





# A multi-centre randomized controlled trial comparing connective tissue graft with collagen matrix to increase soft tissue thickness at the buccal aspect of single implants: 3-Year results

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## Abstract

**Aim:** To compare connective tissue graft (CTG) with collagen matrix (CMX) in terms of increase in buccal soft tissue profile (BSP) when applied at single implant sites.

**Materials and Methods:** Patients with a single tooth gap in the anterior maxilla and horizontal mucosa defect were enrolled in a multi-centre randomized controlled trial. All were fully healed sites with a bucco-palatal bone dimension of at least 6 mm, and received an immediately restored single implant using a full digital workflow. Patients were randomly allocated to the control (CTG) or test group (CMX: Geistlich Fibro-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) to increase buccal soft tissue thickness. Primary endpoints were increase in BSP at T1 (immediately postop), T2 (3 months), T3 (1 year) and T4 (3 years) based on superimposed digital surface models. Secondary endpoints included patient-reported, clinical and aesthetic outcomes.

**Results:** Thirty patients were included per group (control group: 15 males, 15 females, mean age 50.1 years; test group: 14 males, 16 females, mean age 48.2 years) and 50 could be re-examined at T4. The changes in BSP over time were significantly different between the groups ( $p < .001$ ). At T4, the estimated mean increase in BSP amounted to 0.83 mm (95% confidence interval [CI]: 0.58–1.08) in the control group and 0.48 mm (95% CI: 0.22–0.73) in the test group. The estimated mean difference of 0.35 mm (95% CI: 0.06–0.65) in favour of the control group was significant ( $p = .021$ ). No significant differences between the groups could be observed in terms of patients' aesthetic satisfaction ( $p = .563$ ), probing depth ( $p = .286$ ), plaque ( $p = .676$ ), bleeding on probing ( $p = .732$ ), midfacial recession ( $p = .667$ ), Pink Esthetic Score ( $p = .366$ ) and Mucosal Scarring Index ( $p = .438$ ). However, CMX resulted in significantly more marginal bone loss (–0.43 mm; 95% CI: –0.77 to –0.09;  $p = .015$ ) than CTG.

**Conclusions:** CTG was more effective in increasing buccal soft tissue profile and resulted in less marginal bone loss than CMX. Therefore, CTG remains the gold

standard to increase soft tissue thickness at implant sites. *Clinical Trial registration:* This study was registered in ClinicalTrials.gov (NCT04210596).

#### KEYWORDS

collagen matrix, connective tissue graft, dental implant, single tooth

#### Clinical Relevance

*Scientific rationale for study:* Connective tissue graft (CTG) has been well documented to increase buccal soft tissue thickness. However, a second surgical site is needed, which is not required when a collagen matrix (CMX) is used as the grafting material.

*Principal findings:* CMX is less effective than CTG in augmenting soft tissues up to 3 years of follow-up.

*Practical implications:* CTG remains the gold standard to increase soft tissue thickness at implant sites.

## 1 | INTRODUCTION

Soft tissue augmentation is often required to re-establish soft tissue convexity at the buccal aspect of single implants regardless of the timing of implant placement (Cosyn et al., 2024; Wessels et al., 2020). Also, following bone augmentation, loss of the buccal contour is a common finding. In this respect, Schneider et al. (2011) treated 16 single sites with lateral bone augmentation and soft tissue augmentation and demonstrated that the latter contributed to nearly half of the buccal soft tissue contour. Clinical studies comparing augmented and non-augmented sites with clinician- and patient-reported outcomes provide valuable information on the clinical relevance of soft tissue augmentation (Stefanini et al., 2021). A split-mouth randomized controlled trial (RCT) (Wiesner et al., 2010) compared sites augmented with a connective tissue graft (CTG) to non-augmented sites and observed superior aesthetics for augmented sites as rated by both professionals and patients. A prospective cohort study (Hosseini et al., 2020) demonstrated that implant sites that received CTG showed a better mucosal colour-match with adjacent sites when compared to non-augmented sites. Altogether, these findings seem to indicate that soft tissue augmentation is clinically relevant in the aesthetic area. However, additional research is needed given the scarcity of data.

Although CTG is still considered the gold standard for soft tissue augmentation (Thoma et al., 2014), a second surgical site is required for graft harvesting. This may increase patients' morbidity (Griffin et al., 2006). Also, the availability of connective tissue at the donor site may limit the effectiveness of soft tissue augmentation, especially when deep horizontal alveolar defects and/or large edentulous gaps require augmentation (Surdiacourt & Cosyn, 2023). For these reasons, xenogeneic collagen matrices have been developed.

Preclinical (Thoma et al., 2017) and clinical studies (Huber et al., 2018; Naenni et al., 2018; Thoma et al., 2016, 2020, 2023; Zeltner et al., 2017) have been published on a cross-linked porcine-derived collagen matrix (CMX) (Geistlich Fibro-Gide, Geistlich Pharma AG) with promising results up to 5 years. However, its effectiveness needs to be validated because all publications come from the same

group and relate to the same study population of 10 patients per group. Multi-centre RCTs provide the highest external validity because data are delivered by multiple surgeons, thereby providing a large patient sample. Hitherto, two multi-centre RCTs have been conducted comparing CTG with CMX to increase soft tissue thickness at the buccal aspect of single implants (Cosyn et al., 2021, 2022; Hämmerle et al., 2023). The present study reports on the 3-year outcomes of one of these studies (Cosyn et al., 2021, 2022). The primary objective was to compare CTG with CMX in terms of increase in buccal soft tissue profile (BSP) after 3 years when applied at single implant sites showing a minor horizontal alveolar defect.

## 2 | MATERIALS AND METHODS

### 2.1 | Patients

The present study was designed as a follow-up of patients previously enrolled in a multi-centre RCT comparing the superiority of CTG and CMX (Cosyn et al., 2021). Patients requiring a single implant restoration in the premaxilla were screened from September 2019 and treated between January 2020 and September 2020 on the basis of inclusion and exclusion criteria.

Inclusion criteria were as follows:

- At least 21 years old;
- Good oral hygiene, defined as full-mouth plaque score  $\leq 25\%$  (O'Leary et al., 1972);
- Presence of a single tooth gap in the pre-maxilla (15–25) with both neighbouring teeth present;
- Failing tooth removed at least 3 months prior to enrolment;
- At least 5 mm of keratinized mucosa available at the single tooth gap;
- Class I defect at the single tooth gap as clinically assessed (bucco-palatal loss of tissue with a normal apico-coronal ridge height) (Seibert, 1983);

- Bucco-palatal bone dimension of at least 6 mm at the central and crestal aspect of the single tooth gap as assessed by cone-beam computed tomography (CBCT) to ensure complete embedding of an implant by bone;
- Signed informed consent.

Exclusion criteria were as follows:

- Systemic diseases
- Smoking
- Periodontal disease
- Untreated caries lesions
- Need for horizontal bone augmentation at the time of implant placement.

The study was approved by the Ethics Committee of Ghent University Hospital (B670201940413) and registered in ClinicalTrials.gov (NCT04210596). It was conducted in accordance with the ethical standards of the Declaration of Helsinki of 1975, as revised in 2013. The study is reported following the guidelines of the CONSORT (Schulz et al., 2010).

## 2.2 | Randomization, allocation concealment and blinding

Six experienced and calibrated implant surgeons working in different periodontal practices in Belgium were selected to participate in this multi-centre RCT. Details can be found in an earlier paper (Cosyn et al., 2021). Employing block randomization, patients were allocated to either the control group (CTG) or the test group (CMX). The disclosure of group allocation was withheld from the evaluating examiner and statistician to allow for unbiased registrations and analyses, respectively.

## 2.3 | Treatment procedures

Details on treatment procedures and post-operative care have been described in a previous publication (Cosyn et al., 2021). In summary, a low-dose, small-field CBCT and intra-oral scan were taken and imported into designated software (DTX Studio, Nobel Biocare AB, Göteborg, Sweden) to fabricate a stereolithographic surgical guide and a screw-retained CAD/CAM provisional restoration (TempShell, Nobel Biocare AB).

Following full-thickness mucoperiosteal flap elevation, a dental implant (NobelReplace CC PMC TiUnite, Nobel Biocare AB) was placed using a surgical guide. Thereupon, a sealed envelope was opened revealing the assignment to one of two treatment modalities:

- Control group: autogenous CTG, and
- Test group: CMX (Geistlich Fibro-Gide, Geistlich Pharma AG).

In the control group, a CTG was harvested from the palatal mucosa in the premolar region using the single incision technique as described by De Bruyckere et al. (2015). The size of the CTG was customized to fit the dimensions of the defect. A haemostatic gelatin sponge (Spongostan Dental 1 × 1 × 1 cm, Ethicon, Johnson & Johnson, New Brunswick, VS) was applied in the palatal wound and the incision was closed with cross-sutures (Vicryl Plus 4/0, Ethicon, Johnson & Johnson International, Diegem, Belgium). For the test group, CMX was used. Its dimensions were adapted to fit the defect using a scalpel and scissors. After periosteal release, the graft was positioned in the buccal envelope and secured with two single sutures (Seralon 6/0, Serag Wiessner, Naila, Germany) onto the buccal mucosa.

Following the installation of the screw-retained provisional restoration (TempShell, Nobel Biocare AB), tension-free primary wound closure was achieved. Sutures were removed after 2 weeks. The provisional crown was replaced with a permanent crown by the general dentist after 3 months.

## 2.4 | Increase in buccal soft tissue profile

Details on data acquisition can be found in an earlier paper (Cosyn et al., 2021). In brief, an intra-oral scan (Trios, 3shape, Copenhagen, Denmark) was taken at the following time points: T0 (pre-op), T1 (immediately post-op), T2 (3 months), T3 (1 year) and T4 (3 years). The obtained digital surface models in STL (Surface Tessellation Language) were processed using designated imaging software (SMOP, Swissmeda AG, Zurich, Switzerland) by a blinded examiner.

A study-relevant area of interest (AOI) at the buccal aspect was selected for each augmented site. This AOI spanned from 0.5 mm below the soft tissue margin to 4 mm apically and extended in the mesio-distal dimension from the mesial to distal line angle of the implant crown. Although the exact dimensions of the AOI varied among patients because of individual anatomical distinctions, it remained consistent for each patient throughout the different time points.

Comparisons between each time point and the pre-operative model (T0–T1, T0–T2, T0–T3 and T0–T4) were made by aligning the two models using an algorithm that best fitted unchanged adjacent tooth surfaces. Mean volumetric changes were calculated by the software, which were then divided by the AOI size to determine the mean linear increase in BSP (Figure S1).

## 2.5 | Secondary outcomes

### 2.5.1 | Patients' aesthetic satisfaction

Patients' aesthetic satisfaction was assessed using a visual analogue scale (VAS). All patients were asked the following question: 'How satisfied are you with the aesthetic outcome of the soft tissues surrounding the implant?' Patients responded on a 100-mm line with 'most unsatisfied' and 'most satisfied' positions as extremes.

## 2.5.2 | Complications

Complications, biological or technical, were recorded by the treating surgeon. In this paper, only the complications that occurred between 1- and 3-year follow-up are reported.

## 2.5.3 | Marginal bone loss

Peri-apical radiographs were taken with the long-cone paralleling technique at implant placement as well as at 1 year and 3 years. Measurements were performed by a blinded examiner using designated software (DBSWIN Imaging Software, Dürr Dental SE, Bietigheim-Bissingen, Germany). Radiographs were calibrated on the basis of implant length. The distance from the implant–abutment interface to the initial bone-to-implant contact (called bone level) was assessed at the mesial and distal aspects of each implant. Marginal bone loss was calculated by subtracting bone levels at 1 and 3 years from those at implant placement. Mean values were calculated to arrive at one value per implant.

## 2.5.4 | Probing depth, plaque and bleeding on probing

The treating surgeon evaluated plaque and bleeding on probing at four sites around the implant (mesio-buccal, buccal, disto-buccal and oral) at 1 and 3 years after surgery. Each area received a score of 0 or 1, representing the absence or presence of plaque or bleeding on probing. The total score represents the number of sites with plaque or bleeding present.

## 2.5.5 | Peri-implant mucositis and peri-implantitis

The proportion of implants showing peri-implant mucositis and peri-implantitis was determined 3 years after surgery. Case definitions were adopted from the 2017 World Workshop on the classification of periodontal and peri-implant diseases and conditions (Renvert et al., 2018).

## 2.5.6 | Midfacial recession

Midfacial recession was assessed using the same software (SMOP) by a blinded examiner. A reference line, aligned with the implant orientation, was drawn to establish a perpendicular line at the level of the mucosal margin and crown on the post-operative digital surface model (T1). Subsequently, a parallel line was drawn at the mucosal margin on the T2, T3 and T4 models. Comparisons between each time point and the post-operative model (T1–T2, T1–T3 and T1–T4) were conducted by aligning the two models using an algorithm that best fitted unchanged adjacent tooth surfaces. The distance between the reference line and the parallel lines was defined as midfacial recession at

the different time points. Positive values indicated midfacial recession, whereas negative values denoted vertical regrowth.

## 2.5.7 | Pink Esthetic Score and Mucosal Scarring Index

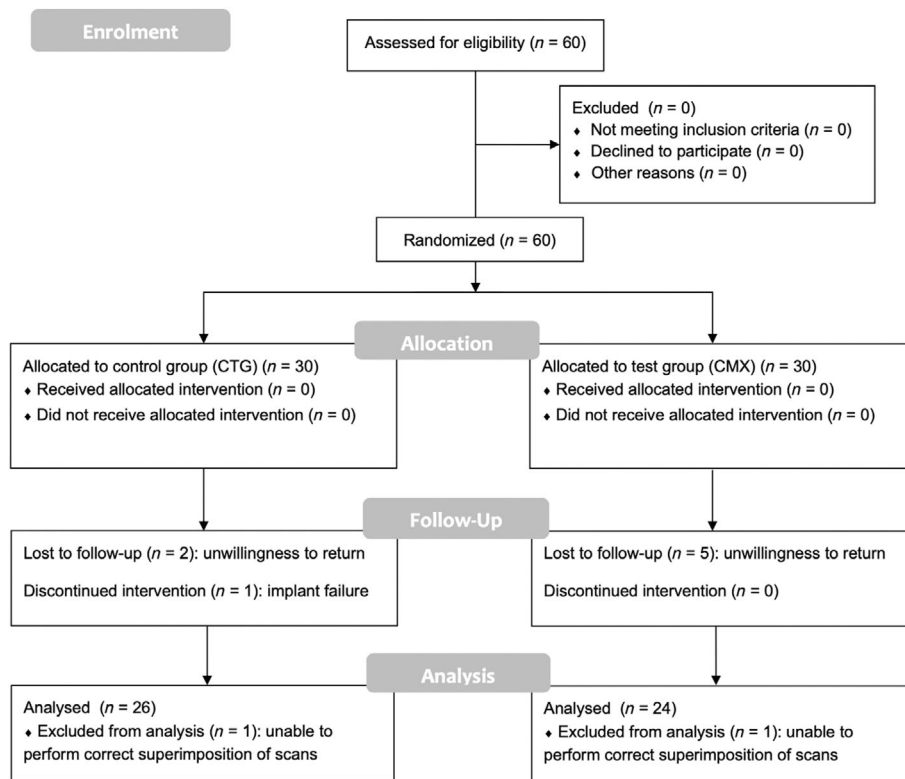
Pink Esthetic Score (PES) (Fürhauser et al., 2005) and Mucosal Scarring Index (MSI) (Wessels et al., 2019) were registered by a trained and blinded examiner using frontal and occlusal clinical pictures taken at 3 years. Prior to assessment, the examiner was calibrated on the basis of clinical images from the 1-year follow-up time point. PES is scored from 0 (worst aesthetic outcome) to 14 (perfect aesthetic outcome), and MSI is scored from 0 (no scar) to 10 (most extreme scar).

## 2.6 | Statistical analysis

The study with a total sample size of 60 patients (30 in each group) was powered to find a mean difference between groups in increase in BSP of at least 0.5 mm. Details on the sample size calculation can be found in an earlier paper (Cosyn et al., 2021). Data analysis was performed using SPSS Statistics 28 (IBM Corp. Released 2021, IBM SPSS Statistics for Windows, version 28.0, IBM Corp, Armonk, NY).

Linear mixed models were used to analyse all outcomes, except for those on the number of sites with plaque or bleeding on probing, for which negative binomial generalized linear mixed models were fitted (with the natural logarithm of the total number of sites as offset variable). Treatment group, time point and their interaction were included as fixed factors in the models, while patient and centre were included as random factors to take into account the repeated measurements within patients and the clustering of patients within centres, respectively. The estimated marginal mean outcome at T4 with 95% confidence interval (CI) was reported for each group, together with the estimated mean difference between groups with 95% CI. Furthermore, the *p*-value from the Type III test of fixed effects for the interactions between group and time points was reported to indicate whether the mean difference between groups was different among any of the time points. Finally, the estimated marginal means with 95% CI were plotted by the treatment group and time point. The Satterthwaite method was used in all models to calculate the degrees of freedom. The analyses included the available information of all subjects (even of those who could not be re-examined at T4) and gave valid inferences under the assumption that outcomes missing at T4 were missing at random. For the primary outcome, the Benjamini–Hochberg method was applied to correct for multiple testing. Therefore, *p*-values from all time points were ranked in an ascending order, each individual *p*-value's Benjamini–Hochberg critical value was calculated and the largest *p*-value with a critical value below 0.05 was identified.

Inter-assessor reliability for PES and MSI was evaluated based on 10 cases scored by two independent and blinded examiners using the two-way mixed, single-rater, absolute agreement intra-class correlation coefficient (ICC).



**FIGURE 1** CONSORT flow diagram. CMX, collagen matrix; CTG, connective tissue graft.

### 3 | RESULTS

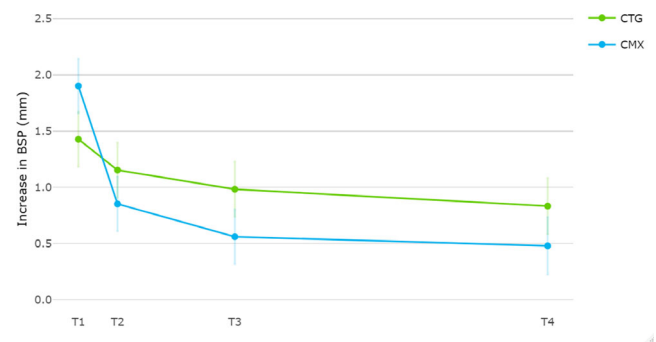
#### 3.1 | Patients

The control group (CTG) included 15 males and 15 females with a mean age of 50.1 years (SD 17.0), while the test group consisted of 14 males and 16 females with a mean age of 48.2 years (SD 16.3). After a 3-year follow-up period, 50 patients could be re-examined (26 in the control group and 24 in the test group). Details on implant positions, length, diameter and initial horizontal defect dimension per group can be found in a previous publication (Cosyn et al., 2021).

In the control group, one implant was lost at 1-week follow-up. No additional implant failures were observed. Seven patients were not willing to return for the 3-year re-assessment, two from the control group and five from the test group. At T4, the primary outcome could not be assessed in one patient from each group because the STL files could not be superimposed. Figure 1 shows the CONSORT flow diagram.

#### 3.2 | Increase in buccal soft tissue profile

The estimated mean difference in BSP increase between the groups was significantly different among the time points ( $p < .001$ ), as can be seen in Figure 2. The Benjamini–Hochberg method was applied to correct for multiple testing when analysing the differences at the four time points and identified



**FIGURE 2** Increase in buccal soft tissue profile (BSP) per treatment group and time point (estimated marginal means; 95% confidence interval). CMX, collagen matrix; CTG, connective tissue graft.

0.035 as the largest  $p$ -value smaller than the critical value of .05. Thus,  $p$ -values  $\leq .035$  indicated significant differences between the groups. At T1, the estimated mean difference was in favour of the test group ( $p = .001$ ) because CMX grafts were thicker than CTGs. The differences at later time points were in favour of the control group (T2:  $p = .035$ ; T3:  $p = .004$ ; T4:  $p = .021$ ). At T4, the estimated mean increase in BSP amounted to 0.83 mm (95% CI: 0.58–1.08) in the control group and 0.48 mm (95% CI: 0.22–0.73) in the test group, pointing to an estimated mean difference of 0.35 mm (95% CI: 0.06–0.65) (Table 1). Four percent of the variability in increase in BSP could be explained by the centre and 11% by the patient.

**TABLE 1** Three-year outcomes.

	Control group (CTG)	Test group (CMX)	Difference	p-Value
Increase in buccal soft tissue profile (mm)	0.83 (0.58–1.08)	0.48 (0.22–0.73)	0.35 (0.06–0.65)	.021
Patients' aesthetic satisfaction (VAS)	89.61 (82.89–96.33)	91.80 (85.02–98.58)	–2.19 (–9.68 to 5.31)	.563
Marginal bone loss (mm)	0.71 (0.40–1.01)	1.13 (0.82–1.44)	–0.43 (–0.77 to –0.09)	.015
Probing depth (mm)	3.17 (2.64–3.71)	3.39 (2.86–3.93)	–0.22 (–0.63 to 0.19)	.286
Plaque (mean no. of sites/4)	0.36 (0.17–0.78)	0.30 (0.13–0.68)	0.06 (–0.25 to 0.37)	.676
Bleeding on probing (mean no. of sites/4)	0.62 (0.28–1.34)	0.55 (0.25–1.21)	0.07 (–0.32 to 0.46)	.732
Midfacial recession (mm)	0.26 (0.01–0.50)	0.19 (–0.07–0.44)	0.07 (–0.24 to 0.38)	.667
Pink Esthetic Score (/14)	10.93 (10.28–11.58)	10.55 (9.88–11.23)	0.38 (–0.45 to 1.20)	.366
Mucosal Scarring Index (/10)	2.14 (1.48–2.79)	1.77 (1.08–2.46)	0.37 (–0.56 to 1.30)	.438

Note: Estimated marginal means at T4 (95% confidence interval), estimated mean difference between groups at T4 (95% confidence interval) and the corresponding p-value.

Abbreviations: CMX, collagen matrix; CTG, connective tissue graft; VAS, visual analogue scale.

### 3.3 | Secondary outcomes

#### 3.3.1 | Patients' aesthetic satisfaction

At T4, the estimated mean VAS for patients' aesthetic satisfaction was 89.61 (95% CI: 82.89–96.33) and 91.80 (95% CI: 85.02–98.58) in the control group and test group, respectively. The estimated mean difference of –2.19 (95% CI: –9.68 to 5.31) between the groups was not significant (Table 1).

#### 3.3.2 | Complications

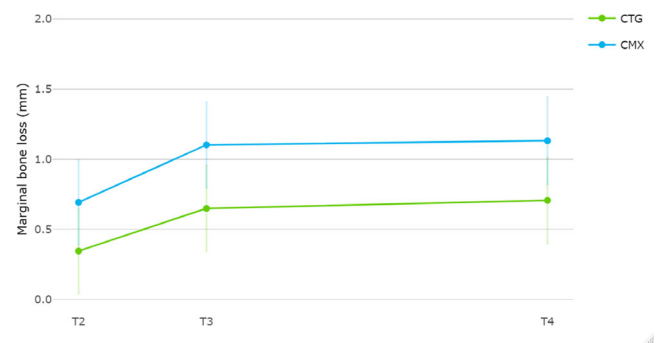
Apart from one crown chipping in the test group, no complications were reported.

#### 3.3.3 | Marginal bone loss

At T4, the estimated mean marginal bone loss amounted to 0.71 mm (95% CI: 0.40–1.01) in the control group and 1.13 mm (95% CI: 0.82–1.44) in the test group. The estimated mean difference of –0.43 mm (95% CI: –0.77 to –0.09) in favour of the control group was significant ( $p = .015$ ) (Table 1). There was no indication that the estimated mean difference between the groups was different among any of the time points ( $p = .821$ ), as can be seen in Figure 3.

#### 3.3.4 | Probing depth, plaque and bleeding on probing

At T4, the estimated mean probing depth amounted to 3.17 mm (95% CI: 2.64–3.71) in the control group and 3.39 mm (95% CI: 2.86–3.93) in the test group. The estimated mean difference of –0.22 mm (95% CI: –0.63 to 0.19) between the groups was not significant ( $p = .286$ ) (Table 1). There was no indication that the estimated mean difference



**FIGURE 3** Marginal bone loss per treatment group and time point (estimated marginal means; 95% confidence interval). CMX, collagen; CTG, connective tissue graft.

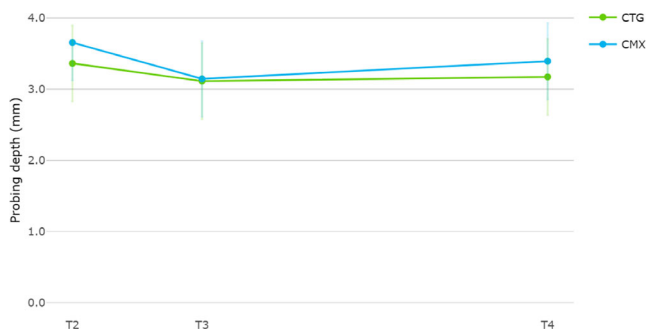
between the groups was different among any of the time points ( $p = .450$ ), as can be seen in Figure 4.

At T4, the estimated mean number of sites with plaque was 0.36 (95% CI: 0.17–0.78) and 0.30 (95% CI: 0.13–0.68) in the control group and test group, respectively. The estimated mean difference of 0.06 (95% CI: –0.25 to 0.37) between the groups was not significant ( $p = .676$ ) (Table 1). There was no indication that the estimated mean difference between the groups was different among any of the time points ( $p = .607$ ).

At T4, the estimated mean number of bleeding on probing sites was 0.62 (95% CI: 0.28–1.34) and 0.55 (95% CI: 0.25–1.21) in the control group and test group, respectively. The estimated mean difference of 0.07 (95% CI: –0.32 to 0.46) between the groups was not significant ( $p = .732$ ) (Table 1). There was no indication that the estimated mean difference between the groups was different among any of the time points ( $p = .989$ ).

#### 3.3.5 | Peri-implant mucositis and peri-implantitis

At T4, 10 implants in the control group and 7 implants in the test group showed peri-implant mucositis. These patients received



**FIGURE 4** Probing depth per treatment group and time point (estimated marginal means; 95% confidence interval). CTG, connective tissue graft; CMX, collagen.

polishing and oral hygiene reinforcement. At T4, none of the implants in the control group, but two implants in the test group, showed peri-implantitis. These patients received non-surgical debridement, polishing and oral hygiene reinforcement. In addition, they were scheduled for re-evaluation 3 months later.

### 3.3.6 | Midfacial recession

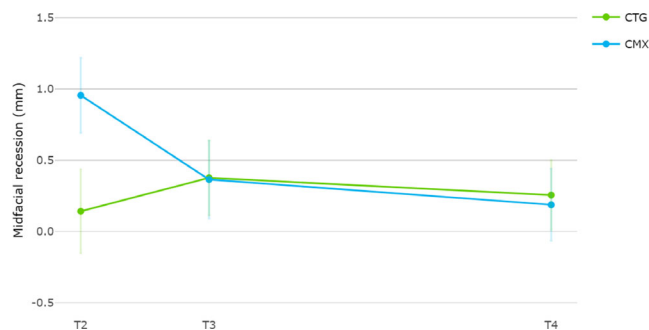
At T4, the estimated mean midfacial recession was 0.26 mm (95% CI: 0.01–0.50) in the control group and 0.19 (95% CI: –0.07 to –0.44) in the test group. The estimated mean difference of 0.07 mm (95% CI: –0.24 to 0.38) between the groups was not significant ( $p = .667$ ) (Table 1). The estimated mean differences between the groups were significantly different among time points ( $p < .001$ ), as can be seen in Figure 5. That is, the estimated mean difference was in favour of the control group at T2 but not at subsequent time points.

### 3.3.7 | Pink Esthetic Score

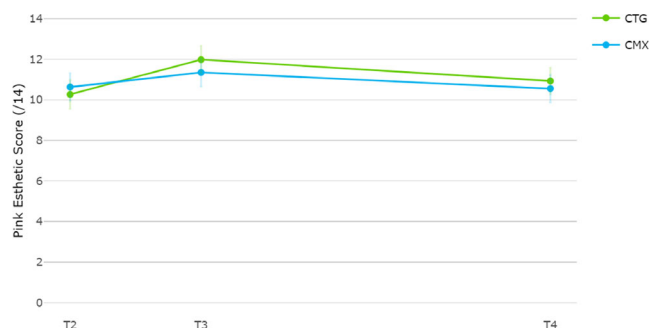
The ICC for assessing inter-assessor reliability on PES was 0.930 (95% CI: 0.640–0.984) suggesting excellent agreement between duplicate measurements. At T4, the estimated mean PES was 10.93 (95% CI: 10.28–11.58) in the control group and 10.55 (95% CI: 9.88–11.23) in the test group. The estimated mean difference of –0.38 (95% CI: –0.45 to 1.20) between the groups was not significant ( $p = .366$ ) (Table 1). There was no indication that the estimated mean difference between the groups was different among any of the time points ( $p = .139$ ), as can be seen in Figure 6.

### 3.3.8 | Mucosal Scarring Index

The ICC for assessing inter-assessor reliability on MSI was 0.960 (95% CI: 0.857–0.990) suggesting excellent agreement between duplicate measurements. At T4, the estimated mean MSI was 2.14 (95% CI: 1.48–2.79) in the control group and 1.77 (95% CI: 1.08–2.46) in the



**FIGURE 5** Midfacial recession per treatment group and time point (estimated marginal means; 95% confidence interval). CMX, collagen; CTG, connective tissue graft.



**FIGURE 6** Pink Esthetic Score per treatment group and time point (estimated marginal means; 95% confidence interval). CMX, collagen; CTG, connective tissue graft.

test group. The estimated mean difference of –0.37 (95% CI: –0.56 to 1.30) between the groups was not significant ( $p = .438$ ) (Table 1). There was no indication that the estimated mean difference between the groups was different among any of the time points ( $p = .783$ ).

## 4 | DISCUSSION

This multi-centre RCT confirms the effectiveness of soft tissue augmentation at the buccal aspect of single implants up to 3 years of follow-up. However, a significant impact of the grafting material was found. After 3 years of follow-up, buccal soft tissues were on average 0.35 mm thicker for CTG when compared to CMX, which is in accordance with recent systematic reviews (Cairo et al., 2019; Tavelli, Barootchi, Avila-Ortiz, et al., 2021). Whether this difference is clinically relevant may be a matter of debate. In this context, the final increase in BSP is relevant to consider, which amounted to only 0.48 mm for CMX. One could question if an increase of such magnitude is relevant enough, given the cost for the patient. On the other hand, CMX simplified surgical procedures and reduced surgery time (Cosyn et al., 2021). In addition, the difference in effectiveness failed to have a significant impact on aesthetic parameters. From the patients' perspective, aesthetic satisfaction was high both for CTG and CMX, yet no significant difference could be observed between

the groups. Similarly, midfacial recession was less than 0.3 mm, PES surpassed 10 and MSI was below 2.5 for both CTG and CMX. No significant difference between the groups could be observed for any of these parameters. These findings corroborate that CTG and CMX may lead to favourable aesthetic outcomes. Because a second surgical site is not required for CMX, patient-reported outcomes (PROMs) were expected to be clearly in favour of CMX. Surprisingly, no significant differences could be observed in post-operative bleeding, pain, intake of analgesics and oedema between CTG and CMX during the early stages of healing (Cosyn et al., 2021). In contrast, PROMs were generally in favour of CMX in another multi-centre RCT (Hämmerle et al., 2023), even though the single incision technique had been used for CTG harvesting in both studies. Possibly, differences in graft dimensions and palatal wounds can explain the discrepancy in PROMs between the two multi-centre trials. Indeed, CTGs had an average dimension of 240 mm<sup>3</sup> and were applied at the buccal and occlusal aspects using a two-stage approach in the study of Hämmerle et al. (2023). In the present study, CTGs had an average dimension of 152 mm<sup>3</sup> and were applied only at the buccal aspect using a one-stage approach. In this context, it is noteworthy that CTG dimensions have a relevant impact on the willingness of patients to undergo surgery again (Burkhardt et al., 2015; Tavelli, Barootchi, Di Gianfilippo, et al., 2021; Zucchelli et al., 2010). In addition, a palatal island flap was coronally advanced in the study of Hämmerle et al. (2023), making the surgery more invasive and leaving an area on the palate for secondary healing. This may have had an impact on pain perception. Altogether, the findings of the present study suggest that patients may cope well with possible discomfort due to CTG harvesting, at least when used for the treatment of minor defects. This is in accordance with a recent systematic review on soft tissue augmentation at implant sites describing similar PROMs for CTG and CMX (Stefanini et al., 2021).

Looking at the changes in BSP over time, similar dynamics could be observed for both grafting materials. Although CMX was, on average, thicker than CTG at the time of application, most volume loss was seen during the early stages of healing in both groups, resulting in only minute loss after 1 year of follow-up. This is in accordance with other studies on the same comparison (Thoma et al., 2020, 2023).

Apart from effectiveness and aesthetic parameters, clinical outcomes are always relevant to consider. At 3 years of follow-up, there were no significant differences between the groups in terms of plaque, bleeding on probing or probing depth. However, marginal bone loss was significantly higher for CMX at all time points. These differences may reflect more inflammation at CMX-treated sites during the early stages of healing due to cross-linking of the matrix (Rothamel et al., 2014; Thoma et al., 2012). In that respect, clinical parameters such as bleeding on probing and probing depth may be more reversible, whereas marginal bone loss may be more permanent. In any case, marginal bone loss is an important parameter in the long term, as it is the main diagnostic criterion for peri-implantitis.

Based on all parameters, CTG remains the gold standard for soft tissue augmentation of minor horizontal alveolar defects. Because CMX simplifies surgical procedures, specific indications may justify its use. These include soft tissue augmentation in pain-sensitive patients, and in patients requiring concise surgery due to anxiety or medical reasons.

For a correct interpretation of the present study, the following limitations need to be acknowledged. First, CMX was, on average, thicker than CTG at the time of application, which may be considered a bias. This relates to the fact that CMX is offered in 6 mm thickness by the manufacturer, whereas the thickness of the palatal mucosa sets a limit to what can be harvested. Second, the sample size calculation was based on the primary outcome, which renders this study possibly underpowered for other parameters. Third, plaque, bleeding on probing and probing depth were assessed by the treating surgeon, which could have introduced information bias. Finally, radiographs were not standardized, which could have had an impact on the results of marginal bone loss.

Long-term RCTs should include a negative control (no soft tissue augmentation) and a cost-effectiveness analysis. Costs for rehabilitation, supportive care and complication management need to be taken into account in such analysis.

## 5 | CONCLUSION

CTG was more effective in increasing buccal soft tissue profile and resulted in less marginal bone loss than CMX. Therefore, CTG remains the gold standard to increase soft tissue thickness at implant sites.

### AUTHOR CONTRIBUTIONS

**Lenz Surdiacourt:** Data analysis; first, second and final draft. **Véronique Christiaens:** Research protocol; surgeon; data interpretation; second and final draft. **Thomas De Bruyckere:** Research protocol; surgeon; data interpretation; second and final draft. **Stefanie De Buysers:** Data analysis; final draft. **Aryan Eghbali:** Research protocol; surgeon; data interpretation; second and final draft. **Stijn Vervaeke:** Research protocol; surgeon; data interpretation; second and final draft. **Faris Younes:** Research protocol; surgeon; data interpretation; second and final draft. **Jan Cosyn:** Principal investigator; funding; coordinator; research protocol development; surgeon; data interpretation; second and final draft.

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Prof. Cosyn has collaboration agreements with Nobel Biocare AB (Göteborg, Sweden) and Straumann (Basel, Switzerland). Dr. Stijn Vervaeke has a collaboration agreement with Denstply Sirona (Mölnal, Sweden).

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

This study was approved by the Ethics Committee of Ghent University Hospital (B670201940413).

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## SUPPORTING INFORMATION

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