



Volumetric assessment of tissue changes following combined surgical therapy of peri-implantitis: A pilot study

Maria Elisa Galarraga-Vinueza^{1,2} | Karina Obreja¹ | Ricardo Magini² |
Anton Sculean³ | Robert Sader⁴ | Frank Schwarz¹

¹Department of Oral Surgery and Implantology, Johann Wolfgang Goethe-University, Carolinum, Frankfurt, Germany

²Post-Graduate Program in Implant Dentistry (PPGO), Federal University of Santa Catarina (UFSC), Florianópolis, Brazil

³Department of Periodontology, School of Dental Medicine, University of Bern, Bern, Switzerland

⁴Department for Oral, Cranio-Maxillofacial and Facial Plastic Surgery, Medical Center of the Goethe University Frankfurt, Frankfurt am Main, Germany

Correspondence

Frank Schwarz, Department of Oral Surgery and Implantology, Carolinum, Goethe University, Theodor-Stern-Kai 7, 60596 Frankfurt am Main, Germany.
Email: f.schwarz@med.uni-frankfurt.de

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Abstract

Aim: To assess volumetric tissue changes at peri-implantitis sites following combined surgical therapy of peri-implantitis over a 6-month follow-up period.

Materials and Methods: Twenty patients ($n = 28$ implants) diagnosed with peri-implantitis underwent access flap surgery, implantoplasty at supracrestally or buccally exposed implant surfaces and augmentation at intra-bony components using a natural bone mineral and application of a native collagen membrane during clinical routine treatments. The peri-implant region of interest (ROI) was intra-orally scanned pre-operatively (S0), and after 1 (S1) and 6 (S2) months following surgical therapy. Digital files were converted to standard tessellation language (STL) format for superimposition and assessment of peri-implant volumetric variations between time points. The change in thickness was assessed at a standardized ROI, subdivided into three equidistant sections (i.e. marginal, medial and apical). Peri-implant soft tissue contour area (STCA) (mm^2) and its corresponding contraction rates (%) were also assessed.

Results: Peri-implant tissues revealed a mean thickness change (loss) of -0.11 and -0.28 mm at 1 and 6 months. S0 to S1 volumetric variations pointed to a thickness change of -0.46 , 0.08 and 0.4 mm at marginal, medial and apical regions, respectively. S0 to S2 analysis exhibited corresponding thickness changes of -0.61 , -0.25 and -0.09 mm, respectively. The thickness differences between the areas were statistically significant at both time periods. The mean peri-implant STCA totalled to 189.2 , 175 and 158.9 mm^2 at S0, S1 and S2, showing a significant STCA contraction rate of 7.9% from S0 to S1 and of 18.5% from S0 to S2. Linear regression analysis revealed a significant association between the pre-operative width of keratinized mucosa (KM) and STCA contraction rate.

Conclusions: The peri-implant mucosa undergoes considerable volumetric changes after combined surgical therapy. However, tissue contraction appears to be influenced by the width of KM.

Maria Elisa Galarraga-Vinueza and Karina Obreja equally contributed to the present study and are considered joint first authors.

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KEYWORDS

dental implants, peri-implantitis, peri-implantitis therapy, three-dimensional analysis

1 | INTRODUCTION

Peri-implantitis is defined as a biofilm-associated pathological condition that features an inflammatory lesion in the peri-implant mucosa and a loss of the implant supportive bone (Berglundh et al., 2018; Schwarz, Derks, Monje, & Wang, 2018). Non-surgical treatment of peri-implantitis was not effective to prevent disease progression, whereas access flap surgery had a marked effect on further bone loss (Karlsson et al., 2019). Adjunctive resective (i.e. implantoplasty), augmentative (i.e. bone fillers, autogenous grafts with or without guided bone regeneration) or combined (i.e. implantoplasty + augmentative) measures were also shown to be effective on the long term; however, their potential benefit over conventional surgical therapy is yet to be determined (Bianchini et al., 2019; Renvert, Polyzois, & Claffey, 2012; Rocuzzo, Bonino, Bonino, & Dalmaso, 2011; Romeo, Lops, Chiapasco, Ghisolfi, & Vogel, 2007; Schwarz, Bieling, Latz, Nuesry, & Becker, 2006; Schwarz, Claus, & Becker, 2017; Schwarz, John, & Becker, 2015; Schwarz et al., 2007, 2017)

In addition to changes in bleeding on probing (BOP), probing depths (PD) and marginal bone levels (MBL), recent recommendations also underlined the need for the assessment of changes in peri-implant soft tissue levels, which in turn may compromise the aesthetics at respective implant sites (Jepsen et al., 2019). In fact, based on a systematic review and meta-analysis evaluating a total of six studies (10 arms) focusing on augmentative therapy, the change in mucosal recession (MR) within a follow-up period of 12 months amounted to -0.7 mm (95% CI: $-1.0/ -0.3$) (Tomasí, Regidor, Ortiz-Vigón, & Derks, 2019). Apart from a surgical trauma, the occurrence of MR following therapy may also be attributed to a decrease in the horizontal mucosal thickness resulting from a resolution of the inflammatory infiltrate at respective sites (Schwarz et al., 2017). Indeed, MR values were almost compensated when surgical therapy was combined with a simultaneous thickening of the mucoperiosteal flap by means of connective tissue grafts (Schwarz, Sahm, & Becker, 2014). At the time being, there are no data which may allow for a more in-depth evaluation of the dynamics of hard and soft tissue remodelling and maturation following surgical therapy of peri-implantitis.

Therefore, the present study aimed at evaluating the volumetric tissue changes at peri-implantitis sites following combined surgical therapy over a 6-month follow-up period.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

The present pilot study included patients who attended the Department of Oral Surgery and Implantology, Goethe

Clinical Relevance

Scientific rationale of the study: Change in peri-implant hard and soft tissue levels is a critical outcome measure following surgical therapy of peri-implantitis. The present study aimed at further analysing volumetric changes of peri-implant tissues following a combined surgical therapy.

Principal findings: Peri-implant tissues underwent considerable volumetric and soft tissue contour changes over a period of 6 months. The STCA contraction rate was significantly correlated with KM width values at baseline (i.e. the lower the KM width, the higher the contraction rate).

Practical implications: The dimensional changes following combined surgical therapy of peri-implantitis are commonly associated with an aesthetic compromise at respective implant sites. These events may however be influenced by the pre-operative width of KM.

University, Frankfurt, Germany, for the treatment of peri-implantitis.

All selected patients had received the same type of an established and standardized surgical protocol during clinical routine treatments between March and June 2019.

Peri-implantitis was defined as the combination of BOP with or without suppuration, $PD \geq 6$ mm and radiographic MBL (i.e. inter-proximal bone levels ≥ 3 mm apical of the most coronal portion of the intra-osseous part of the implant) (Berglundh et al., 2018). All included implants exhibited an intra-bony defect component of ≥ 3 mm as detected on intra-oral radiographs, were clinically stable (i.e. no mobility at clinical examination) and were scheduled for a combined resective/augmentative surgical therapy.

Peri-implantitis severity was classified (i.e. slight, moderate and advanced) based on the evaluation of the defect length as measured from the implant neck and the ratio of MBL relative to the total implant length (bone loss %) (Monje et al., 2019).

The study protocol (No. 92/19), considering the prospective assessment of clinical and volumetric outcomes of the selected patients over a period of 6 months, was approved by the ethics committee of the Goethe University, Frankfurt, Germany, and conducted in accordance with the Helsinki Declaration as revised in 2013. Each patient had received a detailed information of the study protocol and was required to sign an informed consent form.

The following report considers the checklist items of the STROBE statement.

2.2 | Inclusion criteria

The inclusion criteria for the selection of participants included the following: (a) minimum age of 18 years old, (b) titanium implants diagnosed with peri-implantitis requiring a combined surgical therapy, (c) implants presenting an intra-bony defect component of ≥ 3 mm as detected on radiographs, (d) implants with sufficient keratinized mucosa (KM) (i.e. ≥ 2 mm), (e) adequate oral hygiene as evidenced by a plaque index (PI) < 1 (L oe, 1967), and (f) non-smokers and/or light smokers status (< 10 cig/day).

2.3 | Exclusion criteria

The exclusion criteria considered patients who presented the following: (a) general contraindications for oral surgical treatments, (b) untreated periodontal disease, (c) uncontrolled diabetes (HbA1c > 7), (d) pregnant or lactant women, and (e) autoimmune and/or inflammatory diseases affecting the oral cavity.

2.4 | Treatment procedures

All patients were subjected to pre-operative professional supra-mucosal/gingival implant/tooth cleaning and underwent a single episode of non-surgical therapy employing an Er:YAG laser (KEY3; KaVo, Biberach, Germany) (12.7 J/cm^2). Subsequently, all patients had received the same type of an established and standardized surgical protocol during clinical routine treatments (Schwarz et al., 2014) provided by two experienced surgeons (K.O. and A.B.). Whenever possible, the prosthetic superstructure (i.e. screw-retained restorations and secondary components) was removed to facilitate access and repositioned after the surgical procedure. Under local anaesthesia, full-thickness mucoperiosteal flaps were raised at vestibular and oral aspects. Subsequently, a meticulous and complete removal of granulation tissue was accomplished and the exposed implant surfaces were decontaminated using a titanium brush (Hans Korea Co., Ltd.). Implantoplasty was performed at buccally and/or supracrestally (if present) exposed implant surfaces using diamond burs (ZR Diamonds; Gebr. Brasseler GmbH & Co. KG) and Arkansas stones under copious irrigation with sterile saline. The intra-bony defect compartments were homogeneously filled using a natural bone mineral (Bio-Oss spongiosa granules, particle size 0.25–1 mm; Geistlich, Wolhusen, Switzerland) (NBM) and covered with a native collagen membrane (Bio-Gide; Geistlich). Mucoperiosteal flaps were repositioned and adapted using non-resorbable double sutures. After 10 days of surgery, sutures were removed. All patients had received a perioperative one-shot antibiotic medication (2 g amoxicillin, oral) (Amoxicillin, Aliud Pharma, Laichingen, Germany) and supplementary daily mouthwash using 0.12% chlorhexidine digluconate solution (Corsodyl, GlaxoSmithKline Consumer Healthcare) for 5 days.

2.5 | Clinical examination

The following baseline clinical parameters were assessed as part of the clinical routine documentation at each implant site using a periodontal probe (PCP 12 Hu-Friedy Inc.): (1) KM width, (2) BOP, evaluated as present if bleeding was evident within 30 s after probing, or absent, if no bleeding was noticed within 30 s after probing, (3) PD as measured from the mucosal margin to the bottom of the probable pocket, (4) plaque index (PI) (L oe, 1967) and (5) MR measured from the implant shoulder/restoration margin to the mucosal margin, and suppuration, evaluated as positive if evident after probing. All measurements were performed at 6 aspects per implant: mesio-vestibular, mid-vestibular, disto-vestibular, mesio-oral, mid-oral and disto-oral by 2 calibrated investigators (K.O. and A.B.). PI, BOP, PD, MR and KM values were also assessed at 6 months. Prior to these measurements, both investigators were calibrated by evaluating five patients, each presenting two implants with probing depths ≥ 4 mm and a radiographic MBL > 3 mm on at least one aspect, two times, with 48 hr apart. Calibration was accepted if repeated measurements were within a millimetre at $> 90\%$ of the time.

Pre-operative MBL was assessed through radiological evaluation using a software program (ImageJ, software, 1.52a, Maryland, USA). MBL linear measurements were performed by drawing a digital vertical line, following the long axis of the implant, from the implant shoulder to the bottom of the defect at distal and mesial sites. The numerical scale was set by means of the known implant length. Radiological measurements were performed by one examiner (M.E.G.).

The assessment of the morphology and severity of peri-implantitis bone defects considered an established classification system (Monje et al., 2019).

2.6 | Outcome assessments

The primary endpoint was defined as the vestibular thickness change (mm) at respective implant sites following combined surgical therapy over a 6-month follow-up period. Thickness variations were evaluated at 1 (S1) and 6 (S2) months (Figure 1).

Secondary endpoints considered peri-implant soft tissue contour area (STCA) changes (mm^2) and the corresponding contraction rates (%), wound healing (wound infections (yes/no), changes in clinical parameters (PI, BOP, PD, KM and MR values) and the association between baseline bone loss %, MR, as well as KM width and peri-implant thickness and STCA changes at 6 months.

2.7 | Volumetric analysis

The region of interest (ROI) encompassing the peri-implantitis site was intra-orally scanned using an optical scanner (3 shape TRIOS MOVE, Germany GmbH) before surgery (S0), after 1 (S1)

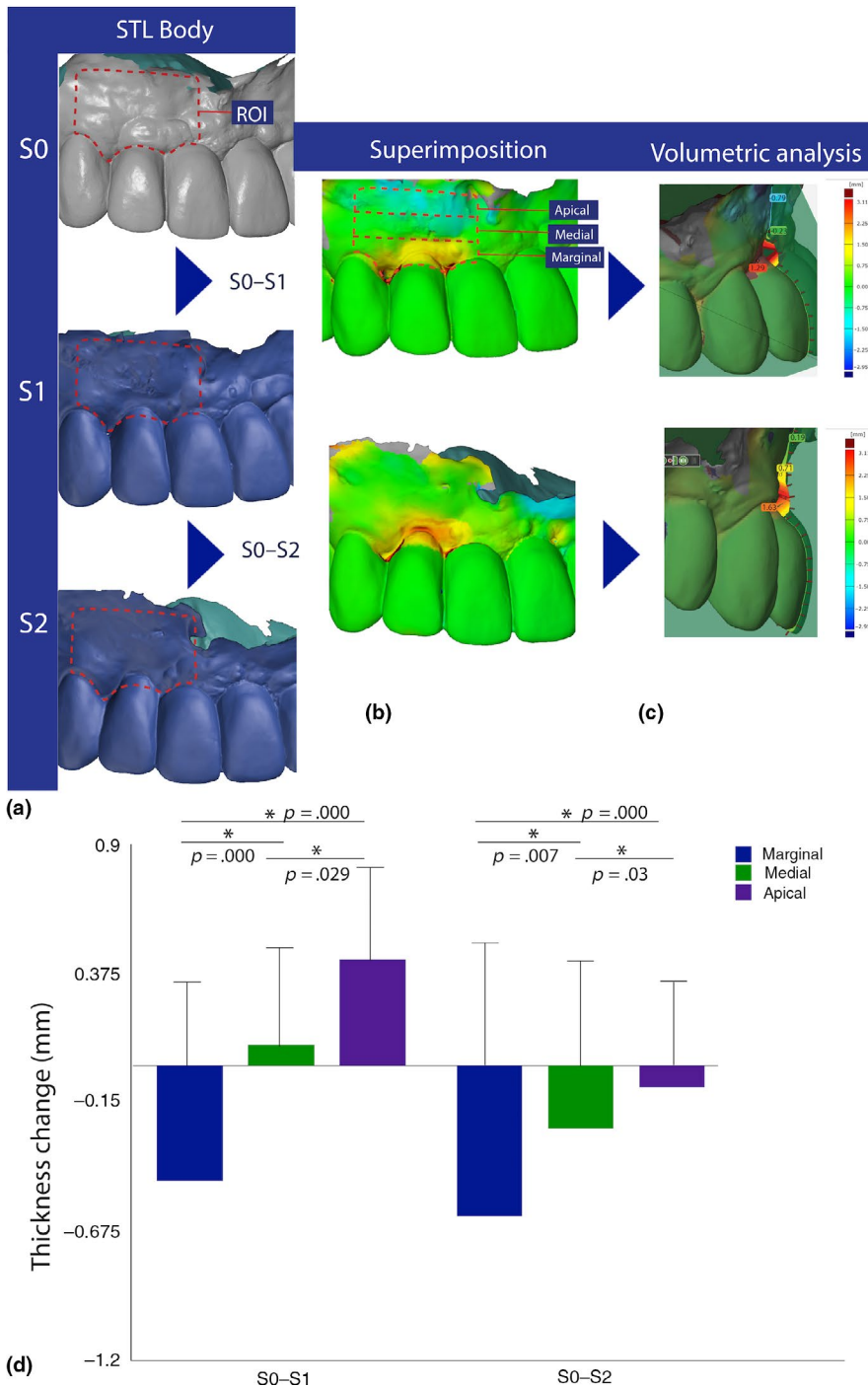


FIGURE 1 Schematic diagram exposing the stages of the study over a 6-month follow-up period. (a) STL files depict the study follow-up visits for the three-dimensional assessments. The standardized ROI encompassing the peri-implant area is enclosed by the red dotted line at S0, S1 and S2 time points. (b) Superimposition of STL files showing volumetric changes. For individual thickness change analysis, the ROI was divided into three equidistant areas (marginal, medial and apical). (c) The superimposed files depict the thickness displacement at the mentioned regions. The colour scale bar shows thickness changes (mm) at the superimposed models, where negative values represent thickness gain and positive values represent loss. (d) Bar diagram depicts the assessed volumetric changes at the specific regions and follow-up periods. Post hoc Tukey's test p values are shown per region comparison, $*p < .05$ was considered statistically significant

and 6 months (S2) of the intervention as elucidated in Figure 1. To evaluate peri-implant volumetric changes, scanned files were converted to STL format. The pre-operative (S0) and postoperative (S1, S2) STL files were aligned and superimposed by selecting 8 reproducible anatomical points in each computer aid design (CAD) body using a software program (Meshlab, ISTI, Italy, 2016). Thickness change computations between the corresponding time points (i.e. S0-S1 and S0-S2) were performed using a software program (GOM inspect 2018, Zeiss Company, Braunschweig, Germany) applying the CAD comparison tool (Figure 1b-a). A standardized ROI (per case) was delimited with a digital pen at

the vestibular aspect. The ROI horizontal extension encompassed both adjacent papillae (mesial and distal), covering the crown/abutment marginal contour and prolonging until the mid-marginal aspect of the contiguous teeth and/or implant. The ROI apical extension was determined by the known implant length (per case). The ROI was additionally subdivided into 3 vertically equidistant regions (i.e. marginal, medial and apical) for individual volumetric assessment (Figure 1b).

For STCA change analysis, digitalized scanned files corresponding to S0, S1 and S2 time points were exported to an image analysis software program (ImageJ, software, 1.52a, Maryland, USA). A

circumference of 15 mm diameter (having as a pivotal point the central-vestibular aspect at the crown/abutment of each implant) was digitally traced. The STCA (within the mentioned circumference) was delineated with a digital pen and then its enclosed area was calculated in mm² (Figure 2a). The crown and/or abutment(s) width at each site served as reference to set up a numerical scale. STCA contraction rate (%) after 1 and 6 months of surgery was calculated applying the following formula: (S0- (evaluated time point)/ S0) × 100.

Each analysis was performed in triplicate by one calibrated examiner (M.E.G.).

2.8 | Statistical analysis

Mean values, standard deviations, medians and confidence intervals for primary and secondary outcomes were calculated using a commercially available software program (SPSS, 19.0). Each implant was followed up with respect to the dimensional changes occurring over the 6-month follow-up; consequently, the implant site was defined as the statistical unit for primary outcome analysis. Shapiro-Wilk test was used to assume normality, considering $p < .05$ significant. Assumption of homogeneity of variance was performed with

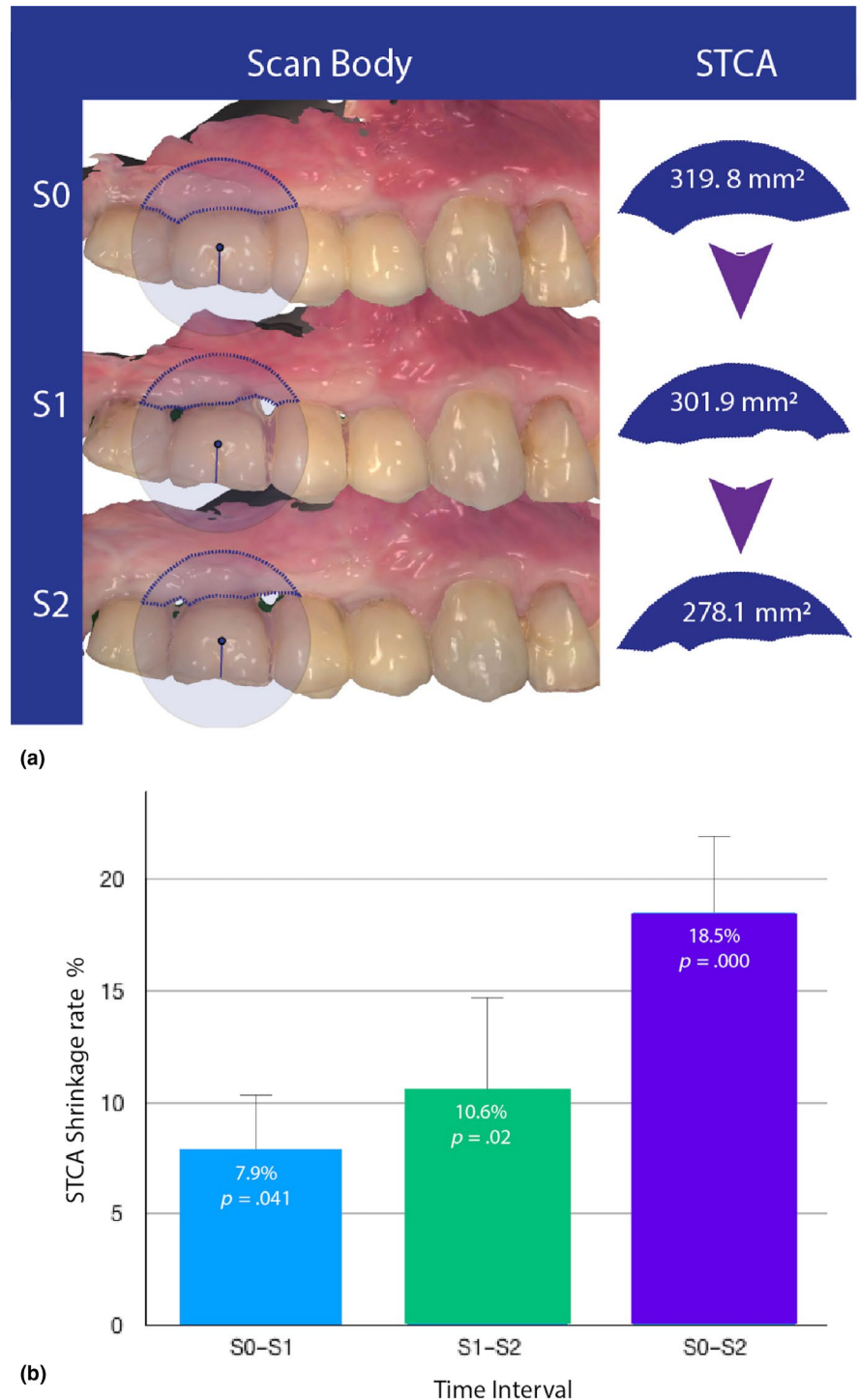


FIGURE 2 Demonstrative scan files depict (a) the delineated STCA perimeter before surgery (S0), after 1 (S1) and 6 (S2) months of surgery. The STCA changes in size and shape are exemplified in the blue regions with its corresponding surface areas (mm²). (b) The STCA contraction rate between the mentioned periods is portrayed on the bar diagram. Post hoc Tukey's test p values are shown per time comparison, $p < .05$ considered for statistical significance

TABLE 1 Description of implant site characteristics and frequency distributions

Site characteristic	Number (n = 28)	Percentage (%)
Region		
Anterior	6	21.4
Posterior	22	78.6
Jaw		
Maxilla	14	50
Mandible	14	50
Bone grafted site		
Yes		
No	4	14.2
Bone grafting procedure (at implant placement)		
External sinus floor elevation		
Lateral ridge augmentation	2	50
Prosthesis type		
Single	8	28.6
Multiple	20	71.4

the Levene test, $p < .05$ significant. The paired t test and one-way ANOVA followed by post hoc Tukey's test were used to analyse clinical parameter changes before and after treatment, within-group changes as well as thickness and STCA changes over time. Linear regression analyses were performed to assess the relationship between the initial bone loss (%), MR, and KM width and thickness variations as well as the STCA changes at 6 months (S2). A value of $p < .05$ was considered statistically significant.

3 | RESULTS

The present analysis included 20 patients (9 males and 11 females) (mean age: 65 years; range: 53 to 79 years) exhibiting twenty-eight implants (mean function time: 10.5 years, SD: 5.8). Soft tissue healing was uneventful in all patients, and no implant loss was noted over the follow-up period. Four (20%) patients had a history of periodontal disease and 5 (25%) reported to be light smokers (i.e. < 10 cigarettes/day). All implants had a Morse taper connection.

3.1 | Clinical assessments

Implant sites characteristics are presented in Table 1. Peri-implantitis severity, defect configuration classification and mean values for MBL and clinical parameters at baseline and after 6 months (i.e. clinical parameters) are presented in Tables 2 and 3.

Mean PI was reduced by 0.05 (implant level) ($p = .3$) and 0.15 (patient level) ($p = .35$) revealing no statistical significance. Mean BOP scores were significantly decreased by 49% (implant level) ($p < .001$) and 53% (patient level) ($p < .001$), and mean PD values were also

TABLE 2 Severity classification, defect configuration, mean MBL and bone loss% for peri-implantitis sites before surgical procedure, at the patient and implant levels

	Implant level n = 28	Patient level n = 20
Severity (%)		
Slight	14.3	15
Moderate	71.4	65
Advanced	14.3	20
Defect configuration (%)		
Ib	3.4	–
Ic	25	–
Ie	14	–
Combined (suprabony and intra-bony components)	57.6	–
MBL (mm) ^a	3.35 ± 1.3	3.65 ± 1.2
Bone loss (%) (MBL/implant length)	37 ± 10	39 ± 12

^aMarginal bone loss.

significantly reduced by 1.26 mm (implant level) ($p < .001$) and 1.34 mm (patient level) ($p < .001$) at 6 months. MR values were significantly increased by 0.61 mm (implant level) ($p < .001$) and 0.83 mm (patient level) ($p < .001$) following 6 months of surgery. Additionally, KM values were as well significantly decreased by 1.4 mm ($p < .05$) (implant and patient level) over the follow-up period.

3.2 | Dimensional assessments

Peri-implant tissues exposed a mean thickness change (loss) of -0.11 (95% CI: -0.4 to 0.02) and -0.28 mm (95% CI: -0.8 to -0.4) after 1 and 6 months following therapy, revealing a significant loss from S1 to S2 ($p = .013$). S0 to S1 volumetric variations resulted in a thickness change of -0.46 (95% CI: -0.5 to -0.3), 0.08 (95% CI: -0.1 to 0.3) and 0.4 mm (95% CI: 0.2 to 0.6) at marginal, medial and apical regions, respectively. Significant differences (post hoc Tukey's test) were noted between marginal and medial regions ($p = .000$), marginal and apical regions ($p = .000$), and medial and apical regions ($p = .029$), respectively.

S0 to S2 analysis resulted in a thickness change of -0.61 (95% CI: -0.8 to -0.4), -0.25 (95% CI: -0.4 to -0.1) and -0.09 (95% CI: -0.2 to 0.04) mm at marginal, medial and apical regions. Significant differences (post hoc Tukey's test) were noted between marginal and medial regions ($p = .007$), marginal and apical regions ($p = .000$), and medial and apical regions ($p = .03$), respectively. Accordingly, the thickness differences between the mentioned areas were statistically significant at both observational periods. Peri-implant volumetric changes are depicted in Figure 1d.

The mean peri-implant STCA totalled to 189.2, 175 and 158.9 mm² at S0, S1 and S2, showing a significant STCA contraction rate of 7.9% (95% CI: 1 to 15.4) (post hoc Tukey's test) ($p = .041$) from

TABLE 3 Clinical parameters (mean, SD and difference values) before surgical procedure and after 6-month follow-up, at the patient ($n = 20$) and implant levels ($n = 28$). * $p < .05$

Clinical parameter	Implant level baseline	Implant level 6 months	Implant level difference	Patient level baseline	Patient level 6 months	Patient level difference
PI (mean) ^a	0.5 ± 0.5	0.45 ± 0.6	0.05 ± 0.5	0.65 ± 0.5	0.5 ± 0.6	0.15 ± 0.5
0 (%)	50%	54.5%	4.5%	65%	50%	15%
1(%)	50%	45.4%	4.6%	35%	50%	15%
2(%)	0	0	0	0	0	0
3(%)	0	0	0	0	0	0
BOP (%) ^b	65 ± 35	16 ± 26	49 ± 25*	73 ± 33	20.5 ± 30	53 ± 28*
PD(mm) ^c	4.66 ± 1.4	3.4 ± 0.9	1.26 ± 1*	4.84 ± 1.4	3.5 ± 1.1	1.34 ± 1.1*
KM (mm) ^d	3.4 ± 1.3	2 ± 1.4	1.4 ± 1*	3.4 ± 1.4	2 ± 1.2	1.4 ± 1.2*
MR(mm) ^e	0.14 ± 0.3	0.75 ± 0.5	0.61 ± 0.4*	0.17 ± 0.34	1 ± 0.6	0.83 ± 0.4*
Suppuration (%)						
Yes	39	0	39	55	0	55
No	61	0	61	45	0	61

^aPlaque Index.^bBleeding on Probing.^cProbing depth.^dKeratinized mucosa.^eMucosal Recession.

S0 to S1 and of 18.5% (95% CI: 11 to 25) from S0 to S2 (post hoc Tukey's test) ($p = .000$) as shown in Figure 2b.

Linear regression analysis revealed a statistically significant association (coef = -0.074 , $R^2 = .19$, $p = .018$) between baseline KM width and STCA contraction rate (%) as exhibited in Figure 3, though the R^2 value was low.

3.3 | Discussion

The present prospective study aimed at assessing volumetric tissue changes at peri-implantitis sites following combined surgical therapy. Within the limitations of a single-arm study, the three-dimensional analysis revealed that peri-implant tissues underwent considerable volumetric changes over a 6-month healing period. This was supported by the assessment of corresponding thickness and STCA alterations also pointing to significant dimensional variations, particularly at marginal regions after 1 and 6 months of healing.

To the authors' knowledge, this is the first study evaluating volumetric tissue changes at peri-implantitis sites following surgical therapy. A previous systematic review and meta-analysis evaluating the efficacy of augmentative therapy at peri-implantitis sites revealed that significant mucosal recessions (MR weighted mean difference = 0.7 mm) occurred over a 12-month follow-up period (Tomasi et al., 2019). Roos-Jansåker, Renvert, Lindahl, and Renvert (2007) reported in a case series assessing regenerative therapy (bovine-derived bone with a resorbable membrane employing submerged healing) at 16 peri-implant defects that MR changes amounted to -2.8 ± 1.4 mm after 1 year of treatment. Another case series evaluating two different regenerative approaches (i.e.

application of nanocrystalline hydroxyapatite versus NBM in combination with CM) at 20 intra-bony defects reported on lower MR values (i.e. -0.4 ± 0.2 and -0.3 ± 0.4 mm) over the same follow-up period (Schwarz et al., 2017). Moreover, a case series reporting on regenerative therapy using a combination of autogenous bone and a demineralized xenogenic bone graft at 36 peri-implantitis defects exhibited a MR that totalled to -1.3 ± 1 mm (Wiltfang et al., 2012), which were comparable to MR changes reported in other studies (Matarasso, Iorio Siciliano, Aglietta, Andreuccetti, & Salvi, 2014; Nart, de Tapia, Pujol, Pascual, & Valles, 2018). A randomized clinical trial assessing the same combined surgical therapy (implantoplasty + NBM + CM) as used in the present study but comparing two different modalities for surface decontamination (i.e. Er:YAG laser versus plastic curettes + cotton pellets + sterile saline) indicated that MR values significantly increased by 0.5 ± 0.4 and 0.4 ± 0.2 mm at 12 months (Schwarz et al., 2012). Also, a prospective study assessing the impact of the defect configuration on the clinical outcome of regenerative therapy (NBM + CM) reported that all 27 augmented defects subdivided into classes Ib ($N = 9$), Ic ($N = 9$) and Ie ($N = 9$), and exhibited MR changes of -0.4 ± 0.7 , -0.5 ± 0.5 and -0.3 ± 0.6 mm at 12 months, respectively (Schwarz, Sahm, Schwarz, & Becker, 2010). Correspondingly, the reported outcomes are comparable with the present results indicating that the mean MR scores increased significantly by 0.61 ± 0.4 mm (implant level) following the mentioned combined surgical therapy (NBM + CM) over a 6-month follow-up period.

When further interpreting the results of the aforementioned studies, it must be kept in mind that MR values had been assessed in one dimension, and these changes may not necessarily correspond to the volumetric outcomes noted in the present analysis.

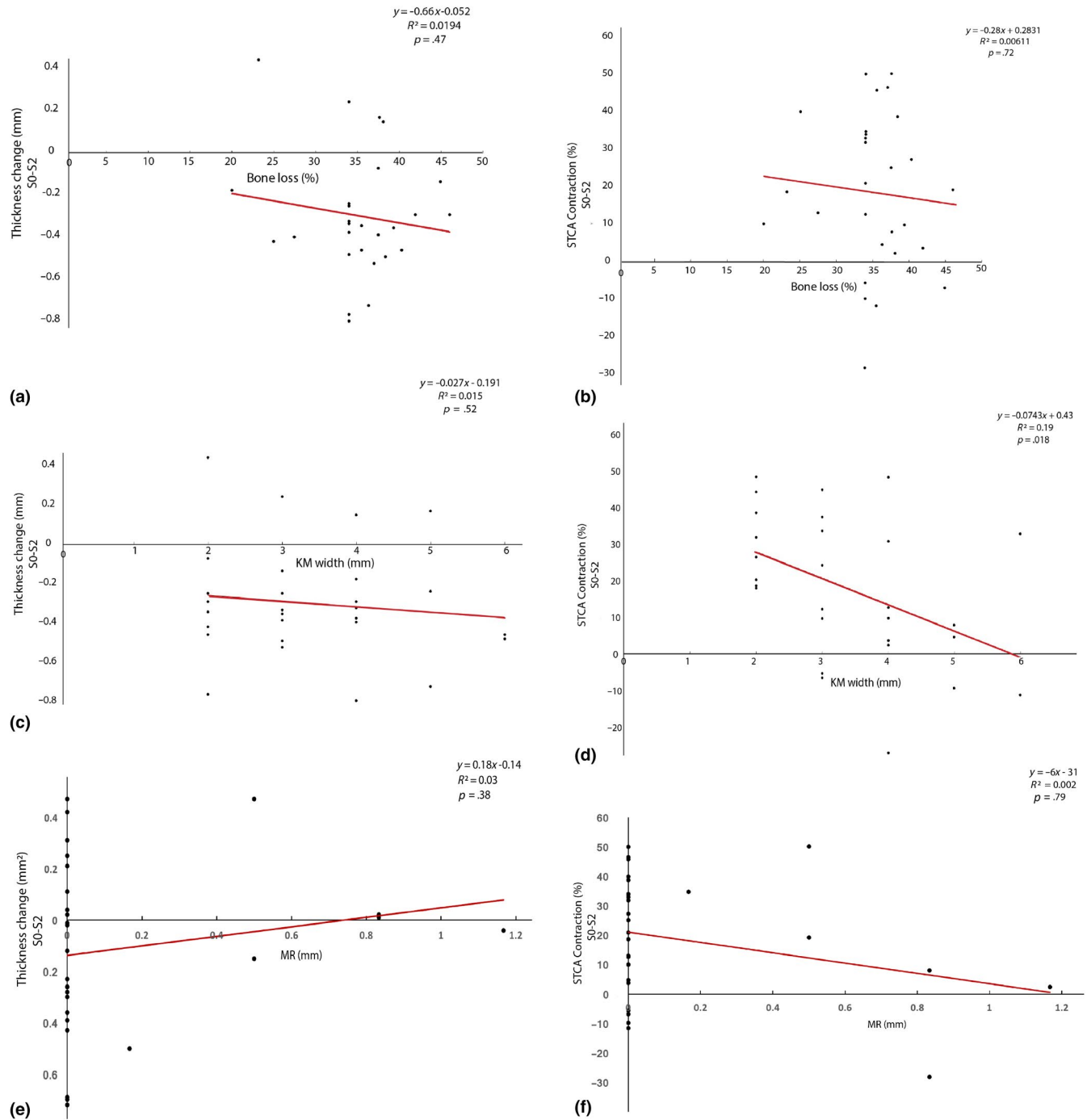


FIGURE 3 Linear regression plots to represent the relationship between baseline bone loss (%) and (a) peri-implant tissue thickness change and (b) STCA (SO-S2), as well as baseline KM width (mm) and (c) peri-implant tissue thickness change and (d) STCA (SO-S2) and baseline MR (mm) and (e) peri-implant tissue thickness change and (f) STCA (SO-S2) at the implant level. $p < .05$ was considered statistically significant

Nevertheless, MR variations may be favoured by the thickness loss that had particularly occurred at the marginal regions after 1 and 6 months of surgery. This loss in thickness may be mainly attributed to the resolution of the inflammatory infiltrate following therapy. In fact, a recent analysis evaluating the horizontal mucosal thickness (hMT) at healthy and diseased implant sites using a validated ultrasonic A-scanner pointed to a median hMT of 1.10 mm at healthy implant sites (Schwarz et al., 2017). These values were significantly

lower at diseased sites, but similar for implants affected by peri-implant mucositis and peri-implantitis (1.68 mm; 1.61 mm). Moreover, hMT values did not markedly differ by implant location (i.e. upper/lower jaws) or position (i.e. anterior/posterior sites) and were also not correlated with PD values (Schwarz et al., 2017).

Even though the present analysis did not assess changes in hMT values, it is assumed that the marked clinical improvements in BOP values noted at 6 months following combined surgical therapy

contributed to the noted marginal thickness changes. Previous clinical data corroborate the clinical efficacy of this treatment approach, also reporting on mean BOP reductions of 47.8 ± 35.5 (Er:YAG laser decontamination) and $55.0 \pm 31.1\%$ (surface decontamination using plastic curettes + cotton pellets + sterile saline) at 6 months after therapy (Schwarz, Sahm, Iglhaut, & Becker, 2011). The biological principle that hMT may be linked with the occurrence of MR has also been demonstrated at healthy implant sites. In particular, after one year of functional loading, there was a significant difference in midfacial MR values noted between implant sites exhibiting either a thin or thick mucosal biotype (Mailoa et al., 2018). These potential correlations are also supported by previous findings of a case series evaluating the clinical outcome of a combined surgical therapy of advanced peri-implantitis lesions with concomitant soft tissue volume augmentation using connective tissue grafts (Schwarz et al., 2014). After 6 months of transmucosal healing, this surgical procedure was associated with a significant reduction in mean BOP ($74.39 \pm 28.52\%$) and PD (2.53 ± 1.80 mm) scores, which were associated with even slight increases in mean mucosal height (0.07 ± 0.5 mm) at the buccal aspects. A slight increase in mean MR was merely noted at two out of 13 implant sites, amounting to 0.3 and 1.0 mm, respectively (Schwarz et al., 2014). The beneficial effect of a volume grafting procedure using connective tissue on peri-implant soft tissue stability was also demonstrated when used along with open flap debridement alone (Dalago et al., 2019).

When further evaluating the present data, it was also noted that particularly the apical regions were initially (i.e. at 1 month) associated with a volume gain, which might be attributed to the grafting procedures performed at the intra-bony defect compartments. At 6 months, however, the apical regions also revealed a thickness loss, most likely due to tissue remodelling and graft consolidation. The latter has been confirmed in a previous report on 5 human re-entry cases (Schwarz, John, & Becker, 2015). In particular, all patients had received a combined surgical treatment of peri-implantitis. The clinical defect resolution at the intra-bony component amounted to $59.4\% \pm 47.59\%$ pointing to a marked consolidation of the grafted area after healing periods of 8 months to 6.5 years (Schwarz, John, & Becker, 2015). In this context, it must be realized that the present volumetric analyses could not differentiate between soft and hard tissues, and therefore, potential differences in the wound healing dynamics at both compartments could not be investigated.

Another relevant finding of the present analysis was related to a significant STCA contraction rate of 18.5% over the 6-month follow-up period, and this outcome links with the significant increase in MR values (measured in one dimensional assessments) reported in this study. The linear regression analyses pointed to a significant association between baseline KM width values and STCA contraction rates, implying that peri-implantitis sites presenting a reduced KM width were more susceptible to the occurrence of MR following combined surgical therapy. Still, this implication should be further evaluated in future studies since this association reported a low R^2 value. While a recent retrospective analysis indicated that the pre-operative width of KM (i.e. < and >2 mm) had no significant influence

on the outcomes of either resective or augmentative treatments of peri-implantitis, its influence on MR changes had not been analysed (Ravida et al., 2020). Accordingly, the need to establish a certain width of KM to limit MR following surgical treatment of peri-implantitis needs to be further investigated (Sculean et al., 2019).

It is imperative to consider that the reliability of this novel method to evaluate thickness and STCA changes through the superimposition and analysis of scan files needs to be further assessed in future clinical investigations. Currently, this is the first study applying a 3-dimensional analysis to assess peri-implant tissue volumetric changes following peri-implantitis therapy; consequently, no data are available for comparison. Furthermore, future research should also consider larger sample sizes, longer follow-up periods and case-control study designs to bring more substantial information on volumetric tissue changes following combined surgical therapy of peri-implantitis.

Within its limitations, the present volumetric analysis suggests that the peri-implant tissues undergo considerable volumetric changes after combined surgical therapy. The tissue contraction, however, was influenced by the width of KM.

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CONFLICT OF INTEREST

The authors report no conflicts of interest related to this study.

ORCID

Maria Elisa Galarraga-Vinueza  <https://orcid.org/0000-0002-4060-0444>

Anton Sculean  <https://orcid.org/0000-0003-2836-5477>

Frank Schwarz  <https://orcid.org/0000-0001-5515-227X>

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