THE EFFECT OF IMMEDIATE IMPLANT PLACEMENT ON ALVEOLAR RIDGE PRESERVATION COMPARED TO SPONTANEOUS HEALING AFTER TOOTH EXTRACTION: SOFT TISSUE FINDINGS FROM A RANDOMIZED CONTROLLED CLINICAL TRIAL.

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ABSTRACT

Aim: to compare soft tissue dimensional changes and relative differences in soft and hard tissue volumes 4 months after single tooth extraction and 3 different treatment modalities: spontaneous healing (SH) and alveolar ridge preservation, with (IMPL/DBBM/CM) or without (DBBM/CM) immediate implant placement.

Materials and Methods: STL files from study casts obtained at baseline and after 4 months were matched to calculate buccal soft tissues linear and volumetric changes. DICOM file from CBCTs were superimposed to STL files allowing the evaluation of soft tissue thickness at baseline and 4 month.

Results: mean horizontal reduction accounted for 1,46 ± 0,20 (SH), 0,85 ± 0,38 (DBBM-CM) and 0,84 ± 0,30 IMPL/DBBM-CM, with no statistically differences. Soft tissue thickness had a significant mean increase of 0.95 for SH group, compared to a non significant mean decrease for DBBM-CM (0.20) and IMPL/DBBM-CM group (0.07).

Conclusion: a preservation technique with DBBM-CM, with or without immediate implant placement, reduced the horizontal linear and volumetric changes at the buccal soft tissue profile 4 months after tooth extraction when compared to spontaneous healing, although differences were not statistically significant. This is due to a significant increase in soft tissue thickness in spontaneous healing sites.

CLINICAL RELEVANCE

Scientific rational for study: the impact of dimensional soft tissue alterations in post-extraction sites has received little attention in clinical research. Moreover the relative contribution of the soft and hard tissue to the total volume and their mutual interplay is poorly understood.

Principal Findings: an alveolar ridge preservation, with or without immediate implant placement, reduced labial soft tissue dimensional changes 4 months after tooth extraction when compared with spontaneous healing, although differences between treatment modalities wer not statistically significant. Soft tissue thickness had a significant increase after 4 months of spontaneous healing.

Practical Implications: on a soft tissue level, treatment modality may be considered less critical in terms of contour alterations than focusing on the preservation of alveolar bone. Spontaneous healing provides an increased amount of keratinized mucosa, which may facilitates primary flap closure for subsequent bone regeneration.

INTRODUCTION

Dimensional changes observed after tooth extractions not only relate to changes in bone morphology but also to those occurring at the surrounding soft tissue architecture (Pietrokovski & Massler, 1967). In fact, since the partial or total resorption of the buccal and palatal wall of an extraction socket, marked alterations of the soft tissue can occur, with a loss of volume in the horizontal dimension that seems amount to 5–7 mm within the first 12 months, approximately corresponding to 50% of the orignal width of the alveolar crest (Schropp et al. 2003).

This may jeopardise the functional and aesthetic outcome of any dental treatment following tooth extraction, as tooth replacement with an implant supported fixed prosthesis as well as a traditional fix bridge with an intermediate pontic.

Different systematic reviews have confirmed the efficacy of an alveolar ridge preservation (ARP) technique in preventing post extraction dimensional changes of the alveolar ridge (Ten Heggler et al. 2011; Vignoletti et al. 2012; Vittorini Orgeas et al. 2013, Horvath et al. 2013; De Risi et al. 2015, MacBeth et al. 2017; Clementini et al. 2015, Avila-Ortiz et al. 2019). However, clinical research related to dimensional change after tooth extraction has mainly focused on the biology of bone, while the impact of soft tissue healing on bone modeling and dimensional changes in post-extraction sites has received little attention.

In recent years, the introduction of soft tissue volumetric analysis using optical scanning and STL image superimposition has allowed the evaluation of changes in tissue contours around teeth and implants (Benic et al. 2012). This validated technique showed a high reproducibility and an excellent accuracy for measuring volume changes with a measurement error below 10 mm (Mehl et al. 1997, Windisch et al. 2007).

Different studies utilized this methodology to investigate the impact of different treatment strategies aimed to counteract dimensional changes after tooth extraction.

Thalmair et al. (2013), investigated soft tissue contour changes after tooth extraction and different alveolar ridge preservation (ARP) surgical procedures. The authors demonstrated that using a xenogenic bone substitute, with or without a free gingival graft, was not able to entirely compensate for the alveolar ridge reduction, while covering the orifice of the extraction socket using a free gingival graft, with or without application of a filler material, was able to somewhat limit the post-operative external contour shrinkage. Another clinical trial on different ARP techniques (Jung et al. 2013) revealed less bone loss in grafted sites compared with extraction alone. Despite that, no significant soft tissue contour changes were observed (Schneider et al. 2014), which implies that soft tissue changes do not seem to completely follow the changes at the alveolar bone level and there are thicker soft tissues in non-grafted sites.

In recent years, the superimposition of DICOM data from CBCT and STL methodology gave insights in experimental and clinical research to better understand the dynamics of tissue healing in a three-dimensional way and also to discern the hard and soft tissue inter-play and the reciprocal role that they may have (Sanz Martin et al. 2017, 2018, 2019). Chappuis et al. (2015), evaluating the fate of buccal soft and hard tissue 8 weeks after extraction and before delayed implant placement, they observed that soft tissue profile did not follow the pronounced resorption pattern of the underlying bone anatomy. The authors reported a 7.5-fold increase in soft tissue thickness after tooth extraction in patients with a thin bio-type and concluded that a rapidly resorbing thin buccal plate favoured soft tissue ingrowth and therefore increased soft tissue thickness.

Very recently, Clementini et al. (2019) investigated the effect of immediate implant placement on alveolar ridge preservation when compared to alveolar ridge preservation alone or spontaneous healing of the socket. Based on radiographic linear measurements from CBCT the authors demonstrated the effectiveness of the alveolar ridge preservation technique, independently of the insertion of the implant, on the reduction of the hard tissue dimensional changes that occurred after spontaneous healing of a tooth extraction. The presence of baseline three-dimensional hard (CBCT) and soft tissue (STL) data allows for the possibility of studying the dynamic changes of tissues over time, so the aim of this report is to compare, soft tissue dimensional changes, 4 months after single tooth extraction, and to compare the relative differences in soft and hard tissue volumes following 3 different treatment modalities: spontaneous healing (SH) and alveolar ridge preservation, with (IMPL/DBBM/CM) or without (DBBM/CM) immediate implant placement.

MATERIALS AND METHODS

Study Design.

This report is based on a prospective controlled, randomized, clinical study (Clementini et al. 2019) performed according to the CONSORT statement (http://www.consort-statement.org/). The study and relative procedures and materials were approved by the local ethical committee (REF: 14-034, 24/07/2015) and monitored following the Good Clinical Practice. The trial was registered at http://www.clinicaltrials.gov/ (REF: NCT03422458).

Population.

The study population consisted of 30 subjects seeking care at the Dental Clinic of San Raffaele Hospital, Vita Salute University, Milan, Italy, between January 2016 and January 2018. All patients signed a written informed consent, according to the ethical principal of Declaration of Helsinki on experimentation involving human subjects, as revised in 2008.

Inclusion criteria

- Adult patients (>18 years old) requiring extraction (for caries, fracture, prosthetic reasons) of one upper or lower single rooted tooth (incisor, canine) or premolar.
- Presence of adjacent (mesial and/or distal) natural teeth.
- The presence of an intact extraction socket (evaluated after a flapped tooth extraction), with a coronal margin of the buccal bone crest that deviated ≤1 mm from the coronal margin of the lingual bone crest and ≤3 mm from the mesial and/or distal interproximal bone crest (evaluated on the preoperative CBCT).
- Systemically healthy patients not smoking more than 10 cigarettes/day.
- Patients with adequate oral hygiene (FMPS < 25%) and periodontal health (FMBS < 10% and absence of PPD > 4 mm with BoP) (Lang & Bartold, 2018).

Exclusion criteria

- Uncontrolled diabetes (HbA1c > 7), osteoporosis or any other systemic or local disease or condition that would compromise post- operative healing.
- Patients with a history of malignancy, radiotherapy or chemotherapy for treatment of malignancy.
- Pregnant patient or intending to become pregnant or nursing at the time of study inclusion.
- Patients taking medications or having treatments with an effect on healing in general (e.g., steroids, large doses of anti-inflammatory drugs, bisphosphonates).

Randomization process and allocation concealment.

A person not involved in the study prepared a computer-generated randomization list. After tooth extraction, an opaque sealed envelope was opened and the allocation in one of the three groups accomplished.

Treatment procedures.

Details of the surgical procedures are reported in Clementini et al. 2019. In brief, after the elevation of a full thickness flap and atraumatic tooth extraction with granulation tissue removal, the integrity of the bone plates was assessed and patients were randomly assigned to:

• Test group (IMPL/DBBM/CM): immediate implant placement (TTi WINSIX®, Biosafin, Ancona, Italy), plus a collagenated bovine bone mineral (Geistlich Bio-Oss Collagen; Geistlich Pharma AG, 6110 Wolhusen, Switzerland) grafted into the gap up to the buccal bone crest, sealed with a collagen porcine matrix (Geistlich Mucograft Seal; Geistlich Pharma AG).

• Control group (DBBM/CM): collagenated bovine bone mineral (Geistlich Bio-Oss Collagen; Geistlich Pharma AG, 6110 Wolhusen, Switzerland) grafted into the socket up to the buccal bone crest, sealed with a collagen porcine matrix (Geistlich Mucograft Seal; Geistlich Pharma AG).

• Negative control group (SH): spontaneous healing.

Patients were provided with oral hygiene instructions (rinsing twice a day, starting the day after surgery, with 0.2% chlorhexidine) and drugs prescriptions (1g of Augmentin twice a day for 6 days and Ibuprofen 600 mg, if needed, for analgesic use).

Sutures were removed 7 days after the surgical procedures. Patients then followed their individual maintenance programme according to the individual periodontal and caries risk assessment. Four months after the surgery, all patients were recalled for a follow-up.

Clinical measurements.

The following clinical parameters were assessed by a single blinded calibrated examiner (A.A.): full-mouth plaque score (FMPS) (O'Leary, Drake, & Naylor, 1972), full- mouth bleeding score (FMBS) (Muhlemann & Son, 1971) and keratinized tissue height (KTH), were recorded with a periodontal probe (PCP UNC 15, Hu-Friedy) at baseline and 4 months. Moreover, tissue thickness (TT clinical) was assessed at baseline and 4 months, as de- scribed in Clementini, Discepoli, Danesi, & de Sanctis, 2018.

STL image acquisition.

For each patient, dental impressions were obtained using a polyether impression material (Impregum™ Penta™, 3M ESPE Dental Products, Seefeld, Germany) at two different time-points: after tooth extraction at the end of the surgical procedure (Baseline, BL) and 4 months after surgery (4M). Afterwards, cast models were made with dental stone (Zeus Stone®, Zeus®, Industria Zingardi S.r.l., Novi Ligure, Italy) and optically scanned using a 3D scanner (Cerec Omnicam, Dentsply Sirona, York, PA, United States) in order to be digitized for creating stereolithography (STL) files.

Soft tissue linear and volumetric measurements.

STL files superimpositions and soft tissue dimensional change measurements were performed by one calibrated and blinded examiner (V.C.), adopting a methodology similar to the one reported by Sanz-Martin I. et al. (2018). BL and 4M STL files of each patient were superimposed and matched using a digital volume compare software program (SMOP, Swissmeda AG, Zurich, Switzerland). After importing the STL files of dental models (BL and 4M) to the software, the matching of STL files was made by defining corresponding point pairs from the occlusal tooth surfaces of the BL and 4M digital models and then the software automatically aligned the models.

Superimposed STL files were used to assess linear and volumetric soft tissue dimensional changes which occurred after 4 moths of healing following the three different treatment modalities (IMPL/DBBM/CM; ARP DBBM/CM; SH):

- linear soft tissue contour changes were assessed on the superimposed models using the cross section representing the mesio-distal centre of the edentulous crest, in order to carry out linear measurement. Using an image analysis software program (ImageJ, National Institutes of Health. Maryland, USA), three parallel lines were drawn at 1, 3 and 5 mm below the most coronal point of soft tissue contour at BL and horizontal linear measurements were performed. The linear horizontal soft tissue contour changes were calculated by subtracting the horizontal measurement of the alveolar soft tissue width at BL to the 4M measurement and were expressed in mm. (Total horizontal 1, 3, 5 mm.). The linear buccal soft tissue contour changes were calculated by measuring the horizontal linear distance between the buccal soft tissue contour at BL to 4M and were expressed in mm (Buccal Horizontal 1, 3, 5 mm.)
- volumetric buccal soft tissue changes were analysed with the same software program used for STL files superimposition (SMOP, Swissmeda AG, Zurich, Switzerland),

selecting a well-defined area on the superimposed digital models. According to Schneider et al. (2014), the area was delimited apico-coronally by the gingival margin and the mucogingival line and mesio-distally by the middle of interdental papillae. Subsequently, the software automatically computed the mean linear distance in mm. (MD) and the volume change in mm^3 (Volume) between BL and 4M buccal surfaces of the selected area.

Soft tissue thickness measurements (DICOM—STL image superimposition).

STL file of the soft tissue profile at BL and 4M were superimposed to the DICOM files of the hard tissue respectively at BL and 4M, as described in Sanz Martin et al. 2017, 2018, 2019. Using an image analysis software program (ImageJ, National Institutes of Health. Maryland, USA), a common vertical axis was selected for both the BL and 4M images, then the buccal tissue thickness was assessed by measuring the distance between the buccal bone and the buccal soft tissue profile perpendicularly to the vertical axis at 1, 3 and 5 mm below the most coronal point of soft tissue contour at BL and 4M (TT digital 1, 3, 5)

Statistical analysis.

Observed values were summarized by means and standard deviations. In order to assess differences among groups, a one-way ANOVA allowing for different variances was used. P-values were, then, adjusted for False Discovery Rate. In order to assess differences within group a paired t-test was performed. All the analyses were performed using R statistical software (R Development Core Team, 2016). The significance threshold was set at 0.05.

RESULTS

From January 2015 to January 2018 a total of 30 subjects were recruited, randomized and included in the clinical trial: 10 allocated to the SH group, 10 allocated to DBBM-CM group, and 10 allocated to IMPL/DBBM-CM group, respectively.

No significant differences between groups were observed when analyzing baseline characteristics (**table 1).** Clinical outcomes were reported in Clementini et al. 2019

Soft tissue linear changes

One millimeter apical to the most coronal soft tissue margin of the baseline STL file, the soft tissue bucco-lingual dimension decreased 2,60±0,32 mm (27,51±5,04 %), 1,60±0,27 mm (15,38±2,78%), 1,66±0,25 mm (16,28±2,90 %) in the SH, DBBM/CM and IMPL/DBBM/CM groups, respectively. Three millimeters apical to the soft tissue margin the variations were 2,79±0,31 mm (21,52±5,20%), 1,42±0,30 mm (16,91±3,07%), 1,55±0,48 mm (16,07±2,78%) in the SH, DBBM/CM and IMPL/DBBM/CM groups, respectively. At the 5 millimeters level of the analysis dimensional changes were 3,21±0,34 mm (21,64±4,59 %), 1,94±0,26 mm (18,76±4,19 %), 1,91±0,26 mm (17,94±3,71 %) in the SH, DBBM/CM and IMPL/DBBM/CM groups, respectively. No statistically significant differences were assessed between groups (**table 2**).

When analyzing soft tissue superimpositions only on the buccal side, at 1 millimeter level of the analysis, the dimensions decreased 1,50±0,23 mm, 0,80±0,27 mm, 0,72±0,23 mm in the SH, DBBM/CM and IMPL/DBBM/CM groups, respectively. Three millimeters apical to the soft tissue margin, dimensional variations were 1,48±0,29 mm, 0,83±0,29 mm, 0,75±0,26 mm in the SH, DBBM/CM and IMPL/DBBM/CM groups, respectively. Soft tissue changes 5 millimeters apical to the tissue margin were 1,66±0,26 mm, 1,02±0,31 mm, 0,85±0.26 mm in the SH, DBBM/CM and IMPL/DBBM/CM groups, respectively. When comparing changes between the control group and the two test groups, differences were statistically significant only at 5mm. apical to the most coronal soft tissue margin ($p<0,001$)

Soft tissue volumetric changes

Observed changes in mean linear distance (MD) from the two STL surfaces were -1,46±0,20 mm for the SH group, -0,85±0,38 for DBBM-CM mm group and -0,84±0,30 mm for IMPL / DBBM-CM group. No statistically significant differences were assessed between groups. (**table 2**)

When volumetric analysis was performed, despite a difference in favor of the two test groups (42,57±17,36 mm³ for SH group, 33,99±9,55 mm³ for DBBM-CM group and 32,50±11,69 mm³ for IMPL / DBBM-CM group,) no statistically significant differences were observed. (**table 2**)

Soft tissue thickness changes (DICOM—STL image superimposition)

Four months after extraction and treatment procedures, only tissue thickness at 3 and 5 mm. could be assessed, since the absence of bone at 1 mm below the most coronal point of soft tissue contour. At 3mm. soft tissue thickness had a significant mean increase of 0.95 for SH group ($p<0,05$), compared to a non-significant mean decrease for DBBM-CM group (0.20) and IMPL/DBBM-CM group (0.07). These changes results in a significant differences ($p<0,05$) in soft tissue thickness between control and test groups. None of the changes values for soft tissue thickness at 5 mm reached a statistical significance (**table 3**).

DISCUSSION

This randomized clinical study reported soft tissue findings following three different surgical procedures after tooth extraction: spontaneous healing (SH) and alveolar ridge preservation, with (IMPL/DBBM/CM) or without (DBBM/CM) immediate implant placement.

Linear and volumetric measurements using STL data demonstrated after 4 months a more pronounced reduction of the ridge contour for spontaneous healing compared to a smaller reduction when an alveolar ridge preservation technique was performed, irrespective of the insertion of an immediate implant. However, the only statistically significant difference between test groups (ARP with or without immediate implant placement) and control group (natural healing) was observed for linear measurement 5 mm apical to the most coronal soft tissue margin at the labial site. This lack of difference in the most coronal aspect may be explained in part by the small sample size of each group and in part by the relative absence at this point of keratinised tissue. Cells from this tissue are able to occupy the available space in the coronal area of an extraction socket and form a granulation tissue rich in fibroblast. These cells may differentiate into myofibroblasts, stabilising wound margin and increasing tissue thickness (Chappuis et al. 2015).

A part from this observation, no significant differences were found between test groups and control group. This is in accordance with recent randomized control clinical trials (Thalmair et al. 2013, Tomasi et al. 2018) demonstrating that alveolar ridge preservation using a xenogenic bone substitutes, was not able to entirely prevent soft tissue contour alterations 4 months after tooth extraction.

Findings from STL analysis are in contrast with previous radiographic results obtained from the same pool of patients. That study (Clementini et al. 2019) demonstrated the effectiveness of the alveolar ridge preservation technique, independently of the insertion of the implant, in reducing the hard tissue dimensional changes that occurred 4 months after spontaneous healing of a tooth extraction. Similarly, Schneider et al (2014), comparing the effect of different techniques for ridge preservation with spontaneous healing on a soft tissue contour level, demonstrated that soft tissue changes do not seem to completely follow the changes at the alveolar bone level when recorded in the same patients (Jung et al. 2013).

One other possible explantation might be that in the radiographic study the region of interest was located more apically (one, three and five millimetres from the initial alveolar crest) as compared to the region of interest for soft tissue contour measurements.

The presence of baseline and 4 months three-dimensional hard (CBCT) and soft tissue (STL) data allowed for the possibility of studying the dynamic changes of tissues over time. Soft tissue thickness had a significant mean increase (+0.95) after 4 months for SH group at 3mm., while no significant difference was found for DBBM-CM group and IMPL/DBBM-CM group. Hence, It appears evident that the more pronounced contraction of the bone crest observed at the natural healed ridge is compensated by an increase of the soft tissue thickness.

These findings are in agreement with Chappuis et al. (2015), in which a significant spontaneous soft tissue thickening can be observed after 8 week of healing in thin and thick bone wall phenotypes. Interestingly, in thin bone phenotypes, the facial soft tissue thickness showed a 7.5-fold increase and did not follow the pronounced resorption pattern of the underlying bone anatomy. Similar results were reported in a recent preclinical investigation studying the three-dimensional dynamics of hard and soft tissues after immediate implantation with a xenograft a xenogenic collagen matrix and imemdiate loading (San Martin et al., 2018). In this study, the buccal bone volume resoprtion after extraction was compensated by an increase in soft tissue thickness below the implant shoulder.

One factor that has been considered as of outmost importance in the healing process of a fresh extraction socket is the thickness of the buccal cortical bone. In the study by Chappuis et al. (2015) the increase in soft tissue thickness was observed only at sites that presented a thin (less than 1 mm) buccal bone. In the present study the mean thickness was 1.2mm, 1.3mm. and 1.3mm in spontaneous healing group, DBBM-CM group and IMPL/DBBM-CM group, respectively, corroborating in part previous findings.

Furthermore, it must be considered that after 4 months of healing of an extraction site a further modelling of the healing crest may be still expected and hence differences may appear after a longer healing period. Indeed, a radiographical study by Misawa (2016) demonstrated almost 30% area resorption of the socket as compared to the healed crest after 1 year. Nevertheless, according to Schropp et al. (2003) major tissue alterations occur within the first 3 months, although various amounts of additional resorption of the ridge are expected to occur in the 6- to 12-month interval.

One of the main limitation of this study is the limited number of patients in each group. Further clinical investigation should be conducted to recruit a larger population to increase the statistical power of this clinical investigations. Furthermore, longer follow up are claimed, in order to compare different surgical options after tooth extraction with evaluation not only of hard and soft tissues volumetric changes but also aesthetics, implant related outcomes, PROMs (morbidity and patient preference) and cost-effectiveness analyses.

CONCLUSION

Four months after tooth extraction horizontal linear and volumetric changes occur at the buccal soft tissue profile. A preservation technique with DBBM-CM, with or without immediate implant placement, reduced the amount of resorption compared to spontaneous healing, although differences were not statistically significant. This is due to a significant increase in soft tissue thickness in spontaneous healing sites.

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TABLES AND FIGURES.

Table 1. *Baseline demographic and clinical data of included patients. FMPS: full mouth plaque score; FMBS: full mouth bleeding score; KTH: keratinized tissue height; TT clinical: tissue thickness clinically measured*

Baseline characteristics	**Spontaneous Healing**	**DBBM-CM**	**IMPL / DBBM-CM**
Age (years)	50.5 (12.2)	55.5 (11.6)	52.5 (7.5)
Male/Female	7/3	4/6	3/7
Maxilla/Mandible	8/2	6/4	8/2
	5/5	5/5	6/4
Reason for extraction (endo/fracture/prosthetic/roo t resorption)	5/1/4	5/2/2/1	4/3/2/1
FMPS (%)	15.3 (1.3)	15.1 (1.9)	14.9 1.5)
FMBS (%)	8.9 (0.4)	8.3 (0.6)	8.6 (0.5)
KTH (mm)	2.70 (1.25)	3.70 (0.95)	4.00 (1.41)
TT clinical (mm)	1.40 (0.57)	1.30 (0.59)	1.30 (0.42)
Ridge width 1 mm	10.97 (0.94)	10.97 (0.77)	10.94 (0.49)
Ridge width 3 mm	14.10 (0.72)	13.85 (1.50)	13.48 (1.38)
Ridge width 5 mm	15.87 (0.70)	14.00 (1.01)	15.26 (2.02)

Table 2. *Linear and volumetric soft tissue changes over 4 months among the three treatment modalities. MD: mean linear distance between the two STL surfaces;*

	Spontaneous Healing	**DBBM-CM**	**IMPL / DBBM-CM**	*P-value*
Changes	Mean (SD)	Mean (SD)	Mean (SD)	
Buccal Horizontal 1 mm	-1.50 (0,23)	- 0.80 (0,27)	- 0.72 (0,23)	0.20
Buccal Horizontal 3 mm	-1.48 (0,29)	- 0.83 (0,29)	- 0.75 (0,26)	0.20
Buccal Horizontal 5 mm	-1.66 (0,26)	- 1.02 (0,31)	- 0.85 (0,27)	0.006
Total horizontal 1 mm	-2.60 (0,32)	- 1.60 (0,27)	- 1.66 (0,25)	0.13
Total horizontal 3 mm	-2.79 (0,31)	- 1.42 (0,30)	- 1.55 (0,48)	0.16
Total horizontal 5 mm	-3.21(0,34)	- 1.94 (0,26)	-1.91 (0,26)	0.16

	Spontaneous Healing	DBBM-CM	IMPL / DBBM-CM	*P-value*
Changes	Mean (SD)	Mean (SD)	Mean (SD)	
MD (mm)	-1,46 (0,20)	-0,85 (0,38)	-0,84 (0,30)	0.89
Volume (mm³)	42,57 (17,36)	33,99 (9,55)	32,50 (11,69)	0.86
Area (mm²)	40,31 (11,74)	39,60 (9,53)	39,95 (8,84)	1

Table 3. *Baseline and 4 month follow-up linear soft tissue thickness (digitally measured) among the three treatment modalities. TT: tissue thickness; BL: baseline; 4M: 4 month follow-up.*

Supplementary figure 1. *CONSORT diagram.*

Supplementary figure 2. *Superimposition and matching of baseline (yellow) and 4 month follow-up (green) STL files were performed by using an image analysis software (SMOP, Swissmeda Ltd©, Zurich, Switzerland).*

	Spontaneous Healing			**DBBM-CM**			**IMPL / DBBM-CM**			*P-value intergroup BL*	*P-value intergroup 4M*
	BL Mean (SD)	4M Mean (SD)	*P-value*	BL Mean (SD)	4M Mean (SD)	*P-value*	BL Mean (SD)	4M Mean (SD)	*P-value*		
TT digital 1 mm.	1.69 (0.57)	n.r.	*n.r.*	1.65 (0.58)	n.r.	*n.r.*	1.66 (0.51)	n.r.	n.r.	*0.89*	*n.r.*
TT digital 3 mm.	1.30 (0.46)	2.25 (0.94)	***0.01***	1.20 (0.51)	1.00 (0.91)	*0.75*	1.22 (0.54)	1.15 (0.93)	0.87	*0.66*	***0.01***
TT digital 5 mm.	1.21 (0.53)	1.10 (0.73)	*0.27*	1.17 (0.63)	0.9 (0.71)	*0.48*	1.18 (0.64)	0.9 (0.72)	0.45	*0.78*	*0.6*

Figure 1. *Occlusal view of superimposed models and sagittal measurements of soft tissue changes. (a) Spontaneous healing, (b) DBBM-CM, (c) IMPL / DBBM-CM.*

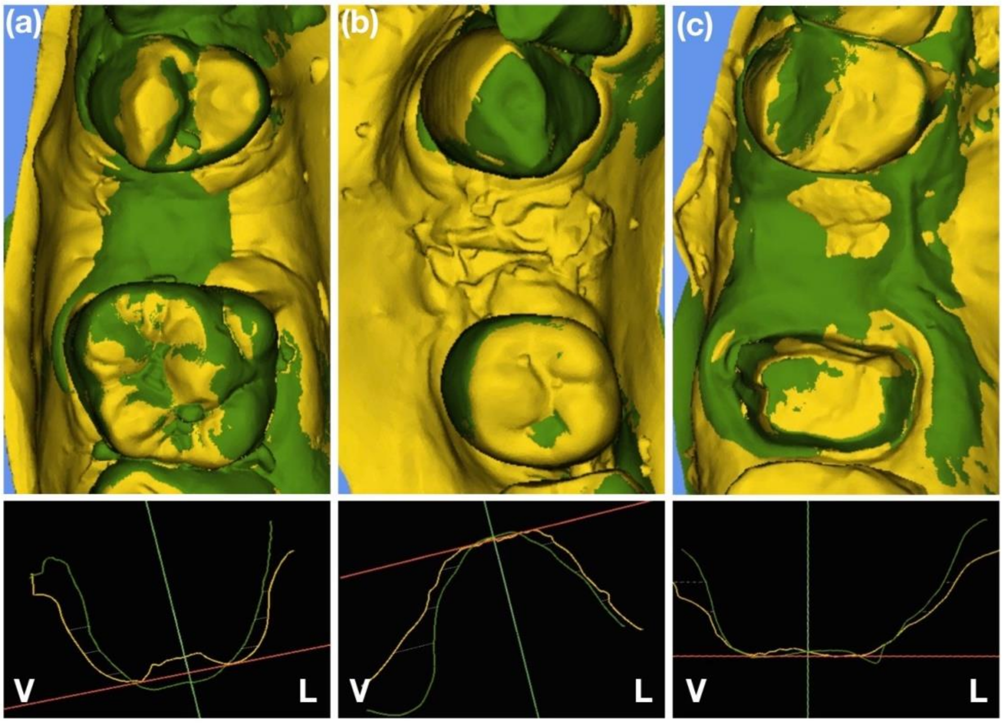

Figure 2. *Volumetric analysis by superimposition of STL files. (1) Spontaneous healing site: (a) baseline, (b) 4 months healing, (c) superimposition showing loss of volume (orange), (d) superimposition showing gradients of volumetric variations. (1) DBBM-CM site: (e) baseline, (f) 4 months healing, (g) superimposition showing loss of volume (orange), (h) superimposition showing gradients of volumetric variations. (3) IMPL / DBBM-CM site: (i) baseline, (j) 4 months healing, (k) superimposition showing loss of volume (orange), (l) superimposition showing gradients of volumetric variations.*

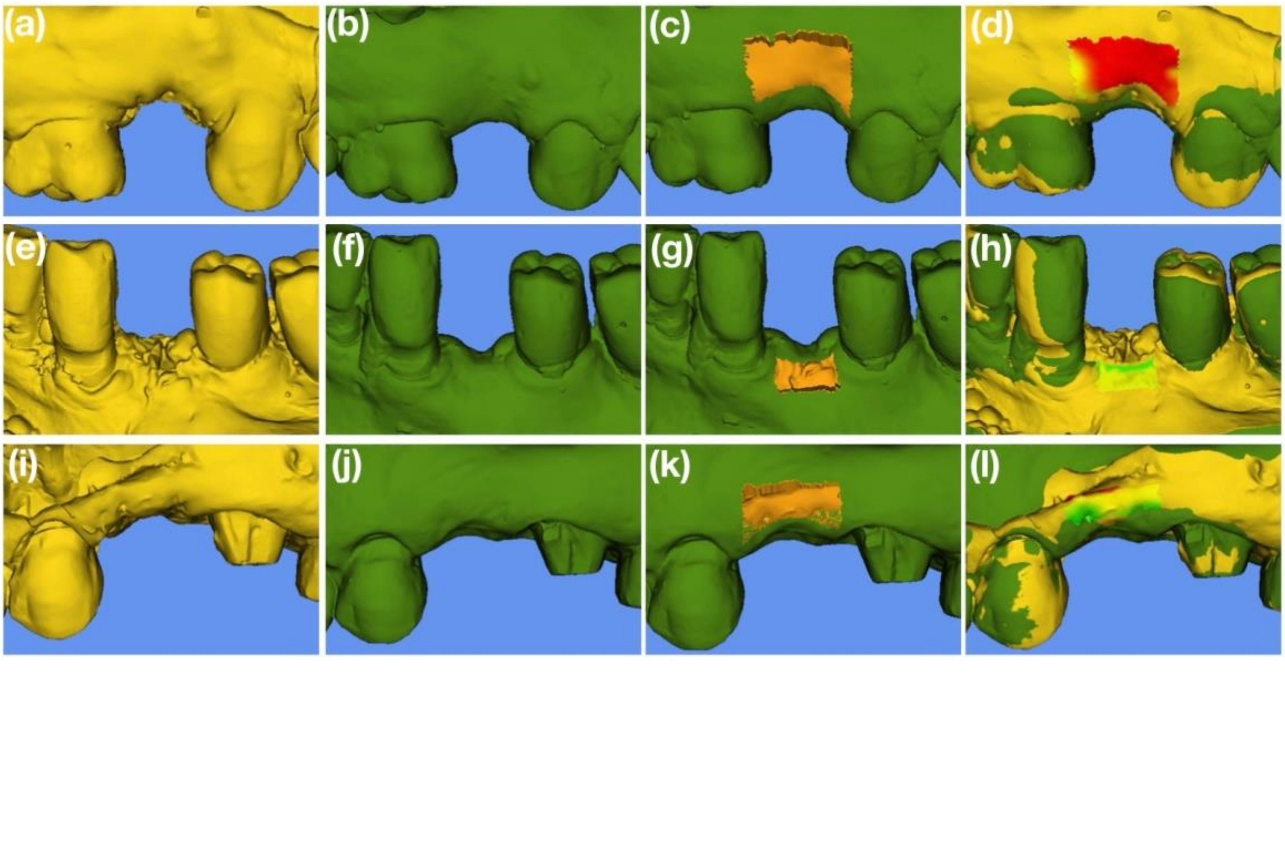

Figure 3. *Superimpositions of hard and soft tissue (purple line) in the three treatment modalities. (1) Spontaneous healing site: (a) baseline, (b) 4 months healing. (2) DBBM-CM site: (c) baseline, (d) four months healing. (3) IMPL / DBBM-CM site: (e) baseline, (f) four months healing.*