

Barootchi Shayan (Orcid ID: 0000-0002-5347-6577)  
Mancini Leonardo (Orcid ID: 0000-0002-7030-155X)  
Mendonca Gustavo (Orcid ID: 0000-0003-2290-4046)  
Wang Hom-Lay (Orcid ID: 0000-0003-4238-1799)

## **Early Soft tissue changes following implant placement with or without soft tissue augmentation using a xenogeneic cross-link collagen scaffold: a volumetric comparative study**

Lorenzo Tavelli<sup>1,2,3</sup>, DDS, MS, Shayan Barootchi<sup>1,2</sup>, DMD, Maria Vera Rodriguez<sup>1</sup>, DDS, Leonardo Mancini<sup>4</sup>, DDS, Priscila Ceolin Meneghetti<sup>1,5</sup>, DDS, MS, DDS, Gustavo Mendonça<sup>6</sup>, DDS, MS, PhD, Hom-Lay Wang<sup>1</sup>, DDS, MSD, PhD

<sup>1</sup> Department of Periodontics & Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA

<sup>2</sup> Center for clinical Research and evidence synthesis In oral TissuE RegeneratION (CRITERION), Ann Arbor-Boston, USA

<sup>3</sup> Department of Oral Medicine, Infection, and Immunity, Division of Periodontology, Harvard School of Dental Medicine, Boston, MA, USA

<sup>4</sup> Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy

<sup>5</sup> Escola de Ciencias de Saúde e da Vida, Pontificia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brasil

<sup>6</sup> Department of Biologic and Materials Sciences, Division of Prosthodontics, University of Michigan School of Dentistry, Ann Arbor, MI, USA

### **Correspondence**

Lorenzo Tavelli, DDS, MS

Department of Oral Medicine, Infection, and Immunity, Division of Periodontology

Harvard School of Dental Medicine (HSDM)

188 Longwood Avenue, 02115 Boston, USA

Tel. +1 734-604-4364

Email: [lorenzo\\_tavelli@hsdm.harvard.edu](mailto:lorenzo_tavelli@hsdm.harvard.edu)

**Figures and Tables:** 3 figures and 1 table

**Disclosure statement.** The authors do not have any financial interest in the companies whose materials are included in this article.

**Acknowledgments.** The study was self-funded. The authors would like to thank Datum Dental for donating the collagen scaffolds utilized in this study.

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

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/jerd.12856](https://doi.org/10.1111/jerd.12856)

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<sup>1</sup> Department of Periodontics & Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA

<sup>2</sup> Center for clinical Research and evidence synthesis In oral TissuE RegeneratION (CRITERION), Ann Arbor-Boston, USA

<sup>3</sup> Department of Oral Medicine, Infection, and Immunity, Division of Periodontology, Harvard School of Dental Medicine, Boston, MA, USA

<sup>4</sup> Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy

<sup>5</sup> Escola de Ciências de Saúde e da Vida, Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brasil

<sup>6</sup> Department of Biologic and Materials Sciences, Division of Prosthodontics, University of Michigan School of Dentistry, Ann Arbor, MI, USA

## Correspondence

Lorenzo Tavelli, DDS, MS

Department of Oral Medicine, Infection, and Immunity, Division of Periodontology

Harvard School of Dental Medicine (HSDM)

188 Longwood Avenue, 02115 Boston, USA

Tel. +1 734-604-4364

Email: [lorenzo\\_tavelli@hsdm.harvard.edu](mailto:lorenzo_tavelli@hsdm.harvard.edu)

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## ABSTRACT

**Objective.** Soft tissue augmentation at implant sites has the potential of improving peri-implant health, esthetics, and marginal bone level stability. The present study aimed at evaluating the volumetric changes occurring following implant placement in sites that received soft tissue augmentation compared to non-augmented sites.

**Methods.** Twenty-six subjects received a dental implant in a posterior edentulous site. Simultaneous soft tissue augmentation with a xenogeneic cross-linked collagen scaffold was performed for the first thirteen patients, while the remaining subjects served as the negative control. An intraoral optical scanner was used at baseline and at 12 weeks to generate digital models.

**Results.** The mean volume (Vol) gain of the test group was 38.43 mm<sup>3</sup>, while a mean Vol of -16.82 mm<sup>3</sup> was observed for the control group ( $p < 0.05$ ). The mean thickness of the reconstructed volume ( $\Delta D$ ) was 0.61 mm and -0.24 mm, for the test and control group, respectively ( $p < 0.05$ ). Higher linear dimensional changes were observed for the test group ( $p < 0.05$ ), while no significant differences were observed in terms of keratinized mucosa width and pocket depth changes between the two groups.

**Conclusions.** Simultaneous soft tissue augmentation with xenogeneic collagen scaffold obtained statistically significant higher volumetric outcomes compared to the non-augmented group.

### **Clinical significance.**

Soft tissue augmentation at the time of implant placement using a xenogeneic cross-linked collagen scaffold can prevent remodeling of the ridge during the first 12 weeks, as compared to non-grafted implant sites.

**Keywords:** collagen matrix, dental implant, soft tissue augmentation, tissue graft, three-dimensional analysis

## INTRODUCTION

It has been well demonstrated that volumetric changes occur at implant sites <sup>1,2</sup>. Volumetric variations around dental implants have increasingly become a topic of interest in the scientific literature <sup>1,2</sup>. Different methods have been used for assessing volumetric changes at implant sites, including cone-beam computed tomography (CBCT), transgingival probing/piercing, ultrasonography and optical-scanning based digital technology <sup>3-5</sup>. Among them, optical scanners have several advantages, such as non-invasiveness, reproducibility, and the possibility of obtaining multiple outcomes of interest <sup>6,7</sup>. Digital impressions can be obtained with an intraoral scanner or with a desktop/laboratory scanner on dental casts <sup>7</sup>. The generated STL (Standard Tessellation Language) file is then imported in a specific software that matches the STL of two, or more time points, allowing for the calculation of volumetric and linear dimensional changes. Recent advancements of these optical scanners and metrology software have contributed to the high accuracy of this technology and its use in different scenarios, such as immediate implant placement, implant placement with guided bone regeneration and peri-implant soft tissue augmentation, among others <sup>8,9</sup>. A recent systematic review from our group highlighted that most of the available clinical studies assessing volumetric changes at implant sites employed optical scanning-based digital technologies <sup>2</sup>.

Interestingly, several studies showed a certain amount of volume loss following implant placement <sup>10-13</sup>. It can be speculated that volume loss following implant surgery is due to physiological bone remodeling that may also negatively affect the soft tissue component <sup>14</sup>. Soft tissue augmentation (STA) at the time of implant placement may compensate for physiological peri-implant bone remodeling, preventing volume loss at the implant site.

Therefore, the aim of the present prospective comparative study was to evaluate volumetric changes at implant sites with or without simultaneous soft tissue augmentation.

## **MATERIAL AND METHODS**

### **Study design and participants**

The present study was designed as a comparative prospective study assessing volumetric changes around dental implants that received simultaneous soft tissue augmentation (STA), with XCCS compared to implants that did not receive any augmentation procedure. It was decided that the assignment would be performed on a consecutive basis such that, the first thirteen patients would receive STA, while the remaining thirteen subjects would not, serving as the negative control.

Twenty-six non-smoking systemically and periodontally healthy patients with an isolated posterior edentulous site planned for rehabilitation with a dental implant were recruited at the Department of Periodontics and Oral Medicine, School of Dentistry, the University of Michigan, USA. All patients provided informed consents and the study protocol was in full accordance with the Helsinki Declaration of 1975, as revised in 2013.

Inclusion criteria were: i) Edentulous area in a premolar or molar site, ii) presence of both teeth adjacent to the edentulous site, iii) full-mouth plaque score and full-mouth bleeding score, iv) patients being able to maintain good oral hygiene, v) bone augmentation not required neither before nor at the time of implant placement. Subjects were excluded if: i) compromised general health or taking medications (e.g. bisphosphonate) that could influence normal wound healing, ii) pregnancy or attempting to get pregnant (self-reported), iii) untreated periodontal disease, iv) smokers, v) buccal bone thickness prior to/after implant placement  $< 1.5$  mm<sup>15</sup>, vi) buccal bone dehiscences  $> 1$  mm or buccal bone fenestration prior to/after implant placement, vii) cases requiring submerged healing and viii) known allergy to collagen-based medical products.

The study flowchart is depicted in Figure 1. After recruitment, patients underwent implant placement (T<sub>0</sub>) and were followed at 2 weeks (T<sub>1</sub>), 4 weeks (T<sub>2</sub>) and 12 weeks (T<sub>3</sub>, prior to crown delivery).

### **Intervention**

Patients received a single dental implant (Zimmer TSV, diameter 3.7, 4.1 or 4.7 mm, 10 or 11.5 mm in length) in a molar or premolar area. After implant placement, the buccal bone was assessed to determine the eligibility of the case. Sites with less than 1.5 mm of buccal bone thickness, with a buccal bone dehiscence  $> 1$  mm or with buccal bone fenestration were excluded. The healing abutment was inserted in all the cases. For sites allocated to STA (test group), a xenogeneic cross-linked collagen scaffold (XCCS, Ossix Volumax, Datum Dental, Dentsply Sirona, Charlotte, USA) was utilized for augmenting the facial mucosal thickness. The XCCS was trimmed based on the mesio-distal width of the edentulous area, while its height was kept to 15 mm and its thickness was fully preserved. After releasing the buccal flap with periosteal scoring to obtain a tension-free flap, the XCCS was folded on itself and then inserted underneath the envelope flap on the facial aspect of the implant. The graft material was stabilized together with the flap utilizing simple and sling sutures (6/0 polypropylene Ethicon, Johnson & Johnson, Somerville, USA) aiming for a healing by primary intention. Care was taken to achieve a

complete closure of the buccal and palatal/lingual flaps, without exposure of the graft (Figure 2). For sites allocated to the control group, no STA was performed, and the buccal and lingual flap were approximated with simple and sling sutures (6/0 polypropylene Ethicon, Johnson & Johnson, Somerville, USA).

Oral and written post-operative instructions were provided to the patients. Ibuprofen (600 mg) every 4-6 hours as needed, Amoxicillin (500 mg) 3 times a day for 7 days and Chlorhexidine mouth rinse (0.12%) twice daily for 2 weeks were prescribed. Suture removal occurred at 2 weeks, when patients receive further instructions regarding the type of toothbrush and brushing technique <sup>16</sup>.

### **Study outcomes**

The primary outcome of the study was to evaluate and compare the volumetric changes between the test (STA with XCCS) and control (no STA) groups. Secondary outcomes included assessment of possible complications or adverse reaction to the XCCS, including patient-reported swelling during the first two weeks. Clinical measurements, such as keratinized mucosa width (KMW) change between T<sub>2</sub> and T<sub>3</sub> and pocket depth (PD) at the last follow-up visit (T<sub>3</sub>), were also evaluated.

### **Volumetric outcome assessment**

An intraoral optical scanner (Trios, 3Shape, Denmark) was utilized at baseline (prior to implant placement (T<sub>0</sub>)), at 12 weeks (T<sub>3</sub>, prior to crown delivery) to generate digital models that were saved as STL files and imported in an image analysis software (GOM Inspect, GOM, Germany). A semi-automated alignment, based on the selection of reproducible points on the digital models and on a best-fit algorithm, was used to superimpose the STL files <sup>2</sup>. The region of interest (ROI) was defined as previously described <sup>2</sup>. The volumetric outcomes of interest were: i) volume change in mm<sup>3</sup> (Vol), ii) the mean distance between the surface/mean thickness of the reconstructed volume in mm ( $\Delta D$ ), and iii) linear dimensional (LD) changes from 1 to 7 mm from the soft tissue margin <sup>2</sup>.

### **Data analysis**

Means and standard deviations (SD) were obtained for descriptive presentation of outcome measures. The volumetric data was obtained as variations between T<sub>0</sub> and T<sub>3</sub>. Means and standard deviations (SD) were also computed to display KMW and PD changes. Paired t tests were used for statistical inferences regarding the volumetric changes and the clinical outcomes within the two groups. A p value of 5% was set for statistical significance.

## **RESULTS**

Twenty-six patients (mean age 48.4 ± 15.3, 17 women) each contributing a single implant site were recruited and completed the study. Among them, the first thirteen received simultaneous STA with

XCCS, while STA was not performed in the remaining subjects. The healing was uneventful in all the cases, with no serious complications or adverse events in either group. Three patients of the test group (23.1%) reported bruising following the implant surgery, while no subjects in the control group referred this event. Post-operative swelling was noticed by six subjects in the test group and 3 patients in the control group.

The digital analysis evaluating volumetric changes between  $T_3$  and  $T_0$  showed that twelve out of thirteen sites (92.3%) of the test group (STA with XCCS) exhibited Vol gain, while six implants (50%) in the control group displayed loss of Vol. The mean Vol of the test group was  $38.43 \text{ mm}^3$ , while a mean Vol of  $-16.82 \text{ mm}^3$  was observed for the control group, differences which yielded statistical significance ( $p < 0.05$ ). The mean  $\Delta D$  for the test group was 0.61 mm, while for the control group was -0.24 mm ( $p < 0.05$ ). The test group obtained higher LD changes compared to the control group (Table 1) (Figure 3). No differences were noticed between the augmented and non-augmented sites in terms of changes in KMW between  $T_2$  and  $T_3$  (mean KMW change 0.15 mm vs 0.12 mm, respectively), as well as PD at the last follow-up (mean PD 3.15 mm vs 3.08 mm, respectively) ( $p > 0.05$  for both comparison).

## DISCUSSION

The present study investigated the volumetric changes following implant placement, comparing soft tissue augmented and non-augmented sites. We observed that implant placement without STA resulted in a certain amount of volume loss, which was, however, within 0.3 mm when measured as a linear dimensional change. On the other hand, the sites that received STA at the time of implant placement exhibited a mean Vol of  $38.43 \text{ mm}^3$  and a mean  $\Delta D$  of 0.61 mm at  $T_3$ . It can be assumed that STA with a XCCS was able to compensate the physiological tissue remodeling occurring following implant placement.

Assessing volumetric changes with optical scanning-based technologies is non-invasive, and relatively easy to use and it allows for multiple comparisons over time <sup>6,7</sup>. Nevertheless, superimposing STL digital files do not allow to establish whether the obtained volume change occurred only in the peri-implant mucosa only, buccal bone or both. Other technologies, such as ultrasonography and cone-beam computed tomography (CBCT) are more indicated to assess this aspect <sup>17,18</sup>. In particular, a recent article described the combination of STL and DICOM file, obtained from intraoral scanner and CBCT, respectively, for identifying and measuring peri-implant soft and hard structures <sup>19</sup>. Nevertheless, this method implies a certain dose of radiations that may not be necessary for every implant case.

Previous studies observed volume loss at non-augmented implants. Benic and coworkers observed a mean contour reduction of 0.09 - 0.17 mm within the first 3 months around dental implant sites that did not receive any augmentation <sup>20</sup>. Another study reported a mean  $\Delta D$  of -0.12 mm after 1 year for two-piece dental implants, while no volumetric changes were observed at one-piece dental implants <sup>12</sup>. The



authors reported that volume loss was more pronounced over time, but it was still within 0.4 mm after 5 years, which may be considered negligible <sup>12</sup>.

It has been considered that several factors may contribute to volumetric changes, including thickness of the cortical plate, soft tissue thickness, and the amount of keratinized mucosa width <sup>21</sup>. Inadequate buccal bone thickness is more likely to undergo physiological remodeling, and pathological bone loss <sup>15,22</sup>. Similarly, the role of the soft tissue component on peri-implant tissue stability has been largely discussed <sup>23,24</sup>. In addition, a minimum of 2 mm of mucosal thickness has been advocated for avoiding discoloration of the peri-implant mucosa due to the underlying implant component <sup>25,26</sup>. Therefore, STA at the time of implant placement can also play a role in the esthetic outcomes of implant therapy. This can be achieved with different approaches, that can mainly be categorized as autogenous and non-autogenous grafts, with the latter including allogeneic and xenogeneic matrices <sup>27,28</sup>. At the present moment, it appears that autogenous graft is still the gold standard approach for soft tissue related procedures in natural dentition and at implant sites <sup>28</sup>. Nevertheless, some studies have shown that, in certain conditions, graft substitutes may provide comparable clinical and volumetric outcomes to the ones obtained with autogenous grafts, however with the clear advantage of reducing patient morbidity and surgical time <sup>4,5</sup>.

In fact, recent systematic reviews have demonstrated that bilaminar approaches for increasing mucosal thickness have beneficial effects on marginal bone levels compared to non-augmented sites <sup>23,24</sup>. Therefore, the rationale of STA at the time of implant placement includes not only preventing possible volume loss during the early stages of healing, but also improving esthetics, and peri-implant bone level stability.

In the present study we utilized a novel XCCS for STA, due to its properties of slow resorption, good biocompatibility <sup>29</sup> and ease in handling and stabilization. The graft was found to be safe, well-tolerated by the patients and effective in increase tissue thickness. This study is one of the first clinical studies evaluating the volumetric outcomes following STA at the time of implant placement with this scaffold. Future studies would be needed to further assess the safety and the efficacy of XCCS in STA, with direct comparisons with autogenous grafts and/or other matrices.

Among the limitations of the present study, the relatively short follow-up, and the lack of assessment of peri-implant health-related parameters should be mentioned. Nevertheless, the aim of this pilot study was to compare the volumetric changes following STA with a collagen matrix compared to non-augmented sites from the time of second stage to crown delivery. Indeed, it has been shown that implant restoration can further result in volumetric variation <sup>30</sup>, and this would have prevented to draw conclusions on the efficacy of STA with XCCS in increasing soft tissue thickness at implant placement in comparison to non-augmented sites.

## CONCLUSIONS

Within its limitations, the present study described the volumetric changes occurring following implant placement in sites augmented with a XCCS vs non-augmented sites. The test group showed statistically superior volumetric outcomes compared to the control group, while no significant differences were observed for keratinized mucosa width and pocket depth changes. Further studies are needed to evaluate the long-term behavior of the augmented peri-implant mucosa, together with the effects of the augmentation on peri-implant health-related parameters.

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**Table and Figures**

**Table 1.** 3D volumetric outcomes within the two groups

**Figure 1.** Study flowchart

**Figure 2.** Implant placement (Zimmer TSV 4.7 mm in diameter and 10 mm in length, Zimmer Biomet, Warsaw, IN, USA) with and without soft tissue augmentation (STA). A) Xenogeneic cross-linked collagen scaffold (XCCS) inserted underneath the flap. B) The scaffold was stabilized together with the flap around the healing abutment and the lingual flap. C) Healing at 3 months. D) Implant placement without STA. E) Flap closure by primary intention. F) Healing at 3 months.

**Figure 3.** Clinical and volumetric outcomes following STA with XCCS. A) Baseline. B) implant placement. C) XCCS prior to its trimming and folding. D-E) Insertion of the XCCS underneath the flap. F) Flap Closure. G) Healing at 3 months. H) Follow-up with the implant-supported restoration. I-L) Digital analysis following the superimposition of the STL files obtained at  $T_0$  and  $T_3$ .

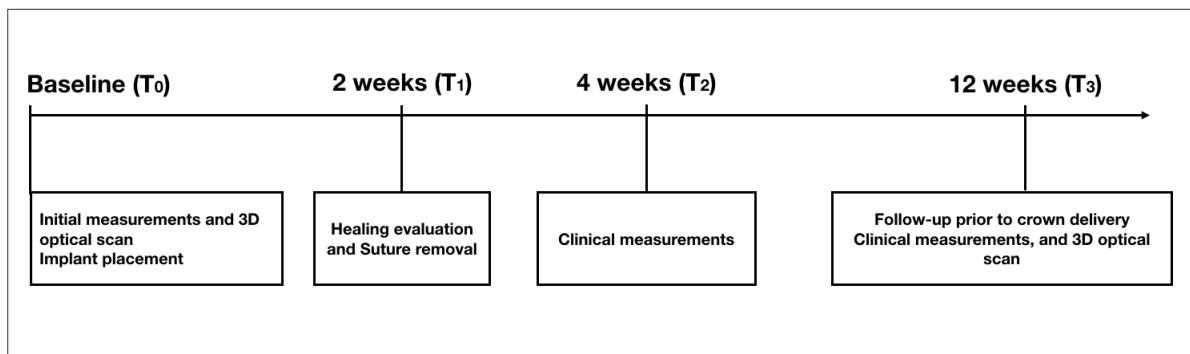
**Table 1.** 3D volumetric outcomes within the two groups between T<sub>3</sub> and T<sub>0</sub>.

<b>3D Volumetric outcomes</b>	<b>Test group (STA with XCCS) (N = 13)</b>	<b>Control group (no STA) (N = 13)</b>
Vol (mean ± SD) (mm <sup>3</sup> )	38.43 ± 11.27*	-16.82 ± 8.24
ΔD (mean ± SD) (mm)	0.61 ± 0.12*	-0.24 ± 0.11
LD1 (mean ± SD) (mm)	0.45 ± 0.05*	-0.04 ± 0.02
LD2 (mean ± SD) (mm)	0.62 ± 0.11*	-0.07 ± 0.04
LD3 (mean ± SD) (mm)	0.58 ± 0.18*	-0.28 ± 0.11
LD4 (mean ± SD) (mm)	0.69 ± 0.21*	-0.29 ± 0.12
LD5 (mean ± SD) (mm)	0.54 ± 0.15*	-0.21 ± 0.11
LD6 (mean ± SD) (mm)	0.47 ± 0.19*	-0.04 ± 0.03
LD7 (mean ± SD) (mm)	0.47 ± 0.11*	0 ± 0

**Legend.** LD: linear dimensional changes between T<sub>1</sub> and T<sub>2</sub> (measured at different apico-coronal distance from the soft tissue margin, i.e. LD 1 is measured 1 mm below the soft tissue margin). N: number of subjects/implants. SD: standard deviation. STA: soft tissue augmentation. Vol: volume changes in mm<sup>3</sup> between T<sub>1</sub> and T<sub>2</sub>. XCCS: xenogeneic cross-linked collagen scaffold. ΔD: mean distance between the surface/mean thickness of the reconstructed volume in mm between T<sub>1</sub> and T<sub>2</sub>.

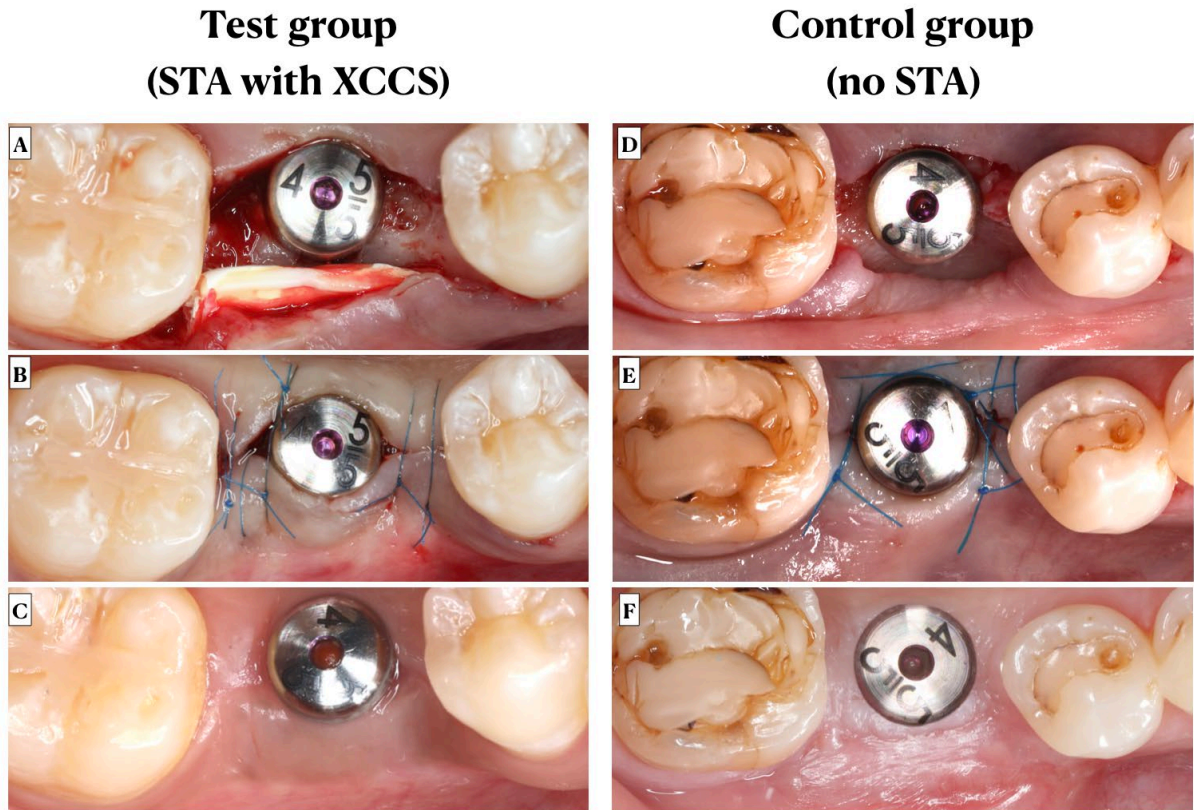
\* denotes a p-value < 0.05 comparing to the other group.

**Figure 1.** Study flowchart.

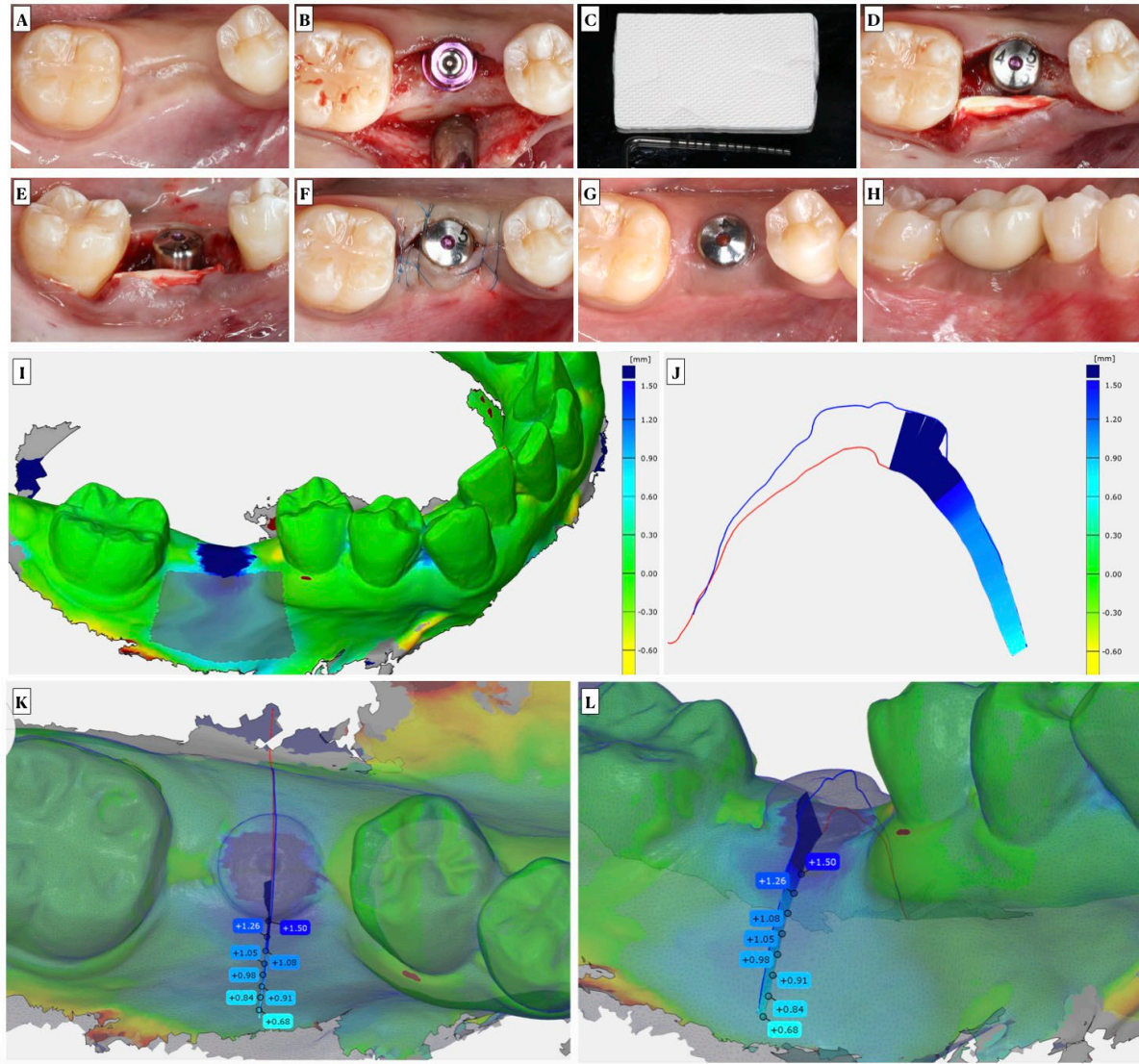


**Legend.** STA: soft tissue augmentation. XCCS: xenogeneic cross-linked collagen scaffold.

**Figure 2.** Implant placement (Zimmer TSV 4.7 mm in diameter and 10 mm in length, Zimmer Biomet, Warsaw, IN, USA) with and without soft tissue augmentation (STA). A) Xenogeneic cross-linked collagen scaffold (XCCS) inserted underneath the flap. B) The scaffold was stabilized together with the flap around the healing abutment and the lingual flap. C) Healing at 3 months. D) Implant placement without STA. E) Flap closure by primary intention. F) Healing at 3 months.



**Figure 3.** Clinical and volumetric outcomes following STA with XCCS. A) Baseline. B) implant placement. C) XCCS prior to its trimming and folding. D-E) Insertion of the XCCS underneath the flap. F) Flap Closure. G) Healing at 3 months. H) Follow-up with the implant-supported restoration. I-L) Digital analysis following the superimposition of the STL files obtained at  $T_0$  and  $T_3$ .



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