0.94)
Recession width (RW)	4.10 (0.93)	2.01 (1.72)	2.27 (1.75)	4.08 (0.89)	1.89 (1.84)	2.15 (1.86)
Width of keratinized tissue (KT)	2.00 (1.22)	2.40 (0.93)	2.57 (1.15)	1.97 (1.13)	2.59 (1.28)	2.90 (1.29)
Thickness of gingival tissue (GT)	0.89 (0.34)	1.17 (0.46)	1.23 (0.46)	0.89 (0.28)	1.37 (0.47)	1.48 (0.46)
Clinical attachment level (CAL)	4.82 (1.09)	2.22 (1.33)	2.21 (1.25)	4.79 (1.01)	2.14 (1.15)	2.09 (1.14)
Probing pocket depth (PPD)	1.48 (0.65)	1.33 (0.60)	1.19 (0.58)	1.33 (0.46)	1.30 (0.62)	1.22 (0.67)

Table 2. Changes in clinical parameters between baseline (BL) and 3 and 6 months

Mean (SD)	Control (CAF)		Test (CAF + CM)		Test/Control	*p*-value
	BL – 3M	BL – 6M	BL – 3M	BL – 6M	Change difference BL – 6M	
% Root coverage (RC)	76.44 (26.83)	72.66 (26.19)	76.11 (26.81)	75.29 (26.68)	2.63 (21.19)	0.1693
% Defects with 100% coverage (CRC)	38	31	38	36		0.3870
Recession depth (REC) reduction	2.46 (1.06)	2.32 (0.99)	2.61 (1.09)	2.59 (1.11)	0.27 (0.92)	0.0175
Recession width (RW) reduction	2.09 (1.57)	1.84 (1.48)	2.19 (1.67)	1.91 (1.73)	0.07 (1.54)	0.3925
Increase in width of keratinized tissue (KT)	0.40 (1.04)	0.57 (0.98)	0.62 (1.12)	0.93 (1.15)	0.37 (1.18)	0.0360
Increase in thickness of gingival tissue (GT)	0.28 (0.53)	0.34 (0.55)	0.48 (0.46)	0.59 (0.44)	0.24 (0.63)	0.0035

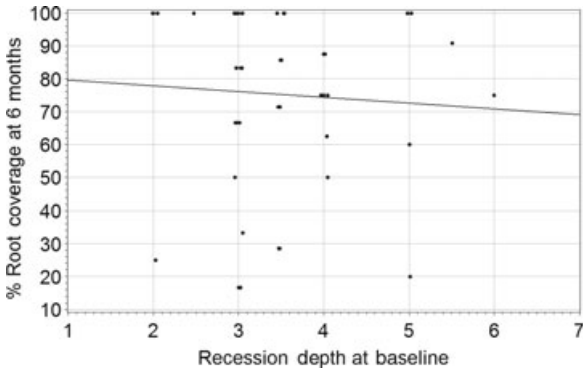

Fig. 4. Scatterplot of % Root Coverage (RC) at 6 months *versus* Recession Depth (REC) at Baseline for Defects treated with coronally advanced flap (CAF) + xenogeneic collagen matrix (CM).

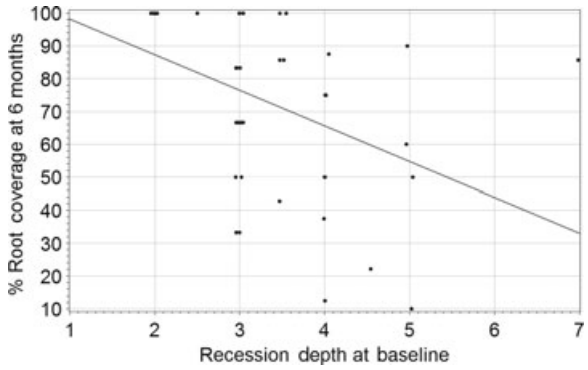

Fig. 5. Scatterplot of % Root Coverage (RC) at 6 months *versus* Recession Depth (REC) at Baseline for Defects treated with coronally advanced flap (CAF) alone.

The collagen matrix utilized in this clinical trial has shown clinical efficacy for widening the width of keratinized tissue, both around teeth and dental implants when used in a non-submerged healing environment (Sanz et al. 2009). Its use has also been reported for the treatment of recession defects when used in a submerged environment in combination with the CAF procedure (McGuire & Scheyer 2010, Cardaropoli et al. 2012). McGuire & Scheyer (2010) in a split-mouth designed clinical trial compared the use of CM + CAF *versus* the gold-standard treatment (CAF + CTG). Although the results in terms of aesthetic outcomes and patient satisfaction were good in both groups, the percentage of root coverage was significantly superior for the CAF + CTG procedure (99.3% *versus* 88.5%). These excellent results for the CTG procedure are, however, superior than the mean %RC reported in systematic reviews, ranging from 64.7% to 97.3% and from 34.0% to 86.7% for CAF alone (Cairo et al. 2008, Chambrone et al. 2010). The % RC result reported in the present clinical trial for the CM + CAF was 75.3%, which is within the range of the scientific evidence for the use of connective tissue grafts, although inferior to the mentioned comparative studies (McGuire & Scheyer 2010, Cardaropoli et al. 2012).

One reason for this discrepancy was the fact that this study was designed as a multicentre randomized clinical trial employing six surgeons in a variety of different settings, what might have influenced the extent of the results, but also highlights its external validity and hence, the generalizability of the results obtained. In the preparation of the study, the examiners had been trained, but not calibrated with regard to an assessment of the intra- and inter-examiner reproducibility of their recordings. This is certainly a weakness of this study and it may only be speculated that any systematic error would have been compensated to some extent by the split-mouth design of the study. Interestingly though, no centre effect on the treatment outcomes could be statistically demonstrated.

Another factor could be the mean baseline recession depth, which was smaller in both studies when compared with this investigation. Although our data showed that for CAF alone, recession coverage correlated inversely with initial recession depth, no such correlation was seen with the use of CAF + CM, indicating that deeper defects would benefit more from the additional application of CM. Indeed, when in a subanalysis 10 patients with shallow recessions (<3 mm) were excluded,

significantly better results with regard to % RC, gain in KT and GT were found for CAF + CM.

As alternative treatments to the use of autogenous grafts, allogeneic materials have also been studied for the treatment of recession defects. The most studied material, acellular dermal matrix (ADM), showed in the meta-analyses a mean % RC for CAF + ADM between 50% and 99% (Cairo et al. 2008, Chambrone et al. 2010). However, these studies did not show a significant additional benefit over CAF alone in terms of complete root coverage, recession reduction or KT gain. These findings are in contrast with those obtained in this investigation, where a higher gain of keratinized tissue was found when CM + CAF was compared to CAF alone. Using CM + CAF, the mean gain in width of keratinized gingiva was 0.93 mm. These results are similar to those obtained in previous studies (McGuire & Scheyer 2010, Cardaropoli et al. 2012), reporting a gain of 1.3 mm and 1.2 mm respectively. In one of these studies (Cardaropoli et al. 2012), the increase in gingival thickness was measured, reporting a mean gain of 1.0 mm at 12 months in the CM group, which is somewhat more than the mean gain of 0.6 mm reported in this study at 6 months, but significantly higher than for CAF alone. This gingival thickness augmentation might improve the long term predictability of this procedure, by diminishing post-surgical relapse and thus providing longer term stability.

There is no evidence from human histology available to demonstrate the quality of the healing following the application of CM. However, results from a recent animal experiment with recession-type defects demonstrated that the CM in conjunction with the CAF procedure attained significantly better regenerative outcomes than the CAF procedure alone. The healing in the CM + CAF group was characterized by a shorter epithelial interphase and a larger dimension of new cementum formation (Vignoletti et al. 2011).

Within the limitations of this study, the following conclusions can be drawn:

- CM + CAF was not superior to CAF in providing a consistent reduction of the baseline recession.
- The shorter chair time could indicate the use of a CAF alone when this issue is of primary importance for the patient.
- If the therapeutic objectives are the increase of gingival thickness and gain of keratinized gingiva,

Table 3. Clinical parameters for patients ($n = 35$) with initial recession depth (REC) $\geq$ 3 mm at baseline (BL) and 6 months

Mean (SD)	Control (CAF)		Test (CAF + CM)	
	BL	6M	BL	6M
Recession depth (REC)	3.63 (0.90)	1.27 (1.09)	3.66 (0.84)	1.01 (0.99)
Recession width (RW)	4.20 (0.99)	2.79 (1.56)	4.27 (0.82)	2.52 (1.82)
Width of keratinized tissue (KT)	2.03 (1.24)	2.54 (1.22)	2.06 (1.22)	3.11 (1.35)
Thickness of gingival tissue (GT)	0.91 (0.35)	1.27 (0.46)	0.87 (0.28)	1.54 (0.48)
Clinical attachment level (CAL)	5.00 (1.11)	2.53 (1.18)	4.96 (0.93)	2.29 (1.15)
Probing pocket depth (PPD)	1.37 (0.56)	1.26 (0.53)	1.30 (0.47)	1.27 (0.68)

Table 4. Changes in clinical parameters between baseline (BL) and 6 months for patients ($n = 35$) with initial recession depth (REC) $\geq$ 3 mm

Mean (SD)	Control (CAF)	Test (CAF + CM)	Test/Control	
	BL – 6M	BL – 6M	Change differences BL – 6M	*p*-value
% Root coverage (RC)	66.16 (25.7)	72.03 (26.85)	5.87 (19.25)	0.0430
% Defects with 100% coverage (CRC)	17	29	12	0.1445
Recession depth (REC) reduction	2.36 (1.10)	2.64 (1.18)	0.29 (0.82)	0.0380
Recession width (RW) reduction	1.42 (1.31)	1.74(1.77)	0.32 (1.47)	0.1145
Increase in width of keratinized tissue (KT)	0.51 (1.00)	1.06 (1.22)	0.54 (1.18)	0.0055
Increase in thickness of gingival tissue (GT)	0.36 (0.55)	0.67 (0.40)	0.31 (0.65)	0.0030

Table 5. Results of patient questionnaire for post-operative pain and discomfort (Question: "How was the postoperative course?")

	Day 7 ($n = 45$)						Day 14 ($n = 44$)					
	Test only		Control only		Tied		Test only		Control only		Tied	
	N	%	N	%	N	%	N	%	N	%	N	%
Pain	1	2.2	0	0.0	44	97.8	2	4.6	2	4.6	40	90.9
Swelling	0	0.0	2	4.4	43	95.6	1	2.3	1	2.3	42	95.5
Unable to chew	0	0.0	0	0.0	45	100.0	1	2.3	1	2.3	42	95.5
Bleeding	3	6.7	3	6.7	39	86.7	0	0.0	0	0.0	44	100.0
Other	4	8.9	0	0.0	41	91.1	1	2.3	0	0.0	43	97.7

Test = collagen matrix + coronally advanced flap, control = coronally advanced flap.

Table 6. Results for pain evaluation by visual analogue scale (VAS)

Visit	Treatment	N	Mean	SD
7 days	Test	45	2.32	2.08
	Control	45	2.04	1.82
14 days	Test	43	0.68	1.21
	Control	42	0.59	0.91

Test = collagen matrix + coronally advanced flap, control = coronally advanced flap.

the use of CM under a CAF should be considered.

- In recession defects ≥ 3 mm, the CM + CAF could improve recession coverage and gingival augmentation compared to CAF alone.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. methods

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Address:
Karin Jepsen
Dept. of Periodontology,
Operative and Preventive Dentistry
University of Bonn
Welschnonnenstr. 17, 53111 Bonn, Germany
E-mail: jepsen@uni-bonn.de

Clinical Relevance

Scientific rationale for the study: Recently, a new xenogeneic collagen matrix has been introduced as a soft tissue substitute and has been evaluated compared with the connective tissue graft. However, there are no data available regarding a possible added benefit when compared to the standard coronally advanced flap procedure for the treatment of recessions.

Principal findings: The combination of a new collagen matrix with the coronally advanced flap yielded similar recession coverage and improved soft tissue augmentation when compared to coronally advanced flap alone.

Practical implications: A new collagen matrix can enhance the outcomes of recession therapy with a coronally advanced flap, and may be an option for the coverage of larger defects.