Received: 2 March 2022 | Revised: 8 June 2022 | Accepted: 12 June 2022

DOI: 10.1111/jcpe.13685

ORIGINAL ARTICLE

Journal of Clinical Periodontology WILEY

Soft and hard tissue changes after immediate implant placement with or without a sub-epithelial connective tissue graft: Results from a 6-month pilot randomized controlled clinical trial

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Funding information
BioSAF IN Srl

Abstract

Aim: The present pilot RCT aimed to investigate the influence of a connective tissue graft (CTG) in combination with the immediate implant placement (IIP) on hard and soft tissue healing, without a bone replacement graft in the gap between the implant and the socket walls.

Materials and Methods: Thirty patients requiring extraction of one anterior tooth (from premolar to premolar) were randomly assigned to one of the two treatment groups (test: IIP + CTG; control: IIP). Cone-beam computed tomography and optically scans were performed before tooth extraction and at 6-month follow-up. Then, DICOM files were superimposed in order to allow the evaluation of osseous ridge and buccal bone changes, while the superimposition of DICOM and Standard Tessellation Language files allowed for evaluating of soft tissue contour. For testing the differences between the two groups, the non-parametric test as Wilcoxon rank-sum test, was used.

Results: Twenty-six of the 30 enrolled patients attended the 6-month follow-up visit. The four patients of the control group that were lost to follow-up were analysed under the intention-to-treat principle. No statistically significant differences between the groups were observed for the vertical buccal bone resorption ($p = .90$), as well as for the horizontal buccal bone resorption at all measured levels. Significant differences were found between the test and control groups in the horizontal dimensional changes of osseous ridge at the most coronal aspect ($p = .0003$ and $p = .02$). Changes in tissue contour were between −0.32 and −0.04 mm in the test group and between −1.94 and −1.08 mm in the control group, while changes in soft tissue thickness varied between 1.33 and 2.42 mm in the test group and between −0.16 and 0.88 mm in the control group, with statistically significant differences for both variables at all measured levels. At 6 months, the mean volume increase was 6.76 ± 8.94 mm^3 and 0.16 ± 0.42 mm^3 in the test and control groups, respectively, with a statistically significant difference.

Conclusions: The findings of the present study indicate that the adjunct of a CTG at the time of IIP, without bone grafting, does not influence vertical bone resorption.

Within the limits of this study, it can be suggested that the adjunct of a CTG at the time of IIP, without bone grafting, reduces the horizontal changes of the alveolar ridge. Moreover, it allows maintenance of the tissue contour due to an increase in soft tissue thickness.

KEYWORDS
bone changes, connective tissue graft, immediate implant placement, soft tissues management

Clinical relevance

Scientific rationale for study: No clinical study has evaluated the effect of a connective tissue graft (CTG) per se at the time of immediate implant placement (IIP). Hence, it is unknown whether the CTG may influence the hard and soft tissue changes that occur.

Principal findings: Minor dimensional changes in the horizontal ridge dimension were observed in the IIP + CTG group at the most coronal aspect. Moreover, a minor reduction in tissue contour was reported in the test group, due to a pronounced soft thickness gain.

Practical implications: IIP plus a CTG may be a valid treatment option, to compensate for hard tissue morphological changes and to maintain the tissue contour.

1 | INTRODUCTION

Immediate implants have shown to be a predictable treatment for the replacement of non-restorable teeth (Lang et al., 2012; Vignoletti & Sanz, 2014a, 2014b). The surgical protocol presents clear advantages in terms of reducing the number of interventions, and the overall treatment time. However, compromised aesthetic has been anticipated especially when utilized in the upper anterior maxilla (Sanz et al., 2010; Cosyn et al., 2013; Cecchinato et al., 2015). There are several factors that may influence aesthetic outcomes, being the buccal bone wall integrity and thickness (Sanz et al., 2010; Ferrus et al., 2010; Tomasi et al., 2010), implant position (Evans & Chen, 2008), and the use of bone grafts within the gap (Sanz et al., 2017), among the most relevant. Hence, it should be considered as a complex surgical procedure that should only be performed in case of ideal anatomic conditions (Tonetti et al., 2019). Several studies demonstrated that immediate implant placement (IIP) fails to prevent the horizontal and vertical ridge alterations following tooth extraction (Araujo et al., 2005; Discepoli et al., 2015; Vignoletti, Discepoli et al., 2012; Vignoletti & Sanz, 2014a, 2014b). Although Several studies demonstrated that immediate implant placement (IIP) fails to prevent the horizontal and vertical ridge alterations following tooth extraction (Araujo et al., 2005; Discepoli et al., 2015; Vignoletti, Discepoli et al., 2012; Vignoletti & Sanz, 2014a, 2014b). Although it has been suggested that these bone dimensional changes are compensated by soft tissues during early healing (Chappuis et al., 2017), nevertheless the reduction of soft tissue contour on long-term follow-up may greatly affect the aesthetic outcome of the prosthetic reconstruction. In a recent study, Sanz-Martín et al. (2019) investigated the interplay between hard and soft tissues after flapless IIP in combination with a buccally inserted xenogeneic bovine bone graft and a xenogeneic porcine collagen matrix in the aesthetic area. The authors reported an overall horizontal osseous ridge resorption (ORR) of about 50% of the original dimension. This was in part compensated by an increase in thickness of the buccal soft tissues. Notwithstanding this fact, a mean of 0.67 ± 0.65 mm of linear horizontal soft tissue reduction as compared to baseline was observed.

Therefore, it becomes apparent that soft tissue management with the use of connective tissue graft (CTG) around implants is of outmost importance to mimic natural ideal conditions, and for this reason, it has become a topic of growing interest for clinicians.

To the best of the authors' knowledge, no randomized controlled clinical trial has compared the outcome of a CTG on buccal bone changes following immediate implant positioning without a bone replacement graft in the implant–socket gap.

Recently in the literature, there is a growing body of evidence suggesting that the soft tissue thickness can exert a protective activity towards bone resorption. This effect was proposed for implant inserted in healed sites, where the soft tissue thickness demonstrated an influence over crestal bone changes at 1 year (Linkevicius et al., 2009; Puisys & Linkevicius, 2015). In a recent systematic review with meta-analyses on the efficacy of soft tissue augmentation procedures and their impact on peri-implant health, authors stated that bilaminar techniques with CTG or collagen matrix showed beneficial effects on marginal bone-level stability (Tavelli et al., 2021). Similar conclusions were described by De Angelis et al. (2021) in a systematic review of the effect of soft tissue augmentation on the clinical and radiographical outcomes following IIP: authors reported that a statistically significant reduced change of the marginal bone loss and vestibular recession is associated with soft tissue augmentation. Nevertheless, the 6th EAO Consensus on soft tissue management at implants stated that "the present scientific evidence does not consistently demonstrate a benefit of soft tissue augmentation procedures in terms of marginal bone level changes" (Thoma et al., 2021).

Therefore, the purpose of the present pilot RCT was to investigate the influence of a CTG in combination with the IIP

on hard and soft tissue healing, without a bone replacement graft in the gap between the implant and the socket walls. The primary objective was to evaluate radiologically the vertical buccal bone dimensional changes, whereas the secondary objectives were to evaluate horizontal dimensional changes of buccal bone and of osseous ridge and linear and volumetric soft tissue changes.

2 | MATERIALS AND METHODS

2.1 | Study design

The study was designed as a pilot randomized controlled clinical trial with a parallel design and single-blinded approach, performed at the Dental Department of San Raffaele Hospital (Milan, Italy). The study protocol was approved by the Ethical Committee of San Raffaele Hospital (with number of protocol "Winsix 1"—EC Reg. N. 71/INT/2017), registered on ClinicalTrial.gov (NCT03784430) and performed in accordance with the Helsinki Declaration of Human Studies. All subjects gave written informed consent.

2.2 | Patient samples

Adults (≥18 years of age) were screened on the basis of having a single hopeless tooth candidate for extraction in the maxillary or mandibular area (from second premolar to second premolar) in need of a single implant-supported fixed prosthetic rehabilitation.

Patients were selected on the basis of fulfilment of the following inclusion criteria:

- The presence of the intact walls of the socket after tooth extraction, or presenting a maximum of 3 mm of buccal dehiscence;
- The distance between interdental bone crest and buccal bone crest ≤3 mm after tooth extraction.

Patients were excluded if they had any of these conditions: general contraindications for dental and/or surgical treatments; inflammatory and autoimmune disease of oral cavity; uncontrolled diabetes; concurrent or previous immunosuppressant, bisphosphonate, or high-dose corticosteroid therapy; concurrent or previous radiotherapy of head area; smokers (>10 cigarettes a day); pregnancy; or lactating women.

2.3 | Randomization, allocation concealment, blinding, and calibration

Patients were assigned to one of the two treatment groups with the use of computer-generated randomization table (test group: immediate implant + CTG; control group: immediate implant). Treatment assignment was concealed to the treating surgeon by opaque envelopes that were opened only after completion of tooth extraction and final assessment of the feasibility of IIP. Clinical and radiographic measures and statistical analyses were performed blind with respect to treatment assignment.

For calibration of clinical measurements, the examiner (G.L.D.D.) measured the keratinized tissue width of 10 patients twice, at 1 week interval. After repeated measurements, the inter-class correlation coefficients for intra-examiner reliability were 0.958 (95% CI: 0.664, 0.955).

All radiographic measurements were carried out by one calibrated and blinded examiner (V.C.), who superimposed and measured baseline and 6-month cone-beam computed tomography (CBCT) and Standard Tessellation Language (STL) images of 10 randomly selected cases twice, at 1 week interval. After repeated measurements, the inter-class correlation coefficient was 0.978 (95% CI: 0.884–0.966).

2.4 | Study interventions

Surgeries were performed by one surgeon (D.G.) at the Dental Clinic of the San Raffaele Hospital.

After local anaesthesia, a buccal split-full-split-thickness envelope flap, as described for the treatment of multiple gingival recessions by Zucchelli and de Sanctis (2000), was elevated, and the tooth was extracted atraumatically.

The flap was incised according to the indications of Zucchelli and de Sanctis (2000), utilizing the site of implant positioning as the center of rotation of the flap. The mesial and distal anatomic papillae were maintained in place.

The osteotomy was prepared with the surgical drill of the surgical kit (Winsix, BioSAF IN Srl, Ancona, Italy) at 1200 rpm under saline irrigation. An implant (Winsix KE, Winsix, BioSAF IN Srl) was immediately inserted with 1 mm of its transmucosal portion positioned under the buccal bone crest, as suggested by previous pre-clinical and clinical studies (Caneva et al., 2010; Vignoletti & Sanz, 2014a, 2014b; Calvo-Guirado et al., 2018; Linkevicius et al., 2020).

In the test group, a CTG resulting from the extra-oral de-epithelialization of a free gingival graft harvested from the palate was positioned coronal to the buccal bone crest and anchored to the anatomic papillae. It was carefully positioned in contact with the implant surface, in such a way that it completely covered the buccal gap, and the buccal crest 2 mm in the apical direction.

In both groups of implants, healing abutments were positioned. The buccal flap was coronally advanced by means of deep and superficial split-thickness incisions and the flap was tightly adapted to the healing abutment. Modified sling sutures were performed to accomplish an accurate adaptation of the buccal flap and to stabilize every single surgical papilla over the inter-dental connective tissue bed of the anatomical papilla.

Examples of the two treatment groups are shown in Figure 1.

Patients were instructed to rinse twice a day (starting the day after surgery) with 0.2% chlorhexidine and received antibiotics (amoxicillin with clavulanic acid 1 g) twice a day for 6 days and analgesic medication (ibuprofen 600 mg) if needed.

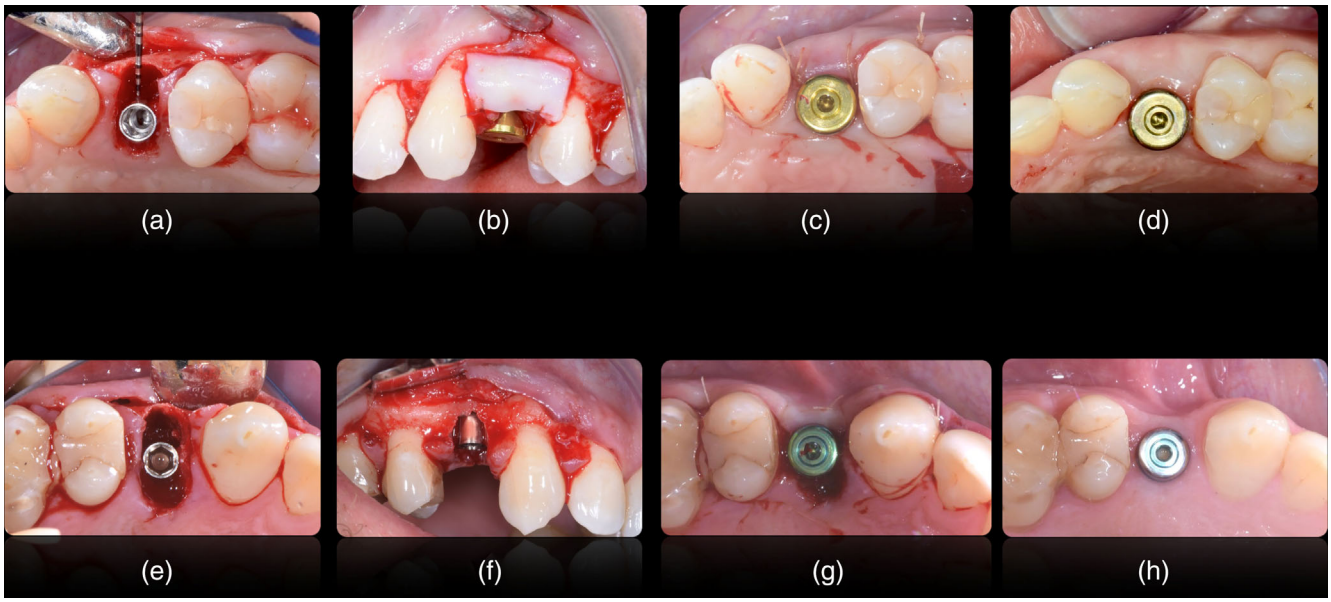

FIGURE 1 Intra-operative view of the two treatment modalities. Clinical case from the test group depicting: (a) the implant placed in the fresh extraction socket, (b) the connective tissue graft sutured to the anatomic papillae, (c) the suture of the flap, and (d) the implant site at 6 months of follow-up. Clinical case from the control group depicting: (e) the occlusal view of the implant placed in the fresh extraction socket, (f) the buccal view of the implant, (g) the suture of the flap, and (h) the implant site at 6 months of follow-up

No implant-supported temporary restorations were used for the first 6 months.

At 6 months after the implant placement, the patient returned for the clinical and radiographic evaluation.

2.5 | Outcomes and study power

The primary outcome of the study was the comparison of the vertical buccal bone resorption (VBBR) at 6 months following IIP in the test and control groups. The study was powered to detect a minimum clinically significant difference in radiographic changes of buccal bone height on CBCT of 1 mm using $\alpha = .05$, a power of 80%, and a hypothesized within-group sigma of 0.9 mm, obtained from previous studies (Jung et al., 2013). As a minimum, 14 patients per treatment arm were selected for power analysis calculation. To compensate for missing data and attrition, a sample size of 30 was selected.

Secondary outcomes included the following: (i) comparison of horizontal buccal bone resorption (HBBR) and osseous ridge resorption (ORR); (ii) comparison of changes in soft tissues parameters—width of keratinized mucosa, soft tissue contour, soft tissue thickness, soft tissue volume; and (iii) comparison of patient experience with the surgical procedures, using a visual analogue scale (VAS) score.

2.6 | Clinical measurements

Clinical measurements were performed at the time of implant placement by a blind and calibrated examiner (G.L.D.D.) to the nearest millimetre using a periodontal probe (Hu-Friedy Diagnostic Probe UNC15 Qulix, Hu-Friedy Mfg. Co. Inc.).

The width of keratinized tissue (KT width) was measured at the buccal aspect, prior to tooth extraction. After the extraction and flap elevation, the thickness of the buccal bone wall (BC thick), was measured 2 mm apical of the most coronal buccal bone crest using a calliper (Iwanson calliper, DP720; Bontempi snc, Quirurgical Bontempi, Barcelona, Spain).

After implant placement, a gap occurred between the implant surface and the buccal bone wall of the extraction socket. The following measurements were taken (Figure 2):

- S-IC, internal horizontal buccal gap dimension, that is, the width of the gap between the implant surface and the inner surface of buccal bone crest;
- S-OC, horizontal buccal crest dimension (bucco-lingual dimension), that is the distance between the implant surface and the outer surface of the buccal bone crest;
- R-B, vertical distance between the implant shoulder to top of the buccal bone crest. Since the implants were placed 1 mm below the buccal bone plate, this measure had a value of −1 mm for all the implants.

2.7 | Hard tissue measurements

For each patient, a CBCT scan (NewTom VGi evo, QR S.r.l., Verona) of the relevant site was performed prior to tooth extraction (BL) and

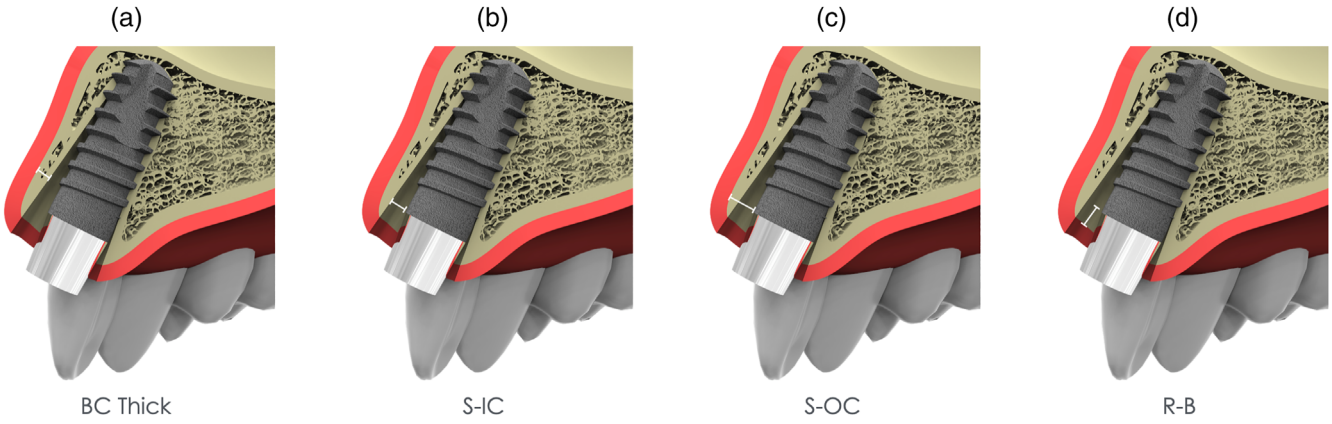

FIGURE 2 Clinical measurements. (a) BC thick: Thickness of the buccal bone. (b) S-IC: Internal horizontal buccal gap dimension. (c) S-OC: Horizontal buccal crest dimension (bucco-lingual dimension). (d) R-B: Vertical distance between the implant shoulder to top of the buccal bone crest

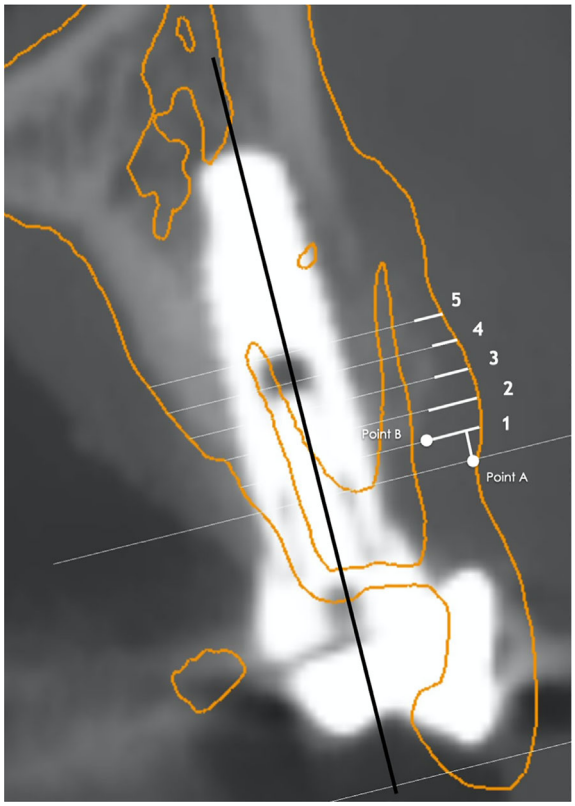

FIGURE 3 Superimposition of baseline DICOM (orange) and 6-month follow-up. Horizontal white lines represent the assessment of the horizontal buccal bone resorption (HBBR) at 1, 2, 3, 4, and 5 mm below the most coronal point of the buccal osseous ridge (point A). Vertical white line represents the measurement of vertical buccal bone resorption (VBBR)

6 months after implant placement (6M), to evaluate hard tissue dimensional changes.

Baseline DICOM files were first converted into an STL file and then superimposed to 6M DICOM file, by selecting common reference points from the adjacent tooth surfaces. The screenshot representing the mesio-distal center of the dental implant was selected to perform linear measurements, using an image analysis software program (ImageJ, National Institutes of Health, MD, USA). All radiographic superimpositions and measurements were carried out as described by Sanz-Martín et al. (2019), by one calibrated and blinded examiner (V.C.).

The following landmarks were identified in the cross-sectional image:

- point A, the most coronal point of the buccal crest of the baseline socket;
- point B, the most coronal point of the buccal crest at 6 months after implant insertion.

Five parallel lines were drawn perpendicular to a line coinciding with the longitudinal axis of the implant and at 1, 2, 3, 4, and 5 mm below to the point A and the following parameters were recorded (Figure 3):

- VBBR, which was calculated by measuring the vertical linear distance from point A to point B.
- HBBR, which was the horizontal linear distance between the outer surface of buccal bone at BL and that at 6M (measurements were expressed in mm and %);
- ORW, osseous ridge width, which was the horizontal linear distance from the outer surface of buccal bone to the outer surface of palatal/lingual bone, measured at baseline and at 6 months. The ORR in millimetres (mm) and in percentage (%ORR) were also calculated.

2.8 | Soft tissue measurements

The relevant upper/lower jaw segment was optically scanned using a 3D scanner (Cerec Omnicam, Dentsply Sirona, York, PA, USA) in order to create STL files and assess soft tissue dimensional changes occurring between BL examination and 6 months after implant placement.

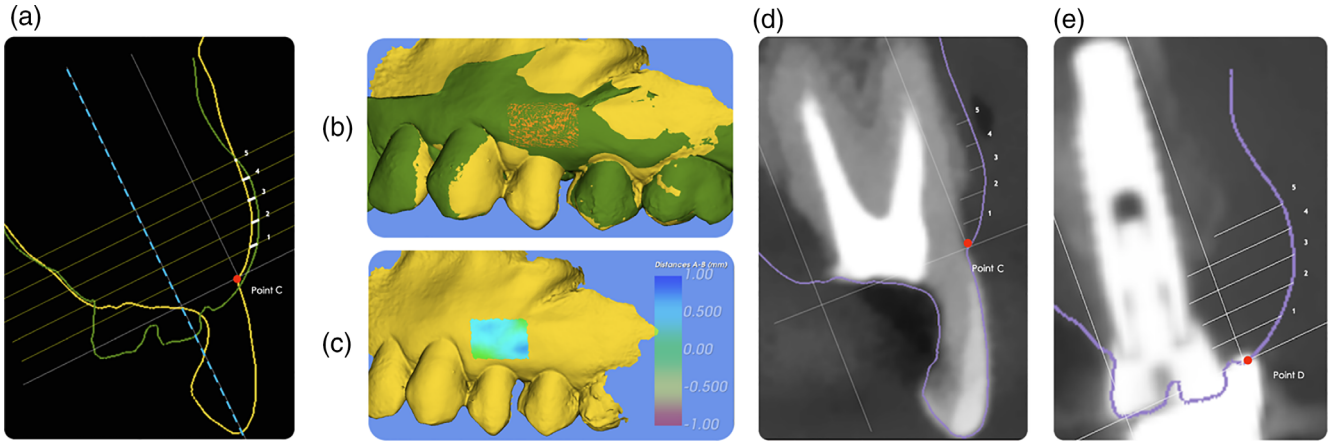

FIGURE 4 Soft tissue measurements. (a) Cross-sectional view of superimposition of baseline (yellow) and 6-month (green) Standard Tessellation Language (STL) files. White lines represent the linear measurements made 1, 2, 3, 4, and 5 mm below the gingival margins (point C). (b) Superimposition of baseline (yellow) and 6-month (green) STL files showing the area of interest for volumetric analysis (orange). (c) Superimposition showing gradients of volumetric variations. (d) Baseline DICOM and STL files superimposed allowing for the evaluation of baseline soft tissue thickness. White lines represent the soft tissue thickness 1, 2, 3, 4, and 5 mm below the gingival margin (point C). (e) Six-month DICOM and STL files superimposed allowing for the evaluation of baseline soft tissue thickness. White lines represent the soft tissue thickness 1, 2, 3, 4, and 5 mm below the gingival margin (point D)

2.8.1 | Soft tissue contour

STL file superimpositions and soft tissue dimensional changes measurements were executed by one calibrated and blinded examiner (V.C.), using a volume comparative software program (SMOP, Swissmeda AG, Zurich, Switzerland) and an image analysis software program (ImageJ, National Institutes of Health. Maryland, USA), as described by Sanz-Martín et al. (2019).

Linear measurements were performed by selecting the cross section representing the mesio-distal center of the tooth crown. A screenshot of the selected cross section was uploaded to five parallel lines drawn perpendicular to a line coinciding with the longitudinal axis of the tooth crown and at 1, 2, 3, 4, and 5 mm apical to the BL gingival margin (point C). Then, the buccal soft tissue contour changes (Δ STC) were calculated by measuring at these different heights, the horizontal linear distance between the buccal soft tissue contour at BL to the one at 6M and were expressed in millimetres (Figure 4).

Volumetric measurements were performed by selecting an area of interest delimited apico-coronally by the gingival margin of the tooth and the mucogingival line and mesiodistally by a vertical line passing through the center of inter-dental papillae (Figure 4). The software calculated the volume changes in cubic millimetres.

2.8.2 | Soft tissue thickness

Superimposition of DICOM file, representing hard tissue volume, to STL file representing soft tissue contour, was used to measure the buccal soft tissue thickness in the two different treatment groups. DICOM-STL analysis were performed by one calibrated and blinded examiner (V.C.) adopting a methodology reported by Sanz-Martín et al. (2019).

DICOM files at BL and 6M were matched to STL file respectively at BL and 6M using the same digital imaging software mentioned for STL files superimposition (SMOP, Swissmeda AG, Zurich, Switzerland). Screenshots of the cross-section images representing the mesio-distal center of the tooth at BL and the mesio-distal center of the implant at 6M were then exported to the previously mentioned image processing software program (ImageJ, National Institutes of Health, MD, USA).

A common vertical axis was selected for both the BL and 6M cross-section images. Five parallel lines were drawn perpendicular to this axis at 1, 2, 3, 4, and 5 mm respectively apical to the BL and 6M gingival margin (points C and D, respectively). The buccal soft tissue thickness (STT) was then evaluated by measuring at these different heights, the linear distance between the buccal soft tissue outline to the buccal bone at BL and 6M and was expressed in millimeteres (Figure 4).

2.9 | Statistical analysis

Mean and standard deviation for continuous variables were used as indices of centrality and dispersion of the variable distribution. For testing the differences between the two groups, the non-parametric test as Wilcoxon rank-sum test was used.

The Spearman rank correlation coefficient was used to test the strength and direction of association that may exist between the percentage of osseous ridge resorption (%ORR) and the following variables: BC thick, S-IC, S-OC, soft tissue total thickness (that includes STT at baseline and the CTG thickness), and CTG thickness. When testing the null hypothesis of no association, the probability level of error at two tails was 0.05.

All analyses were based on the intention-to-treat principle with mean imputation technique (ITT analysis, i.e., the mean value of a

variable is used in place of the missing data value for that same variable). Primary and secondary endpoints were also evaluated in the per-protocol collective (PP analysis).

Statistical computations were made using StataCorp 2021 (Stata Statistical Software: Release 17, StataCorp LLC, College Station, TX).

3 | RESULTS

3.1 | Study population

Patient recruitment was conducted from November 2018 to December 2020. The causes for the tooth extraction were several and included root fracture, caries, root resorption, or endodontic failure.

Thirty patients were enrolled; of these, four patients of the control group did not complete the follow-up evaluation. Hence, a total of 26 patients attended the 6-month follow-up visit. The four patients who were lost to follow-up were analysed under the intention-to-treat principle. In this way, all 30 patients were included in the statistical analysis.

The sample consisted of 17 women and 13 men with a mean age of 53.4 ± 12.2 years (range: 34–74 years) (Figure 5).

Twenty-four implants were placed in the maxilla and six in the mandible. Five implants (1 central incisor, 2 lateral incisors, 1 canine) were located at anterior sites and 23 at premolar sites. Twenty-four implants were 3.8 mm in diameter (the corresponding diameter of the endo-osseous portion was 4.0 mm), while six implants were 4.5 mm (the corresponding diameter of the endo-osseous portion was 4.7 mm) (Table 1). A CTG was applied in 15 implants (test group).

3.2 | Clinical outcomes

At baseline, the thickness of the buccal bone measured at 2 mm from bone margin ranged from a minimum of 0.2 mm to a maximum of 1.9 mm, but did not reveal any statistically significant differences between the two treatment groups (ITT analysis—test group: 0.84 [0.39] mm, control group: 1.03 [0.49] mm, $p = .16$; PP analysis—test group: 0.84 [0.39] mm, control group: 1.04 [0.58], $p = .41$).

After IIP, the mean horizontal buccal gap (S-IC) was 2.59 ± 0.77 and 2.73 ± 0.90 mm, in the control and test group, respectively. The difference between the groups was not statistically significant ($p = .70$).

All implants healed adequately without any complications.

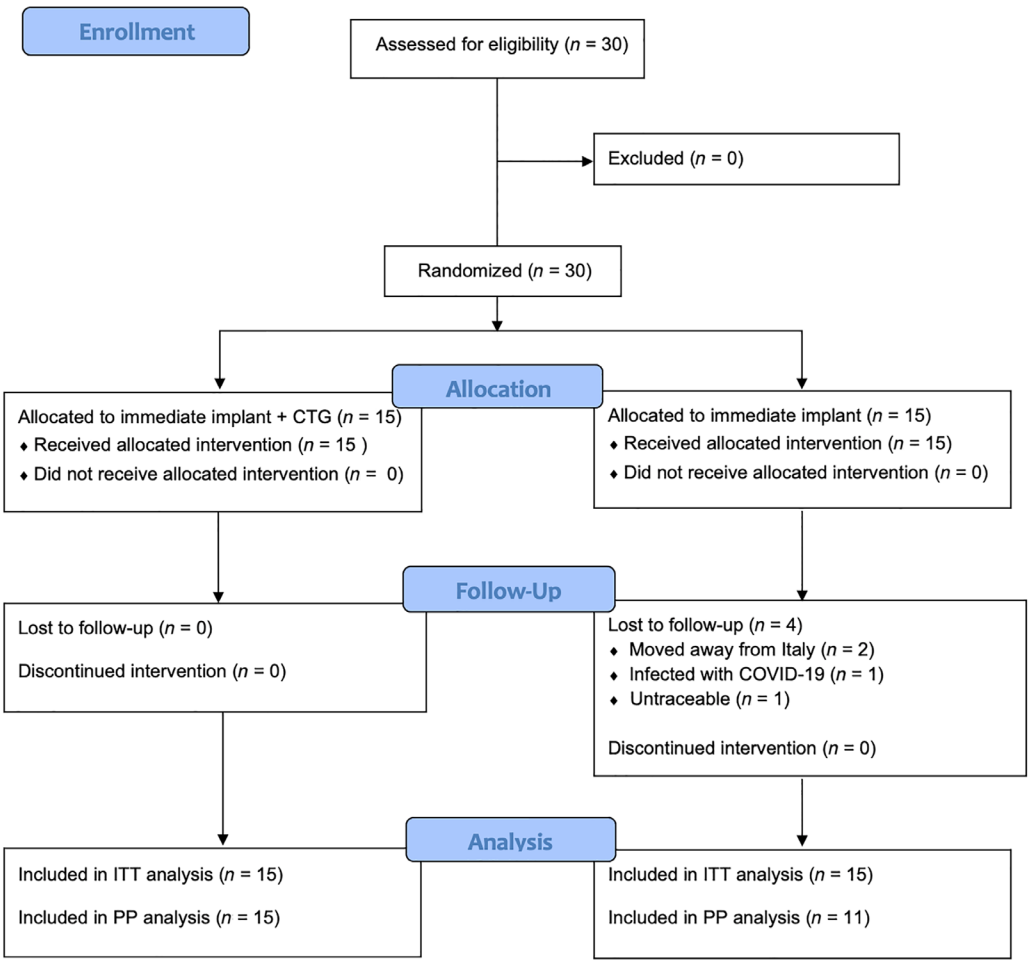

FIGURE 5 CONSORT flow diagram

TABLE 1 Characteristics of the implants

	Per-protocol analysis		Intention-to-treat analysis	
	Control group ($n = 11$)	Test group ($n = 15$)	Control group ($n = 15$)	Test group ($n = 15$)
Arch (upper/lower)	9/2	13/2	12/3	12/3
Position (anterior/premolar)	0/11	3/12	2/13	3/12
Diameter (3.8/4.5 mm)	8/3	12/3	12/3	12/3
Length (9/11/13/15 mm)	2/6/3	0/6/7/2	2/10/3	0/6/7/2

TABLE 2 Changes in horizontal and vertical dimensions of buccal bone (HBBR and VBBR) and in osseous ridge width (ORR) among the two treatment groups

	Per-protocol analysis			Intention-to-treat analysis		
	Control group ($n = 11$)	Test group ($n = 15$)	p value*	Control group ($n = 15$)	Test group ($n = 15$)	p value*
VBBR (mm)	−0.66 (0.75)	−0.66 (0.53)	.75	−0.66 (0.63)	−0.66 (0.53)	.90
HBBR 1 (mm)	−1.59 (0.63)	−1.36 (1.17)	.13	−1.59 (0.54)	−1.36 (1.17)	.05
HBBR 2 (mm)	−1.13 (0.47)	−0.89 (0.70)	.19	−1.13 (0.4)	−0.89 (0.70)	.10
HBBR 3 (mm)	−0.96 (0.44)	−0.73 (0.53)	.18	−0.96 (0.37)	−0.73 (0.53)	.13
HBBR 4 (mm)	−0.79 (0.40)	−0.69 (0.39)	.55	−0.79 (0.34)	−0.69 (0.39)	.37
HBBR 5 (mm)	−0.7 (0.40)	−0.66 (0.45)	.27	−0.78 (0.34)	−0.66 (0.45)	.14
HBBR 1 (%)	44.62 (19.86)	38.82 (26.56)	.55	44.6 (16.8)	38.82 (26.56)	.20
ORR 1 (mm)	−2.08 (0.65)	−1.16 (0.5)	.003**	−2.09 (0.53)	−1.16 (0.5)	.0003**
ORR 2 (mm)	−1.66 (0.95)	−1.03 (0.66)	.084	−1.66 (0.79)	−1.03 (0.66)	.02**
ORR 3 (mm)	−1.45 (0.89)	−0.95 (0.6)	.244	−1.45 (0.76)	−0.95 (0.6)	.10
ORR 4 (mm)	−1.13 (0.69)	−1.05 (0.68)	.721	−1.13 (0.59)	−1.05 (0.68)	.72
ORR 5 (mm)	−1.06 (0.58)	−0.94 (0.56)	.443	−1.06 (0.49)	−0.94 (0.56)	.31
ORR 1 (%)	22 (6)	14 (6)	.018**	22 (5)	14 (6)	.006**
ORR 2 (%)	17 (9)	11 (7)	.095	17 (7)	11 (7)	.04**
ORR 3 (%)	15 (8)	10 (6)	.239	15 (7)	10 (6)	.10
ORR 4 (%)	12 (7)	11 (7)	.678	12 (6)	11 (7)	.69
ORR 5 (%)	11 (6)	10 (5)	.467	11 (5)	10 (5)	.42

Abbreviations: HBBR, horizontal buccal bone resorption; ORR, osseus ridge resorption; VBBR, vertical buccal bone resorption.
*Wilcoxon rank-sum test (Mann–Whitney). ** Statistically significant.

3.3 | Hard tissue dimensional changes

3.3.1 | Vertical changes

The mean loss in height (VBBR) amounted to −0.66 ± 0.53 mm in the test group and −0.66 ± 0.53 mm in the control group, with no significant differences ($p = .9$). For results of the PP analysis, see Table 2.

3.3.2 | Horizontal changes

The majority of the horizontal changes of the buccal bone (HBBR) occurred at 1 mm below the most coronal aspect of the buccal wall with similar changes between the two treatment groups (Table 2). Changes were in fact −1.59 ± 0.54 mm for the control group and −1.36 ± 1.17 mm for the test group, without statistically significant differences ($p = .05$).

When evaluating the ORR, that is, the mean reduction of the alveolar crest in the bucco-lingual width (measured as difference between ORW at baseline and ORW at 6 months), the results indicated −2.09 ± 0.53 mm and −1.16 ± 0.5 mm of horizontal dimensional changes at 1 mm and −1.66 ± 0.79 mm and −1.03 ± 0.66 mm at 2 mm, in control and test groups, respectively. These differences

TABLE 3 Spearman correlation between bone and soft tissue baseline dimensions and osseus ridge resorption at 1 mm (%)

	Per-protocol analysis ($n = 26$) %ORR 1*	Intention-to-treat analysis ($n = 30$) %ORR 1*
BC thick	0.04 (0.42)	−0.084 (0.68)
S-IC	0.14 (0.49)	0.19 (0.33)
S-OC	0.13 (0.53)	0.07 (0.70)
Soft tissue total thick	−0.464 (0.02)**	−0.597 (0.0012)**
CTG thick	−0.457 (0.02)**	−0.57 (0.002)**

Abbreviations: CTG; connective tissue graft; %ORR, percentage of osseus ridge resorption.
*ρ, Rho di Spearman and p value.
**Statistically significant.

TABLE 4 Changes in linear and volumetric soft tissue contour (Δ STC) and in soft tissue thickness (Δ STT) among the two treatment groups

	Per-protocol analysis			Intention-to-treat analysis		
	Control group ($n = 11$)	Test group ($n = 15$)	p value*	Control group ($n = 15$)	Test group ($n = 15$)	p value*
Δ STC 1 (mm)	−1.94 (0.99)	−0.32 (0.97)	.002**	−1.94 (0.83)	−0.32 (0.97)	.0007**
Δ STC 2 (mm)	−1.85 (0.92)	−0.04 (0.74)	<.0001**	−1.85 (0.78)	−0.04 (0.74)	.00003**
Δ STC 3 (mm)	−1.57 (0.75)	0.11 (0.66)	<.0001**	−1.57 (0.63)	0.11 (0.66)	.00001**
Δ STC 4 (mm)	−1.30 (0.75)	0.18 (0.70)	.0002**	−1.30 (0.64)	0.18 (0.70)	.00006**
Δ STC 5 (mm)	−1.08 (0.80)	0.13 (0.81)	.003**	−1.08 (0.80)	0.13 (0.81)	.004**
Δ STC volume (mm^3)	0.16 (0.49)	6.76 (8.94)	.002**	0.16 (0.42)	6.76 (8.94)	.0015**
Δ STT 1 (mm)	−0.16 (0.72)	1.47 (1.08)	.0001**	−0.16 (0.61)	1.47 (1.08)	.00005**
Δ STT 2 (mm)	0.12 (0.83)	2.04 (1.18)	.0002**	0.12 (0.70)	2.04 (1.18)	.00008**
Δ STT 3 (mm)	0.81 (1.14)	2.42 (1.63)	.007**	0.81 (0.96)	2.42 (1.63)	.003**
Δ STT 4 (mm)	0.88 (1.05)	2.07 (1.22)	.02**	0.88 (0.88)	2.07 (1.22)	.008**
Δ STT 5 (mm)	0.11 (0.90)	1.33 (1.17)	.01**	0.11 (0.76)	1.33 (1.17)	.005**

*Wilcoxon rank-sum test (Mann–Whitney).
**Statistically significant.

were statistically significant ($p = .0003$ and $p = .02$, respectively). The corresponding values in percentage were 22 ± 5% and 14 ± 6% at 1 mm and 17 ± 7% and 11 ± 7% at 2 mm, in control and test groups, respectively (Table 2).

3.3.3 | Factors influencing bone resorption

The correlation analysis identified only a significant (negative) relationship between the resorption of osseous ridge width (% ORR) and the soft tissue total thickness, which includes STT at baseline and the CTG thickness ($r = -0.464$, $p = .02$) (Table 3). Scatterplots of the different correlations tested are shown in the Supplementary file 1.

3.4 | Soft tissues dimensional changes

3.4.1 | Tissue contour

At 6-month follow-up examination, a horizontal reduction in the dimensions of the tissue contours was observed in both test and control groups. This change in horizontal dimension was between −0.32 and −0.04 mm in the test group, and between −1.94 and −1.08 mm in the control group. The pairwise analysis showed statistically significant differences between the two groups at all levels (Table 4).

At 6 months, the mean volume increase was 6.76 ± 8.94 mm^3 and 0.16 ± 0.42 mm^3 in the test and control groups, respectively, with statistically significant difference ($p = .0015$). For results of the PP analysis, see Table 4.

3.4.2 | Soft tissue thickness

After 6 months, the test group experienced significantly more tissue thickness gain at 1, 2, 3, 4, and 5 mm from the gingival margin than the control group compared with baseline. This change ranged between 1.33 and 2.42 mm in the test group, and between −0.16 and 0.88 mm in the control group (Table 4).

3.4.3 | KT width

At 6-month follow-up, the mean keratinized width was 3.64 ± 1.29 mm and 4.53 ± 1.36 mm in the control and test groups respectively, with no statistically significant difference ($p = .14$). There was a gain in the dimension of KT, which was of 0.14 ± 1.28 mm and of 0.6 ± 1.71 mm in the control and test groups, respectively ($p = .51$).

3.5 | Patient-reported outcomes

Post-operative pain and discomfort were evaluated with questionnaires using VAS at the 1-week post-operative appointment. Although both procedures were well tolerated, a significant difference was observed comparing the two procedures (ITT analysis—test group: 2.73 [1.62]; control group: 1.07 [0.70]; $p = .0009$; PP analysis—test group: 2.73 [1.62]; control group: 1.09 [0.83]; $p = .0049$).

4 | DISCUSSION

4.1 | Hard tissue dimensional changes

IIP was introduced in order to reduce the number of surgical procedures and potentially limit physiological reduction of the ridge dimensions following tooth extraction (Schulte & Heimke, 1976; Lazzara, 1989). The present study confirms findings from previous investigations that this procedure fails to prevent the horizontal and vertical ridge alterations (Araujo et al., 2005; Vignoletti, Discepoli, et al., 2012; Vignoletti,

Matesanz, et al., 2012; Vignoletti & Sanz, 2014a, 2014b; Discepoli et al., 2015).

Data of the current study reveal a reduction of the bone height at 6 months of 0.6 mm, both in test (SD 0.53 mm) and control groups (SD 0.75 mm). These data suggest that the height of the bone is only slightly modified during the healing phases, that is, a stable clinical bone-to-implant relation can be achieved even in the presence of a thin buccal socket wall (<1 mm). These data are in agreement with the study by Sanz et al. (2017), which reported 0.3 mm of vertical changes at the buccal crest both in the test and the control groups.

When evaluating horizontal ridge resorption, results of the present study show a reduction of 2.09 ± 0.53 mm (22 ± 5%) for the control group and 1.16 ± 0.51 mm (14 ± 6%) for the test group, with statistically significant differences. The amount of horizontal ORR observed in the control sites is comparable to the data reported by previous studies, namely Sanz et al. (2017) (16%).

On the other hand, results from the test group are similar to the results obtained with the use of a bone substitute graft in the gap between the implant surface and the bone wall: Sanz et al. (2017) reported horizontal mean changes of −1.26 ± 1.75 mm (11%), whereas Clementini et al. (2019) reported a change of −1.29 ± 0.38 mm (14.9 ± 4.9%). Therefore, it is conceivable that the CTG will exert a protective effect on the crestal bone loss, both augmenting the STT and providing a precise closure of the gap.

Neither initial buccal bone thickness nor horizontal gap width are significantly correlated with the amount of ORR. These results are in agreement with previous findings (Tomasi et al., 2010; Morimoto et al., 2015; Sanz et al., 2017). As a matter of fact, in the current study bucco-lingual dimensions of the alveolar crest were only influenced moderately by soft tissue total thickness, which includes the gingival thickness at baseline and the CTG thickness. This result is in contrast with the suggestion that the surgical intervention utilized for the application of the CTG could induce higher buccal bone loss because of the disruption in the vascularization between the mucosa and periosteum (Zuiderveld et al., 2021). On the contrary, the utilization of the proposed surgical technique, the modified coronal advanced flap a with split-full-split approach, maintains the integrity of the periosteal vascularization in to the flap and it is ideal for flap closure that should be passive and tension-free. Also, this technique presents other advantages due to the absence of vertical incisions, which will improve both flap vascularization and stability (Zucchelli et al., 2009), while the coronal position of the margin will reduce the risk of flap shrinkage (Baldini et al., 2010). Also, it must be underlying that interdental papillae were not elevated, but maintained in position, this could be another factor could explain the buccal bone protective effect.

In the current study, the mean buccal bone loss found is 44.6 ± 16.8% for the control group and 38.82 ± 26.56% for the test group, without statistically significant difference. The control group data are similar to the results of Sanz et al., which showed 38% of buccal hard tissue loss in the non-grafted sites, and to those of Botticelli et al., which found 56% of buccal bone loss (Botticelli et al., 2004; Sanz et al., 2017).

Our results are not in accordance with Zuiderveld et al.: in their work the connective tissue grafted sites showed higher buccal bone loss resorption when compared to control ones (Zuiderveld et al., 2021). The difference between the two studies could be explained by the different surgical modalities (bone graft was used to fill the gap in both groups) and by the different measurement methodologies; in fact, the buccal bone resorption was measured from the neck of the implant, while in the current study the reference point for the measurement is the most coronal point of buccal bone.

4.2 | Soft tissue findings

Volumetric measurements using STL data demonstrated a pronounced augmentation in tissue contour for the CTG group (6.76 ± 8.94 mm^3) when compared to control sites (0.16 ± 0.42 mm^3) at 6-month follow-up visit.

The observed loss of tissue volume that occurred in the control group may be due to the reduction in width of the osseous ridge, which was not completely compensated by the physiological increase in STT (Chappuis et al., 2015).

The tissue contour in the test group was maintained at all level of the measurements, including in the most coronal zone: this result can be explained due to the position of the CTG, which was sutured to the anatomical papillae, at the level of implant shoulder, so to cover the gap between implant and buccal bone wall, in contrast with Sanz-Martín et al.'s studies (2018, 2019).

When comparing the effect of a CTG on tissue contours after IIP, it should be taken into account that all previous investigations have utilized bone grafting in the gap. Nevertheless, results from the current study were comparable to a recent study by Jiang et al. (2020), which showed a similar contour reduction for the test groups, although bone grafting was used.

Because extraction process itself may cause transient changes in the dimension of the bone and soft tissues (Chappuis et al., 2015), in the present study, we considered data before tooth extraction as the baseline data to allow a more precise evaluation.

STT had a statistically significant increase for CTG sites when compared to control group at 6-month follow-up. Hence, it appears clear that the placement of a CTG maintained the tissue contour and compensated for bone resorption.

When considering the keratinized tissue dimension, it is interesting to notice that although the utilization of CTG, in the test group the KT width did not differ from the control group. This finding is in accordance with the study by Tavelli et al. (2021), which suggests that the absence of the effect could be due to the different composition of peri-implant soft tissues and vascularization when compared with teeth. The absence of the increment of KT could also be explained by the absence of shrinkage of the buccal flap.

For a correct interpretation of the present study, the following limitations need to be taken into account. The present RCT is a pilot study, due to the lack of previous articles at the time of this protocol design, which compare the effect of a CTG on radiographic vertical buccal bone loss after IIP. The primary outcome and the corresponding sample size calculation were based on vertical bone loss, which could explain the lack of significant differences in some secondary outcomes (HBBR) between both treatment groups.

At the same time though, significant differences were found for soft tissue findings, although the power analysis does not apply to them. Hence, these findings should be interpreted with caution until further studies are performed.

In addition, four subjects in the control group did not complete the follow-up and an intention-to-treat analysis was performed in order to overcome this bias.

Furthermore, the present results should be interpreted considering the limited sample size analysed and a skewed distribution of the implant location in the premolar region, which could have an influence on the evaluation of hard tissue changes.

Data showing whether the bone resorption and the soft tissue contour remain stable over the time, as well as data on the aesthetic appearance and acceptance by the patient, should be included in the future trials conducted with long-term follow-up on homogeneous sample.

5 | CONCLUSIONS

The findings of the present study indicate that the adjunct of a CTG at the time of IIP, without bone grafting, does not influence vertical bone resorption. Nevertheless, the use of CTG seems to reduce the horizontal changes of the alveolar ridge that occur. Moreover, it allows maintenance of the tissue contour due to an increase in STT. Nevertheless, data from the present study have to be considered cautiously due to the dimensional limitation. Further trials with long-term follow-up and a larger sample of patients are needed.

AUTHOR CONTRIBUTIONS

Davide Guglielmi: data acquisition (surgery); study design. **Giovanna Laura Di Domenico**: data acquisition; data interpretation; manuscript revision. **Sofia Aroca**: study conception. **Fabio Vignoletti**: data acquisition. **Vincenzo Ciaravino**: data acquisition. **Rossella Donghia**: data analysis. **Massimo de Sanctis**: study design, manuscript revision, final approval.

CONFLICT OF INTEREST

The authors report no conflicts of interests related to the study.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The project "Winsix 1" was approved by the Ethical Commettee of San Raffaele Hospital (Milan, Italy) and it was partially supported by a grant from BioSAF IN Srl (Ancona, Italy).

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REFERENCES

Araújo, M. G., da Silva, J. C. C., de Mendonça, A. F., & Lindhe, J. (2015). Ridge alterations following grafting of fresh extraction sockets in man. A randomized clinical trial. *Clinical Oral Implants Research*, *26*(4), 407–412. https://doi.org/10.1111/clr.12366

Araujo, M. G., Sukekava, F., Wennstrom, J. L., & Lindhe, J. (2005). Ridge alterations following implant placement in fresh extraction sockets: An experimental study in the dog. *Journal of Clinical Periodontology*, *32*, 645–652. https://doi.org/10.1111/j.1600-051X.2005.00726.x

Baldini, A., Zucchelli, G., & de Sanctis, M. (2010). A novel surgical technique for soft tissue in a aesthetic areas of the mouth at implant placement. *Journal de Parodontologia & d'Implantologie Orale*, *29*(4).

Botticelli, D., Berglundh, T., & Lindhe, J. (2004). Hard-tissue alterations following immediate implant placement in extraction sites. *Journal of Clinical Periodontology*, *31*(10), 820–828. https://doi.org/10.1111/j.1600-051X.2004.00565.x

Calvo-Guirado, J. L., López-López, P. J., Pérez-Albacete Martínez, C., Javed, F., Granero-Marín, J. M., Sánchez, M., de Val, J. E., & Ramírez Fernández, M. P. (2018). Peri-implant bone loss clinical and radiographic evaluation around rough neck and microthread implants: A 5-year study. *Clinical Oral Implants Research*, *29*(6), 635–643. https://doi.org/10.1111/clr.12775

Caneva, M., Salata, L. A., de Souza, S. S., Baffone, G., Lang, N. P., & Botticelli, D. (2010). Influence of implant positioning in extraction sockets on osseointegration: Histomorphometric analyses in dogs. *Clinical Oral Implants Research*, *21*(1), 43–49. https://doi.org/10.1111/j.1600-0501.2009.01842.x PMID: 20070746.

Cecchinato, D., Lops, D., Salvi, G. E., & Sanz, M. (2015). A prospective, randomized, controlled study using OsseoSpeedTM implants placed in maxillary fresh extraction socket: Soft tissues response. *Clinical Oral Implants Research*, *26*, 20–27.

Chappuis, V., Araújo, M. G., & Buser, D. (2017). Clinical relevance of dimensional bone and soft tissue alterations post-extraction in esthetic sites. *Periodontology 2000*, *73*(1), 73–83. https://doi.org/10.1111/prd.12167

Chappuis, V., Engel, O., Shahim, K., Reyes, M., Katsaros, C., & Buser, D. (2015). Soft tissue alterations in esthetic postextraction sites: A 3-dimensional analysis. *Journal of Dental Research*, *94*(9 Suppl), 187S–193S. https://doi.org/10.1177/0022034515592869

Clementini, M., Agostinelli, A., Castelluzzo, W., Cugnata, F., Vignoletti, F., & De Sanctis, M. (2019). The effect of immediate implant placement on alveolar ridge preservation compared to spontaneous healing after tooth extraction: Radiographic results of a randomized controlled clinical trial. *Journal of Clinical Periodontology*, *46*, 776–786. https://doi.org/10.1111/jcpe.13125

Cosyn, J., DeBruyn, H., & Cleymaet, R. (2013). Soft tissue preservation and pink aesthetics around single immediate implant restorations: A 1-year prospective study. *Clinical Implant Dentistry and Related Research*, *15*, 847–857.

De Angelis, P., Manicone, P. F., Gasparini, G., De Angelis, S., Liguori, M. G., De Filippis, I., & D'Addona, A. (2021). Influence of immediate implant placement and provisionalization with or without soft tissue augmentation on hard and soft tissues in the esthetic zone: A one-year retrospective study. *BioMed Research International*, *5*, 8822804. https://doi.org/10.1155/2021/8822804

Discepoli, N., Vignoletti, F., Laino, L., de Sanctis, M., Munoz, F., & Sanz, M. (2015). Fresh extraction socket: Spontaneous healing vs. immediate implant placement. *Clinical Oral Implants Research*, *26*, 1250–1255. https://doi.org/10.1111/clr.12447

Evans, C. D., & Chen, S. T. (2008). Esthetic outcomes of immediate implant placements. *Clinical Oral Implants Research*, *19*(1), 73–80. https://doi.org/10.1111/j.1600-0501.2007.01413.x

Ferrus, J., Cecchinato, D., Pjetursson, E. B., Lang, N. P., Sanz, M., & Lindhe, J. (2010). Factors influencing ridge alterations following immediate implant placement into extraction sockets. *Clinical Oral Implants Research*, *21*, 22–29.

Jiang, X., Di, P., Ren, S., Zhang, Y., & Lin, Y. (2020). Hard and soft tissue alterations during the healing stage of immediate implant placement and provisionalization with or without connective tissue graft: A randomized clinical trial. *Journal of Clinical Periodontology*, *47*(8), 1006–1015. https://doi.org/10.1111/jcpe.13331

Jung, R. E., Philipp, A., Annen, B. M., Signorelli, L., Thoma, D. S., Hämmerle, 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*(1), 90–98. https://doi.org/10.1111/jcpe.12027

Lang, N. P., Pun, L., Lau, K. Y., Li, K. Y., & Wong, M. C. (2012). A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. *Clinical Oral Implants Research*, *23*(Suppl 5), 39–66. https://doi.org/10.1111/j.1600-0501.2011.02372.x

Lazzara, R. G. (1989). Immediate implant placement into extraction sites: Surgical and restorative advantages. *International Journal of Periodontics and Restorative Dentistry*, *9*(5), 332–343.

Linkevicius, T., Apse, P., Grybauskas, S., & Puisys, A. (2009). The influence of soft tissue thickness on crestal bone changes around implants: A 1-year prospective controlled clinical trial. *The International Journal of Oral & Maxillofacial Implants*, *24*(4), 712–719.

Linkevicius, T., Puisys, A., Linkevicius, R., Alkimavicius, J., Gineviciute, E., & Linkeviciene, L. (2020). The influence of submerged healing abutment or subcrestal implant placement on soft tissue thickness and crestal bone stability. A 2-year randomized clinical trial. *Clinical Implant Dentistry and Related Research*, *22*(4), 497–506. https://doi.org/10.1111/cid.12903

Morimoto, T., Tsukiyama, Y., Morimoto, K., & Koyano, K. (2015). Facial bone alterations on maxillary anterior single implants for immediate placement and provisionalization following tooth extraction: A superimposed cone beam computed tomography study. *Clinical Oral Implants Research*, *26*(12), 1383–1389. https://doi.org/10.1111/clr.12480

Puisys, A., & Linkevicius, T. (2015). The influence of mucosal tissue thickening on crestal bone stability around bone-level implants. A prospective controlled clinical trial. *Clinical Oral Implants Research*, *26*(2), 123–129. https://doi.org/10.1111/clr.12301

Sanz, M., Cecchinato, D., Ferrus, J., Pjetursson, E. B., Lang, N. P., & Lindhe, J. (2010). A prospective, randomized-controlled clinical trial to evaluate bone preservation using implants with different geometry placed into extraction sockets in the maxilla. *Clinical Oral Implants Research*, *21*(1), 13–21. https://doi.org/10.1111/j.1600-0501.2009.01824.x

Sanz, M., Lindhe, J., Alcaraz, J., Sanz-Sanchez, I., & Cecchinato, D. (2017). The effect of placing a bone replacement graft in the gap at immediately placed implants: A randomized clinical trial. *Clinical Oral Implants Research*, *28*(8), 902–910. https://doi.org/10.1111/clr.12896

Sanz-Martín, I., Encalada, C., Sanz-Sánchez, I., Aracil, J., & Sanz, M. (2019). Soft tissue augmentation at immediate implants using a novel xenogeneic collagen matrix in conjunction with immediate provisional restorations: A prospective case series. *Clinical Implant Dentistry and Related Research*, *21*(1), 145–153. https://doi.org/10.1111/cid.12696

Sanz-Martín, I., Permuy, M., Vignoletti, F., Nuñez, J., Muñoz, F., & Sanz, M. (2018). A novel methodological approach using superimposed micro-CT and STL images to analyze hard and soft tissue volume in immediate and delayed implants with different cervical designs. *Clinical Oral Implants Research*, *29*(10), 986–995. https://doi.org/10.1111/clr.13365

Schulte, W., & Heimke, G. (1976). The Tübingen immediate implant. *Die Quintessenz*, *27*(6), 17–23.

Tavelli, L., Barootchi, S., Avila-Ortiz, G., Urban, I. A., Giannobile, W. V., & Wang, H. L. (2021). Peri-implant soft tissue phenotype modification and its impact on peri-implant health: A systematic review and network meta-analysis. *Journal of Periodontology*, *92*(1), 21–44. https://doi.org/10.1002/JPER.19-0716

Thoma, D. S., Cosyn, J., Fickl, S., Jensen, S. S., Jung, R. E., Raghoebar, G. M., Rocchietta, I., Roccuzzo, M., Sanz, M., Sanz-Sánchez, I., Scarlat, P., Schou, S., Stefanini, M., Strasding, M., & Bertl, K. (2021). Soft tissue management at implants: Summary and consensus statements of group 2. The 6th EAO consensus conference 2021. *Clinical Oral Implants Research*, *32*(Suppl. 21), 174–180. https://doi.org/10.1111/clr.13798

Tomasi, C., Sanz, M., Cecchinato, D., Pjetursson, B., Ferrus, J., Lang, N. P., & Lindhe, J. (2010). Bone dimensional variations at implants placed in fresh extraction sockets: A multilevel multivariate analysis. *Clinical Oral Implants Research*, *21*, 30–36. https://doi.org/10.1111/j.1600-0501.2009.01848.x

Tonetti, M. S., Jung, R. E., Avila-Ortiz, G., Blanco, J., Cosyn, J., Fickl, S., Figuero, E., Goldstein, M., Graziani, F., Madianos, P., Molina, A., Nart, J., Salvi, G. E., Sanz-Martin, I., Thoma, D., Van Assche, N., & Vignoletti, F. (2019). Management of the extraction socket and timing of implant placement: Consensus report and clinical recommendations of group 3 of the XV European workshop in periodontology. *Journal of Clinical Periodontology*, *46*(Suppl 21), 183–194. https://doi.org/10.1111/jcpe.13131

Vignoletti, F., Discepoli, N., Muller, A., de Sanctis, M., Munoz, F., & Sanz, M. (2012). Bone modelling at fresh extraction sockets: Immediate implant placement versus spontaneous healing. An experimental study in the beagle dog. *Journal of Clinical Periodontology*, *39*, 91–97. https://doi.org/10.1111/j.1600-051X.2011.01803.x

Vignoletti, F., Matesanz, P., Rodrigo, D., Figuero, E., Martin, C., & Sanz, M. (2012). Surgical protocols for ridge preservation after tooth extraction. A systematic review. *Clinical Oral Implants Research*, *23*(Suppl 5), 22–38. https://doi.org/10.1111/j.1600-0501.2011.02331.x

Vignoletti, F., & Sanz, M. (2014a). Immediate implants at fresh extraction sockets: From myth to reality. *Periodontology 2000*, *66*(1), 132–152. https://doi.org/10.1111/prd.12044

Vignoletti, F., & Sanz, M. (2014b). Immediate implants at fresh extraction sockets: From myth to reality. *Periodontology*, *2000*(66), 132–152. https://doi.org/10.1111/prd.12044

Zucchelli, G., & De Sanctis, M. (2000). Treatment of multiple recession-type defects in patients with esthetic demands. *Journal of Periodontology*, *71*(9), 1506–1514. https://doi.org/10.1902/jop.2000.71.9.1506

Zucchelli, G., Mele, M., Mazzotti, C., Marzadori, M., Montebugnoli, L., & De Sanctis, M. (2009). Coronally advanced flap with and without vertical releasing incisions for the treatment of multiple gingival recessions: A comparative controlled randomized clinical trial. *Journal of Periodontology*, *80*(7), 1083–1094. https://doi.org/10.1902/jop.2009.090041

Zuiderveld, E. G., van Nimwegen, W. G., Meijer, H. J. A., Jung, R. E., Muhlemann, S., Vissink, A., & Raghoebar, G. M. (2021). Effect of

connective tissue grafting on buccal bone changes based on cone beam computed tomography scans in the aesthetic zone of single immediate implants: A 1-year randomized controlled trial. *Journal of Periodontology*, *92*, 553–561. https://doi.org/10.1002/JPER.20-0217

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How to cite this article: Guglielmi, D., Di Domenico, G. L., Aroca, S., Vignoletti, F., Ciaravino, V., Donghia, R., & de Sanctis, M. (2022). Soft and hard tissue changes after immediate implant placement with or without a sub-epithelial connective tissue graft: Results from a 6-month pilot randomized controlled clinical trial. *Journal of Clinical Periodontology*, *49*(10), 999–1011. https://doi.org/10.1111/jcpe.13685