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DOTTORATO DI RICERCA IN MEDICINA MOLECOLARE

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Development and validation of novel procedures for peri-implant bone augmentation

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“*Dedicato a tutte le notti, le facce, le voci, le corna al cielo*
che danno un senso a questa palude”
(Una Palude, Ministri)

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II. TROMBELLI L, PRAMSTRALLER M, SEVERI M, SIMONELLI A, FARINA R (2020a)

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Chapter 1
General introduction

Peri-implant bone dehiscence

Definition and clinical implications

Peri-implant bone dehiscence (BD) is the exposure, on the buccal or oral aspect of the implant, of the rough threaded titanium surface of the implant. BDs are a common finding when standard diameter implants (i.e. 4 mm) are placed in anatomical regions of the oral cavity such as maxillary and mandibular posterior areas (Farina et al., 2011, Bressan et al. 2016, Pramstraller et al.,2018), in particular when a prosthetically-driven, rather than a bony-driven, implant placement is adopted to enhance functional and esthetic results (Grunder et al.,2005). Due to the combination of the pattern of bone resorption after tooth extraction and the prosthetically ideal implant tridimensional position, BDs are more probably located at the buccal aspect of the implant (Chappuis et al., 2015), and this has to be taken into account since the integrity of the peri-implant buccal bone plate (PPBP) is crucial for both functional (Monje et al.,2019) and esthetic reasons (Grunder et al., 2005).

Moreover, even when an implant is completely surrounded by bone at placement, a buccal BD may arise during the initial healing phase of the implant as a consequence of the horizontal and vertical resorption of the PBBP as a consequence of the surgical trauma for implant placement (Spray at al., 2000, Mehreb et al., 2014, 2017, Monje et al. 2019).

In this respect, a horizontal PBBP reduction of 0.31 mm between implant placement and 12 months after prosthetic rehabilitation, regardless of a thin (<1 mm) or thick (≥ 1 mm) PBBP at implant placement (Merheb et al.,2017). Consequently, when placing an implant, either the integrity and thickness of the PBBP have to be taken into account to reduce the occurrence of a BD during the initial healing phase. A PBBP thickness, at implant placement, ranging

between 1.5 and 1.8 mm seems to be a protective factor for the occurrence of a BD during the initial healing phase, as observed in both a large-scale retrospective (Spray et al. 2000) and an animal study (Monje et al. 2019).

The presence of a residual BD after a reconstructive procedure has been associated with a higher incidence of peri-implant biological complications such as peri-implant mucositis and peri-implantitis (Schwarz et al. 2012). Moreover, when a peri-implantitis lesion was inducted after the initial healing phase, its progression was faster at implants presenting a BD when compared to implants completely surrounded by bone (Monje et al. 2019).

A randomized controlled trial compared the 18 months peri-implant clinical and radiological peri-implant tissue conditions of implants where a BD was left untreated compared to implants where a BD was treated with a bone reconstructive procedure. Despite similar healthy conditions of peri-implant soft tissues between study groups, a higher interproximal radiographic bone loss was observed around implant where the BD was left untreated (Jung et al. 2017).

Collectively, these findings seem to indicate the need for BD correction at implant placement to avoid i) a higher incidence and a faster progression of peri-implantitis and ii) a higher interproximal bone loss possibly leading to the occurrence of a peri-implantitis lesion (Berglundh et al. 2018).

Reconstructive approaches to correct peri-implant bone dehiscence

The correction of a BD is commonly performed by reconstructive surgical procedures aimed at re-establishing the integrity and the thickness of the PBBP. The most documented and

validated approach for bone reconstruction is the Guided bone regeneration (GBR) (Dahlin et al. 1988).

GBR is based on the so-called PASS principle, which includes primary wound closure, angiogenesis, space creation and stability of the wound (Wang et al. 2006). Technically, it consists in the combination of a resorbable/non-resorbable membrane used alone or in combination with a bone graft, submerged by a mucoperiosteal flap to create a secluded space preventing fibroblasts and other soft connective-tissue cells from entering the bone defect thus allowing the slower-migrating cells with osteogenic potential, coming from the blood vessels of the defect and embedded in a blood clot, to repopulate the defect and repair it with newly formed bone (Dahlin et al. 1988). The efficacy and effectiveness of GBR, performed with different combination of regenerative devices, in correcting a BD was previously observed (Dahlin et al. 1991a, Dahlin et al.1991b, Zitzmann et al. 1997, Jung et al. 2003).

The most used and validated GBR procedure to correct a BD is the combination of a resorbable collagen membrane and a deproteinized bovine bone mineral (DBBM) graft (Sanz-Sanchèz et al. 2015, Thoma et al. 2019). A mean and percentage BD reduction of 4.2 mm and 81.3% were reported from a recent systematic review of controlled clinical trials and randomized controlled trials (Thoma et al. 2019).

However, the use of a barrier membrane is related to an incidence of complications of 16.8% and an incidence of membrane exposure of 18.3% and 17.6% for resorbable and non-resorbable membranes, respectively (Lim et al. 2017). Membrane exposure is outmost important since it is related with a reduction of BD correction of 1.01 mm at implants where a membrane exposure occurred compared to implant healed uneventfully (Sanz-Sanchèz et al. 2015). A possible explanation for the significant incidence of GBR complications may be

related to the exclusion of the periosteum from the healing process. Although the creation of a well-defined and secluded space underneath a membrane has been shown of biological and clinical relevance to enhance bone formation (Wikesjo e al. 1999), the need to exclude the innate osteogenic potential of the periosteum from the wound area by a membrane barrier may be questioned (Linde al. 1993).

Periosteum role in new bone formation

Periosteum anatomy

The periosteum is specialized fibrous tissue in a form of fibro-vascular membrane that covers the external surface of most bones (Jee 2001). It consists of an outer, fibrous, firm layer (collagen and reticular fibres) and an inner, proliferative layer (cambium) which lies adjacent to bone and contains osteoblast and osteoprogenitor cells. Cambium is capable of: i) forming normal lamellar bone apposition and ii) forming primary, woven bone after a fracture (Hotrop et al. 1975, Tang et al.1986, Tonna et al. 1975). The outer fibrous layer provides elasticity and flexibility, whereas the inner cambium is the osteogenic layer and contains three or four cell layers, including osteoblasts and preosteoblastic cells (Chavanaz et al. 1995, Squier et al. 1990). A preclinical study showed how quiescent osteoprogenitor cells residing in the cambium layer may differentiate in osteoblasts when a tensile strain is applied to the periosteum (Kanno et al. 2005).

Periosteum is highly vascularized and its blood vessels network is an important part of bone nutritive system. Moreover, when injured, periosteal vascular network rapidly proliferates and

re-establishes its connections with the bone vessels (Nobuto et al. 2005). All these findings together suggest that periosteum may act as a cell font, as well as a source for growth factors.

Preclinical applications of periosteum in bone augmentation

The use of periosteum in bone reconstruction has been evaluated by various medical branches, including orthopedic, plastic and maxillofacial surgeons.

In an animal study, a non-containing critical defect, i.e. defect without spontaneous reparative potential, was created in the middle portion of a dog femur and subsequently stabilized with a orthopedic fixation. Defects were left for spontaneous and submerged with a dermal flap alone or covered with femoral periosteum and then submerged with a dermal flap (Fig. 1).

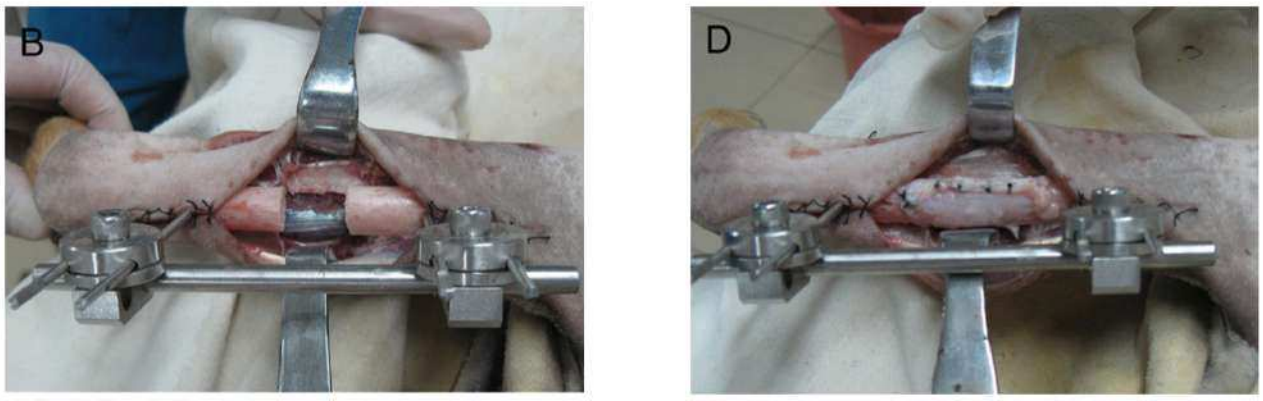

Fig. 1. Critical defect left for spontaneous healing (left) or covered with femoral periosteum (right)

The 20-weeks radiographic examination showed no bone formation in the spontaneous healing group whereas a complete bone filling in all defects was observed in the periosteum

group, underlining role of periosteum in inducing and regulating bone reparative processes (Yu et al. 2015).

A similar experiment was performed at the mandible of a canine model. Initially, a mandible segment was resected to create a critical defect. Subsequently, defects were stabilized by mean of a porous titanium mesh alone or in combination with coral hydroxyapatite or autologous bone, respectively (Fig.2).

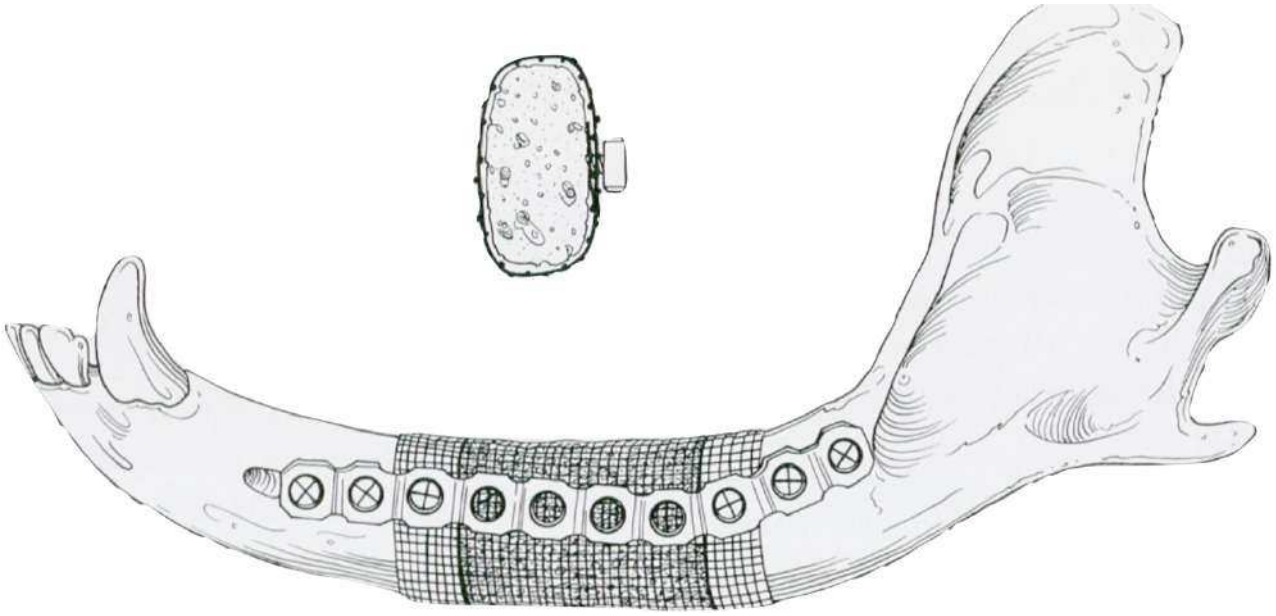

Fig.2

In all groups, the coronal portion of the defects was then covered with periosteum and submerged with a dermal flap, thus providing conditions for regeneration, whereas in the apical portion of defects periosteum was absent. At the 4 months histomorphometrical analysis, the group where titanium mesh alone was covered by periosteum showed a statistically higher rate of defect bone filling, with a mean filling of 50% (Fig. 3). Interestingly, the apical portion of the defects, not covered with periosteum, showed no new bone formation, suggesting the

paramount importance of periosteum in enhancing the osteogenic capacity of a bone defect (Lemperle et al. 1998).

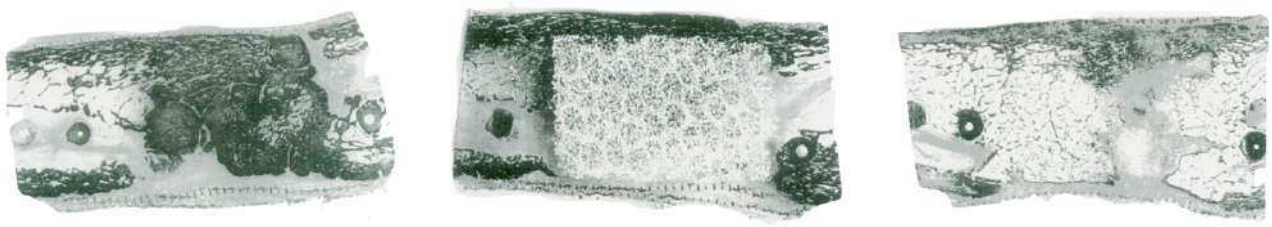

Fig.3 Titanium mesh alone (left), combined with hydroxyapatite (center) or autologous bone (right)

A recent study evaluated the capacity of periosteum in inducing peri-implant vertical bone formation. In a pig model, frontal bone was exposed by mean of a full thickness flap and titanium fixtures were inserted leaving a supracrestal exposed portion of 5 or 10 mm. In a group of animals, the flap was repositioned and sutured over the exposed implants thus creating a secluded space delimited by the frontal bone apically and by periosteum coronally (test group), whereas in another group, implants were isolated by mean of a polidioxanone capsule before flap suture, in order to exclude periosteum from wound healing (control group) (Fig. 4).

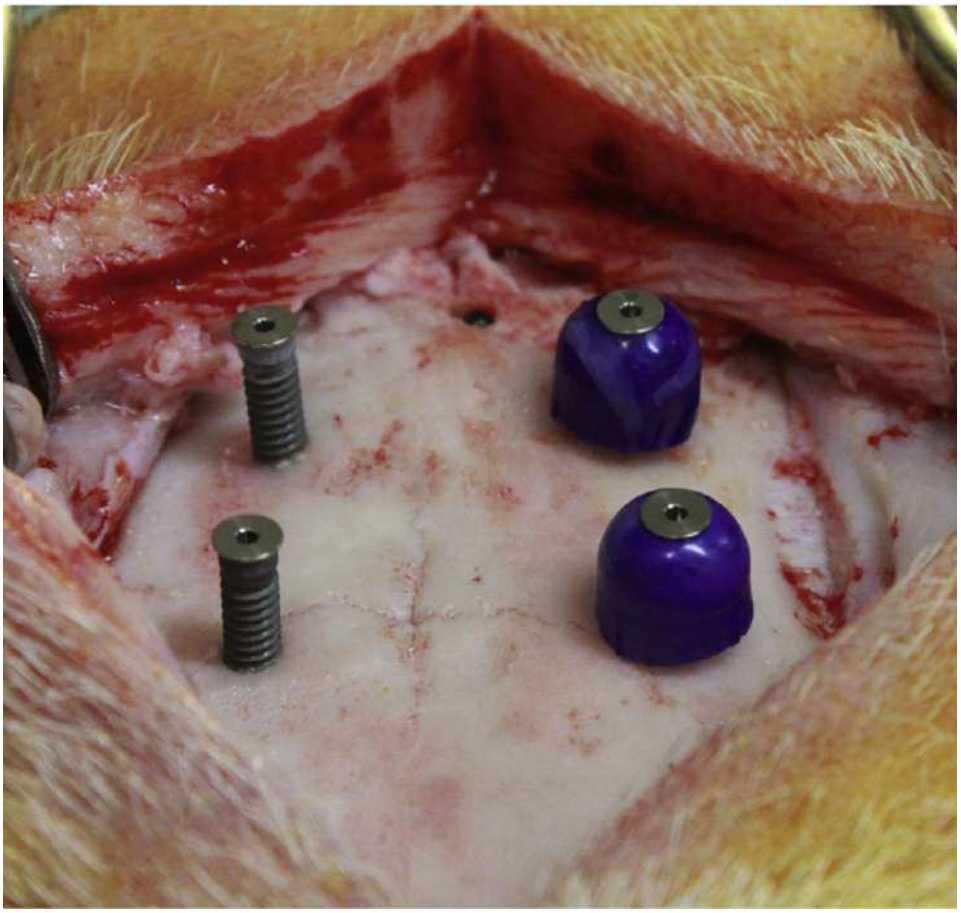

Fig.4 Implants covered with the flap (left) and isolated by mean of a polydioxanone capsule.

Histological exam at 20, 40 and 60 respectively showed a progressive new bone formation reaching the head of the implant in the test group, while in the control group the space under the polydioxanone capsule was completely filled by dense connective tissue and limited new bone formation was observed. Interestingly, in the control group, progressively increasing bone formation was observed between periosteum and the coronal margin of the capsule.

Micro-CT evaluation revealed a statistically higher vertical bone growth, 50.3.- 51.6% of vertical periosteal elevation, in test group whereas in control group the vertical growth was limited to 12.1-16.1%. The authors concluded that periostal elevation may be a suitable means of inducing supracortical peri-implant bone formation, and therefore is a possible treatment alternative to vertical peri-implant augmentation of atrophic alveolar bone (Lutz et a.l 2017).

A novel periosteum-based reconstructive approach

Sub-periosteal Peri-implant Augmented Layer technique

Recently, a novel simplified soft tissue management, namely the Sub-Periosteal Augmented Layer (SPAL) technique was proposed to increase (horizontal and/or vertical) hard tissue dimensions at the most coronal portion of a dental implant simultaneously with implant plcament (Trombelli et al. 2018).

The technique starts with a partial thickness crestal incision, made by a 15C scalpel blade and a mesial partial-thickness releasing incisions, made to obtain better visibility and avoid tension on the flap. A split-thickness flap is then raised on the buccal aspect by sharp dissection (namely, the mucosal layer) and leaving the periosteal layer on the edentulous ridge intact. After separation between the mucosal and periosteal layer to allow for a tension-free, coronal advancement of the mucosal layer, a second crestal incision reaching the bone crest is performed to allow the periosteal layer elevation was from the bone crest to create a secluded pocket that could accommodate an adequate extension and volume of the bone graft material. A full-thickness flap is elevated on the oral (lingual/palatal) aspect.

Subsequently, prosthetically guided implant-placement is performed and a titanium mplant is placed. If implant placement resulted in a BD or a PBBP thickness < 1 mm, a DBBM xenograft is used as a space-making device to fill the surgically-created space between the periosteal layer to completely correct the BD, if present, and to increase PBBP thickness to at least 2 mm.

The periosteal layer is then sutured to the oral mucoperiosteal flap by means of internal mattress sutures. The mucosal layer is coronally advanced and sutured tension-free by

horizontal internal mattress and interrupted sutures to submerge both the graft and the implants.

A case report on the SPAL technique, performed on a 61-years old patient presenting a PBBP thickness < 1 mm at two implants in position 4.5 and 4.6, reported an increase in the PPBP thickness (> 2 mm) of the buccal peri-implant hard tissue and no BD at the 4-months surgical re-entry. This result, although anecdotical, indicated tha SPAL technique may represent a valuable surgical option in the horizontal augmentation of peri-implant tissue thickness.

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AIM OF THE THESIS

The general purpose of this Ph.D. thesis was to evaluate the effectiveness of a novel surgical soft tissue management (the Sub-periosteal Peri-implant Augmented Layer, SPAL; Trombelli et al. 2018).

The following studies were performed in order to answer specific research/clinical questions:

1. What is the clinical effectiveness of SPAL technique in the preventing or correcting a peri-implant bone dehiscence or at implant placement?
2. Is there any difference in peri-implant tissue conditions on the short-term at patients receiving SPAL technique compared to patients with adequate thickness (≥ 2 mm) of PBBP at implant placement?
3. May bone augmentation be performed successfully at peri-implant dehiscence sites with a combination of SPAL and a deproteinized bovine bone mineral (DBBM) block?
4. What is the clinical effectiveness of SPAL technique in the regenerative treatment of peri-implantitis bone defects?

CHAPTER 2

A simplified soft tissue management for peri-implant bone augmentation

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ABSTRACT

Purpose: The present case series illustrates a simplified soft tissue management, namely the Sub-Periosteal Augmented Layer (SPAL), to increase hard and soft tissue dimensions at the most coronal portion of an implant.

Methods: Twenty-seven implants in 16 patients presenting either a buccal bone dehiscence or a thin (< 1 mm) buccal cortical bone plate (BCBP) were consecutively treated. Briefly, a split-thickness flap (namely, the mucosal layer) was raised on the buccal aspect. Then, the periosteal layer was elevated from the bone crest. A full-thickness flap was elevated on the oral aspect. After implant site preparation, a xenograft was used to fill the space between the periosteal layer and the BCBP and/or exposed implant surface and, if present, to completely correct the bone dehiscence. The periosteal layer was sutured to the oral flap. The mucosal layer was coronally advanced and sutured to submerge both the graft and the implants. At 3-6 months, a re-entry procedure for implant exposure was performed.

Results: Healing was uneventful, with no signs of infection in all cases. A wound dehiscence was observed in 3 implants at 2 weeks post-surgery. Out of 15 implants showing an initial bone dehiscence, 12 implants (80%) showed a complete resolution, with a sub-periosteal tissue thickness (SPTT) at the time of re-entry of 3.1 ± 1.0 mm. Three implants presented a residual dehiscence of 1 mm (2 implants) or 2 mm (1 implant), with a SPTT of at least 2 mm. Out of 12 implants showing a thin BCBP at implant placement, 10 implants (90%) revealed a SPTT≥ 2 at the time of re-entry. Two implants revealed a SPTT of 1 mm.

Conclusion: SPAL technique represents a valuable simplified surgical approach associated with a low rate of complications in the treatment of peri-implant bone dehiscence and in the horizontal augmentation of peri-implant tissue thickness.

INTRODUCTION

Insufficient bone volume with respect to implant dimension may lead to a deficiency of peri-implant tissues, thus calling for hard and/or soft tissues reconstructive procedures. In particular, prosthetically-driven implant placement in a reduced horizontal bone dimension often results in a peri-implant bone dehiscence or fenestration. Even in presence of an intact but thin cortical bone plate, trauma and consequent bone remodeling following surgical procedure for implant placement may result in a vertical bone loss with the exposure of the coronal part of the implant at uncovering (1).

The presence of a buccal bone dehiscence has been shown to be associated with greater mucosal recession on the long-term. Also, a greater risk for the occurrence of mucosal bleeding upon probing was reported for implants with dehiscences deeper than 1 mm compared to implants without dehiscence (2). Therefore, bone dehiscence or fenestration around implants are commonly corrected by bone augmentation, soft tissue augmentation or combination. The most documented procedure consists of the use of a resorbable/non-resorbable membrane combined with a graft according to Guided Bone Regeneration (GBR) principles. Experimental studies revealed a greater augmented bone area for groups treated with GBR compared to non-GBR controls (3). However, recent data shows that the complete

resolution of a bone dehiscence around implants is limited to 33% of GBR treated defects (2). A vertical bone loss 6 months after implant insertion was observed in 20% of implants with a shallow (< 5mm) dehiscence treated with GBR (4). In addition, a substantial incidence of membrane exposure has to be expected for resorbable and non resorbable membranes following GBR to correct peri-implant fenestrations/dehiscences (5), thus leading to substantially less bone regeneration compared to non-exposed sites (6, 7).

GBR principles that support new bone formation by the use of a barrier membrane imply the concept of “cell-exclusion” and “space-making” (8). Although the creation of a well-defined and stable compartment underneath a membrane has been repeatedly shown of biological and clinical relevance to enhance bone formation (9), the need to exclude the innate osteogenic potential of the periosteum from the wound area by a membrane barrier has been questioned (10). In this respect, a possible explanation for the observed insufficient bone augmentation following GBR may relate to the exclusion of the contribution of the periosteum in the bone healing process.

Different techniques for grafting buccal plates without barrier membranes for horizontal augmentation have been reported in the literature (11, 12, 13, 14, 15). One of these techniques, esthetic grafting, consists of interposing a graft biomaterial directly between the exposed implant surface and the buccal (thick) mucoperiosteal flap. The procedure has been shown effective to treat peri-implant buccal bone dehiscence occurred at the time of implant placement (11, 16). More recently, a novel bone augmentation procedure based on the utilization of the periosteum as a barrier membrane and space-making “device” has been

successfully used to enhance the horizontal bone dimension prior to implant placement (17). Consistently, the use of a laparoscopic approach to deliver a growth factor/xenograft combination into a subperiosteal pouch resulted in predictable and consistent bone regeneration (18). The biologic rationale for the use of the “periosteum layer” was recently confirmed by an experimental study where the peri-implant osteogenic potential of the periosteum in determining vertical bone augmentation around implants has been histologically reported (19). Collectively, these findings indicate that pre- and peri-implant tissue augmentation may be enhanced by surgical procedures where the periosteum is left intact although detached from the underlying bone, and a secluded space between the periosteum and the bone or implant is warranted.

The purpose of the present study is to produce proof-of-principle evidence on the effectiveness of a simplified soft tissue management, namely the Sub-Periosteal Augmented Layer (SPAL). SPAL technique is proposed to increase (horizontal and/or vertical) hard and soft tissue dimensions at the most coronal portion of an implant. Cases where either a bone dehiscence (with exposed implant threads) or a thin buccal cortical bone plate (BCBP) was present are presented.

MATERIALS AND METHODS

Study population

Sixteen systemically healthy patients (7 men and 9 women; 2 patients both smoking 4 cigarettes/day and 1 former smoker), aged 39 to 72 years (mean 57 ± 10 years), in need for

implant supported rehabilitation were consecutively included at the Research Centre for the Study of Periodontal and Peri-implant Diseases, University of Ferrara, Italy, and one private practice in Ferrara, from December 2015 to September 2017. When needed, patients had undergone active periodontal therapy for the treatment of periodontitis and were enrolled in a professional recall program prior to implant placement. Treatment plan was based on 3D radiographic assessment, and a surgical stent was fabricated on diagnostic wax-up when deemed necessary.

Patients were included only when the preliminary clinical and radiographic evaluation suggested the presence of a thin (< 1 mm) BCBP or a bone dehiscence was detected at the time of implant placement. Twenty-seven implants in 16 patients were included for analysis. All patients signed a written informed consent.

Surgical procedure

SPAL technique represents a soft tissue management procedure aimed at increasing the horizontal and vertical dimensions of the sub-periosteal tissues at peri-implant sites where BCBP is missing or thin (Figure 1 and 2, respectively).

At implant placement, patients were administered 2 g of amoxicillin + clavulanic acid (Augmentin, GlaxoSmithKline, Verona, Italy) one hour prior to surgery. Local anesthesia was attained using articaine with 1:100,000 epinephrine administered by local infiltration. Attention was paid not to infiltrate the area where the split-thickness flap has to be performed.

A partial thickness mid-crestal incision was made by a 15C blade. For single implants, the incision was extended intra-sulcularly one tooth mesial and one tooth distal to the area of interest, thus outlining an envelope flap. In case of multiple implants, one (mesial) or two (mesial and distal) partial-thickness releasing incisions were made to obtain better visibility and avoid tension on the flap. A split-thickness flap was raised on the buccal aspect by sharp dissection (namely, the mucosal layer) and leaving the periosteal layer on the edentulous ridge intact. After separation between the mucosal and periosteal layer to allow for a tension-free, coronal advancement of the mucosal layer, a second crestal incision reaching the bone crest was performed, and the periosteal layer was elevated from the bone crest. Sharp dissection of the mucosal layer was performed by a 15C blade as well as tunneling knives (KPAX, TKN1X and TKN2X, Hu Friedy, Chicago, Illinois) with varying angulated sharp edges according to the anatomical location, while the periosteal layer was elevated by a periosteal elevator (PTROM, Hu-Friedy, Chicago, Illinois) thus creating a pocket that could accommodate an adequate extension and volume of the bone graft material. A full-thickness flap was elevated on the oral (lingual/palatal) aspect.

Implant site preparation was made with ceramic burs according to manufacturer's instruction, and tissue-level implants (Thommen Medical, Grenchen, Switzerland) were placed with the polished collar (varying from 0.5 to 1 mm) above the bone crest. In all cases, healing cap were used. A xenograft (Bio-Oss® spongiosa granules, particle size 0.25-1.0 mm; Geistlich Pharma, AG, Wolhusen, Switzerland) was used as a space-making device to fill the surgically-created space between the periosteal layer and the BCBP and/or exposed implant surface and, if

present, to completely correct the bone dehiscence up to the implant polished collar. No perforations of the buccal plate were performed.

The periosteal layer was sutured to the oral mucoperiosteal flap by means of internal mattress sutures. The mucosal layer was coronally advanced and sutured tension-free by horizontal internal mattress and interrupted sutures to submerge both the graft and the implants. For both mucosal and periosteal layers, a resorbable 6/0 suture (Vicryl 6/0, Ethicon, Somerville NJ, USA) was used.

Patients were instructed not to wear any removable prostheses to avoid compression onto the surgical site for at least 3-4 weeks, and not to chew or brush in the treated area for approximately 2 weeks. The home use of a 0.12% chlorhexidine solution (Curasept ADS Trattamento Rigenerante®; Curaden Healthcare, Saronno, Italy) was prescribed for chemical plaque control (1-minute rinse b.i.d. for 3 weeks). Sutures were removed at 2-weeks post-surgery.

At 3-6 months following implant placement, a re-entry procedure for implant exposure was performed. Timing of re-entry was based on the size of the peri-implant bone defect at implant placement, i.e. the larger the defect the later the re-entry. A buccal split-thickness flap was performed to position the healing abutment, attention was paid to leave a substantial thickness of tissue to protect the coronal part of the implant. The flap was designed to be apically positioned or laterally displaced in order to achieve ideal gingival dimensions (height, thickness) at buccal aspect. When necessary (i.e. in absence of an adequate amount of buccal

peri-implant mucosa and/or when no keratinized tissue could be obtained from adjacent areas), a gingival graft was positioned at the most coronal portion of the implant.

Clinical measurements

The evaluation of SPAL procedure was focused on its potential to augment the horizontal dimension of the crest, assessed as the change in sub-periosteal tissue thickness (SPTT) at the most coronal portion of the implant (immediately apical to the polished collar) from the time of implant placement to the re-entry procedure. Also, the increase in the vertical dimension of the bone crest was determined as the change in the depth of the buccal bone dehiscence (BBD), when present. All measurements were performed by a single, calibrated examiner using a periodontal probe (PCPUNC 15, Hu Friedy, Chicago, Illinois) placed perpendicular or parallel to the long axis of the implant (for SPTT and BBD, respectively) at the buccal aspect of each implant.

At the time of implant placement, SPTT was recorded as the thickness of the BCBP measured at the level of the most visible apical portion of the polished collar of the implant. When a buccal bone dehiscence was present, SPTT was recorded as 0. Also, BBD was measured from the most apical portion of the polished collar to the most apical position of the BCBP at the dehiscence. After graft positioning and suturing of the periosteal layer, SPTT was recorded as the buccal thickness of BCBP (if present) plus the graft and the periosteal layer at the most visible apical portion of the polished collar. SPTT and BBD were finally measured following the partial-thickness dissection of the mucosal layer at the time of re-entry. In presence of a

residual dehiscence, SPTT was measured in the most coronal portion of the non-exposed buccal implant surface.

Measurements were performed by a periodontal probe and rounded at the nearest mm. Data are presented as mean ± standard deviation (SD). The implant was the statistical unit.

RESULTS

At implant positioning, SPTT was either <1mm (12 implants) or 0 due to a buccal bone dehiscence (15 implants) (Table 1). BBD was 2.5 ± 1.5 mm (Figure 3). At completion of the grafting of the sub-periosteal space, SPTT and BBD were 3.0 ± 0.9 mm and 0 mm, respectively.

Healing was uneventful, with no signs of infection in all cases. A wound dehiscence was observed in 2 non-smoker patients (3 implants) at 2 weeks post-surgery, with partial implant exposure in one case (2 implants). Patients were maintained with a 0.2% chlorhexidine mouthrinse regimen for 6 weeks and seen monthly until re-entry.

The re-entry procedure was performed after a period of at least 3 months (3.6 ± 1.0 months). At re-entry, all implants were stable. SPTT at re-entry amounted to 2.6 ± 0.9 mm. 25 implants (92.6%) revealed a SPTT ≥ 2 mm (Table 1). A slight decrease (0.4 ± 1.0 mm) in SPTT was observed from intrasurgery to re-entry.

The postoperative increase in SPTT as measured at most apical visible portion of the polished implant collar in implants either without initial buccal bone dehiscence or with initial buccal bone dehiscence completely corrected is shown in Table 1. Out of 15 implants showing an initial bone dehiscence, 12 implants (80%) in 9 patients showed a complete resolution with a SPTT at the time of re-entry of 3.1 ± 1.0 mm. Three implants in 2 patients presented a residual dehiscence of 1 mm (2 implants) or 2 mm (1 implant) with a SPTT of at least 2 mm (range 2-4 mm). No dehiscence was observed at re-entry on implants where a thin, but present, BCBP was recorded at implant placement. Out of 12 implants showing a thin (<1 mm) BCBP, 10 implants (90%) in 7 patients revealed a SPTT≥ 2 at the time of re-entry (2.2 ± 0.4 mm). Two implants in 2 patients revealed a SPTT of 1 mm.

Out of 27 implants included in this study, 1 implant presented a buccal fenestration of 2 mm, completely resolved at the time of re-entry.

Since the buccal soft tissues had been coronally displaced during first stage surgery, at re-entry soft tissues were managed in order to re-establish proper dimensions of the peri-implant mucosal unit. More specifically, in 10 patients (15 implants) either an apically positioned or a laterally displaced flap was performed, whereas in 6 patients soft tissue augmentation in the most coronal portion of the implant was achieved by a free gingival graft (11 implants in 5 patients) or by a bilaminar connective tissue graft (1 implant in 1 patient).

DISCUSSION

SPAL technique originates from the Double Flap incision as originally proposed (20). This design includes a partial-thickness flap elevation leaving the periosteal layer on the edentulous

ridge and separation of the mucosal layer of the flap. The periosteal layer is then used to stabilize the regenerative site using periosteal sutures. Various regenerative devices, such as non-resorbable/resorbable membrane and titanium mesh with different size and locations, were used for both horizontal and vertical implant site development (20). More recently, a similar flap design was reported (17) to perform GBR for horizontal bone augmentation prior to implant placement. A periosteal pocket was created by splitting a mucosal from a periosteal layer, and the created sub-periosteal space was then filled with bone substitute materials and covered by a resorbable membrane. At 6 months, a substantial increase of horizontal bone crest dimensions was recorded.

SPAL technique benefits by the advantages of the two previous techniques, in terms of flap design (20) and creation of a sub-periosteal space aimed at receiving an osteoconductive scaffold (17). However, our proposal is characterized by two major technical differences that simplify the procedure while leading to predictable results: i) the increase in SPTT is performed at the time of implant placement in presence of either a bone dehiscence or a thin (< 1mm) BCBP; ii) enhanced horizontal dimension and bone dehiscence correction merely relies on the osteogenetic potential inherent to the periosteum without use of membranes. Our results indicate that this technique is effective in i) correcting small (≤ 5 mm) bone dehiscence associated with implant placement, and ii) creating at least 2 mm of sub-periosteal tissue thickness in the most coronal portion of the implant, in the great majority (80% and 81%, respectively) of treated implants. Only 2 implants in 1 patient experienced an early wound dehiscence which resulted in a limited (< 2 mm) residual bone dehiscence. Although encouraging, these findings must be considered as preliminary due to the nature of the study

design (case series) and the limited sample size and, therefore, need to be corroborated with other trials.

SPAL technique resulted in an overall increase of SPTT from implant placement to re-entry even at implants with bone dehiscence. These findings contrast with those recently reported by a study where similar bone dehiscence have been either treated by GBR or left to spontaneously healing (4). Our novel flap approach to horizontal bone augmentation is based on the so-called PASS principle that includes primary wound coverage, angiogenesis, space creation, and wound stability (21).

Space is needed for the osteogenic cells to creep into the wound site, differentiate into osteoblasts, and form woven bone. Stability of the secluded space containing the graft biomaterial acting as scaffold for blood clot formation and maturation has been repeatedly emphasized in GBR, and various devices/techniques aimed at stabilizing the membrane-contained graft have been proposed (22). In our technique, space provision was warranted by i) creating a sub-periosteal pocket which is open only in its coronal portion, while not detached by underlying bone on the mesial, apical and distal aspects; and ii) the use of slow-resoption xenograft inserted and stabilized with limited dispersion and minimal micromovements.

Deproteinized bovine bone particles may have create a suitable osteoconductive scaffold for new bone formation while mechanically maintaining the periosteal layer elevated from the overlying implant and bone surface. Previous studies have shown that periosteal elevation by means of titanium mesh (23), degradable devices (24), or dental implant (19) resulted in

induction of supracortical peri-implant bone formation. Moreover, the application of tensile strain on the periosteum activates the expression of osteogenic and angiogenic factors (25). The periosteum layer may not only represent a source of osteogenetic cells, but also effectively contributes to angiogenesis which is a prerequisite for new bone formation (26). Although the clinical measurement of SPTT did not qualify the nature of the augmented tissues, human histology derived form a similar procedure where a sub-periosteal pouch was surgically created revealed xenograft particles surrounded by newly formed bone (18).

Our flap design allows for soft tissue mobilization leading to tension-free primary closure, a condition which is regarded as essential to achieve undisturbed bone regeneration. Primary closure was facilitated by two factors: i) the amount of horizontal bone resorption is positively correlated with soft tissue thickness (27). In this respect, a substantial (buccal) bone remodeling leads to an increased soft tissue thickness that can be easily manipulated by a split thickness dissection; ii) grafting was limited to the most coronal portion of the implant and rarely exceeded 4 mm in thickness.

Similar to the periosteal pocket flap (PPF) technique (17) and the Double Flap Incision Design (20), SPAL technique determined a complete primary intention healing in 91% of treated implants. In contrast, a recent systematic review showed that soft tissue complications following GBR procedure, including membrane exposure, soft tissue dehiscence, and acute infection/abscess, may reach an incidence of 45% (mean 16.8%) (5) . In GBR, wound dehiscence unavoidably results in membrane exposure which in turn jeopardize the amount of regenerated bone. Previous reports indicating that membrane exposure may lead to 50%-80%

less regenerated bone compared to non-exposed sites (28, 29). Notably, in the sole case where a substantial wound failure occurred, a limited residual bone dehiscence associated with SPTT increase was recorded. The limited adverse consequences observed in our technique compared to GBR may be ascribed to a less detrimental effect of bacterial contamination of the surgical area following SPAL technique compared to bacterial contamination of an exposed membrane.

An overall decrease in SPTT was observed from intrasurgery to re-entry. This reduction can be partly explained by post-surgery graft remodeling, with the variability in SPTT change observed among implants being partly explained by differences in the timing for re-entry. The augmented volume obtained with graft during bone reconstructive procedures was shown to undergo a progressive reduction starting from the first postoperative weeks (30). The extent of this shrinkage is dependent on the different physical and chemical characteristics of the graft material, and, for DBBM, amounted to more than 60% of the initial grafted volume at 2 years post-surgery (30). An alternative explanation may involve the horizontal and vertical bone loss associated with implant placement in presence of either a thin BCBP (1) or a bone dehiscence (4), which may have partly counterbalanced the amount of newly formed bone due to the osteogenetic capacity occurred at the sub-periosteal pocket.

In conclusion, SPAL technique represents a valuable simplified surgical approach associated with a low rate of complications in the treatment of peri-implant bone dehiscence and in the horizontal augmentation of peri-implant tissue thickness. Further longitudinal studies are

needed to evaluate whether and to what extent this procedure may ensure long-term stability of the buccal mucosal profile and healthy conditions of peri-implant tissues.

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TABLES

Table 1. Sub-periosteal tissue thickness (SPTT) and depth of the buccal bone dehiscence (DBD) at each observation interval.

		immediately after implant placement		immediately after graft placement and suturing the periosteal layer		timing for re-entry for implant uncovering	at re-entry for implant uncovering	
Patient number	**Implant position** (tooth number)	**SPTT** * (mm)	**DBD** ♀ (mm)	**at re-entry for implant uncovering**	**DBD** ^ (mm)	(months)	**SPTT** § (mm)	**DBD** ♀ (mm)
1	3.4	0	5	2	0	4	2	2
1	3.5	0	4	2	0	4	3	1
2	4.6	0	2	2	0	3	2	0
3	3.4	0	3	3	0	5	3	0
3	3.5	0	3	4	0	5	5	0
3	3.6	0	4	3	0	5	3	0
4	4.5	0	1	4	0	3	4	0
4	4.6	0	2	3	0	3	3	0
5	2.4	<1	0	2	0	4	2	0
5	2.5	0	4	3	0	4	3	0
6	1.1	<1	0	4	0	4	2	0
6	2.1	<1	0	2	0	4	1	0
6	2.3	<1	0	2	0	4	2	0
7	1.5	0	1	4	0	2	4	0
8	4.5	<1	0	4	0	4	3	0
8	4.6	<1	0	3	0	4	2	0
9	3.6	0	1	2	0	3	3	0
10	4.6	0	2	3	0	2	1	0
10	4.7	<1	0	3	0	2	2	0
11	1.4	<1	0	2	0	6	2	0
12	1.3	<1	0	3	0	4	3	0
13	3.6	0	2	3	0	4	4	1
14	2.2	<1	0	3	0	3	2	0
14	2.3	<1	0	3	0	3	2	0
15	4.6	0	2	3	0	4	3	0
16	2.4	<1	0	6	0	3	3	0
16	2.5	<1	0	4	0	3	2	0

SPPT: sub-periosteal tissue thickness; DBD: depth of the buccal bone dehiscence.

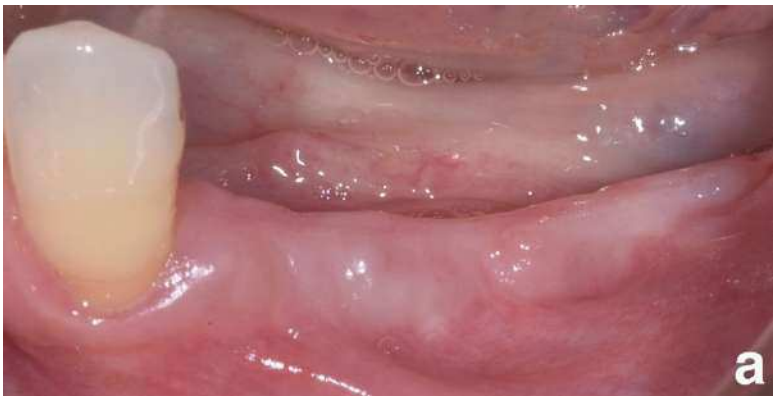
* recorded as the thickness of the buccal cortical bone plate at the level of the most apical visible portion of the polished implant collar. When a buccal bone dehiscence was present, SPTT was recorded as 0.

recorded as the thickness of buccal cortical bone plate (if present) plus the graft and the periosteal layer at the most apical visible portion of the polished implant collar;

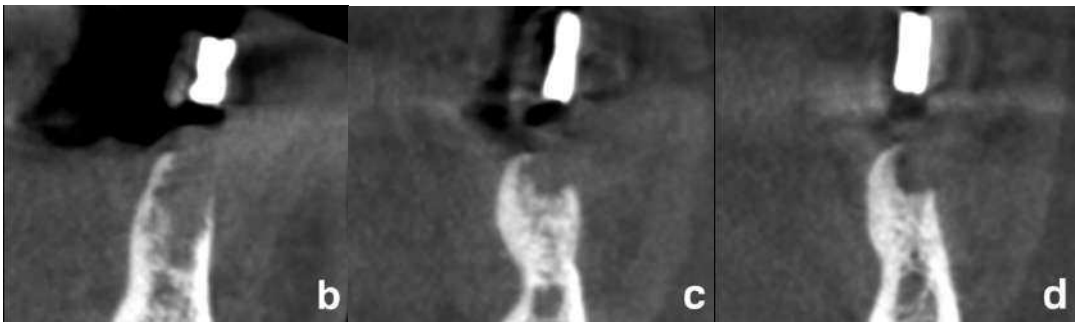
§ recorded following the partial-thickness dissection of the mucosal layer at the time of re-entry. In presence of a residual dehiscence, SPTT was measured in the most coronal portion of the non-exposed buccal implant surface;
ϛ measured from the most apical portion of the polished collar to the most apical position of the BCBP at the dehiscence;
^ measured from the most apical portion of the polished implant collar to the most coronal extension of the graft.

FIGURES

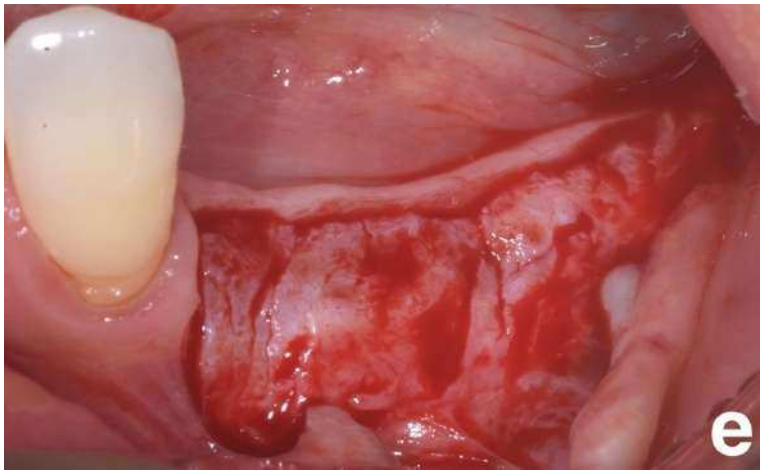
Figure 1. Sub-Periosteal Augmented Layer (SPAL) technique at multiple sites with buccal bone dehiscence.



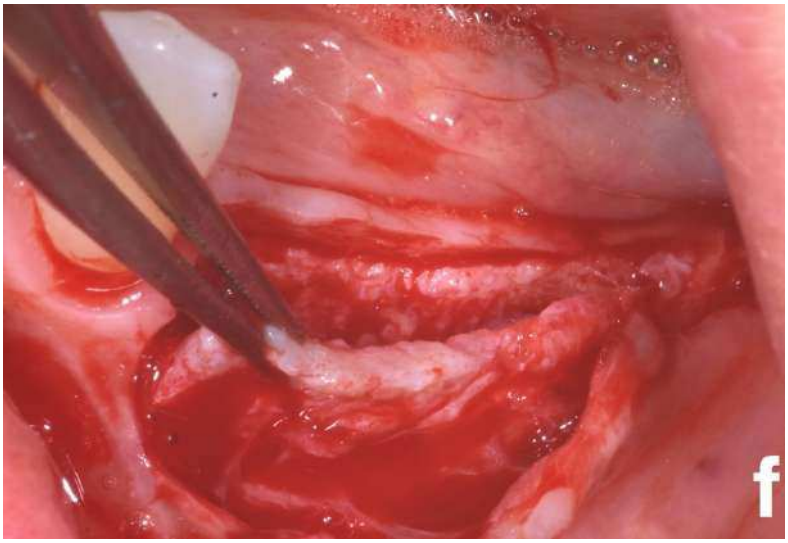
a. Preoperative view of an atrophic, edentulous mandibular posterior region.



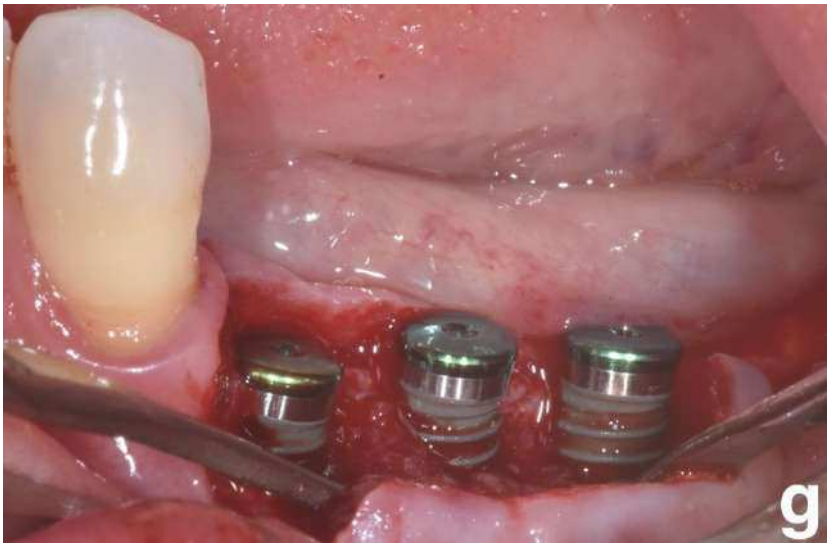
b-d. Tomographic scans show insufficient bucco-lingual width of the residual crest at first premolar, second premolar and first molar sites, respectively.



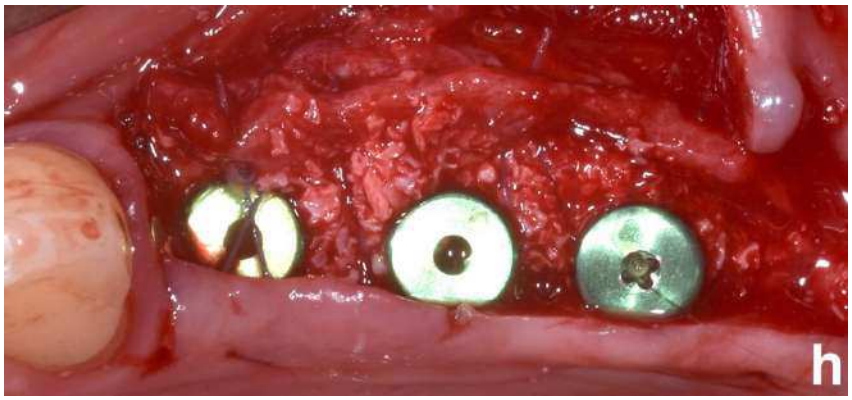
e. A split-thickness flap with releasing incisions is raised on the buccal aspect by sharp dissection, leaving the periosteal layer on the edentulous ridge intact.



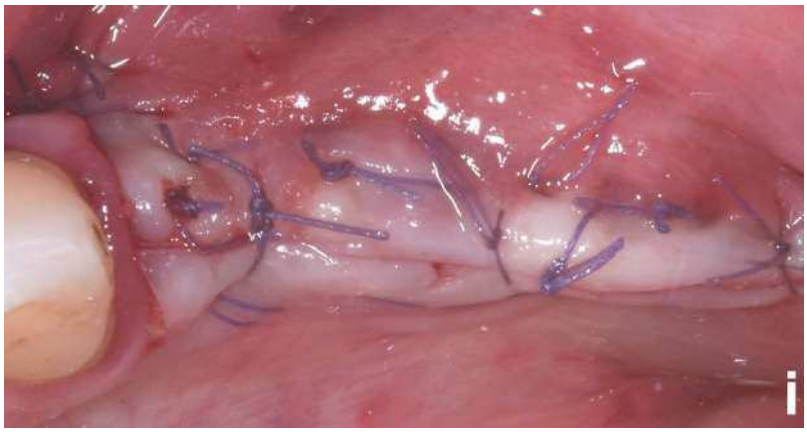
f. The periosteal layer is elevated from the buccal bone plate.



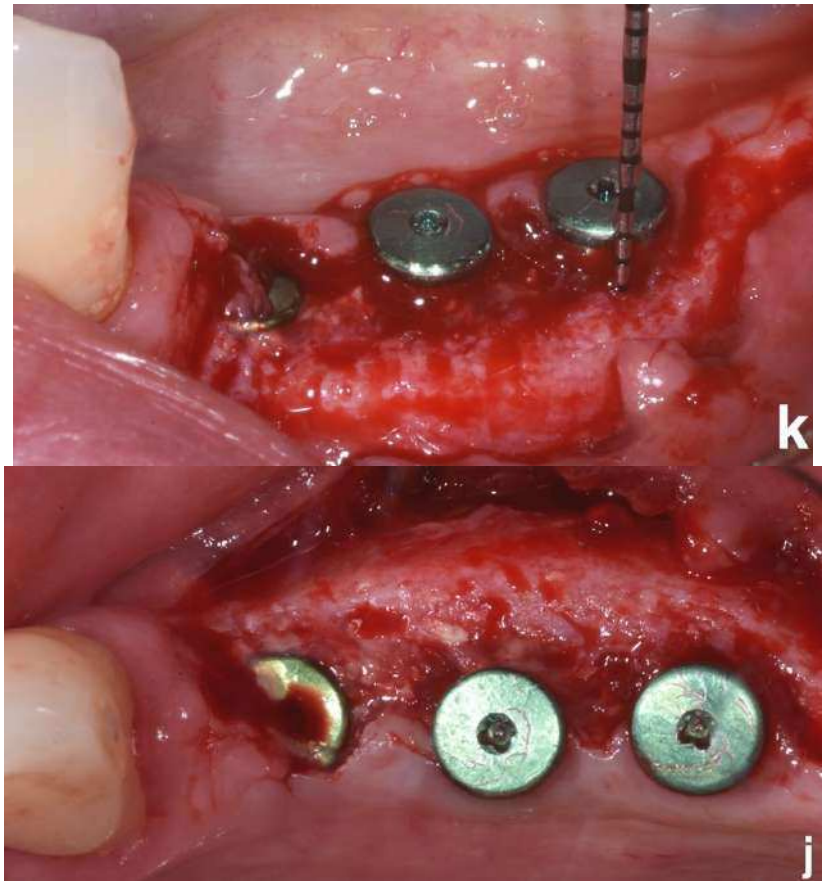
g. After placement, all implants show dehiscence defects at the buccal aspect.



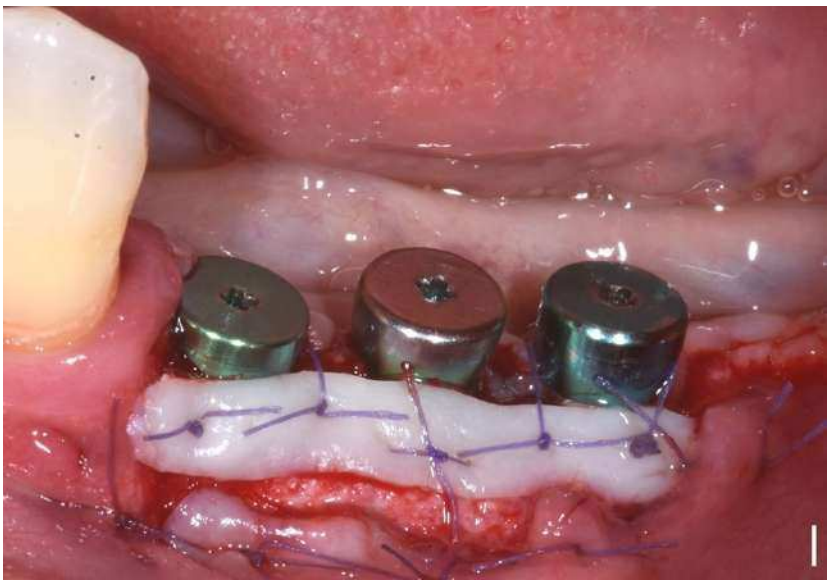
h. A xenograft is positioned into the pocket underneath the periosteal layer. The periosteal layer is sutured to the lingual flap by means of internal mattress sutures.



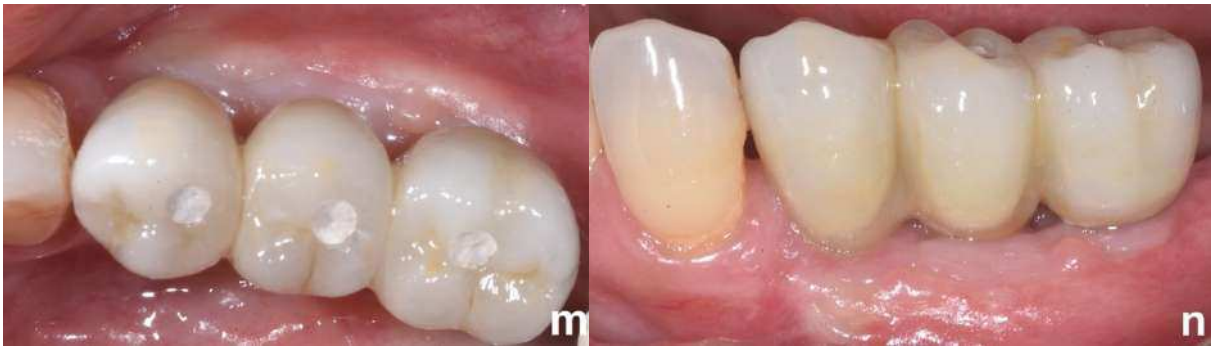
i. The mucosal layer is coronally advanced and sutured tension-free by horizontal internal mattress and interrupted sutures to submerge both the graft and the implants.



j,k. Occlusal and buccal view at re-entry for implant uncovering (4 months).

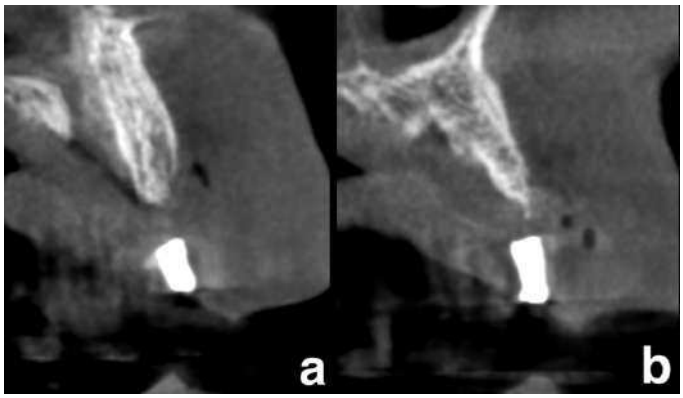


l. A free gingival graft is performed to augment the amount of peri-implant keratinized tissue.

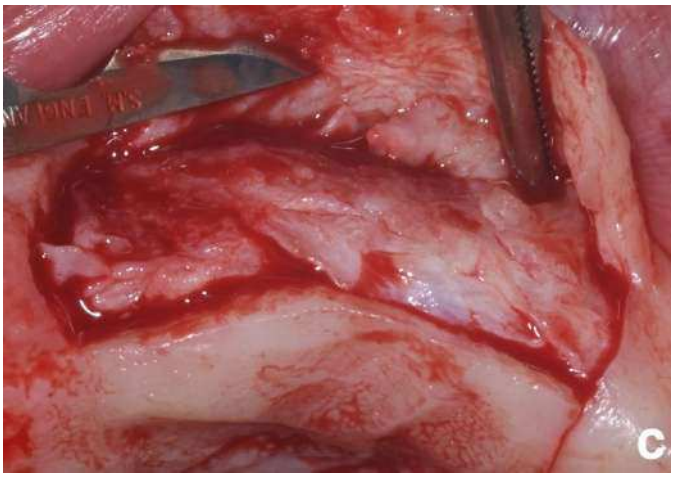


m,n. Occlusal and buccal view at prosthetic rehabilitation.

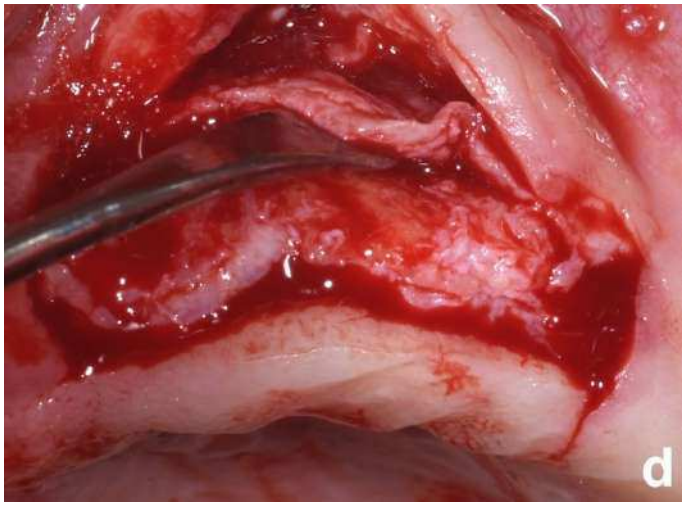
Figure 2. Sub-Periosteal Augmented Layer (SPAL) technique at multiple sites with thin buccal cortical bone plate and fenestration.



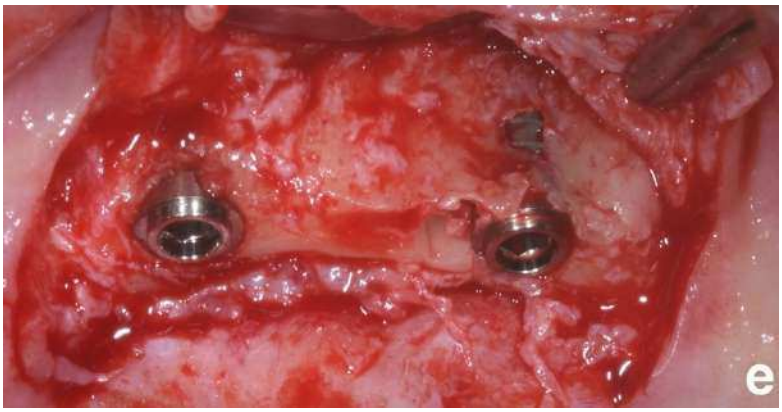
a,b. Tomographic scans show insufficient bucco-lingual width of the residual crest at an edentulous maxillary left central incisor (a) and canine (b) region.



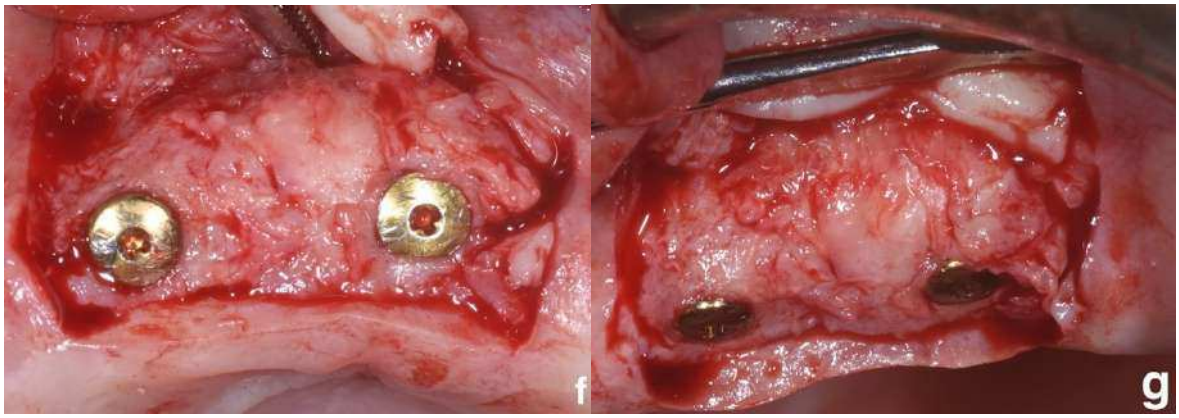
c. Elevation of a split-thickness flap with releasing incisions on the buccal aspect.



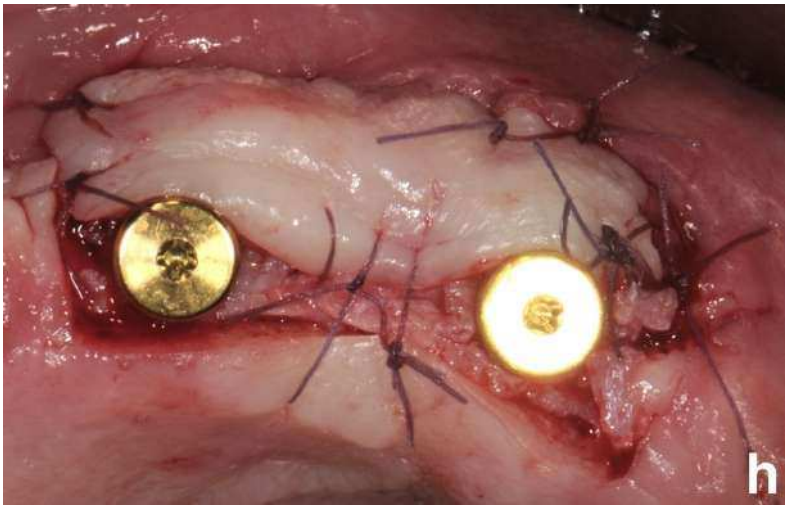
d. The periosteal layer is elevated from the bone crest.



e. After placement, both implants show a thin buccal cortical bone plate. A fenestration-type defect is also present on one implant.



f,g. At 4-month re-entry, a thick band of sub-periosteal tissues is evident at the most coronal portion of both implants.



h. An apically positioned flap is performed to increase keratinized tissue dimensions.

CHAPTER 3

Peri-implant tissue conditions at implants treated with Sub-periosteal Peri-implant Augmented Layer technique: A retrospective case series

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Abstract

Objectives: To assess peri-implant tissue conditions on the short term in patients receiving the Sub-periosteal Peri-implant Augmented Layer (SPAL) technique and in patients with adequate thickness (≥2 mm) of the peri-implant buccal bone plate (PBBP) at placement.

Methods: Patients where either a dehiscence defect or thin PBBP at implant place- ment was corrected by SPAL technique (SPALdehiscence and SPALthin groups, respec- tively) and patients presenting a residual PBBP thickness ≥2 mm at implant placement (control group) were retrospectively selected. The number of peri-implant sites positive to bleeding on probing (BoP) at 6 months following prosthetic loading was the primary outcome. Also, height of keratinized mucosa, marginal soft tissue level, Plaque Index, peri-implant probing depth, suppuration on probing, and interproximal radiographic bone level (RBL) were evaluated.

Results: Thirty-four patients (11 in the SPALdehiscence group, 11 in the SPALthin group, and 12 in the control group) were included. In each SPAL group, 10 patients (90.9%) showed peri-implant tissue thickness ≥2 mm at the most coronal portion of the im- plant at uncovering. The prevalence (number) of BoP-positive sites was 2, 1, and 0 in the SPALdehiscence, SPALthin, and control groups, respectively. RBL amounted to 0.3 mm in the SPALdehiscence group, 0.2 mm in the SPALthin group, and 0 mm in the control group.

Conclusion: After 6 months of prosthetic loading, patients treated with SPAL tech- nique show limited peri-implant mucosal inflammation in association with shallow PD and adequate KM. At implants receiving SPAL technique, however, interproximal RBL was found apical to its ideal position.

INTRODUCTION

Prosthetically driven implant placement in a reduced horizontal bone dimension often results in a peri-implant bone dehiscence or fenestration. Even in the presence of an intact but thin buccal cortical bone plate, surgical trauma and consequent bone remodeling following implant placement may lead to a vertical bone loss with the exposure of the coronal part of the implant at uncovering (Merheb et al., 2017, Monje, et al., 2019, Spray, Black, Morris, 2000). Although the amount of bone remodeling following implant insertion was shown to be similar at both thin and thick buccal bone plates (Merheb et al., 2017), such remodeling may have a different impact on the integrity of peri-im- plant buccal bone plate (PBBP). In this respect, an increased risk of esthetic and biological complications following implant placement at sites with either a dehiscence defect or a thin PBBP compared to thick PBBP has been shown in preclinical (Monje, et al., 2019) and clinical (Schwarz, Sahm, Becker, 2012, Jung et al., 2017) studies. Collectively, these findings underline the relevance of the integrity and thickness of PBBP at implant placement in favoring stable, healthy conditions of peri-implant tissues over time (Sanz-Sánchez et al., 2018).

The most documented and efficacious procedure to surgically correct a dehiscence-type defect is based on the use of barrier membranes combined with bone replacement grafts according to guided bone re- generation (GBR) principles (Sanz-Sánchez, Ortiz-Vigón, Sanz-Martín, Figuero, Sanz, 2015). The reduction or resolution of peri-implant bone dehiscence reported following GBR (Thoma, Bienz, Figuero, Jung, Sanz-Martín, 2019) seems to positively impact on long-term implant conditions, in terms of implant survival rate and peri-implant tissue stability (Sanz-Sánchez et al., 2018). Unfortunately, whether and to what extent an increased

amount of peri-implant bone thickness associated with complete coverage of the exposed implant surface may support peri-implant health has not been entirely elucidated.

Recently, a simplified bone augmentation procedure, namely the Sub-periosteal Peri-implant Augmented Layer (SPAL) technique, based on the use of the periosteum as a barrier membrane and a graft as space-making “device” for bone augmentation concomitant to implant placement, has been described (Trombelli, Severi, Pramstraller, Farina, 2018). The effectiveness of this technique to correct a peri-implant bone dehiscence and/or to augment the thickness of peri-implant bone was previously reported (Trombelli, Severi, Pramstraller, Farina, 2019), and its application has also been explored in the treatment of peri-implantitis defects (Trombelli et al. 2020). The aim of the present retro- spective case series was to assess peri-implant tissue conditions on the short term in patients receiving SPAL technique compared to patients with adequate thickness (≥2 mm) of PBBP at implant placement.

MATERIAL AND METHODS

Study design and ethical aspects

The present study was designed in accordance with the STROBE guideline Appendix S1. The protocol was approved by the Ethical Committee of Area Vasta Emilia Centro, Italy (protocol no.637/2018/ Oss/UniFe, date of approval 12.12.2018). Each patient had provided a written informed consent prior to surgical treatment. All the clinical procedures had been performed in accordance with the Declaration of Helsinki and the Good Clinical Practice (GCP) Guidelines.

Study population

The record charts of patients undergone implant-supported pros- thetic rehabilitation in the period December 2015–July 2018 at the Research Centre for the Study of Periodontal and

Peri-implant Diseases, University of Ferrara, and one private dental office in Ferrara were screened to determine patient eligibility for the study.

Patient inclusion into the study was subordinated to the following criteria:

- Non-smokers or smokers ≤10 cigarettes/day at the time of surgery;
- Non-diabetics or well-controlled diabetics (HbA1c ≤ 7%) at the time of surgery;
- Availability of clinical parameters and radiographic examinations for the study (see "Study parameters" for details).
- Not taking drugs influencing osseous metabolism (e.g., bisphosphonates, corticosteroids);
- Undergone implant placement entirely in native bone (with a residual PBBP thickness ≥2 mm after implant insertion) or concomitantly with SPAL technique.

Implant inclusion into the study was subordinated to the following criteria:

- Placement in healed ridge (type IV implants, Hämmerle, Chen, Wilson, 2004);
- Primary stability, as assessed by insertion torque.

Based on the conditions of PBBP at the time of implant placement and on its clinical management, patients were categorized into three groups:

- Patients with implant/s presenting a residual PBBP thickness ≥2 mm after implant insertion (control group);
- Patients with implant/s treated with SPAL technique for correcting a peri-implant bone dehiscence ≥3 mm concomitantly with implant placement ($SPAL_{dehiscence}$ group);

- Patients with implant/s treated with SPAL technique for augmenting a thin (≤1 mm) PBBP concomitantly with implant placement ($SPAL_{thin}$ group).

Clinical procedures

Prior to implant placement, all patients had undergone active therapy for treating carious lesions and periodontal diseases and had been enrolled in a professional maintenance with frequency of recalls scheduled according to the PerioRisk assessment tool (Trombelli, Farina, Ferrari, Pasetti, Calura, 2009, Trombelli et al., 2017).

All the surgical procedures were performed by two experienced periodontists (L.T. and M.P.). Patients were administered 2 g of amoxicillin + clavulanic acid (Augmentin, GlaxoSmithKline) one hour prior to surgery. Local anesthesia was attained using articaine with 1:100,000 epinephrine administered by local infiltration.

Surgical procedures—SPAL groups

In patients where either a dehiscence defect or thin PBBP at placement was corrected by SPAL technique (Figures 1 and 2, respectively), surgical access to the bone crest was performed as previously described (Trombelli, Severi, Pramstraller, & Farina, 2018). Briefly, a mucosal layer was raised on the buccal aspect by split-thickness dis- section with a 15C blade as well as tunneling knives (KPAX, TKN1X, and TKN2X, Hu-Friedy) with varying angulated sharp edges according to the anatomical location. Then, the periosteal layer was elevated from the bone with a periosteal elevator (PTROM, Hu-Friedy), creating a pouch that could accommodate a graft. A full-thickness flap was elevated on the oral (lingual/palatal) aspect.

Tissue-level implants (SPI ElementTM; Thommen Medical) were inserted. A bovine-derived xenograft (Bio-Oss® spongiosa granules, particle size 0.25–1.0 mm; Geistlich Pharma, AG) was used alone or in combination with autogenous cortical bone particles to fill the surgically created space between the periosteal layer and either thin buccal bone plate or exposed implant surface. In the presence of a dehiscence, grafting was performed to completely correct the peri-implant defect up to the polished collar. In all cases, the sub-periosteal graft provided at least 2 mm of thickness at the most coronal portion of the implant. The coronal portion of the periosteal layer was stabilized to the oral mucoperiosteal flap by means of resorbable internal mattress sutures (Vicryl 6/0, Ethicon). The mucosal layer was then coronally advanced and sutured tension-free by horizontal internal mattress and interrupted sutures to submerge both graft and implants.At re-entry procedure for implant uncovering, a buccal split-thickness flap was dissected to position the healing abutment. To provide adequate dimensions of keratinized peri-implant mucosa, either an apically positioned flap or a free gingival graft was performed (Trombelli, Severi, Pramstraller, & Farina, 2019).

Surgical procedures—control group

A buccal and lingual/palatal full-thickness flap was raised to expose the bone crest. The implant site was prepared according to the manufacturer's instructions, and tissue-level implants (SPI ElementTM;Thommen Medical) were inserted. Due to the presence of a residual PBBP thickness ≥2 mm, no bone augmentation procedure was performed. In all cases, the flap was trimmed and positioned around the healing abutment by resorbable sutures (Vicryl 6/0, Ethicon). Flap design and manipulation as well as suture technique were performed to ensure adequate dimensions (height, thickness) of keratinized peri-implant mucosa.

Postoperative procedures

Patients were instructed not to wear any removable prostheses to avoid compression onto the surgical site for at least 4 weeks and not to chew or brush in the treated area for approximately 2 weeks. The home use of a 0.12% chlorhexidine solution (Curasept ADS Trattamento Rigenerante®; Curaden Healthcare) was prescribed for chemical plaque control (1-min rinse b.i.d. for 3 weeks). Sutures were removed at 2 weeks post-surgery. Timing of prosthetic rehabilitation

Prosthetic rehabilitation was started at 3–4 months after implant placement in the control group whereas at least 4 weeks following implant uncovering in the SPAL groups.

Study parameters

Clinical parameters

After 6 months of prosthetic loading, a trained examiner (M.S.) who had been involved in previous studies on the SPAL technique (Trombelli, Severi, Pramstraller, Farina, 2019) performed the following clinical measurements with a UNC-15 periodontal probe in the following chronological sequence:

• Height of keratinized mucosa (KM): measured at the mid-buccal aspect of the implant as the distance between the buccal peri-implant mucosal margin and the mucogingival junction, and recorded to the nearest millimeter;

• Marginal soft tissue level (MSTL) (Zitzmann, Schärer, Marinello, 2001): measured at the mid-buccal aspect of the implant as the distance between the buccal peri-implant mucosal margin

and the implant-abutment junction, and recorded to the nearest millimeter. MSTL was recorded as positive or negative when the abutment margin was located above or below the mucosal margin, respectively;

• Plaque Index (PII; O'Leary, Drake, Naylor, 1972): recorded at the mesiobuccal, mid-buccal, distobuccal, mid-lingual/palatal implant aspects as supragingival plaque present or absent after exploring the juxtagingival prosthetic margin with the probe tip;

• Probing depth (PD): measured from mucosal margin to deepest probe penetration at six sites (mesiobuccal, mid-buccal, distob- uccal, disto-lingual, mid-lingual, and mesiolingual) using a force of 0.2–0.3 N, and recorded to the nearest millimeter;

• Bleeding on probing (BoP; Ainamo and Bay, 1975): recorded as present or absent at PD assessment;

• Suppuration on probing (SoP): recorded as present or absent at PD assessment.

Radiographic bone level

Non-standardized periapical radiographs taken with the long-cone parallel technique at 6 months after prosthetic loading were digitized and analyzed using a specifically designed software (NIS elements v4.2; Nikon Instruments, Campi Bisenzio). Radiographic bone level (RBL) was measured as the distance (approximated to the nearest 0.1 mm) between the apical margin of the implant polished collar and the bone crest at the mesial (mRBL) and distal (dRBL) aspect of each implant using a 10x–15x magnification. A reference mark 1-mm high present on digital radiograph was used for calibration. One examiner (A.S.) performed the radiographic measurements. The examiner was involved in a calibration session on a sample of radiographs obtained from patients not selected for the present study. The calibration

session consisted of two sessions of RBL measurements, performed at a 7-day interval, and allowed for reaching an excellent intra-examiner agreement (k score = 0.89), with a mean difference between paired measurements of 0.04 ± 0.15 mm.

Statistical analysis

The patient was regarded as the statistical unit. If two or more im- plants in the same patient were eligible for the study, only one im- plant was randomly included for analysis. Data were described using mean and standard deviation (SD), median and interquartile range (IR), minimum–maximum values for quantitative variables, and fre- quency and percentage for categorical variables. The median number of BoP-positive sites as assessed at 6 months following implant loading was the primary outcome variable of the study. Median values of PD, KM, MSTL, RBL, number of PII-positive sites, and number of SoP-positive sites were secondary outcome variables. Due to the limited sample size, no inferential statistics were per- formed and the results were reported with a narrative approach. However, effect size (ES) was computed for each outcome variable according to non-parametric Kruskal–Wallis test. ES was classi- fied as small (d = 0.1–0.3), medium (d = 0.3–0.5), or large (d ≥ 0.5) (Cohen, 1988).

RESULTS

Study population

Thirty-four patients with 34 implants (11 in the $SPAL_{dehiscence}$ group, 11 in the $SPAL_{thin}$ group, and 12 in the control group) were included for analysis. The vast majority of the patients were non-smokers (90.9% in the $SPAL_{dehiscence}$ group, 90.9% in the $SPAL_{thin}$ group, and 75% in the control group). Implants in the $SPAL_{dehiscence}$ group were predominantly located in the

mandible, whereas implants in the $SPAL_{thin}$ and control group were predominantly placed in the maxilla (Table 1). No patients or implants were lost during the follow-up period.

In the $SPAL_{dehiscence}$ group, 1 patient revealed wound dehiscence after 2 weeks, with partial exposure of the implant threads. The patient was seen monthly until re-entry, and the site was locally disinfected with a 0.12% chlorhexidine solution at each recall visit. In both the $SPAL_{dehiscence}$ and $SPAL_{thin}$ groups, re-entry was performed at 3–6 months after implant placement (median: 4.0 months in both groups; p = 1; Table 1). Thickness of peri-implant bone and height and width of the peri-implant bone dehiscence recorded for the $SPAL_{dehiscence}$ and $SPAL_{thin}$ groups are reported in Tables 2 and 3, respectively. In each SPAL group, 10 patients (90.9%) showed absence of peri-implant dehiscence combined with peri-implant bone thickness ≥2 mm (Tables 2 and 3). One patient in the $SPAL_{dehiscence}$ group presented a residual dehiscence of 2 mm (Table 2), which was covered with a free gingival graft. One patient in the $SPAL_{thin}$ group presented a peri-implant bone thickness of 1 mm without dehiscence (Table 3).

In the $SPAL_{dehiscence}$ group, 8 implants supported a fixed partial prosthesis, 2 implants were restored with a single crown, and 1 implant was part of an overdenture. In the $SPAL_{thin}$ group, 9 implants supported a fixed partial prosthesis, 2 implants were restored with a single crown, and 1 was part of an overdenture. In the control group, 4 implants were part of a fixed partial prosthesis and 8 implants were restored with a single crown.

Study outcomes

Data related to clinical outcomes (i.e., PD, BoP, SoP, PII, MSTL, and KM) and RBL as assessed at 6 months following implant loading are reported in Table 4.

The median prevalence (number) of BoP-positive sites was 2, 1, and 0 in the $SPAL_{dehiscence}$, $SPAL_{thin}$, and control groups, respectively. The median number of PII-positive sites was 1 in all groups. SoPwas negative at all implant sites. The mucosal margin was located 1 mm ($SPAL_{dehiscence}$ group) or 2 mm ($SPAL_{thin}$ and control groups) above the implant–abutment junction in all groups, and study groups presented a median KM of at least 3 mm. Radiographic bone level amounted to 0.3 mm in the $SPAL_{dehiscence}$ group, 0.2 mm in the $SPAL_{thin}$ group, and 0 mm in the control group. ES was small for the number of BoP + sites (d = 0.137) and PII (d = 0.198), medium for KM (d = 0.309), PD (d = 0.432) and MSTL (d = 0.680), and large for RBL (d = 0.975) (Table 4).

DISCUSSION

The aim of the present retrospective case series was to assess peri- implant tissue conditions on the short term at patients receiving SPAL technique and in patients with adequate thickness (≥2 mm) of PBBP at implant placement. The results indicated that patients treated with SPAL technique showed low number of peri-implant in- flamed sites and shallow PD (<4 mm) at 6 months of prosthetic loading. Also, the interproximal bone level was found apical (although to a limited extent) to the implant polished collar only in SPAL groups.

Bleeding on probing was selected as primary outcome since (a) the assessment of BoP is currently identified as the clinical measure to distinguish between peri-implant health and disease, being an invariable diagnostic element of peri-implant mucositis and peri-implantitis (Renvert, Persson, Pirih, Camargo, 2018, Berglundh et al., 2018), and (b) its absence is associated with stability of peri-implant tissue conditions (Jepsen, Rühling, Jepsen, Ohlenbusch, Albers, 1996, Luterbacher, Mayfield, Brägger, Lang, 2000). The proportion of

inflamed peri-implant sites as recorded in the study groups compares with previous findings evaluating BoP prevalence on 289 implants (Farina, Filippi, Brazzioli, Tomasi, Trombelli, 2017). Also, similar peri-implant inflammatory conditions were reported at 18 months following GBR (Jung et al., 2017).

In our study, a low frequency of inflamed peri-implant mucosal sites was observed in all study groups. This may be partly due to similar characteristics for factors shown to influence BoP around implants, such as low presence of juxtagingival plaque (Pontoriero et al., 1994; Salvi et al., 2012), shallow PD (Farina, Filippi, Brazzioli, Tomasi, & Trombelli, 2017), and adequate amount of KM (Chung, Oh, Shotwell, Misch, Wang, 2006, Perussolo et al., 2018). Our findings are consistent with those stemming from a recent systematic review on biological complications of dental implants placed either in pristine or in augmented sites. Meta-analysis showed a similar prevalence of peri-implant mucositis at patient either receiving (19.6%; 95% CI: 0%–40%) or not receiving (22.4%; 95% CI: 6%–38%) procedures for alveolar ridge preservation and/or vertical/lateral ridge augmentation (Salvi, Monje, Tomasi, 2018). Also, similar inflammatory conditions were reported at implants placed in native bone compared to implants placed concomitantly with a GBR procedure (Benic, Jung, Siegenthaler, Hammerle, 2009; Benic, Bernasconi, Jung, Hammerle, 2017).

It is noteworthy to consider that at re-entry, the great majority of patients receiving SPAL technique showed a peri-implant bone thickness ≥2 mm at the most coronal portion of the implant. Although the measurement of PBBP was not available at re-entry for the control group (one-stage procedure), the integrity of PBBP following post-insertion peri-implant bone remodeling may be assumed based on preclinical (Monje, et al., 2019) and clinical (Spray, Black, Morris, & Ochi, 2000) data on critical dimensions of buccal bone plate. Collectively,

available data seem to suggest that adequate vertical and horizontal dimensions of peri-implant tissues achieved by means of augmentation procedures may favor conditions to limit peri-implant tissue inflammation. However, the association of the integrity of PBBP up to the most coronal portion of the implant and the severity of peri-implant mucosal inflammation is not entirely clear (Jung et al., 2017).

At 6 months of prosthetic loading, a different position of the inter- proximal peri-implant bone level was observed among groups, with a more apical RBL in the SPAL groups. Noteworthy, in the SPAL groups tissue-level implants were positioned slightly subcrestally (Figures 1 and 2). Although it may have facilitated the grafting of the periosteal pouch up to the most coronal part of the implant as well as primary intention closure, subcrestal positioning might also have contributed interproximal bone remodeling (Saleh et al., 2018). Moreover, since implants receiving SPAL technique underwent additional surgery for uncovering including an apically positioned flap or a free gingival graft, interproximal bone remodeling in the SPAL groups may be also partly ascribed to the detrimental effect of flap elevation on local blood supply. Consistently, marginal, peri-implant bone loss has been reported between re-entry for uncovering and final prosthesis delivery by other authors (Cardaropoli, Lekholm, Wennstrom, 2006, Nader et al., 2016). It should also be considered that, in some patients of the $SPAL_{dehiscence}$ group, grafting was extended to the mesial and/or distal implant aspects due to an interproximal extension of the peri-implant bone defect. In the $SPAL_{dehiscence}$ group, therefore, the extent of graft remodeling at interproximal sites may have negatively impacted on RBL values. Recent data have shown that even slowly resorbable graft biomaterials, such as DBBM, are associated with a substantial reduction of the grafted area at 12-month radiographic evaluation following endosinusal augmentation procedures (Franceschetti et al.,

2019). However, the magnitude of RBL observed in the present study is limited compared to that reported for implants placed with concomitant GBR or in native bone (Urban et al., 2019) and implants presenting an untreated buccal dehiscence (Jung et al., 2017).

A slightly lower KM and MSTL was observed for the $SPAL_{dehiscence}$ group. This occurred despite peri-implant soft tissue manipulation was adequately performed to provide adequate dimensions of keratinized peri-implant mucosa and a subgingival position of the prosthetic margins. This finding may be somewhat correlated with the increased bone remodeling (RBL) observed in the $SPAL_{dehiscence}$ group, which may also have involved the regenerated buccal bone plate. A recent systematic review correlated the remodeling of the buccal bone with the occurrence of peri-implant soft tissue recession (Aizcorbe-Vicente, Peñarrocha-Oltra, Canullo, Soto-Peñaloza, & Peñarrocha-Diago, 2020).

In the $SPAL_{dehiscence}$ group, 1 patient (9.1%) experienced a wound dehiscence at 2 weeks that lead to partial exposure of the implant threads at re-entry. This finding compares with incidence of wound dehiscence and consequent membrane exposure following GBR procedures to correct peri-implant bone dehiscence at placement, as reported in a recent meta-analysis conducted on both prospective and retrospective studies (Garcia et al., 2018). In particular, membrane exposure occurred with an incidence ranging from 16.7% (Tawil, El-Ghoule, & Mawla, 2001) to 62.8% (Gher, Quintero, Assad, Monaco, & Richardson, 1994), and was associated with a significantly lower dehiscence coverage (Garcia et al., 2018).

The limitations of this preliminary report include the retrospective design, small sample size, and short follow-up time of 6 months after restoration of the implants. Also, the impact of patient-related factors (e.g., soft tissue thickness at edentulous area, smoking habit, diabetes) and surgery-related complications (e.g., perforations of the periosteal and/or mucosal layer) on

clinical outcomes has not been comprehensively analyzed. Moreover, specific clinical conditions (i.e., thin PBBP or peri-implant bone dehiscence of limited vertical dimension) have been selected for SPAL treatment. Further studies are needed to assess which clinical conditions/lesions may be effectively treated with SPAL technique or a more conventional treatment (e.g., GBR) should be preferred.

In conclusion, the results of the present study showed that, after 6 months of prosthetic loading, patients treated with SPAL technique show limited peri-implant mucosal inflammation in association with shallow PD and adequate KM. At implants receiving SPAL technique, however, interproximal RBL was found apical to its ideal position. Whether and to what extent the favorable short-term results observed following SPAL technique might be beneficial for long-term healthy conditions of peri-implant tissues and stability of the buccal mucosal profile needs to be assessed.

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CONFLICT OF INTERESTS

The authors have no conflict of interest to declare with regard to the present study.

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TABLES

Table 1. Patient and implant characteristics in $SPAL_{dehiscence}$, $SPAL_{thin}$ and CONTROL group. Categorical variables are described using count and percentage, and numerical

variables are expressed as mean, standard deviation (SD), median, interquartile range (IR) and minimum-maximum (min-max) range.

Patient characteristics		**SPAL$_{dehiscence}$** (11 patients)	**SPAL$_{thin}$** (11 patients)	**CONTROL** (12 patients)
Age (years)	Mean (SD)	57.5 (13.7)	63.8 (8)	62.5 (14.1)
	Median (IR)	57.0 (52.0 – 71.0)	66.0 (55.0 – 71.0)	65.5 (55.5 – 72.5)
	Minimum-maximum range	30.0 – 72.0	50.0 – 74.0	28.0 – 79.0
Males/ Females	Frequency	5/6	5/6	6/6
	Percentage	45,5 / 54,5	45,5 / 54,5	50 / 50
Smokers / non-smokers	Frequency	1/10	1/10	3/9
	Percentage	9 / 91	9 / 91	25 / 75
N° cigarettes/day **(averaged only for smokers)**	Mean (SD)	10	4	10 (0)
	Median (IR)	10	4	10 (10 – 10)

Table 2. Peri-implant tissue thickness, dehiscence height and width (DH and DW, respectively) in each patient of the $SPAL_{dehiscence}$ group.

Patient	Peri-implant tissue thickness at re-entry for implant uncovering (mm)	DH (mm)		DW (mm)	
		Placement	Re-entry	Placement	Re-entry
$SPAL_{dehiscence}$ #1	0	5	2	4	4
$SPAL_{dehiscence}$ #2	3	4	0	4	0
$SPAL_{dehiscence}$ #3	3	5	0	4	0
$SPAL_{dehiscence}$ #4	2	3	0	4	0
$SPAL_{dehiscence}$ #5	3	4	0	4	0
$SPAL_{dehiscence}$ #6	2	4	0	3.5	0
$SPAL_{dehiscence}$ #7	3	4	0	4	0
$SPAL_{dehiscence}$ #8	3	5	0	4	0
$SPAL_{dehiscence}$ #9	2	3	0	4	0
$SPAL_{dehiscence}$ #10	3	3	0	4.2	0
$SPAL_{dehiscence}$ #11	3	6	0	3.5	0

Table 3. Peri-implant tissue thickness, dehiscence height and width (DH and DW, respectively) as assessed at re-entry for implant uncovering in each patient of the $SPAL_{thin}$ group.

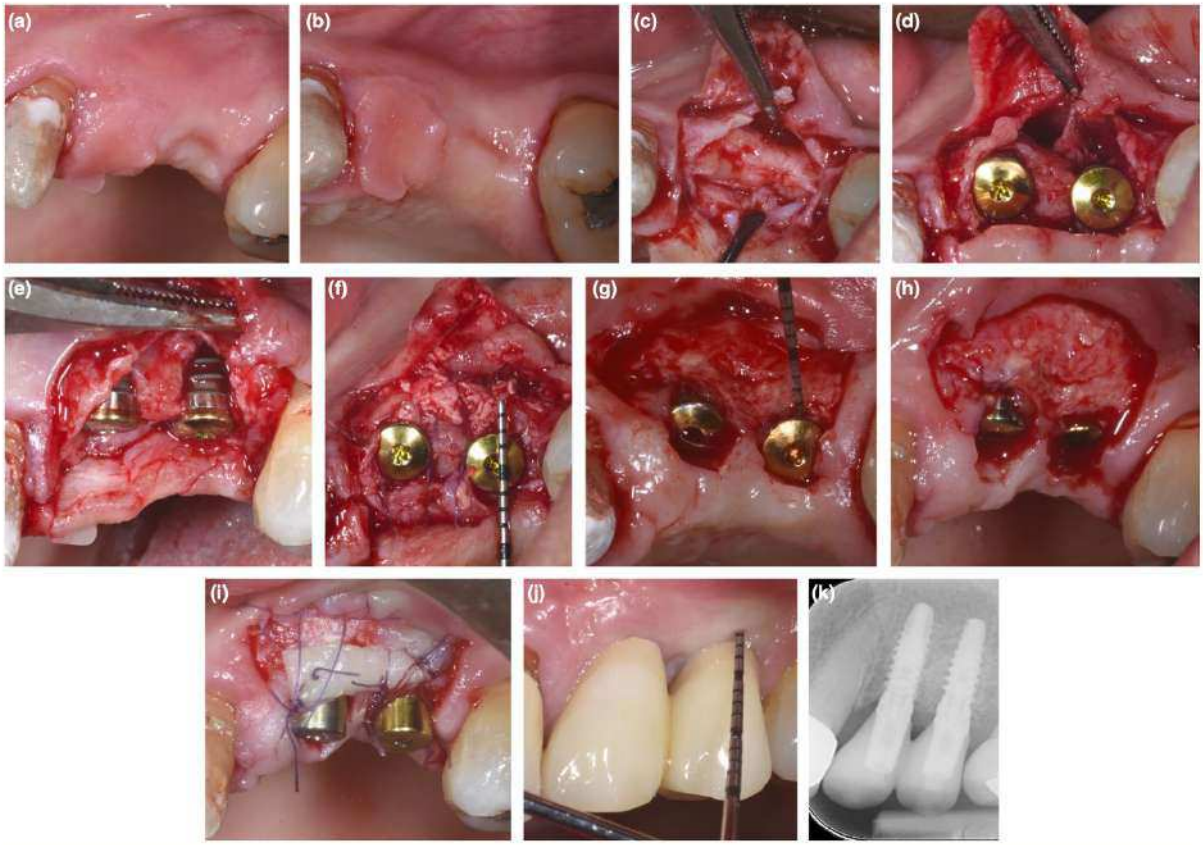
Patient	Peri-implant tissue thickness (mm)	DH (mm)	DW (mm)
$SPAL_{thin}$ #1	3	0	0
$SPAL_{thin}$ #2	2	0	0
$SPAL_{thin}$ #3	2	0	0
$SPAL_{thin}$ #4	1	0	0
$SPAL_{thin}$ #5	2	0	0
$SPAL_{thin}$ #6	2	0	0
$SPAL_{thin}$ #7	2	0	0
$SPAL_{thin}$ #8	2	0	0
$SPAL_{thin}$ #9	2	0	0
$SPAL_{thin}$ #10	2	0	0
$SPAL_{thin}$ #11	3	0	0

Table 4. Clinical outcomes (i.e., probing depth, PD; bleeding on probing, BoP; suppuration on probing, SoP; Plaque Index, mPII; marginal soft tissue level, MSTL; and width of keratinized mucosa, KM) and radiographic bone level (RBL) as assessed at 6 months following implant loading. Data are expressed at the patient-level as mean, standard deviation (SD), median, interquartile range (IR) and minimum-maximum (min-max) range.

	Study outcome		$SPAL_{dehiscence}$ (11 patients)	$SPAL_{thin}$ (11 patients)	CONTROL (12 patients)
Primary outcome variable	**n° of BoP-positive sites per implant (n)**	Mean (SD)	1.9 (1.7)	1.5 (1.6)	1.0 (1.7)
		Median (IR)	2 (1 – 3)	1 (1 – 2)	0 (0 – 2)
		Min - Max	0 – 6	1 – 6	0 – 5
Secondary outcome variables	**PD** (mm)	Mean (SD)	2.6 (0.5)	2.5 (0.4)	2.3 (0.7)
		Median (IR)	2.5 (2.2 – 3.0)	2.3 (2.2 – 2.8)	1.9 (1.8 – 2.6)
		Min - Max	2.0 – 3.7	2.0 – 3.3	1.7 – 4.0
	n° of SoP-positive sites per implant (n)	Mean (SD)	0 (0)	0 (0)	0 (0)
		Median (IR)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)
		Min - Max	0 – 0	0 – 0	0 – 0
	n° of PII-positive sites per implant (n)	Mean (SD)	1.4 (1.5)	1. 2 (1.1)	0.7 (0.7)
		Median (IR)	1 (0 – 2)	1 (1 – 1)	1 (0 – 1)

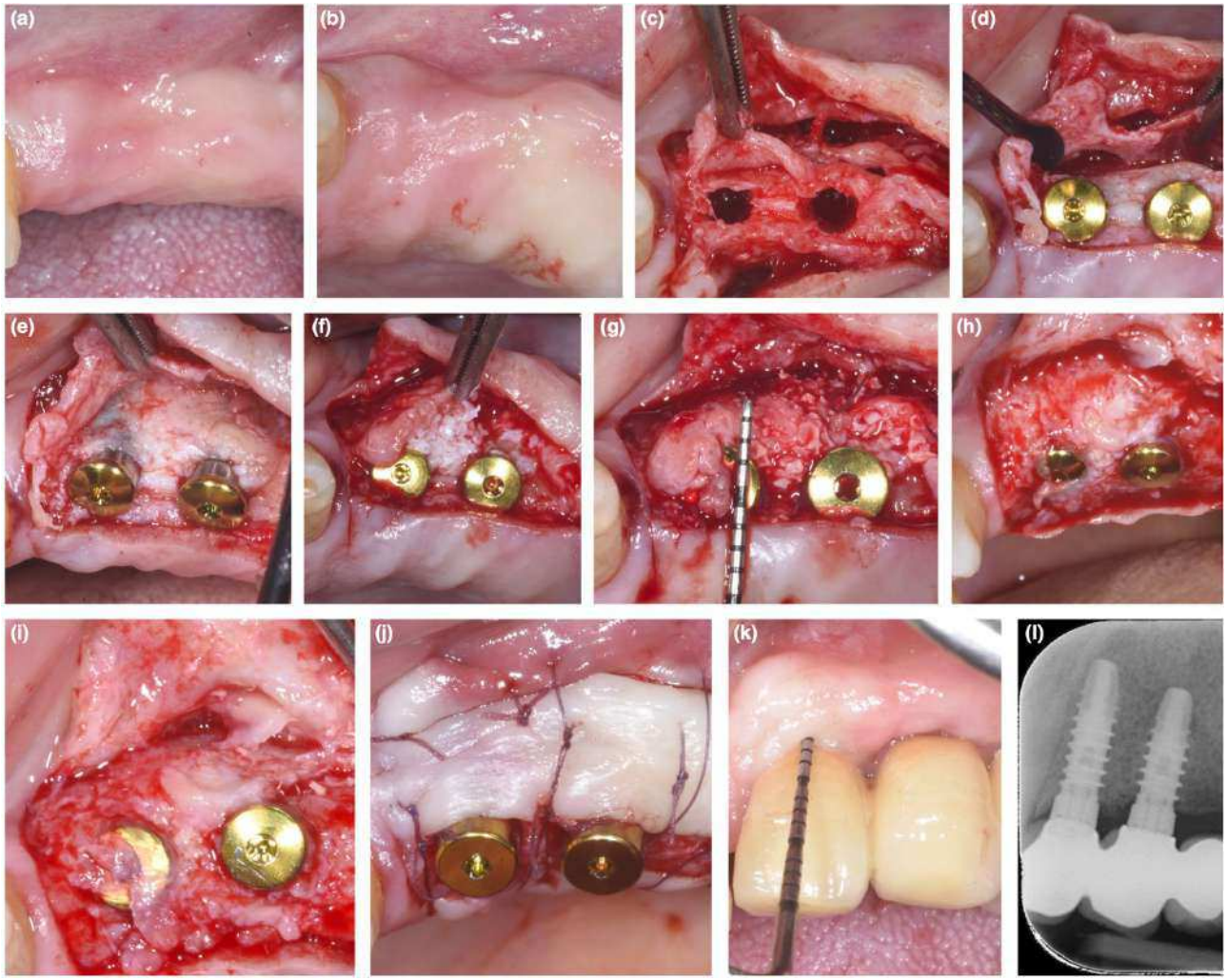
FIGURES

Figure 1. SPAL technique for correcting a peri-implant bone dehiscence concomitantly with implant placement ($SPAL_{dehiscence}$ group).



a-b. Buccal and occlusal view of an atrophic maxillary premolar region. **c.** The mucosal layer was raised on the buccal aspect by split-thickness dissection. Then, the periosteal layer was elevated from the bone and implant sites were prepared. **d-e.** After placement, the implant in position 2.5 showed a buccal dehiscence with a depth ≥ 3 mm. **f.** Buccal dehiscence was corrected using a deproteinized bovine bone mineral graft and periosteal layer was sutured to the oral flap. **g-i.** At re-entry, the implant presented an adequate thickness of the buccal bone and the buccal dehiscence was completely corrected. A free gingival graft was used to obtain adequate dimensions of peri-implant keratinized mucosa. **j-k.** Clinical and radiographic view at 6 months after prosthesis delivery.

Figure 2. SPAL technique for augmenting a thin (≤ 1 mm) peri-implant buccal bone plate concomitantly with implant placement ($SPAL_{thin}$ group).



a-b. Buccal and occlusal view of an atrophic maxillary anterior region. **c.** Implant site was prepared after mucosal and periosteal layer elevation. **d-e.** After placement, the implant in position 2.2 showed an intact but thin buccal peri-implant buccal bone plate (PBBP). **f-g.** Thin PBBP was augmented using deproteinized bovine bone mineral, that was stabilized by the periosteal layer. The periosteal layer was then sutured to the oral flap. **h-j.** At re-entry, the implant presented a peri-implant tissue thickness of 2 mm at the most coronal portion of the implant. An apical positioned flap was then used to obtain adequate dimensions of peri-implant keratinized mucosa. **k-l.** Clinical and radiographic view at 6 months after prosthetic loading.

CHAPTER 4

Peri-implant bone augmentation by the Sub-periosteal Peri-implant Augmented Layer (S.P.A.L.) technique combined with a bovine-derived bone block: a case report

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Abstract

Background: the Sub-periosteal peri-implant augmented layer (SPAL) technique combined with deproteinized bovine bone mineral (DBBM), delivered as a particulate, was effective in completely correcting up to 92% of peri-implant buccal bone dehiscences. The use of a DBBM block (bDBBM), however, may result in an improvement of the peri-implant bone dehiscence as well as a relevant lateral bone augmentation, since its mechanical properties may ensure a better dimensional stability at flap manipulation than particulate DBBM. The aim of the present a proof-of-principle case report is to investigate if bone augmentation may be performed successfully at peri-implant dehiscence sites with a combination of SPAL and bDBBM.

Case presentation: lateral bone augmentation around two dehiscent implants was performed using the SPAL technique. A partial-thickness flap was elevated, leaving the periosteal layer on the buccal cortical bone plate. The periosteal layer was in turn elevated to create a pouch, which was used to stabilize a bDBBM graft at the peri-implant buccal bone dehiscences. At re-entry, exposed implant surfaces were completely covered by new thick hard tissue up to their most coronal portion. A free epithelial-connective tissue graft was used to augment the peri-implant soft tissue phenotype.

Conclusion: the combination of SPAL and bDBBM may be successfully used to achieve an increase in buccal tissue thickness at the most coronal portion of an exposed implant.

Key words: dental implant, dehiscence, surgical flaps, bone regeneration, xenograft

BACKGROUND

A simplified technique to augment the osseous component of the peri-implant phenotype[1] at implant placement, namely the Sub-periosteal Peri-implant Augmented Layer (SPAL), was recently proposed[2]. SPAL is based on the separation of the buccal flap into two layers: a periosteal layer, which creates an “osteogenic”, protected space to stabilize a graft at a thin or deficient peri-implant buccal bone plate, and a mucosal layer, which is mobilized to provide primary intention healing[2]. Previous studies have shown that SPAL may result in a substantial dehiscence correction[3,4], thus providing conditions for peri-implant health at the treated implants4. Also, SPAL has been shown effective in treating Class Ib and Ic peri-implantitis defects5.

In all treated cases, SPAL has been combined with deproteinized bovine bone mineral (DBBM), delivered as a particulate. Although proved effective as a space-making osteoconductive scaffold at most dehiscent implants with up to 92% of complete dehiscence coverage, however, particulate DBBM might result in limited increase in thickness of the buccal bone plate[6,7,8.]

Preclinical[6,7] and clinical[8] studies seem to suggest that the use of a DBBM block (bDBBM) may result in an improvement of the peri-implant bone dehiscence as well as a relevant lateral bone augmentation when applied according to the principles of Guided Bone Regeneration (GBR).

The present study consists a proof-of-principle case report aimed at investigating if bone augmentation may be performed successfully at peri-implant dehiscence sites with a combination of SPAL and bDBBM.

Ethical aspects

The present report was approved by the Ethical Committee of Area Vasta Emilia Centro, Italy (protocol n°637/2018/Oss/UniFe, date of approval 12.12.2018). The patient provided a written informed consent prior to surgical treatment. All the clinical procedures have been performed in accordance with the Declaration of Helsinki and the Good Clinical Practice Guidelines (GCPs).

Clinical Presentation, Case Management, and Clinical Outcomes

On October 2020, a 50 year-old, non-smoker, systemically healthy female patient presented for the rehabilitation of an edentulous area (#18 and #19) (Fig.1a-b). After treatment for stage III periodontitis, the patient presented a bleeding on probing (BoP) score9 <10% and no sites with probing depth (PD) ≥ 5 mm, and was enrolled in a supportive periodontal care program. An implant-supported rehabilitation was programmed in the #18 and #19 area.

Implant position was planned digitally§ on a CBCT exam, and a surgical guide was fabricated (Fig). Digital planning previewed the formation of a buccal dehiscence at placement of both implants, suggesting the need for horizontal bone augmentation procedure (Fig. 1c-d).

The patient was administered 2 g of amoxicillin + clavulanic acidǁ one hour prior to surgery. Local anesthesia was attained using articaine with 1:100,000 epinephrine administered by local infiltration.

At the buccal aspect, a split-thickness flap (creating the “mucosal layer”) was raised, leaving the periosteal layer on the edentulous ridge intact (Fig. 1e) Then, the periosteal layer was elevated from the bone crest by means of a microsurgical periosteal elevator ¶ and tunneling knives # with varying angulated sharp edges[2,3] (Fig. 1f). At the lingual aspect, a full-thickness flap was elevated. The elevation was extended in an apical direction to detach the superficial fibers of the mylohyoid muscle and obtain a tension-free lingual flap.

Implant sites were prepared using the computer-aided surgical guide (Fig. 1g), and two tissue-level implants** were positioned (Fig. 1h). Implants presented a buccal dehiscence of 3 mm at #19 and 2 mm at #18. Cortical perforations were performed using a carbide bur.

bDBBM†† was trimmed using a high-speed diamond bur in order to obtain a homogeneous thickness of 3-4 mm and was adapted beneath the periosteal layer to completely cover the exposed implant surface (Fig. 1i).

Using a resorbable 6/0 suture‡‡, the periosteal layer was stabilized to the lingual flap by means of internal mattress sutures (Fig 1j). The mucosal layer was coronally advanced to achieve primary closure of the wound (Fig 1k).

The patient was instructed to avoid any compression of the surgical site and not to chew or brush in the treated area for 2 weeks. A 0.12% chlorhexidine mouthrinse§§ was prescribed (1-minute rinse b.i.d. for 3 weeks). Sutures were removed at 2-weeks post-surgery.

At 6 months following implant placement (Fig. 1l), a re-entry procedure for implant exposure was performed using a buccal split-thickness flap. Previously exposed implant surfaces were completely covered by new hard tissue, and peri-implant buccal tissue thickness ≥ 3 mm was present at the most coronal portion of both implants (Fig. 1m-o). A free epithelial-connective tissue graft was used to augment the peri-implant soft tissue phenotype1. (Fig. 1p).

A digital impression was taken 4 weeks after implant exposure to digitally plan final restoration shape and emergency profile. Two splinted crowns were milled from a zirconia monoblock[lll] and cemented[¶¶] on the titanium inserts[##] according to manufacturer's instructions. Final restoration was screwed 4 weeks after impression.

Peri-implant tissue conditions appeared adequate at both clinical and radiographic examination (Fig. 1q-r).

§ RealGUIDE 5.0 pro, 3DIEMME, Figino Serenza, Como, Italy

ll Augmentin, GlaxoSmithKline, Verona, Italy

¶ PTROM, Hu-Friedy, Chicago, Illinois

KPAX, TKN1X and TKN2X, Hu Friedy, Chicago, Illinois

** SPI Element RC, Thommen Medical, Grenchen, Switzerland

†† Bio-Oss® Block, size 2 x 1 x 1 cm; Geistlich Pharma, AG, Wolhusen, Switzerland

‡‡ Vicryl 6/0, Ethicon, Somerville NJ, USA

§§ Curasept ADS Trattamento Rigenerante®; Curaden Healthcare, Saronno, Italy

lll Upcera Explore Esthetic, Shenzhen Upcera Dental Technology Co., Ltd, Shenzhen, Guangdong, China

¶¶ Nobil Fix, Nobil-Metal, Villafranca d'Asti, Italy

Ti-base, Thommen Medical, Grenchen, Switzerland

DISCUSSION

The present case report suggests that the use of bDBBM in combination with SPAL technique may represent a suitable alternative to particulate DBBM for correcting a peri-implant bone dehiscence with a substantial increase in buccal bone thickness.

In the SPAL technique, graft stabilization into the sub-periosteal space is ensured by suturing its most coronal part and subsequent coverage by the mucosal layer. One of the potential drawbacks when using particulate DBBM is the potential displacement and/or compression of the graft particles around the coronal portion of the implant at suturing. This consideration is well substantiated in the literature for the association of particulate DBBM and GBR [6,7,8,10,11]. In contrast, bDBBM may act as an efficacious osteoconductive scaffold while its mechanical properties would ensure a better dimensional stability at flap manipulation. Previous preclinical[6,7,11] and clinical[8] seems to corroborate our findings. On the other hand, the stiffness of the block graft calls for an ideal passive adaptation of the mucosal layer to minimize the risk for flap perforation and graft exposure.

Although a thick bone-like tissue was found on the previously exposed implants at re-entry, the histological nature of the newly formed tissue still has to be determined. Available data stemming from experimental studies[6,7] and 6-month human histologic samples[12] where bDBBM was used for lateral bone augmentation showed a more limited new bone formation, mainly located at the native bone-bDBBM interface[13], compared to particulate DBBM. These observations seem to reinforce the need to improve the osteogenic conditions of the wound (e.g. cortical perforations[14], use of additional growth factors[15]) and/or wait for longer maturation time prior to implant uncovering when a bDBBM is used.

CONCLUSION

The present proof-of-principle case report indicates that the combination of SPAL and bDBBM may be successfully used to achieve an increase in buccal tissue thickness at the most coronal portion of an exposed implant.

SUMMARY

Why is this case new information?	- to assess whether and to what extent SPAL technique may benefit from the use of bDBBM.
What are the keys to successful management of this case?	- Careful dissection of both the mucosal and the periosteal layer to maintain their integrity - Trimming the xenogenic bone block to maintain the space between the periosteal layer and the exposed implant surface - On the other hand, the stiffness of the block graft calls for an ideal passive adaptation of the mucosal layer to minimize the risk for flap perforation and graft exposure - Elevation of a tension-free lingual flap
What are the primary limitations to success in this case?	- Thin buccal peri-implant mucosa, not allowing the separation of mucosal and periosteal layers - Limited mesio-distal extension of the flap limiting the possibility of placing an adequate amount of xenogenic bone block

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L.T. received grants and fee for lectures and courses by Geistlich Pharma, AG, Wolhusen, Switzerland and Thommen Medical, Grenchen, Switzerland.

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FIGURES LEGEND

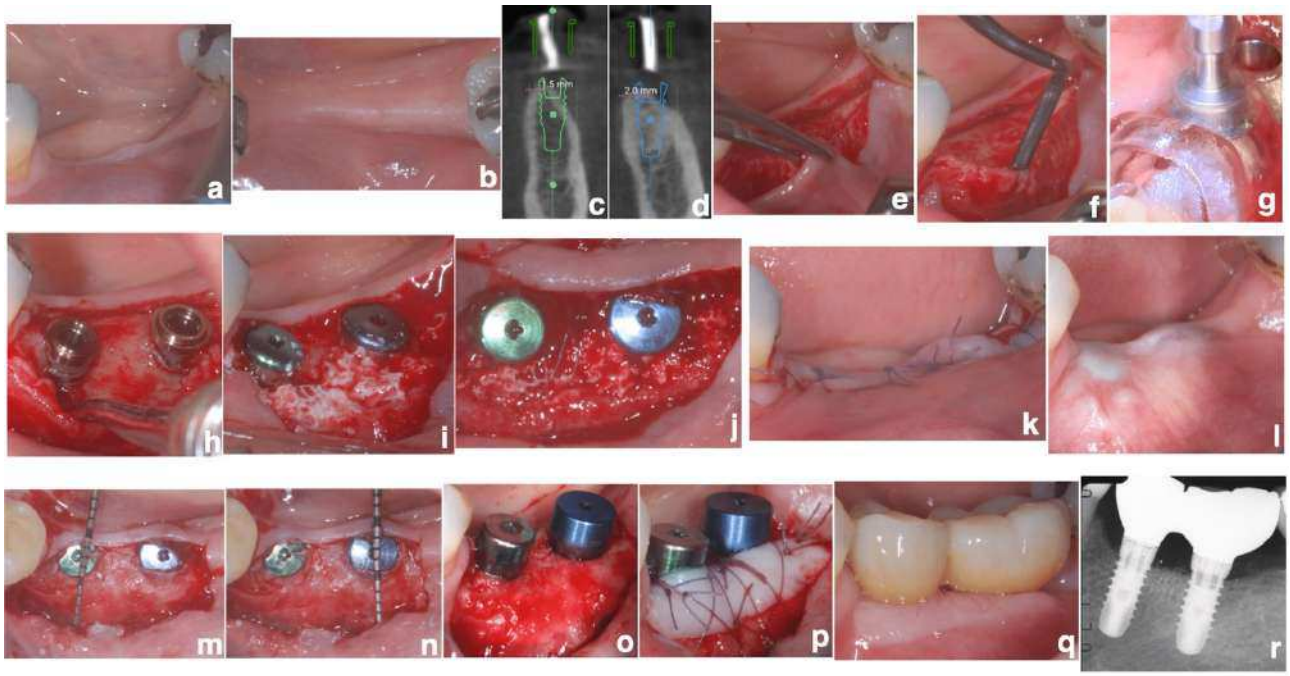

Figure 1a-b. Buccal and occlusal view of the edentulous region #18-#19 **1c-d**. Digital implant planning, suggesting the need for lateral bone augmentation **1e**. Mucosal layer obtained after partial-thickness dissection **1f**. Periosteal layer elevation from the bone crest by mean of an angulated sharp knife **1g**. Digitally guided implant site preparation **1h**. Both the implants in position #18 and #19 presented a peri-implant bone dehiscence **1i**. DBBM block adapted beneath the periosteal layer to completely cover the exposed implant surface. **1j**. Stabilization of the periosteal layer by mean of internal mattress sutures. **1k**. Coronal advancement of the mucosal layer submerging both the graft and the implants. **1l**. Buccal view of the region #18-#19 before re-entry procedure. **1m-o**. 6-months re-entry: previously exposed implant surfaces were completely covered by new hard tissue and peri-implant buccal tissue thickness ≥ 3 mm was present at the most coronal portion of both implants. **1p**. Free epithelial-connective tissue graft used to augment the peri-implant soft tissue phenotype. **1q-r**. Final restoration delivery. Peri-implant tissue conditions appeared to be adequate at both clinical and radiographic examination

CHAPTER 5

Sub-Periosteal Peri-implant Augmented Layer technique to treat peri-implantitis lesions

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ABSTRACT

Introduction: The efficacy of surgical regenerative procedures to treat peri-implantitis lesions has been extensively reviewed. Regenerative treatment showed a variable rate of success, in terms of pocket reduction, gain in bone support and elimination of signs of infection/inflammation. The aim of the present case report is to illustrate the use of Sub-Periosteal Peri-Implant Augmented Layer (SPAL) technique to correct peri-implantitis defects

Case series: Surgical treatment of 3 class Ib and 1 class Ic peri-implantitis lesions in 3 patients was performed by mean of the SPAL technique. A partial-thickness flap was elevated, leaving the periosteal layer on the buccal cortical bone plate. The periosteal layer was in turn elevated to create a pouch, which was used to stabilize a bovine-derived xenograft (DBBM) at the peri-implant buccal bone defect. No barrier membrane was used. In case of insufficient dimensions of peri-implant mucosa, a connective tissue graft (CTG) was buccally positioned at the most coronal portion of the implant. Treatment resulted in substantial reconstruction of peri-implant support associated with reduced probing depth and absence of inflammation.

Conclusions: SPAL technique with or without additional CTG may be a suitable option to obtain clinical remission of peri-implantitis defects associated with buccal bone dehiscence.

Key Words: Peri-Implantitis, Dental implants, Bone regeneration, Surgical flaps

BACKGROUND

The efficacy of surgical regenerative procedures to treat peri-implantitis lesions has been extensively reviewed[1,2]. Regenerative treatment showed a variable rate of success, in terms of pocket reduction, gain in bone support and elimination of signs of infection/inflammation, which seems partly dependent on the defect configuration[3] and surgical procedure[4]. Among the proposed surgical options, the use of a deproteinized bovine bone mineral (DBBM) with 10% collagen with or without the additional use of a connective tissue graft (CTG) led to significant clinical improvements at crater-like peri-implant defects[5], even when implant sites were re-evaluated long-term[6].

Recently, a simplified technique for horizontal bone augmentation at implant placement, namely the Sub-periosteal Peri-implant Augmented Layer (SPAL), was proposed[7,8]. SPAL technique is based on the use of periosteum to create a periosteal pouch which is used to stabilize DBBM at the deficient peri-implant buccal bone plate and was successfully used to increase the horizontal dimension of the peri-implant tissues in presence of a bone dehiscence or a thin buccal cortical plate at implant placement[7,8].

This case report illustrates the use of SPAL technique for the treatment of peri-implantitis lesions.

Clinical Presentation, Case Management, and Clinical Outcomes

Each patient provided a written informed consent prior to surgical treatment. All the clinical procedures have been performed in accordance with the Declaration of Helsinki and the Good Clinical Practice Guidelines (GCPs).

Patients were systemically healthy and enrolled in a professional recall program. The persistence of a 5 mm pocket associated with bleeding and/or suppuration and radiographic bone loss > 3 mm were regarded as indication for surgical correction. The morphology of the peri-implantitis defect was diagnosed by bone sounding and periapical radiographs.

Case #1

A 65 y-o, non-smoker male patient presenting a Class Ic peri-implantitis lesion[9] at one rough-surface, tissue-level, cylindrical implant (Fig.1a-c) was treated on June 2018. The patient was treated for a stage IV periodontitis and presents with no residual bleeding sites with probing depth (PDD) ≥ 5 mm.

A partial thickness incision was performed intra-sulcularly at the buccal aspect of the implant and extended mesio-distally on the edentulous ridge. Two partial thickness oblique releasing incisions were then made mesially and distally. The mucosal layer was raised by sharp dissection, leaving the periosteal layer on both implant surface and peri-implant bone crest (Fig. 1d). The periosteal layer was carefully elevated by mean of tunneling knives† as well as by a periosteal elevator‡, thus exposing the peri-implant bone defect and creating a periosteal pouch that could accommodate and stabilize a xenograft (Fig 1e.). A full-thickness flap was elevated on the palatal aspect. After degranulation, the defect was diagnosed as combined class Ic + II [9] (Fig. 1f). The exposed implant surface was carefully debrided by an ultrasonic tip device§ plus a specifically designed rotating titanium brush‖ and finally cleaned with cotton pellets soaked in a 0.2% chlorhexidine solution. DBBM graft ¶ was used to fill the intrabony component, (Fig. 1g). The periosteal layer was then secured to the palatal flap by an internal mattress 6/0 resorbable suture# to contain and stabilize the graft up to the most coronal part of

the peri-implant defect (Fig. 1h). The mucosal layer was then coronally advanced and sutured to provide wound stability (Fig. 1i).

† KPAX, TKN1X and TKN2X, Hu Friedy, Chicago, Illinois

‡ PTROM, Hu-Friedy, Chicago, Illinois

§ EMS Airflow Prophylaxis Master, EMS-Electro Medical System SA, Nyon, Switzerland

‖ i-Brush, Neo Biotech, Rotterdam, The Netherlands

¶ Bio-Oss® spongiosa granules, particle size 0.25-1.0 mm; Geistlich Pharma, AG, Wolhusen, Switzerland

Vicryl 6/0, Ethicon, Somerville NJ, USA

Case #2 and #3

On May 2019, a 50 y-o female patient (case 2) presenting a Class Ib peri-implantitis lesion[9] at a rough-surface, tissue-level, tapered implant (Fig. 2a-c) was treated according to SPAL technique. Patient was affected by stage 2 periodontitis, treated before peri-implantitis surgical therapy.

Due to the lack of graft stability in the most coronal portion of the implant and the limited thickness of keratinized mucosa, a CTG was harvested from the palate [10] and sutured over the coronal part of the xenograft and exposed implant surface (Fig. 2 d-g). The mucosal layer was coronally advanced and sutured to completely submerge the CTG (Fig. 2h).

On May 2018, a 44 y-o male patient, with no history of periodontitis (case 3), presenting two Class Ib peri-implantitis lesions[9] at two rough-surface, tissue-level, cylindrical implants, was treated according to SPAL technique. Due to partial exposure of the DBBM graft coronal to the periosteal pouch following SPAL technique and lack of keratinized peri-implant mucosa, a CTG was harvested and sutured as in Case #2 and left partially exposed supragingivally in order to create a band of keratinized peri-implant mucosa and increase vestibule depth (Fig. 3 a-f).

Postoperative regimen

Patients were instructed not to brush the treated area for 2 weeks. A pain killer‡‡ was prescribed as needed. A 0.12% chlorhexidine solution, 10 ml for 60 seconds b.i.d. was prescribed for 3 weeks. Sutures were removed at 2-weeks post-surgery. Successful therapy, defined as probing depth (PD) ≤4 mm, absence of bleeding/suppuration on probing and substantial radiographic bone gain, was observed at 6-months re-evaluation (Figs. 1 j-l, 2 i-k, 3 g-j and Table 1 and 2).

‡‡ Brufen 600 mg, Abbott Laboratories, Abbott, Texas

DISCUSSION

The selection of SPAL technique to treat Class Ib/Ic peri-implantitis lesions was based on the reported effectiveness in augmenting horizontal bone dimensions at implant placement in presence of an overt implant dehiscence[8]. The stabilization of graft particles by the periosteal layer may have enhanced the conditions for clot stabilization and subsequently bone regeneration either in the intrabony component or at the buccal dehiscence. Moreover, the periosteum layer may have acted as a source of blood and osteogenetic cells, contributing bone formation[11]. The rationale for the use of a DBBM graft only was based on previous studies reporting relevant outcomes when the intrabony component of a peri-implant defect was exposed by a full-thickness flap and grafted by DBBM with [3,12,13] or without [5,6,14] an additional membrane. Although a radiographic bone fill of the peri-implantitis lesions was evident at 6 months, this evidence does not qualify the nature of the augmented tissues.

Previous human histology derived from a similar procedure where a sub-periosteal pouch was surgically created revealed xenograft particles surrounded by newly formed bone[15]

The decision to avoid the use of a membrane was also based on previous data[16] where the application of a membrane to treat a peri-implantitis defect resulted costly, time consuming, technique sensitive and provided no clear added value.

The additional use of a CTG was based on previous studies on surgical regeneration of peri-implantitis defects[3,14] where a full-thickness flap was raised to access the lesion and contaminated implant surface, bone defects were filled with a DBBM graft, and, in case of limited amount of keratinized mucosa, a CTG was used to cover the defect. Although controversial data exists about the importance of keratinized peri-implant soft tissue to ensure peri-implant health, recent systematic reviews support the use of soft tissue augmentation at deficient sites to maintain long term peri-implant hard and soft tissue stability[17]. Overall, our findings seem to suggest that the use of a CTG to SPAL may be of additional benefit since i) it increased mucosa dimensions and (if left exposed) vestibule depth; ii) it contributed the stabilization of the portion of the graft coronal to the periosteal pouch; and iii) it supported the coronal displacement of the mucosal layer, thus enhancing wound stability conditions during tissue maturation phase. Further studies are needed to elucidate this hypothesis.

CONCLUSION

The present proof-of-principle case report indicates that SPAL technique with or without additional CTG may result in the clinical remission of Class Ib/Ic peri-implantitis defects. Whether and to what extent these beneficial effects may be maintained long-term and extended to other defect configurations needs be carefully assessed.

SUMMARY

Why is this case new information?	- A novel surgical procedure, namely the Sub-Periosteal Peri-Implant Augmented Layer (SPAL) technique, is described for the regenerative treatment of peri-implantitis lesions.
What are the keys to successful management of this case?	- Careful dissection of both the mucosal and the periosteal layer to maintain their integrity - Extensive decontamination of implant surface - Management of both periosteal and mucosal layers to stabilize the graft, create conditions for space provisioning and wound stability - Additional use of a connective tissue graft (CTG) to increase dimensions of peri-implant mucosa, when deficient or missing.
What are the primary limitations to success in this case?	- Thin buccal peri-implant mucosa, not allowing the separation of mucosal and periosteal layers - Morphology of the peri-implantitis lesion

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The study was entirely supported by the Research Centre for the Study of Periodontal and Peri-implant Diseases, University of Ferrara, Italy. M. S., R.F. and A. S. declare no conflict of interest. L.T. received grants and fee for lectures and courses by Geistlich Biomaterials and Thommen Medical.

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FIGURES LEGEND

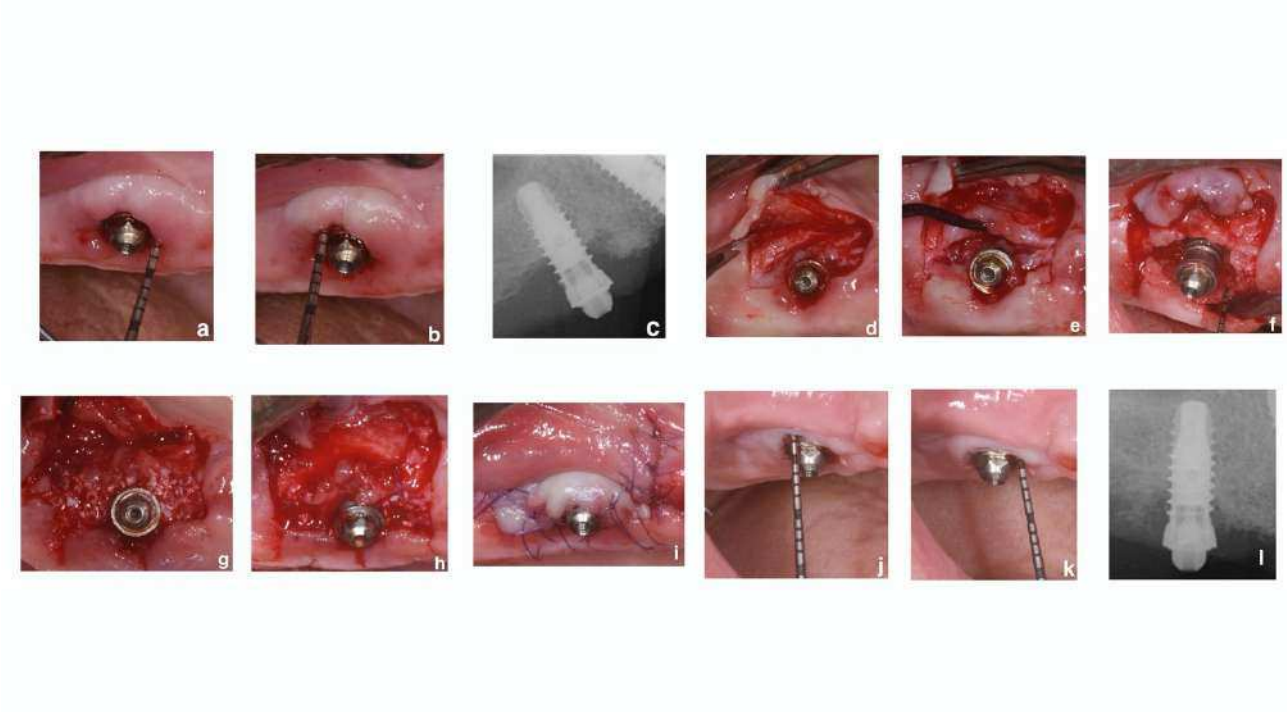

Figure 1. Case #1 a-c. Clinical and radiographic view of an implant in position #4 affected by peri-implantitis. **1d.** Mucosal layer is raised by sharp dissection, leaving the periosteum attached to the bone crest. **1e**. Periosteal layer is elevated from the buccal bone plate creating a pouch where a bone substitute can be grafted. 1**f.** Peri-implant defect characterized by a mesio-palatal-distal infrabony component associated with a buccal dehiscence (class Ic).

1g. Infrabony component, including the palatal extension of the defect, is completely filled with a bovine derived xenograft **1h.** Periosteal layer is sutured to the oral flap to contain and stabilize the graft in the infrabony component. **1i.** The mucosal layer is coronally advanced and sutured around the abutment to provide condition for wound stability. **1j-l**. Clinical and radiographic view at 6-months examination.

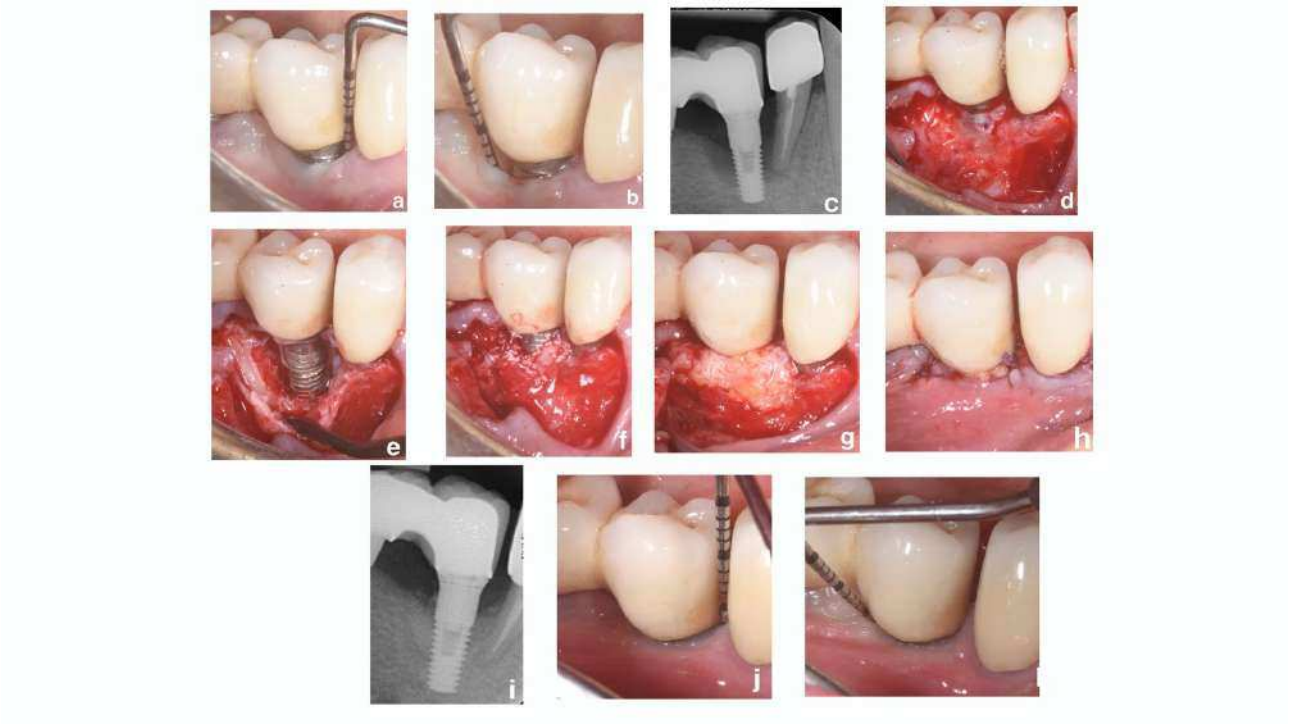

Figure 2. Case #2 a-c. Peri-implant defects associated with bleeding and suppuration upon probing are present on implant in position #29. **2d.** A trapezoidal split-thickness flap is elevated. **2e.** Periosteal layer is elevated from underlying bone and exposed implant surface. A class Ib defect is present, characterized by a mesio-distal infrabony component associated with a buccal dehiscence. **2f.** The periosteal pouch is grafted with xenograft particles to correct the infrabony component of the defect and on the peri-implant bone dehiscence. **2g.** A connective tissue graft (CTG) is sutured over the coronal part of the xenograft and exposed implant surface to enhance wound/graft stability and increase the thickness of the peri-implant mucosa. **2h.** The mucosal layer is coronally advanced to submerge the CTG . **2i-k.** Probing and radiographic assessment at 6-months.

Figure 3. Case #3 a-b. Preoperative examination view of two implants in position #28-#29 affected by peri-implantitis. A non-keratinized, thin peri-implant mucosa associated with implant exposure is present at both implant sites. Peri-implant infrabony defect are visible on the peri-apical radiograph **c.** After reflection of both mucosal and periosteal layers, both implants show class Ib peri-implantitis defects. **3d-e.** Infrabony component of the peri-implantitis defects grafted. Partial exposure of the xenograft coronal to the periosteal pouch is evident**.** A connective tissue graft (CTG) is sutured over the coronal part of the xenograft and exposed implant surface. **3f.** The mucosal layer is coronally advanced, leaving the CTG partially exposed to create a band of keratinized tissue. **3g-j.** Probing and radiographic assessment at 6-months.

CHAPTER 6
General discussion

In the current series of studies, the effectiveness of a novel surgical soft tissue management (the Sub-periosteal Peri-implant Augmented Layer, SPAL; Trombelli et al. 2018), was evaluated both i) at implant placement and ii) in the treatment of peri-implantitis bone defects. Its short-term effect on peri-implant tissue conditions was also investigated.

Findings from these studies will be critically discussed in this chapter, mainly focusing on the following clinical issues:

The following studies were performed in order to answer specific research/clinical questions:

1. What is the clinical effectiveness of SPAL technique in the preventing or correcting a peri-implant bone dehiscence or at implant placement?
2. Is there any difference in peri-implant tissue conditions on the short-term at patients receiving SPAL technique compared to patients with adequate thickness (≥ 2 mm) of PBBP at implant placement?
3. May bone augmentation be performed successfully at peri-implant dehiscence sites with a combination of SPAL and a deproteinized bovine bone mineral (DBBM) block?
4. What is the clinical effectiveness of SPAL technique in the regenerative treatment of peri-implantitis bone defects?

What is the clinical effectiveness of SPAL technique in the preventing or correcting a peri-implant bone dehiscence or at implant placement?

Lateral augmentation procedures are the most documented and validated techniques for peri-implant bone dehiscence treatment (Sanz-Sanchez et al. 2015, Thoma et al. 2019). In this context, SPAL technique was used to correct or prevent a peri-implant bone dehiscence at implant placement (Trombelli et al. 2019). From implant placement to surgical re-entry, the vertical dehiscence height decreased from 2.5 ± 1.5 to 0.3 ± 0.6 mm, and 12 (80%) out of 15 implants showing an initial bone dehiscence, showed a complete resolution. Mean vertical dehiscence reduction amounted to 88%. Three implants in 2 patients presented a residual dehiscence of 1 mm (2 implants) or 2 mm (1 implant). Ten (90%) out of 12 implants showing a thin (<1 mm) BCBP revealed a sub-periosteal tissue thickness (SPTT) ≥ 2 at the time of re-entry (2.2 ± 0.4 mm). No dehiscence was observed at re-entry on implants where a thin, but present, PBBP was recorded at implant placement. Two implants in 2 patients revealed a SPTT of 1 mm. Overall, SPTT at re-entry amounted to 2.6 ± 0.9 mm and 25 out of 27 implants (92.6%) revealed a SPTT ≥ 2 mm. While data on peri-implant bone dehiscence correction were similar to those reported in a recent systematic review (Thome et al. 2019), no comparative data are present on the prevention of a bone dehiscence thereby no comparison could be made.

To maximize the regenerative potential of the SPAL technique, a proper pre-operative diagnosis is mandatory, since it is evident that the SPAL technique may be applied only in

specifical clinical conditions (i.e. horizontal bone deficiencies). Moreover, an adequate stabilization of the graft material by mean of the periosteal layer sutures and a tension free mucosal layer for primary intention closure are crucial to provide conditions for bone regeneration (Wang et al 2006).

In the light of these findings, the SPAL technique seems to be at least as effective as traditional Guided Bone Regeneration procedures in correcting a peri-implant bone dehiscence, even though a direct comparison in high-quality longitudinal studies is still missing.

Is there any difference in peri-implant tissue conditions on the short-term at patients receiving SPAL technique compared to patients with adequate thickness (≥ 2 mm) of PBBP at implant placement?

The results reported in chapter 3 (Trombelli et al. 2020a) indicated that patients treated with SPAL technique showed low number of peri-implant inflamed sites and shallow PD (<4 mm) at 6 months of prosthetic loading. However, in SPAL groups, the interproximal bone level was found apical (although to a limited extent) to the implant polished collar.

The proportion of inflamed peri-implant sites as recorded in the study groups compares with previous findings evaluating BoP prevalence on 289 implants (Farina, Filippi, Brazzioli, Tomasi, Trombelli, 2017). Also, similar peri-implant inflammatory conditions were reported at 18 months following GBR (Jung et al., 2017).

The low frequency of inflamed peri-implant mucosal sites, observed in all study groups, may be partly due to similar characteristics for factors shown to influence BoP around implants, such as low presence of juxtagingival plaque (Pontoriero et al., 1994; Salvi et al., 2012),

shallow PD (Farina, Filippi, Brazzioli, Tomasi, & Trombelli, 2017), and adequate amount of KM (Chung, Oh, Shotwell, Misch, Wang, 2006, Perussolo et al., 2018). These findings are consistent with those stemming from a recent systematic review on biological complications of dental implants placed either in pristine or in augmented sites. Meta-analysis showed a similar prevalence of peri-implant mucositis at patient either receiving (19.6%; 95% CI: 0%–40%) or not receiving (22.4%; 95% CI: 6%–38%) procedures for alveolar ridge preservation and/or vertical/lateral ridge augmentation (Salvi, Monje, Tomasi, 2018). Also, similar inflammatory conditions were reported at implants placed in native bone compared to implants placed concomitantly with a GBR procedure (Benic, Jung, Siegenthaler, Hammerle, 2009; Benic, Bernasconi, Jung, Hammerle, 2017).

It is noteworthy to consider that at re-entry, the great majority of patients receiving SPAL technique showed a peri-implant bone thickness ≥2 mm at the most coronal portion of the implant. Although the measurement of PBBP was not available at re-entry for the control group (one-stage procedure), the integrity of PBBP following post-insertion peri-implant bone remodeling may be assumed based on preclinical (Monje, et al., 2019) and clinical (Spray, Black, Morris, & Ochi, 2000) data on critical dimensions of buccal bone plate. Collectively, available data seem to suggest that adequate vertical and horizontal dimensions of peri-implant tissues achieved by means of augmentation procedures may favor conditions to limit peri-implant tissue inflammation. However, the association of the integrity of PBBP up to the most coronal portion of the implant and the severity of peri-implant mucosal inflammation is not entirely clear (Jung et al., 2017).

At 6 months of prosthetic loading, a different position of the inter-proximal peri-implant bone level was observed among groups, with a more apical RBL in the SPAL groups. Noteworthy, in the SPAL groups tissue-level implants were positioned slightly subcrestally.

Although it may have facilitated the grafting of the periosteal pouch up to the most coronal part of the implant as well as primary intention closure, subcrestal positioning might also have contributed interproximal bone remodeling (Saleh et al., 2018). Moreover, since implants receiving SPAL technique underwent additional surgery for uncovering including an apically positioned flap or a free gingival graft, interproximal bone remodeling in the SPAL groups may be also partly ascribed to the detrimental effect of flap elevation on local blood supply. Consistently, marginal, peri-implant bone loss has been reported between re-entry for uncovering and final prosthesis delivery by other authors (Cardaropoli, Lekholm, Wennstrom, 2006, Nader et al., 2016). It should also be considered that, in some patients of the $SPAL_{dehiscence}$ group, grafting was extended to the mesial and/or distal implant aspects due to an interproximal extension of the peri-implant bone defect. In the $SPAL_{dehiscence}$ group, therefore, the extent of graft remodeling at interproximal sites may have negatively impacted on RBL values. However, the magnitude of RBL observed in the present study is limited compared to that reported for implants placed with concomitant GBR or in native bone (Urban et al., 2019) and implants presenting an untreated buccal dehiscence (Jung et al., 2017).

A slightly lower KM and MSTL was observed for the $SPAL_{dehiscence}$ group. This occurred despite peri-implant soft tissue manipulation was adequately performed to provide adequate dimensions of keratinized peri-implant mucosa and a subgingival position of the prosthetic margins. This finding may be somewhat correlated with the increased bone remodeling (RBL) observed in the $SPAL_{dehiscence}$ group, which may also have involved the regenerated buccal

bone plate. A recent systematic review correlated the remodeling of the buccal bone with the occurrence of peri-implant soft tissue recession (Aizcorbe-Vicente, Peñarrocha-Oltra, Canullo, Soto-Peñaloza, & Peñarrocha-Diago, 2020).

The limitations of this preliminary report include the retrospective design, small sample size, and short follow-up time of 6 months after restoration of the implants. Also, the impact of patient-related factors (e.g., soft tissue thickness at edentulous area, smoking habit, diabetes) and surgery-related complications (e.g., perforations of the periosteal and/or mucosal layer) on clinical outcomes has not been comprehensively analyzed. Moreover, specific clinical conditions (i.e., thin PBBP or peri-implant bone dehiscence of limited vertical dimension) have been selected for SPAL treatment. Further studies are needed to assess which clinical conditions/lesions may be effectively treated with SPAL technique or a more conventional treatment (e.g., GBR) should be preferred.

May bone augmentation be performed successfully at peri-implant dehiscence sites with a combination of SPAL and a deproteinized bovine bone mineral (DBBM) block?

The results from chapter 4 (Trombelli et al. 2021) suggests that the use of a DBBM graft delivered as a block in combination with SPAL technique may represent a suitable alternative to particulate DBBM for correcting a peri-implant bone dehiscence with a substantial increase in buccal bone thickness.

In the SPAL technique, graft stabilization into the sub-periosteal space is ensured by suturing its most coronal part and subsequent coverage by the mucosal layer. One of the potential drawbacks when using particulate DBBM is the potential displacement and/or compression of the graft particles around the coronal portion of the implant at suturing. This consideration is

well substantiated in the literature for the association of particulate DBBM and GBR (Benic et al. 2016, Benic et al. 2017, Benic et al. 2019, Mir-Mari et al. 2015, Naenni et al. 2017). In contrast, bDBBM may act as an efficacious osteoconductive scaffold while its mechanical properties would ensure a better dimensional stability at flap manipulation. Previous preclinical (Benic et al. 2016, Benic et al. 2017, Mir-Mari et al. 2015) and clinical (Benic et al. 2019) seems to corroborate the findings of the study. On the other hand, the stiffness of the block graft calls for an ideal passive adaptation of the mucosal layer to minimize the risk for flap perforation and graft exposure.

Although a thick bone-like tissue was found on the previously exposed implants at re-entry, the histological nature of the newly formed tissue still has to be determined. Available data stemming from experimental studies (Benic et al. 2016, Benic et al. 2017) and 6-month human histologic samples (Laass et al. 2020) where bDBBM was used for lateral bone augmentation showed a more limited new bone formation, mainly located at the native bone-bDBBM interface (Araujo et al 2002), compared to particulate DBBM. These observations seem to reinforce the need to improve the osteogenic conditions of the wound, like cortical perforations (Oda et al. 2009) and the use of additional growth factors (Schwarz et al 2008) and/or wait for longer maturation time prior to implant uncovering when a bDBBM is used.

What is the clinical effectiveness of SPAL technique in the regenerative treatment of peri-implantitis bone defects?

Data from chapter 5 (Trombelli et al. 2020b) seems to indicates that SPAL technique with or without additional CTG may result in the clinical remission of Class Ib/Ic peri-implantitis defects.

The selection of SPAL technique was based on the reported effectiveness in augmenting horizontal bone dimensions at implant placement in presence of an overt implant dehiscence (Trombelli et al. 2019). The stabilization of graft particles by the periosteal layer may have enhanced the conditions for clot stabilization and subsequently bone regeneration either in the intrabony component or at the buccal dehiscence. Moreover, the periosteum layer may have acted as a source of blood and osteogenetic cells, contributing bone formation (Nobuto et al. 2005). The rationale for the use of a DBBM graft only was based on previous studies reporting relevant outcomes when the intrabony component of a peri-implant defect was exposed by a full-thickness flap and grafted by DBBM with (Schwarz et al. 2010, Roos-Jansaker et al. 2007, 2014) or without (Roccuzzo et al. 2011, 2016, 2017) an additional membrane. Although a radiographic bone fill of the peri-implantitis lesions was evident at 6 months, this evidence does not qualify the nature of the augmented tissues. Previous human histology derived from a similar procedure where a sub-periosteal pouch was surgically created revealed xenograft particles surrounded by newly formed bone (Lee et al. 2017)

The decision to avoid the use of a membrane was also based on previous data[16] where the application of a membrane to treat a peri-implantitis defect resulted costly, time consuming, technique sensitive and provided no clear added value.

The additional use of a CTG was based on previous studies on surgical regeneration of peri-implantitis defects (Roccuzzo et al. 2016) where a full-thickness flap was raised to access the lesion and contaminated implant surface, bone defects were filled with a DBBM graft, and, in case of limited amount of keratinized mucosa, a CTG was used to cover the defect. Although controversial data exists about the importance of keratinized peri-implant soft tissue to ensure peri-implant health, recent systematic reviews support the use of soft tissue augmentation at

deficient sites to maintain long term peri-implant hard and soft tissue stability (Thoma et al. 2018). Overall, our findings seem to suggest that the use of a CTG to SPAL may be of additional benefit since i) it increased mucosa dimensions and (if left exposed) vestibule depth; ii) it contributed the stabilization of the portion of the graft coronal to the periosteal pouch; and iii) it supported the coronal displacement of the mucosal layer, thus enhancing wound stability conditions during tissue maturation phase. Further studies are needed to elucidate this hypothesis.

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CHAPTER 7
Conclusive remarks

The general purpose of the studies included in this Ph.D. activity was to evaluate the effectiveness of a novel surgical soft tissue management (the Sub-periosteal Peri-implant Augmented Layer, SPAL; Trombelli et al. 2018).

On the basis of the produced evidence, the following conclusions can be drawn:

1. SPAL technique represents a valuable simplified surgical approach associated with a low rate of complications in the treatment of peri-implant bone dehiscence and in the horizontal augmentation of peri-implant tissue thickness (Chapter 2)
2. After 6 months of prosthetic loading, patients treated with SPAL technique show limited peri-implant mucosal inflammation in association with shallow PD and adequate KM. At implants receiving SPAL technique, however, interproximal RBL was found apical to its ideal position. Whether and to what extent the favorable short-term results observed following SPAL technique might be beneficial for long-term healthy conditions of peri-implant tissues and stability of the buccal mucosal profile needs to be assessed. (Chapter 3)
3. The combination of SPAL and bDBBM may be successfully used to achieve an increase in buccal tissue thickness at the most coronal portion of an exposed implant. (Chapter 4)
4. SPAL technique with or without additional CTG may result in the clinical remission of Class Ib/Ic peri-implantitis defects. Whether and to what extent these beneficial effects may be maintained long-term and extended to other defect configurations needs be carefully assessed. (Chapter 5)

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