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Minimal invasiveness in vertical ridge augmentation

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ABSTRACT

Vertical ridge augmentation (VRA) is one of the most challenging procedures in implant dentistry due to the advanced skills required for the operator and the fact that bone augmentation is aimed outside the bony contour, in a reduced blood supply environment. What is more, the required flap management to ensure soft tissue closure frequently leads to associated comorbidities in terms of swelling and haematomas. For these reasons, and even if autologous onlay block grafts are still the "gold standard", new techniques and biomaterials have favored the development of potentially less invasive approaches. The present work evaluates the most recent strategies in VRA to reduce invasiveness and complications, including diagnostic/treatment planning considerations, surgical techniques, digital tools (e.g. customized Ti-meshes/membranes or bone blocks) and future trends in the field of tissue engineering and cell therapy.

1. Introduction.

The term "minimally invasive surgery" (MIS) first entered the medical literature in 1990 and in the last decades it has been applied with the aim to better preserve structures and function, providing methods to optimize surgical results with less operative trauma and, consequently, minimizing patient discomfort [1,2]
This requires the development of specific methods of preoperative imaging, planning, intraoperative navigation, and special surgical instrumentation. These approaches are quickly evolving thanks to progressively more precise surgical procedures in association with smaller incisions as compared to those traditionally used [3].

The concept of MIS can also be applied in the field of maxillo-mandibular bone regeneration/reconstruction and has become a particularly interesting challenge for clinicians in the last years. The aim of MIS is, on one hand, to simplify procedures and to reduce morbidity and invasiveness to patients, and, on the other hand, to have the same effectiveness in terms of functional and aesthetic outcomes.

In case of vertical bone defects in patients in need of implant-supported prosthetic restorations, the challenge becomes even more complex since vertical ridge augmentation aims to achieve bone regeneration without an osseous wall containment. Consequently, the elevation of an adequate size flap, the releasing incisions to allow a tension-free suture, the need of an adequate quantity of autogenous bone, and certain surgical skills are mandatory to decrease intra- and post-operative complications [4], but may conflict with the concept of mini-invasiveness.

In order to reduce morbidity and complications (such as infection, dehiscence, and neural damage) and to simplify procedures, the use of short implants have been proposed with acceptable clinical results [5-7]. However, when short implants do not guarantee an adequate functional and/or aesthetic result or they cannot be used because of insufficient residual bone volume, the reconstruction of hard and soft tissues in edentulous areas affected by severe bone defects is mandatory before implant placement.

Different bone reconstructive or regenerative techniques have been proposed: i) distraction osteogenesis [8-10]; ii) maxillary sinus floor elevation

[11,12]; iii) onlay grafts with intra-oral and extra-oral autogenous bone blocks [13-21]; iv) guided bone regeneration (GBR) with resorbable or non-resorbable membranes (PTFE) [4,22] in association or not with tending screws; and v) protected bone regeneration with non-customized [23-26] or customized titanium meshes [27-30].

All of the aforementioned surgical techniques require special skills and results are very technique-sensitive [31]). Distraction osteogenesis, even if it makes possible to correct relevant vertical defects, is limited to "pure" vertical augmentation and requires a non-negligible compliance of the patient. Onlay grafting with autogenous bone blocks still represents a versatile and well-documented procedure which allows the correction of any type of defect, with no limitations as regards the defect extent. However, the increased morbidity due to a frequent "double" surgical site (donor and recipient site) must be taken into consideration, and the modelling and fixation phases of the blocks require specific expertise [14-16]. Also GBR represents a well-documented procedure: according to the extent of the vertical defect, GBR can be performed using autogenous bone particles or bone substitutes in association with resorbable or non-resorbable membranes. However, it is worth noting that the use of resorbable membranes, because of their insufficient space-maintaining capacity, might be inadequate for relevant vertical defects. Conversely, non-resorbable membranes offer a very good space-maintaining effect, but are prone, in case of exposure, to a non-negligible risk of infection which may compromise the amount of regeneration [14,17,32]. Moreover, non-resorbable membranes must be trimmed and modelled "in situ" to be adapted to the defect, thus requiring specific skills. Finally, titanium meshes (Ti-meshes) have shown good clinical and radiological results, even if the traditional ones must be trimmed and curved according to the defect to be reconstructed, lengthening surgical times and requiring surgical experience. Moreover, Ti-Meshes may undergo exposure (with or without infection) and may be difficult to remove (because of growth of bone over the mesh or penetration of the inner layer of the soft tissues into the "open" structure of the mesh [23-26].

To minimize complications and post-operative morbidity, different modifications to conventional augmentation methods have been suggested in the last two decades, including: i) the use of soft tissue expanders prior to bone grafting [33,34]; ii) the cortical tenting technique [35]; iii) the split bone blocks technique [36,37]; iv) the tunnel technique [36,38]; v) the computer-guided bone harvesting procedure [39]; vi) the use of a 3D-printed bone

model to pre-shape or produce bone blocks [40-45] pre-shape or produce customized Ti-meshes [27-30,46]; vii) the split-thickness flap design without vertical releasing incisions [47,48] viii) the Vestibular Shifted Flap Design [49]; ix) Tissue engineering and cell therapy [50,51].

The aim of this review is to describe the most recent surgical strategies used in vertical bone augmentation to reduce the invasiveness and complications, as well as to improve patient-related outcome measurements (PROMs). Even if this is a narrative review, a systematic electronic search was performed to analyse comprehensively the scientific literature available in order to cover all the potential manuscripts proposing minimally invasive reconstructive approaches in the treatment of vertical ridge deficiencies.

2. Electronic search

The eligibility criteria for the search were: i) interventions aimed for vertical ridge augmentation (VRA); ii) RCTs, CCTs, prospective/retrospective case series with a minimum of 10 patients (5 per group in controlled studies) with at least data at re-entry/implant placement/implant loading.

The electronic search was performed in Medline via PubMed. The search was limited to human subjects and to studies reported in English. The search strategy was the same than the one previously used for the European Workshop of Periodontology on Bone Regeneration in the systematic review evaluating the effectiveness of VRA interventions [52] adding the term "minimal invasiveness" [i.e. ([MeSH terms]: Alveolar bone loss OR Alveolar bone atrophy OR [Text Words, Title]: ridge atrophy OR ridge atrophies OR ridge deficiency OR ridge deficiencies OR vertical ridge deficiency OR vertical ridge deficiencies OR alveolar ridge atrophy OR alveolar ridge atrophies OR vertical ridge atrophy OR vertical ridge atrophies OR bone atrophy) AND ([MeSH terms]: Alveolar ridge augmentation OR bone regeneration OR bone grafting OR bone replacement material OR [Text Word, Title]: vertical bone augmentation OR vertical ridge augmentation OR vertical ridge regeneration OR vertical bone regeneration OR vertical alveolar ridge augmentation OR vertical alveolar ridge regeneration)].

The initial electronic search identified 274 records in PubMed. However, after screening for title and abstract, just 2 manuscripts focused on minimally invasive approaches in VRA [53-55]. Therefore, we decided to remove the term "minimal invasiveness" from the search strategy and update it from January 2018 to July 2021.

The second electronic search yielded 401 articles published since January 2018. After abstract screening and full-text evaluation, 16 manuscripts fulfilled the inclusion criteria. However, it must be noted that most of these manuscripts did not describe any particular technique that could be considered "minimally invasive" neither evaluate patient reported outcome measures (PROMs). Therefore, we will consider for this review only those manuscripts resulting from our search and the one for the XV European Workshop on Periodontology that propose reconstructive approaches that may be considered minimally invasive or that propose innovative surgical techniques (e.g. subperiosteal tunnels, soft tissue expanders, tent pole technique, etc.), devices (e.g. customized meshes or xenograft/allograft blocks) or adjuncts (e.g. growth factors, cell therapy) that may end up into less morbidity for the patient, independently if it was properly evaluated or not. Further considerations related with pre-operative and/or diagnostic examinations, the incidence of complications and associated morbidity, and the factors influencing the long-term results of VRA procedures will be presented.

3. Evaluation of proposed surgical techniques (e.g. GBR vs. shell-technique, resorbable vs non-resorbable membranes, etc.) and devices (e.g. graft materials, membranes, growth factors, etc.) in terms of their minimal invasiveness.

VRA per se is a complex treatment modality that somehow requires certain invasiveness. However, in order to minimize invasiveness, different strategies can be considered to reduce the risk of complications, improve the patient related outcomes and to optimize treatment success.

Diagnostic phase and patient preparation

Before undergoing any vertical bone augmentation procedure, a meticulous diagnosis and the proper patient preparation should be considered as part of a successful treatment-planning protocol to avoid or minimise the onset of complications associated with bone

augmentation procedures [56]. In the treatment of complex cases, we need to evaluate the objective of the regenerative approach and if there are other less invasive alternatives (e.g. short implants) that may end up with similar treatment outcomes. This is especially relevant in the case of vertical defects, since the more extensive the defect is, the greater the risk of complications [4]. Therefore, the evaluation of bone availability is one of the first steps that should be carried out to determine if we will need to perform a vertical bone augmentation procedure.

The introduction of new technologies and software allows us to be very accurate in the estimation not only of the residual bone, but also to evaluate the amount of bone that a potential donor site would provide if needed [57]. Moreover, the possibility of merging the information of the available bone with the planned prosthetic restoration, give us the opportunity to predict very precisely the type of bone augmentation procedure needed, the amount of bone to be gained and the expected aesthetic outcomes [58]. Therefore, the use of these available tools is highly recommended when planning a VRA procedure to have an overview of what we can reach and what we need to do, and also to choose the less invasive treatment option.

Patient preparation should be also an important step before undergoing any vertical augmentation procedure. First, it is crucial to eliminate any source of potential infection, such as untreated caries, endodontic pathology or active periodontitis, since it is very important to prevent post-operative complications [59]. Also, before starting any complex bone augmentation procedure we must consider the extraction of teeth with a hopeless prognosis or teeth which might have disease recurrence and are close to the regenerated area [31]. Moreover, patients should only receive surgery if they show high standards of oral hygiene [60]. From the patient perspective, smoking cessation is highly recommended, since smoking may be associated with a higher risk of complications [61] and peri-implantitis, especially in the scenario of bone augmentation procedures [62]. Several medical conditions may alter healing of the soft and hard tissues, such as diabetes, in which an impaired healing capacity, ossification deficiencies and vascular alterations are present [63,64]. Therefore, diabetic patients should maintain a strict glycaemic control [65] and patients and clinicians should be aware that major augmentation procedures present an increased risk of failure in this cohort of patients [66].

To achieve success together with the less invasiveness, vertical bone augmentation procedures should be performed by well-trained and experience surgeons. The clinician should carefully follow each step with special attention during flap management and suturing, since it is crucial that the stabilized bone regenerative materials remain covered by the soft tissues [67]. In any case, it is important to follow the recommendations described for each individual technique and to acquire the proper learning curve to achieve successful results with the minimum inconvenience for patients.

Modification of surgical techniques

Several modifications in the surgical techniques have been proposed to reduce and minimize invasiveness and the risk of postoperative complications. VRA is more challenging than horizontal ridge augmentation, since it requires advanced flap management and uncompromised soft tissue coverage of the wound to protect the grafts and to support supracrestal blood clot stabilization [68]. If properly executed, the conventional full-thickness flap design with vertical and horizontal releasing incisions results in tension-free wound closure and subsequent primary intention wound healing (Figure 1), although membrane exposure and/or graft infection is a well-documented complication of this approach [52,59]. As an alternative to the conventional approach, a minimal invasive split-thickness flap without periosteal releasing incisions has been proposed, which could have the same results in a tension-free wound closure but at the same time avoiding the mentioned adverse events related to full-thickness flaps [47]. Briefly, the technique consists on a partial-thickness incision used to separate the mucosal layer of the flap from the periosteal layer on the alveolar ridge. The periosteal layer is reflected and used to stabilize the regenerative site using periosteal sutures. This, so-called *Double-flap incision technique* demonstrated in a clinical trial to obtain greater flap advancement with less patient morbidity (pain and swelling as evaluated by a visual analog scale at 7 days postoperatively) than with conventional periosteal releasing incisions techniques [47]. However, some concerns may arise from this surgical approach. First, it is probably more demanding for the average clinician. Second, it is unlikely that in major VRA the periosteum will be able to cover the entire graft/membrane.

Another approach that has been described to reduce the invasiveness of VRA by means of GBR is the split thickness flap design without vertical releasing incisions [48,69]. The

technique consists on a midcrestal incision on the keratinized mucosa that is continued intracrevicularly at the two adjacent teeth mesially and distally both buccally and orally. In case of posterior edentulism, the midcrestal incision line length is two-thirds of the entire surgical area, and one-third length was continued mesially to the neighboring two teeth. No vertical-releasing incisions are performed and, therefore there is less reduction in blood supply, which may affect graft ossification and increase remodeling capacity [70]. A full-thickness buccal flap is reflected with elevators up to the mucogingival line, followed by split-thickness mucosal flap preparation over the mucogingival line. Subsequently, the underlying periosteal layer is elevated from the bone surface. After the bone augmentation procedure has been done, a double-layer suturing is performed using horizontal mattress sutures in order to cover the membrane with the periosteal layer, and a combination of horizontal mattress and non-interrupted sutures to close the mucosal layer and to reach a tension-free wound closure [48]. The main advantage of this procedure seems to be the bilaminar wound closure, leading to a tension-free flap adaptation thus minimizing post-operative complications related to wound dehiscence. In this prospective case series the split-thickness flap design represented an approach leading to favorable wound healing with low patient morbidity and a low rate of membrane exposure (4.2%). However, in most of the cases included in this manuscript the amount of VRA was minimal as they were dealing mostly with horizontal defects. Furthermore, it is an open question how effective is to split flaps in thin phenotype patients as this may lead to flap necrosis.

In the field of autogenous bone blocks the "three-dimensional" reconstruction or shell technique has been proposed [36,37]. Thin cortical bone blocks are initially used to restore the contours of the alveolar ridge and the remaining gaps are then filled with autogenous bone chips. The resulting accelerated vascularization in the container and the volume stability of the avascular cortical bone plate reduces bone resorption to <10%, so the alveolar ridge contour can be restored with a predictable outcome. The short- and long-term results after augmentation with the aid of the shell technique demonstrated low complication rates and excellent volume stability, even ten years after surgery [37]. The main advantage of this technique is that the grafts are harvested from the external oblique ridge with a micro saw, making the procedure very safe and with low risk of complications. Moreover, since the bone block is split in two thin plates that will serve to

prepare the external walls of the regeneration area, the amount of bone block to be harvested can be reduce considerably, making the procedure much less invasive.

In order to further reduce the invasiveness of this technique, different modifications have been introduced, such as the tunnel technique [38]. The idea is to prepare a tunnel, allowing the maintenance of the integrity of the soft tissue over the graft material. This approach was studied in a prospective case series including ten patients that evaluated vertical bone augmentation with autogenous bone block grafts following the tunnel technique. The block was harvested from the external oblique ridge with the conventional technique. In the recipient area a single vertical incision was done at the distal margin of the mesial tooth to the defect. This incision extended over the mucogingival junction. Through this single vertical incision, a full-thickness flap was raised buccally and lingually, tunnelling the mucosa and the attached gingiva over the defect and reaching the distal portion of the defect. Once the soft tissues were prepared, the first thin bone plate was fixed with titanium screws and stabilized in such a way so as to create a bone bridge between the mesial and distal bone peaks. The second thin bone block was fixed laterally with a titanium screw, closing access to this space once the remaining gaps were filled with autogenous bone chips. No barrier membranes were used. After 4 months of healing, no complications were registered, and the mean vertical bone gain was 6.00±1.29 mm.

The *Cortical Tenting Technique* [35] and the *Tent Pole Technique* [71] have been proposed to increase the ridge width or height using autologous bone blocks or a combination of bone substitutes together with a barrier membrane. Both techniques seek to preserve the space for bone augmentation, in a way the titanium screws maintain this dimension decreasing the pressure of the overlying soft tissue onto the graft, preventing its migration and resorption. This technique may diminish the invasiveness of the procedure if it is used with resorbable collagen membranes, being able to obtain vertical ridge augmentations ≈4.3 mm [52] (Figure 2). However, it should be noted that if major augmentations are sought, the use of non-resorbable membranes or the shell technique with autogenous bone plates is encouraged.

As wound dehiscences are one of the most common complications of horizontal and VRA procedures, soft tissue management is a crucial aspect that impacts upon the outcome of these surgeries. Most commonly in reconstructive procedures, optimal wound seal is

obtained by two suture planes to obtain a deep and a superficial closure by horizontal mattress sutures and single simple sutures. As the palatal flap eversion to couple the first 4 to 5 mm of the buccal flap may be difficult due to the characteristic dense connective tissue of the area, a new technique named Vestibular Shifted Flap Design has been proposed [49]. In this technique, the incision line is shifted towards the buccal side based on defect anatomy and the target of vertical bone augmentation, in a way the palatal flap length extends at least 4 mm coronal to the bone graft level prior to wound closure. This approach may impact invasiveness as it is expected that the optimal adaptation of the inner faces of the flaps results into a lower risk of non-primary wound healing.

The use of soft tissue expanders for vertically atrophied alveolar ridges has been proposed prior to bone grafting [33]. The rationale behind its use is to increase the soft tissue volume before bone grafting allowing for sufficient amount of soft tissue, allowing better graft coverage which will lead to a more stable and effective vertical bone augmentation procedure. Furthermore, several studies demonstrated that soft tissue expansion improved microcirculation and more rapid osseointegration and even new bone formation around the expander in cases of slowly expanding periosteum has been reported [72]. The use of soft tissue expanders have been evaluated in a multi-center randomized clinical trial and compared to conventional GBR to treat vertical ridge deficiencies [73]. Patients in the experimental group received a hydrogel type, self-inflating soft tissue expander that was in place for 28 days. After this one-month period of expansion, the expander was removed, and bone grafting was performed with the tunneling method without full flap reflection using a resorbable membrane together with a xenograft. For the control group, the conventional GBR technique with sufficient periosteal-releasing incisions was performed to achieve a tension-free wound with primary closure. The results showed that only in one out of 23 cases, the expander had to be removed. Moreover, early wound dehiscence after bone grafting did not occur in this group. On the contrary, 2 out of 23 cases in the control group experienced wound dehiscence. Six months after the reconstructive procedure vertical bone gain was significantly greater in the experimental group (5.12 ± 1.25 mm compared to 4.22 ± 1.15 mm) and graft contraction significantly less (30.7% compared to 55.1%) [73].

Staged or simultaneous implant placement?

In theory, the invasiveness of VRA interventions may be limited by reducing the number of surgical interventions, this is, placing implants simultaneously to the ridge

augmentation. However, when evaluating the effectiveness of different VRA procedures on a recent systematic review, the weighted mean effect (WME) of the simultaneous approach was 3.81 mm, while the staged approach achieved a WME of 4.39 mm. This may imply that the amount of augmented bone is somehow limited on simultaneous interventions or that these procedures are carried out whenever the required augmentation is more limited. In any case, the invasiveness is also related somehow with the severity of the complications that may occur. Frequently, graft/membrane exposures and post-operative infections may lead to a bacterial contamination of adjacent implant surfaces if a simultaneous technique is utilized. and in cases of simultaneous VRA. For this reason, a staged approach is preferable whenever there is an important amount of missing bone, the ideal position of the implant according to the future restoration is outside the bony envelope, or primary stability is compromised, especially in the hands of unexperienced clinicians.

Digital tools and materials

With the advent of new technologies, bone grafting procedures have become more efficient, not only in terms of surgical treatment time, but also in relation to patient morbidity [74]. Digital tools can be very useful during the diagnostic phase, treatment planning and surgical execution. Today, there are available softwares that can simulate the amount of bone needed, predicting accurately the bone volume to be gained. This can help the clinician to select the best donor site, to help the patient understanding of the treatment objective and even to estimate the budget more precisely.

An available digital tool is to transform the DICOM files from the Cone Beam Computed Tomography (CBCT) into STL files or another printable format. By doing this, we can have very easily a printed model of the bone. Again, this can be useful to help the patient understanding of the type of bone defect and the aim of the procedure. Furthermore, surgical and prosthetic phases can be virtually simulated by importing 3D data into implant planning software, and ideal implant positions could be planned before surgery according to bone quality and quantity, location of anatomic structures such as nerves, vessels, sinuses, prosthetic demands and aesthetic evaluations [75,76]. Specifically, computer-guided implant placement may be advantageous in cases of limited bone

availability, combining the effects of virtually-aided GBR and computer-guided implantology [77].

Also, it has been proposed that the printed model can be used to trim and preformed a titanium mesh before the augmentation procedure [74]. Traditional titanium meshes have shown to be effective when used to vertically augment the ridge defect, although some drawbacks and complications have been reported [23]. First, the mesh usually has a rectangular shape and must be trimmed and bended according to the defect morphology, requiring clinical skills, expertise and lots of time. Furthermore, irregular and sharp angles and edges may be created during modelling, which may expose soft tissues to mechanical trauma, leading to perforation of the flap and exposure of the mesh. This can be followed by infection and partial or total loss of the initial bone augmentation.

To overcome these disadvantages, laser sintering has been proposed to produce customized titanium meshes by means of CAD-CAM technology (Figure 3). The main advantages are the fabrication of meshes with smooth edges, better adaptation to the bone defect and the possibility to include individual design modifications that can improve all aspects of ridge augmentation procedures, as for example the guidance of where the implants should be placed during the second stage surgery [30,78]. Further advantages could be the reduction of surgical time, the estimation of the amount of bone needed to reconstruct the defect, and the reduction of invasiveness since we can prelude flap extension and anatomical landmarks. In a prospective case series including 21 patients and 30 implant sites this procedure was evaluated. During healing, two mesh exposures occurred and, after removing the exposed part, healing was uneventful. Vertical bone gain above the implant platform was 1.4 mm (average vertical bone gain was 2.5 mm), while the average thickness of the buccal bone width at the implant platform was 2.0 mm (average horizontal bone gain was 4.1 mm). In order to evaluate the feasibility and accuracy of this technology, an accuracy assessment of this digital solution was conducted. Through the volume analysis of virtual augmentation and actual augmentation, the accuracy of this procedure reached 95.82% (range from 88.53% to 99.15%) [46]. A recent retrospective study also evaluated the use of customized Ti-meshes to treat vertical ridge deficiencies in 41 patients [29]. According to the results, this mode of therapy can represent a reliable and a safe tool for GBR of severely atrophic sites, with

simplification of the surgical phases. The applicability of this technique could also be extrapolated to the use of pre-shaped non-resorbable membranes.

Specially interesting is a recently published RCT assessing the 3D bone augmentation of severely atrophied maxillary alveolar ridges using pre-bent Ti-meshes or customized poly-ether-ether-ketone (PEEK) meshes [79]. In this study DICOM files of both groups were imported into a specialized software that allowed the design of the virtual 3D increment of the deficient ridge, and 3D printing technology was used to fabricate the virtually grafted stereolitographic model used for pre-bending the Ti-mesh (control group) or a printed and customized PEEK meshwork designed with a 2 mm thickness covering the buccal, crestal and palatal surfaces of the alveolar bone leaving the space for the grafted area (test group). Wound healing was uneventful in all cases except one in each group (i.e. 1 out of 8 cases in each group) and no differences were observed among them regarding the vertical bone height obtained. Pre-shaping the Ti-mesh or printing a PEEK-mesh could reduce the invasiveness of VRA procedures as long as conforming Ti-meshes or non-resorbable membranes is time consuming during the surgical interventions. Common complications associated with the use of Ti-meshes are mesh exposure due to its stiffness and difficulties in the removal process. This limitations may be overcome by the use of PEEK or other biocompatible materials, that have been widely used in orthopedic and trauma surgery [80], although its efficacy in VRA requires further research.

Computer-guided can also be helpful in the bone harvesting procedures required for the shell technique in order to reduce the risk of anatomical structural damage at the donor site [39]. The technique starts using a planning software that allows to visualize the anatomical structures, such as the alveolar canal, the mental foramina, the mental nerve, and the teeth roots present in the donor site. Through each cross-sectional image, ideal bone-cutting planes are defined taking into consideration the above-mentioned anatomical structures. Then, the bone block length, height and thickness are defined. Once the cutting planes are established, their projection outside the bone/body surface defines the internal faces of the surgical guide. Each face guides the cutting tool direction once the tool is simply leaning against the surface of the surgical guide that has been printed and fixed with mini-screws. The osteotomy can be done with a piezoelectric instrument, which may be safer than a micro-saw. As the cutting direction and the

working depth are unequivocally defined by the surgical guide the risk for injuring important anatomic landmarks disappear. The results from case series showed that this procedure was safe with no complications reported [39].

Another applicability of a 3D-printed bone model is to pre-shape a bone block graft and to plan the fixation screws. The main advantages of this technique are time reduction and ease of graft adaptation. The feasibility and security of this procedure have been reported in several clinical studies, which have also confirmed the related advantages when using allogenic bone blocks manually milled before surgery [40,42].

The same application has been suggested with the use of synthetic grafts together with the shell technique. In summary, a virtual ridge augmentation of a maxillary defect is done, and a 3D-printed model is utilized chairside for extra-oral thermic bending and trimming of an absorbable shell graft (poly-D, L-lactic acid polymer). Then, a tunnel technique is used to fix the shell with osteosynthesis screws, and a mixture of autologous bone chips and xenograft is used to fill the spaces [81]. Invasiveness of the shell technique can also be reduced by using allogenic bone plates, with similar results as compared to autogenous bone, at least as long as autologous bone chips are used to fill the bony envelope [82]. If autologous bone, xenografts and/or synthetic grafts without any addition of autogenous are enough to lead to VBA seems to be unlikely from the biological plausibility perspective. Specifically, as VRA aims to achieve bone augmentation in the absence of osseous walls containments, angiogenesis must reach a certain distance from pre-existing bone, in a way the use of the only graft able to ensure osteogenesis (i.e. autogenous bone) is desirable, which just does not mean other bone substitutes such as xenografts may be useful due to their osteconductive properties in order to reduce the amount of autogenous bone to be retrieved.

The reconstruction of the alveolar ridge dimensions can also be performed digitally, and the graft digitally designed and manufactured by a milling process. This workflow will eliminate the need to have a physical alveolar ridge defect model. One possible way to do it is to mill bone blocks. This approach has been utilized with different graft origins, such as allogeneic [45], alloplastic [43] or xenogeneic [44]. The main advantage when using this customized bone blocks are time reduction, since graft adaptation is much easier, decreased morbidity and increase fitting accuracy of the graft (Figure 4). One clear

advantage of CAD/CAM technology for block grafts over 3D-printing is its potential application on a wide range of grafting materials.

3-D printing has also been developed to produce customized bone blocks from synthetic origin [43]. The advantages associated to this technique include unlimited availability, no risk for disease transmission, high patient acceptance, reduced waste of biomaterial, ability to optimize surface topography and macroporous architecture and reduction of intra-operative time. However, most of the evidence is coming from preclinical studies in animal models and further research in clinical studies is needed to evaluate the real impact of these grafts as an alternative to conventional therapies [83].

Tissue engineering and cell therapy

The future in bone augmentation procedures is tissue engineering. This is a discipline employing the principles of engineering and biological sciences for the fabrication of functional constructs used to restore, maintain or improve tissue functions. Growth factors incorporated in carriers, stimulation of selective production of growth factors using gene therapy and the delivery of expanded cellular constructs (i.e. cell therapy) have been developed for craniofacial regeneration, including VRA [50].

Growth factors such as bone morphogenic proteins (BMPs), platelet-derived growth factor (rh PDGF-BB), transforming growth factor-β 1 (TGF-β1), insulin-like growth factor-1 (IGF-1) and vascular endothelial growth factor (VEGF) have the ability of inducing differentiation of stem cells into osteoblasts (i.e. osteoinduction) [84]. A wide range of results are reported regarding the use of growth factors in GBR procedures, as these are frequently combined with different biomaterials and bone augmentation techniques, making difficult to prove any superiority of their effect [51,85,86].

The use of transplanted cells to promote and direct wound healing is commonly named as *cell therapy*. Cells, factors for tissue induction, and a matrix for seeding cells are the three-key factors of this technology. This combination has proven to allow the growth of tissue *in vitro*, prior to implantation into the subject [87].

Stem cells can differentiate into a wide variety of cell types, including osteogenic cells. The bone marrow stroma contains hematopoietic cells and mesenchymal stem cells that from a single progenitor cell have an important potential of differentiation [88], being able to lead to bone formation in ectopic places [89]. Indeed, bone block allografts impregnated with bone marrow aspirated from the iliac crest has been presented as a predictable and effective treatment of deficient alveolar ridges when compared to harvesting autogenous bone [90]. One of the various sources of mesenchymal stem cells include adipose tissue. For this reason, buccal fat pad has been proposed as a suitable intraoral source of osteoprogenitor cells [91]. Specifically, an exploratory clinical study performed in Iran included 14 patients with atrophic posterior mandible that received buccal fat pad-derived stem cells with DBBM as scaffold for VRA (test group) or a combination of DBBM with particulated autogenous bone (control group) [92]. After 6 months, no differences in the quantitative analysis of CBCT images for new bone formation were observed between groups, showing that the bone formation of buccal fat pad stem cells is comparable to that of particulated autogenous bone when combined with DBBM.

During the different steps of tissue engineering, the design of the scaffold prior to exposure to cells is of vital importance. The main characteristic of the scaffold is that it must present a surface that promotes cell attachment, growth and differentiation, providing at the same time a porous network for tissue growth. 3-D printing has also been proposed to customize these scaffolds in the field of bone augmentation procedures [93]. The most commonly evaluated scaffolds for craniofacial bone regeneration include xenogenic, allogenic and synthetic bone substitutes. However, limitations in their use is related to the lack of degradability or too fast degradability, inability to maintain the desired bone volume under mechanical stimuli, etc. Ideally, these scaffolds should be degradable at a similar rate to that of bone tissue turn-over, with large, interconnected pores allowing for cell incorporation, proliferation and migration, etc. For this reason, future scaffolds will be probably synthetic (e.g. different polymers) and being able to be constructed by CAD-CAM technologies to adapt to bone defects with complex geometries [94].

Another possibility is 3-D bioprinting. This technology is based on the same principles of earlier 3D printing technologies, but has been customized to manufacture permanent implants, biomimetic scaffolds and drug delivery platforms using cells, growth factors

and biomaterials as input materials. The technology can produce objects with controlled morphology and internal structure having highly similar structure to the human body. Currently, the technology is used in various aspects of tissue engineering and regenerative medicine applications including hard and soft tissue printing, cartilage printing, skin printing and tumorous tissue model printing [95]. According to the comprehensive review by Ventola, the major steps in 3D bioprinting include: i) creating a blueprint of the desired organ with its vascular architecture; ii) generating a bioprinting process plan; iii) isolating stem cells and differentiating them into organ-specific cells; iv) preparing bio-ink reservoirs with organ-specific cells, blood vessel cells, and support medium to be loaded into the printer; v) bioprinting the required product; and (vi) placing the bio-printed organ in a bioreactor prior to transplantation [41]. With the development of this technology it is expected that we will have the opportunity to print customized synthetic bone enriched with growth factors and stem cells to reconstruct alveolar ridge defects. Indeed, a proof-of-concept feasibility study was conducted in the University of Michigan to evaluate in a RCT the effect of cell therapy with lxmyelocel-T adsorbed into a gelatin sponge following the GBR principles (test group) versus a GBR group with the gelatin carrier alone (control group) [96]. Histological analyses revealed that biopsy specimens from the test group presented higher density of bone. However, it should be noted that these approaches are expensive and thus limited by now to the research environment. Furthermore, they required to harvest a bone marrow sample from the iliac crest.

Another clinical study evaluated the potential of mesenchymal stem cells in a biphasic calcium phosphate (BCP) scaffold in the reconstruction of large mandibular bone defects [97]. Non resorbable PTFE-d membranes were used to provide a tenting effect, while 5 cm^3 of BCP mixed with 100 million mesenchymal cells were applied below the membrane. After 4-6 months of healing, the regenerated bone volume was adequate to place dental implants and healing was uneventful. It is expected that due to the disadvantages of autologous grafting, which is still the gold standard, future trends will be focused on the development of synthetic scaffolds enriched with stem cells and/or growth factors.

4. Complications, sequelae, and morbidity in vertical ridge augmentation

4.1 Complications

VRA is a complex, technique sensitive intervention, which entails a risk of short and long term complications [14].

Short term complications are the most documented, as they occur during the healing of the reconstructive procedure. These are mainly represented by flap dehiscence and infection of the underlying regenerative biomaterials, and have been described from 1 week up to 6 months after surgery [98-101]. In a recent systematic review on VRA, their weighted mean incidence was 16,9% [52]. Specifically, based on no direct comparison, distraction osteogenesis presented the highest rate (47.3%), followed by the use of bone blocks (23.9%), and guided bone regeneration (GBR) (12.1%) [52].

Among bone blocks, the highest weighted mean incidence of complication was observed with allografts (39,2%), while when using autogenous bone, the shell technique presented less frequent complications than onlay blocks (17,8 vs. 26,1%). These included both wound infection with or without block exposure, incomplete block integration, and block mobilization at the time of implant placement [23,102]. Due to the technical sensitivity of the procedure, a clear heterogeneity was observed among the different studies, with some reporting up to 77% of complications [103] and other reporting less than 10% [16,104] or no complications [105]. While some cases of superficial exposure only required to remove the most coronal portion of the graft [106], others resulted into significant graft resorption with the need of additional grafting at the time of implant placement [107], or into the complete loss of the block graft [103].

Interestingly, among GBR techniques, complications were most frequent when using a resorbable (22.7%) vs. non-resorbable membrane (6.9%), as it was also described in previous systematic reviews [32,108,109]. Such finding may reflect the publication bias observed specifically for the case series included in the aforementioned review and could be explained by the fact that most of the reports are published by a selective group of master clinicians that present outstanding results but with limited external validity to other practitioners. Furthermore, it is expected that a higher degree of caution was carried out in studies applying non-resorbable membranes, as the management of wound dehiscences is more complex when using this type of barriers.

Indeed, in order to provide specific indications for the clinical management of healing complications with non-resorbable membranes, Fontana et al. distinguished 4 classes of contingencies based on the extent of the wound dehiscence and the presence or absence of an underlying infection [110]: i) Class 1: small membrane exposure (≤3mm) without purulent exudate; ii) Class 2: large membrane exposure (>3mm) without purulent exudate; iii) Class 3: membrane exposure with purulent exudate; iv) Class 4: abscess formation without membrane exposure.
Class 1 exposures, being the smallest ones, allow for an attempt to maintain the membrane in place for an additional month, under a strict plaque control regimen, supplemented by the use of local antiseptics. Such indication is provided based on the in vitro evidence that bacterial penetration through PTFE-e membranes requires approximately 3-4 weeks, during which further maturation of the underlying grafting material can occur, before the membrane is removed [111]. Such time could be potentially increased when using PTFE-d membranes, as a higher cell occlusivitiy has been described for this type of barrier [112]. Class 2 to 4 cases, on the other hand, require the immediate removal of the membrane, with the additional curettage of the infected bone particles in class 3 and 4 cases [110].

Exposure rates comparable to the ones of GBR have also been reported with the use of Ti meshes combined with resorbable collagen membranes [22,29]. Specifically, direct comparative data were provided by a RCT from Cucchi et al., which reported no significant differences in the incidence of healing complications when performing VRA in the posterior mandible with PTFE-d membranes (15.0%) vs. non-customized Ti-meshes combined with cross linked collagen membranes (21.1%) [22]. Similarly, a cohort study by Chiapasco et al. reported an exposure incidence of 20,75%, when performing VRA with customized CAD/CAM Ti-meshes combined with a native collagen membrane [29].

Long term complications, on the other hand, are the ones occurring once the regenerated bone receives an implant supported rehabilitation, and mainly consist in the onset of peri-implant diseases. Fewer data are available in this respect, as most studies on VRA did not report the occurrence of biological complications based on specific, unified, case definitions. Urban et al. reported progressive bone loss >2 mm combined with BOP at 3.73% of implants in vertically augmented sites, at 12 to 72 months after loading (Urban et al., 2009), while Merli et al. reported that 0% of the implants had progressive bone loss

>3 mm combined with BOP, 6 years after VRA with GBR [113]. The majority of studies, reported either the occurrence of peri-implantitis without a specific case definition, or based on the bone loss thresholds established by Albrektsson & Zarb, with heterogenous data [8,16,114,115].

4.2 Sequelae and Morbidity of Vertical Ridge Augmentation

VRA aims to reconstruct severely atrophic edentulous ridges where the residual bone volume does not allow the placement of dental implants in their optimal prosthetic position, even if adopting short or narrow implants [52]
Thus, its surgical invasiveness is related with two main factors: the involvement of delicate anatomical structures within the surgical site, and the amount of flap passivation required to achieve primary closure, which is proportionate to the volume of the grafted bone [116]. Further invasiveness can derive from the harvest of autogenous bone grafts, which based on the adopted reconstructive approach, can be performed locally, or at a second intra- or extra-oral site [14].

Involvement of local anatomical structures is a common event when performing VRA in the posterior mandible, as the emergence of the mental nerve is frequently exposed during flap elevation, and a blunt dissection of its main branches is sometimes required to achieve proper flap passivation. Post-operative paresthesia of the mental nerve has been reported in 12 to 27% of mandibular VRA cases, albeit its resolution occurred spontaneously within a short timeframe [23,117,118].

Further anatomical structures which could be exposed during VRA include the nasal floor [119], the maxillary sinus [120], the canalis sinuosus [121], and the inferior alveolar nerve, when severe mandibular atrophies result in its superficialization in the edentulous crest [122]. ,Furthermore, flap passivation in the upper arch can result in the involvement of peripheral branches of the infraorbital nerve [123] and the buccal fat pad [124], while in the lower arch it can expose the submandibular gland and Wharton duct, the mylohyoid muscle and artery [125,126], and the lingual nerve [127].
In order to avoid damage to such anatomical structures, the use of blunt dissection has been advocated during flap passivation, especially in the lingual aspect of the posterior mandible [128,129].

Extensive passivation and coronal advancement of the flaps results in post-operative edema and hematoma, which usually peaks within 48 to 72 hours, diffuses based on the position of muscle insertions, fascia and bone structures, and then resolves in the following days [130-132]. While the use of corticosteroids has been validated as an efficacious mean to reduce swelling after the extraction of impacted third molars, some concerns have been raised with their use in bone reconstructive procedures, as potential interfering effect of corticoids with the incorporation of bone grafts has been described in animal models [133,134].

Finally, postoperative sequelae associated with the harvest of autogenous bone have been described for both intra and extra-oral sites, especially with the harvest of bone blocks. When focusing on intra-oral sites, the linea obliqua externa of the mandible is the most commonly adopted site to harvest autogenous bone (Clavero & Lundgren, 2003; Chiapasco et al. 2009). When adopting a conventional harvesting technique with a combination of burs and microsaws, Khoury et al. reported an incidence of minor alveolar nerve injuries (e.g. hypoesthesia or paresthesia) in 20 out of 3874 cases (0.5%) [37]. Alternatively, the mandibular symphysis has been advocated as an accessible donor site, albeit in presence of the lower incisors, altered sensitivity has been described in a relevant percentage of cases. In the study by Clavero & Lundgren, permanent paresthesia in the mental region was observed in 51.7% of cases [135].

Independently of the site of harvest, the adoption of modern technologies based on piezoelectric surgery and CAD-CAM guides for bone harvesting, seems to be a promising approach to increase the accuracy of the block harvesting procedure and reduce the risk of complications [39]. Also, the use of bone scrapers has been advocated as a less invasive mean to collect particulated autogenous bone compared to the harvest and extra-oral milling of bone blocks, allowing in certain clinical scenarios the collection of smaller bone quantities without the involvement of a second surgical site [136]. Interestingly, evidence from preclinical studies reported similar amounts of osteogenic cells DNA, cell adhesion and proliferation rates, in bone samples harvested with the two techniques, which was superior to the ones achieved with piezo-surgery or a bone trap filter within an aspiration device [137].

5. Factors influencing the outcomes of vertical ridge augmentation procedures (patient & site risk factors)

VRA has been regarded as a highly sensitive intervention, where the operators´ technical skills, patients´ risk profile and site-specific features are pivotal in succeeding. Patient-related risk factors seem to be common regardless the type of intervention. Smoking habit has been suggested to limit the extent of VRA [4], to lead to a higher risk of post-operative complications [36,66] and to increase the rate of implant failure in regenerated bone [138]. The rationale behind this clinical observation is that smoking increases the number of osteoclasts by inhibiting osteoclast apoptosis via the mitochondrial reactive oxygen species and cytochrome C-caspase-3 pathway, also affecting bone marrow cells, leading to an increased formation of osteoclasts [139]. It is encouraged, thus, to restrict smoking at least 3 months before VRA [4]. Moreover, other conditions affecting wound healing such as diabetes mellitus have been identified as detrimental factors for VRA [66]. In these patients it must be noted though, that an appropriate metabolic control may reverse the adverse effect [64]. Therefore, a comprehensive anamnesis is crucial prior to VRA to identify and modify potential patient-related risk factors that may compromise the primary outcome. Although these patient-related features may not affect the invasiveness of VRA, it is critical to disclose them to understand the limitations of this procedure based upon the risk profile

In addition, site-specific factors influencing VRA outcomes have been identified in clinical studies and suggested in expert opinion reviews. These might be of interest to select minimally invasive approaches. For instance, it was proved that bone gain in the maxilla was significantly greater in the posterior compared to the anterior area (mean difference=0.36mm). On the other side, in the mandible, bone gain was greater in the anterior in contrast to the posterior area (mean difference=0.32mm) [140]. Furthermore, it was claimed that optimal results are anticipated in the presence of a concave defect topography neighbored by adjacent bony peaks instead of isolated supra-crestal defects, where attaining space creation is more arduous and demands of higher expertise [4,141]. The former scenarios might be more prone to succeed whenever minimally invasive approaches are applied. Along these lines, it is important to note that tension-free primary closure dictates the extent of achievable VRA and the odds for post-operative complications [142]. In this sense, it is paramount to conceive the nature of the periosteum

and vestibular depth as critical factors to succeed in VRA [143,144]. In order to overcome scenarios exhibiting damaged periosteum or shallow vestibule, technical maneuvers such as the remote/safety/vestibular shifted flap, the papilla shift approach or the periosteoplasty have been recommended [49,143]. In the later scenarios might be more challenging the application of minimally invasive approaches.

6. Long term outcomes of the vertical ridge augmentation procedures

VRA is a well-documented procedure with implant success and survival rates similar to those placed in native bone [108,145]. However, only few studies have reported in the long-term marginal bone level changes around implants placed on vertically augmented sites [16,52,104]. In this context, a recent systematic review identified only 11 investigations evaluating bone level changes at least 12-months after loading. Among these studies, most of them reported marginal bone level changes similar to those around implants placed into native bone. On the contrary, three studies showed that 5.8-20% of the implants placed in vertically augmented sites had bone loss above the criteria defined by Albrektsson & Zarb [8,114,115].

An important factor to be considered is the timing of bone remodeling, since it should be noted that in some cases after VRA there might be more bone loss during the adaptation phase. As an example, Simion and coworkers run a retrospective study reporting on implants with a machined surface 13 to 21 years after loading [146]. It was found that between the first year and the final visit, minimal marginal bone loss occurred (1.02 mm), demonstrating a stability of the crestal bone similar to native bone. However, it must be highlighted that the baseline radiographs were taken 1 year after physiological bone re-modeling, when bone levels were already located 2.11mm below the implant shoulder of Branemark implants. These results suggests that we cannot take for granted that there will be no bone loss around implants placed into vertically augmented bone and that external hex designs may be associated to a greater initial bone remodelling [146,147]. In this context, implant design and surface characteristics may play a role. In order to prevent biological complications due to the exposure of the rough surface secondary to bone loss, the use of one-piece implant designs (such as tissue level implants), hybrid implant surfaces and the subcrestal placement of implants have been proposed [148-153].

In order to minimize the initial bone remodeling associated to VRA procedures, a second protecting layer of bone grafting at the time of implant placement has also been advocated [144]. Results using a mixture of a slowly resorbable xenogenic bone graft and autogenous bone chips covered with a resorbable membrane demonstrated that epi-crestally placed implants into vertically augmented bone exhibited excellent marginal bone stability [154]. Increasing of the soft tissue thickness has also been proposed to prevent marginal bone loss, since VRA procedures may result in stretching and thinning of the soft tissues during regenerative surgeries [51,155]. Additionally, many patients have minimal or no keratinized tissues at the end of regenerative therapy, which has been identified as one important factor impairing oral hygiene and increasing the risk of biological complications. Therefore, soft tissue grafting to increase keratinized tissue should be frequently considered after VRA procedures [51]. In two long-term retrospective studies [16,104], in which patients presenting with edentulous and atrophic ridges were treated with autogenous mandibular or calvarial bone blocks and were rehabilitated with implant-supported prostheses, the use of vestibuloplasty in association with free gingival grafts reduced the incidence of implant failures and peri-implantitis, although the difference was not statistically significant. Nevertheless, these techniques as well as the above-mentioned factors should be investigated in well-designed randomized clinical trials.

Outcomes associated to peri-implant health or disease, such as mucosal or bleeding indexes, as well as probing depths, have been reported scarcely and inconsistently in studies dealing with VRA [52]. This fact, together with the scarcity of long-term reports, hinder to have a clear image of the incidence of biological complications of implants placed into vertically augmented sites using different surgical approaches. Moreover, several factors such as the previous history of periodontitis can influence long term results. Roccuzzo et al. in a long-term clinical study analyzing periodontal indexes and MBLs around non-submerged implants placed after vertical alveolar ridge augmentation, reported a statistically significant greater bone loss in patients whose bone atrophy was consequence of a previous history of periodontitis [156]. Therefore, primary prevention protocols are still the main tool to assure the long-term stability of implants placed in this clinical scenario. Proper maintenance protocols and oral hygiene strategies should be developed and individualized for each patient [157,158].

7. Summary and conclusions

VRA procedures are challenging procedures aimed to reconstruct the alveolar process in situations where no osseous wall containment is present, and therefore, it is questionable that they may be considered "minimally invasive". However, that does not mean that new advances have not been developed to simplify the procedure, making it easier for clinicians and consequently, having an impact on patient´s morbidity (even if PROMs have not been properly evaluated in most of the reports).

Among the most relevant innovations, advances in pre-operative treatment-planning together with digital tools such as CAD/CAM technologies have allowed to customize Ti-meshes or bone/bone substitutes blocks (e.g. computer guided bone harvesting procedures, 3D-printed bone models to pre-shape meshes or allograft plates, 3D-printed allogenic/xenogeneic/alloplastic bone blocks, digitalization and customization of reinforced PTFE meshes, etc.) reducing treatment time and restoring geometrically complex anatomical defects with accuracy and precision. Furthermore, the use of biomaterials instead of autogenous onlay blocks (which are still the "gold standard") reduce the need of a donor site and the potential complications associated to a second surgical site. However, the truth is that these approaches have been presented in only a few short-term case reports, and it remains questionable which are the most suitable biomaterials, their resorption rate or the long-term results of the implants placed in these augmented ridges.

Different surgical designs have been proposed also to reduce the invasiveness and risk of complications in ridge augmentation procedures, including tunnel techniques, different periosteal releasing incisions, apical accesses, absence of vertical releasing incisions, etc. Sadly, these techniques have been described mostly in retrospective case series, and their efficacy have not been tested in properly designed randomized clinical trials, including the evaluation of PROMs.

Probably future trends in VRA will lay on new strategies on regenerative medicine and tissue engineering using stem cells on 3D printed scaffolds. However, their use is limited to research environments by now due to costs and legislation, and it is crucial that they prove to provide additional benefits over current standard therapies (i.e. GBR, shell technique with autogenous bone).

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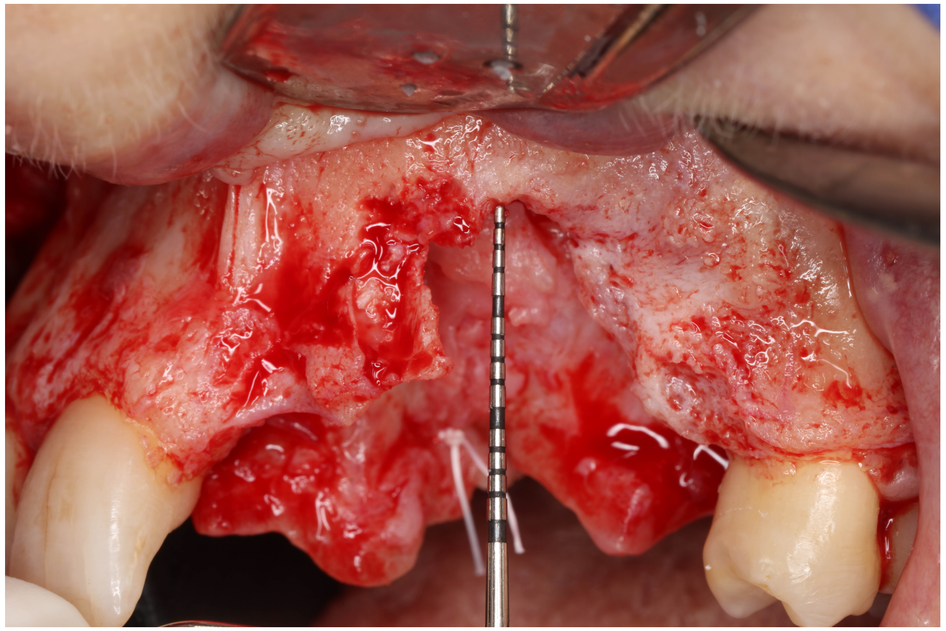

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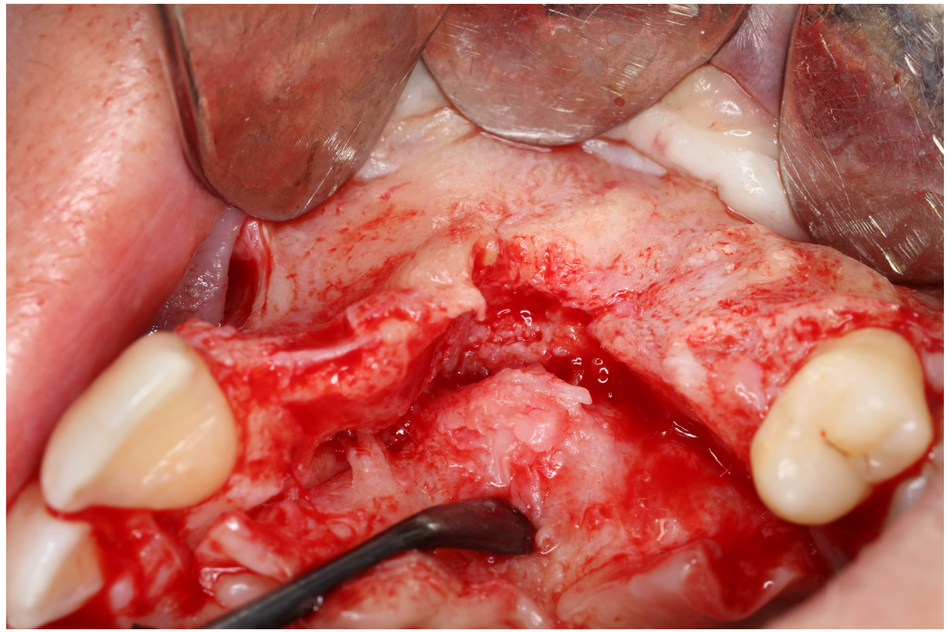

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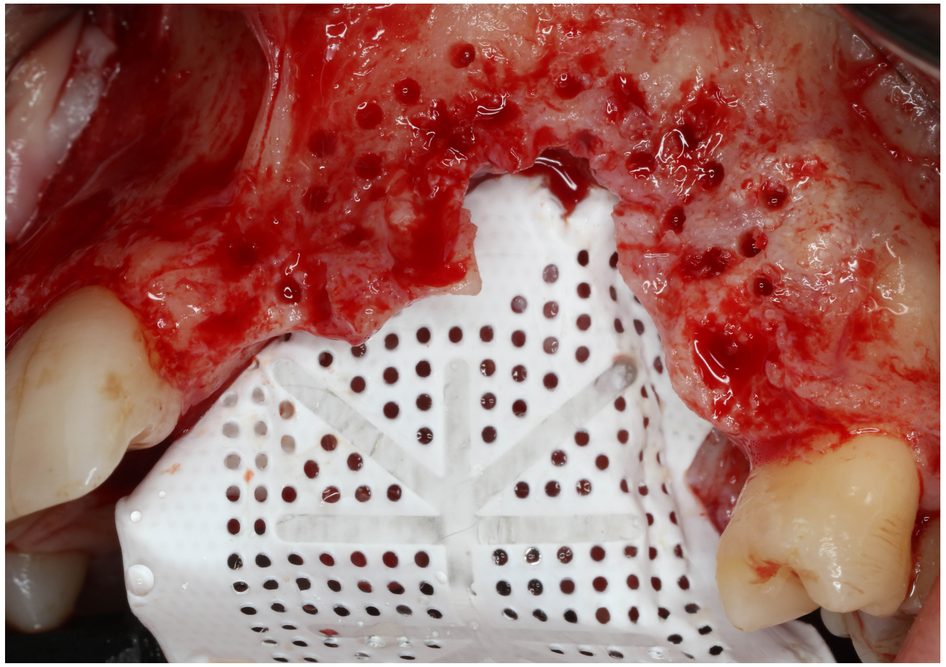

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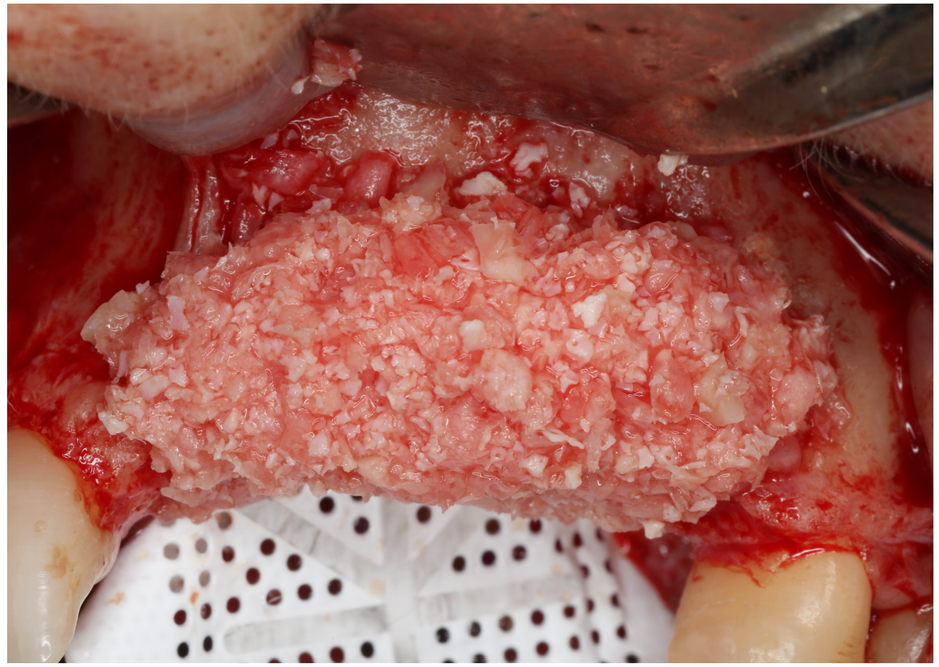

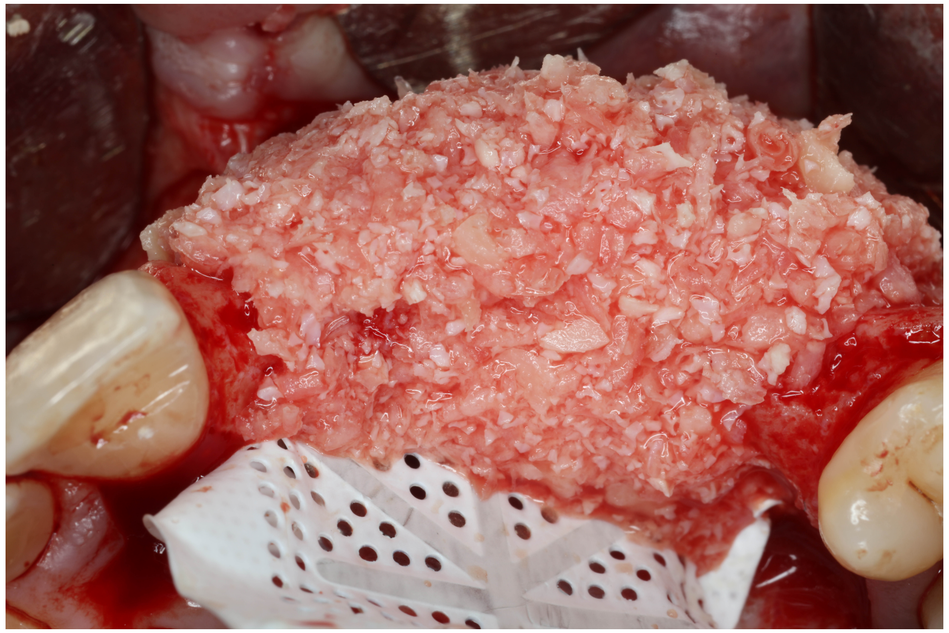

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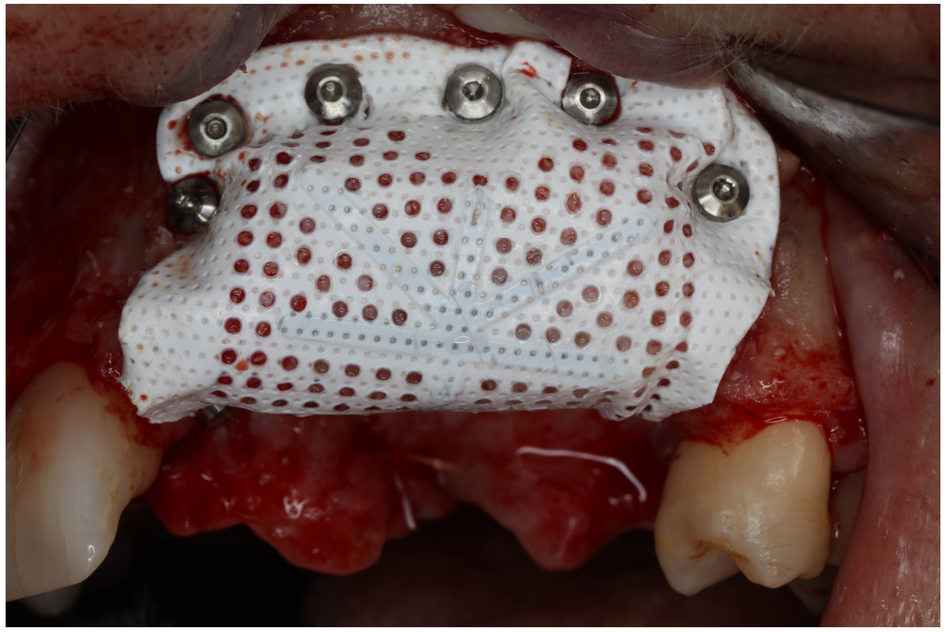

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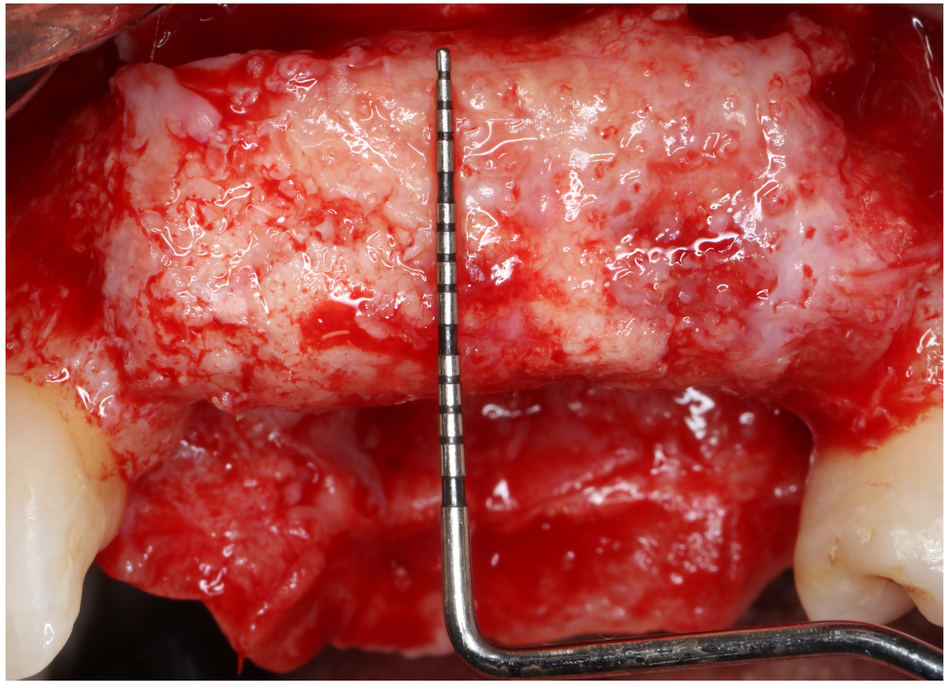

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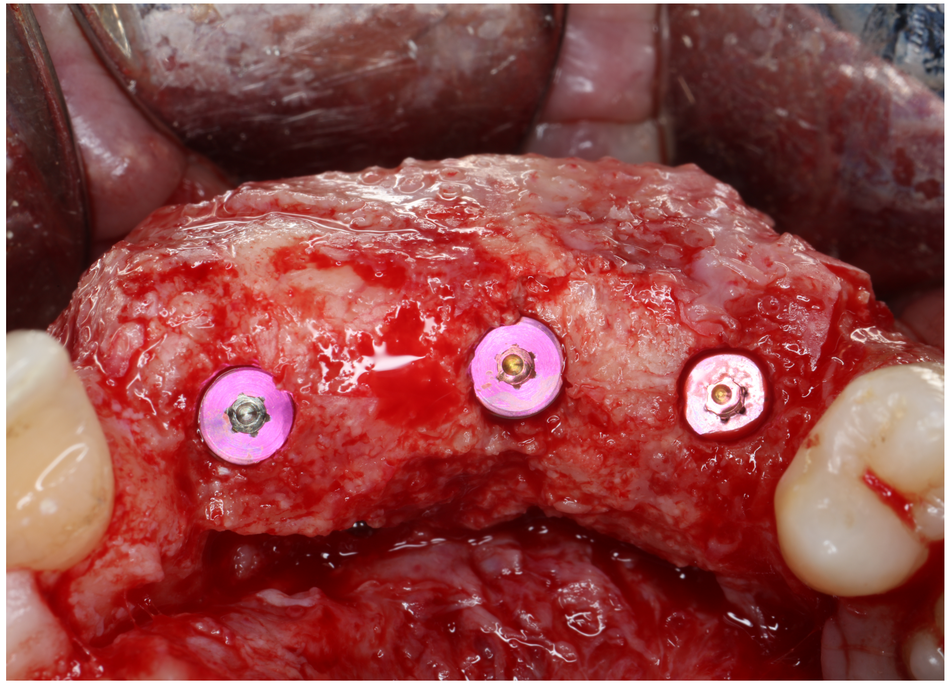

(H)

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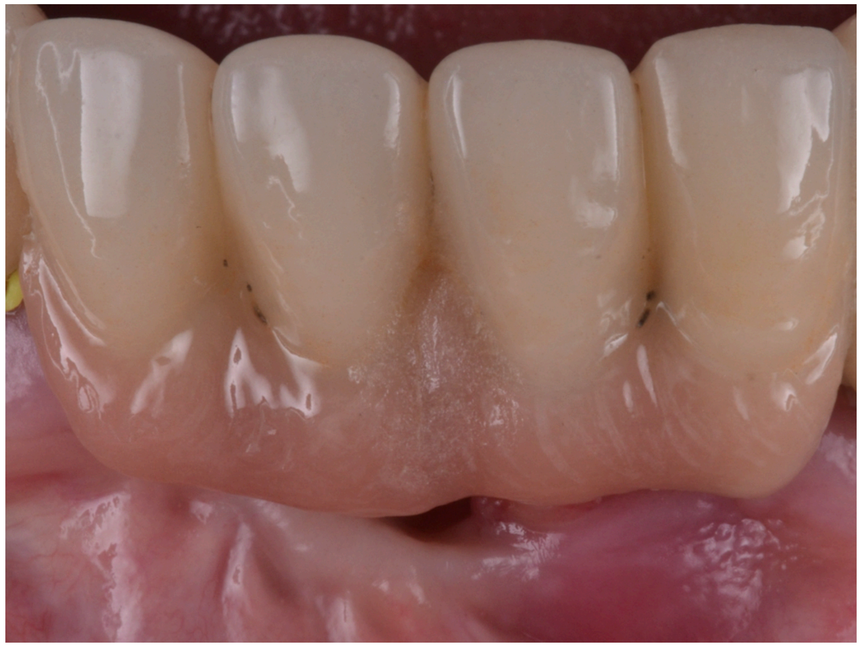

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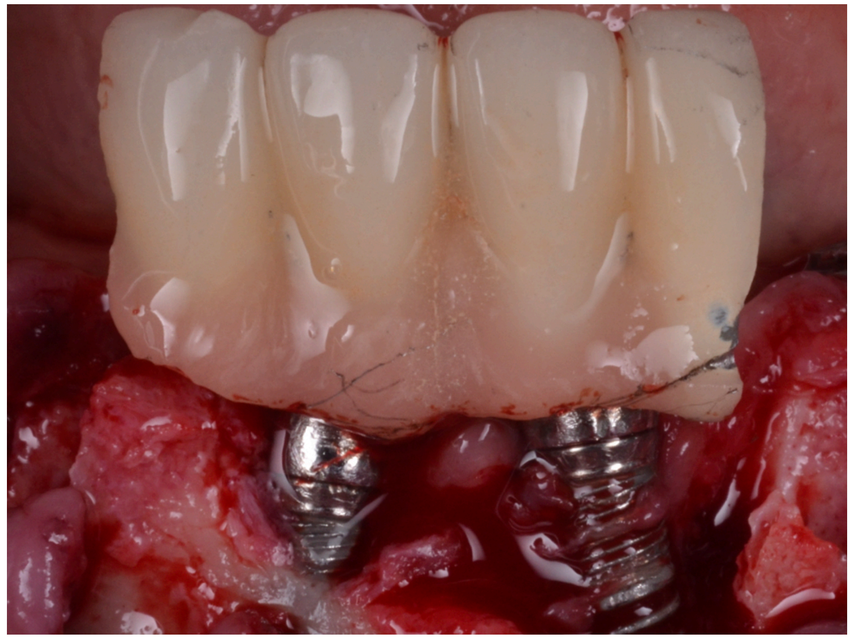

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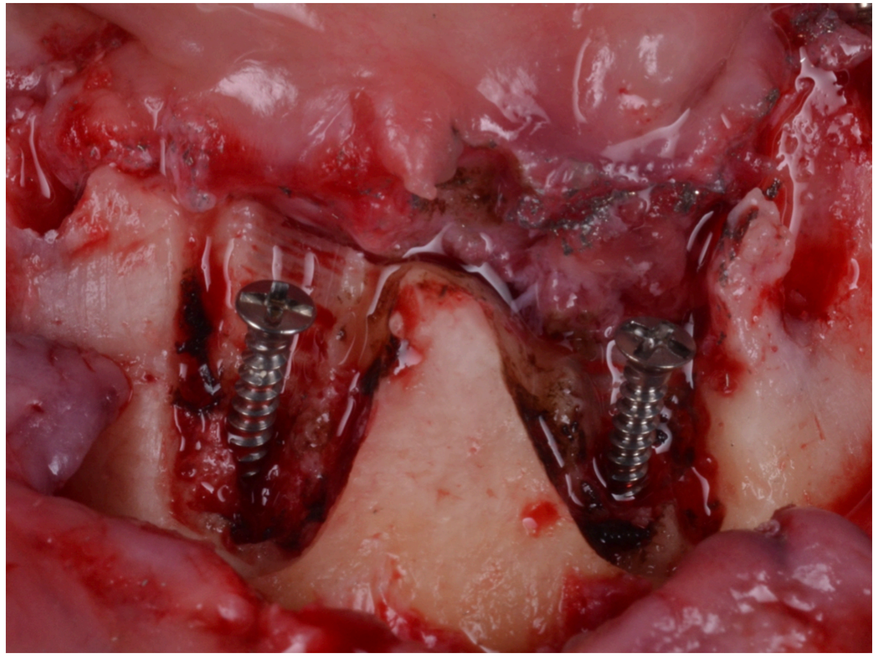

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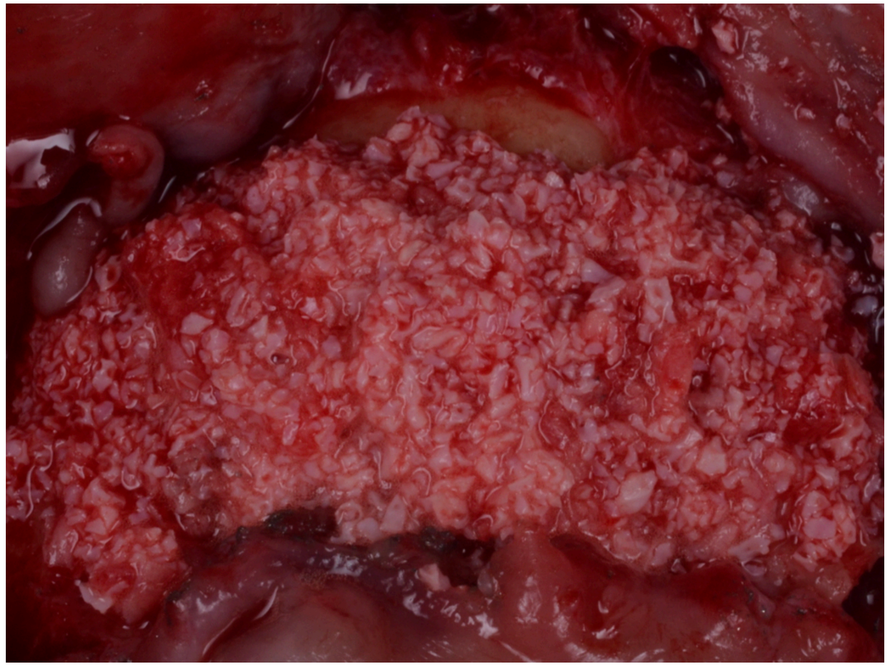

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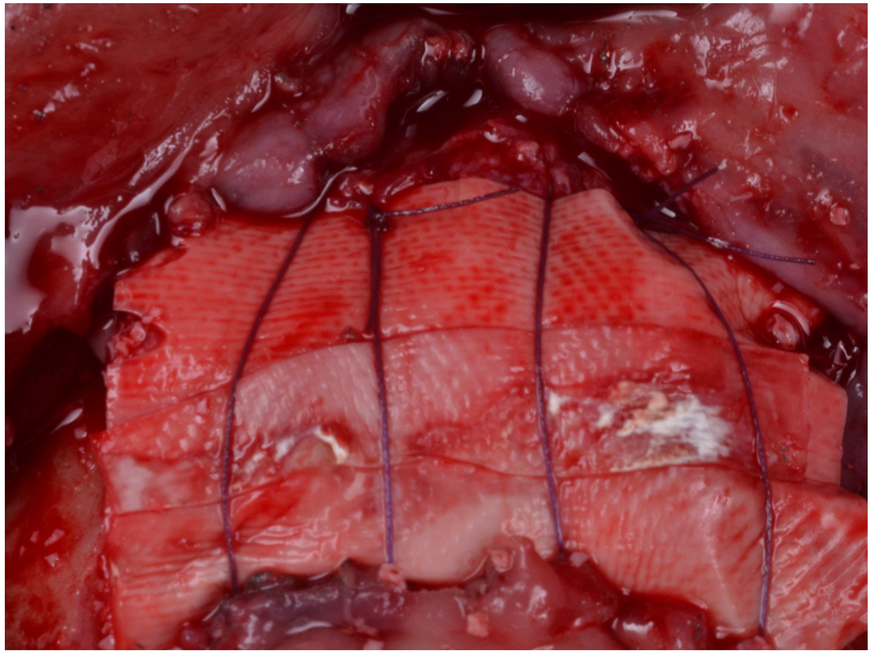

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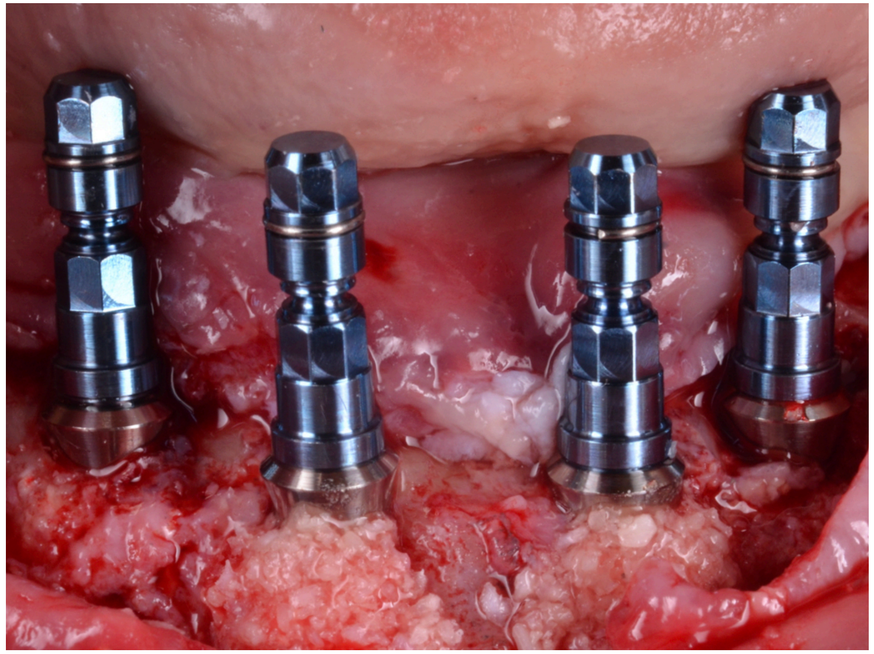

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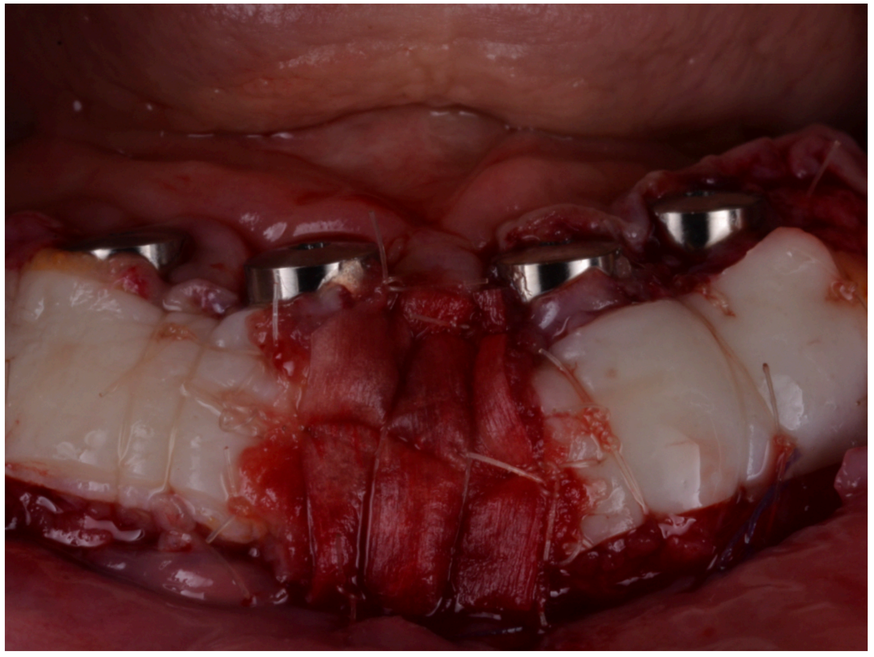

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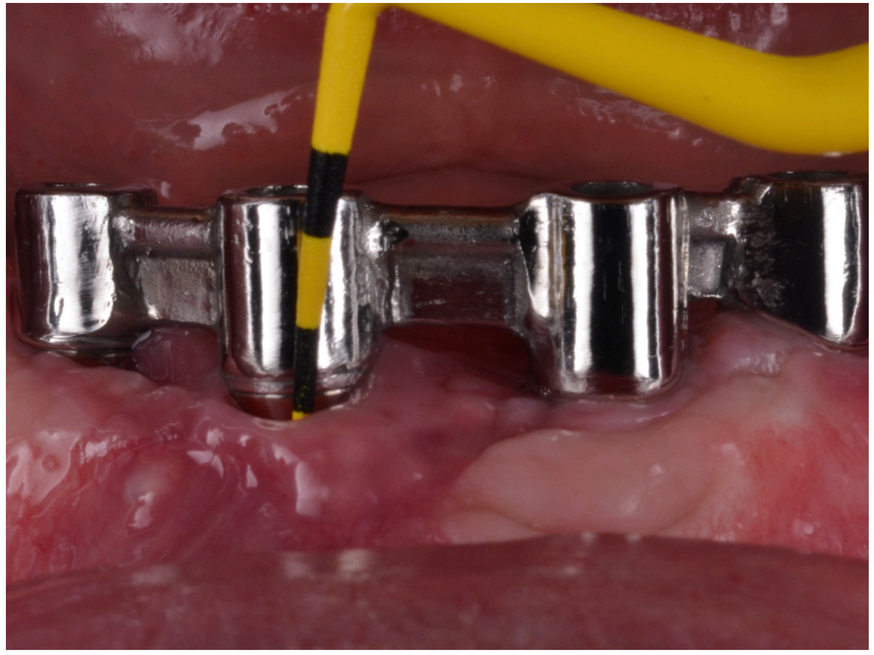

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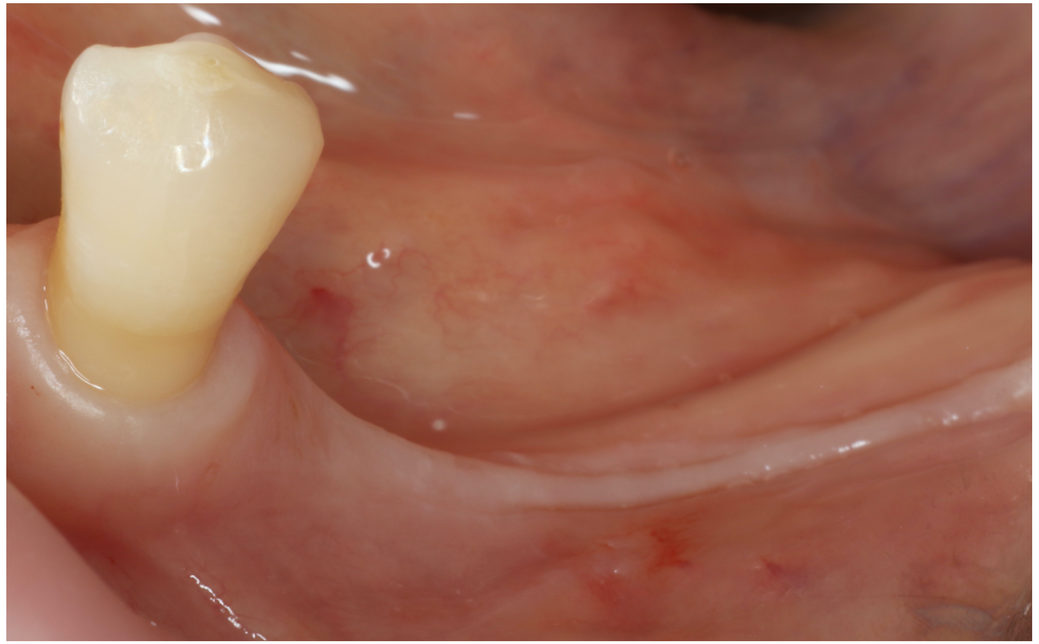

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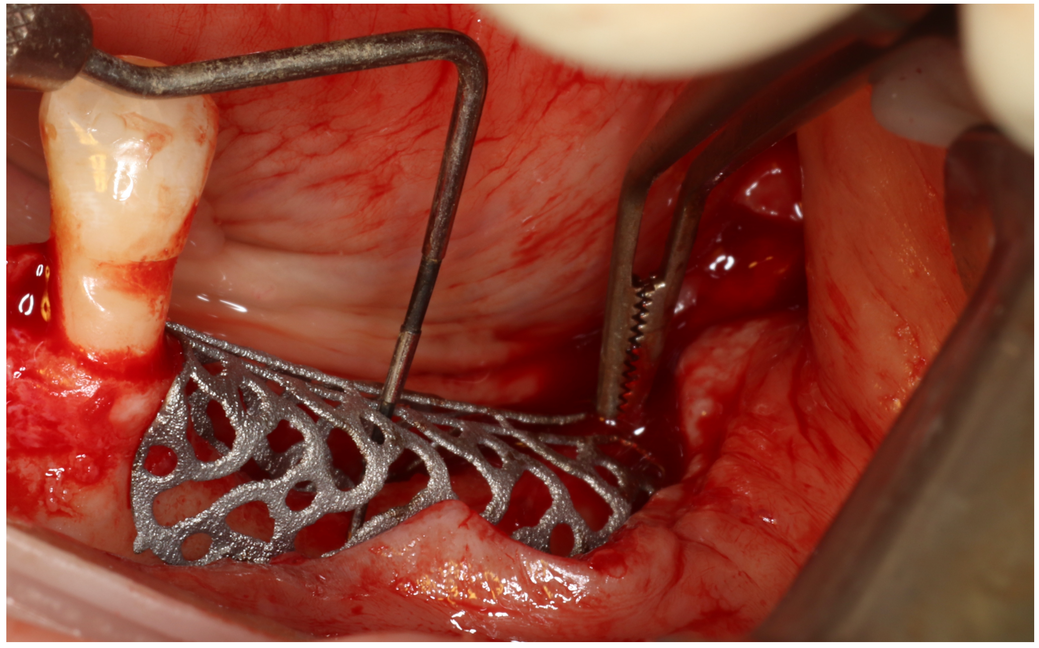

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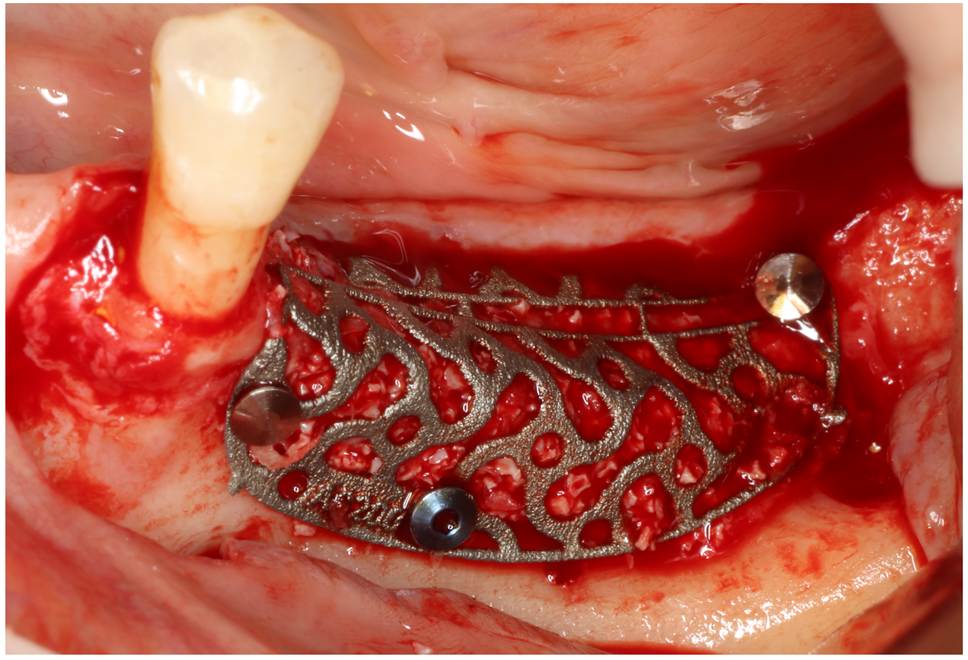

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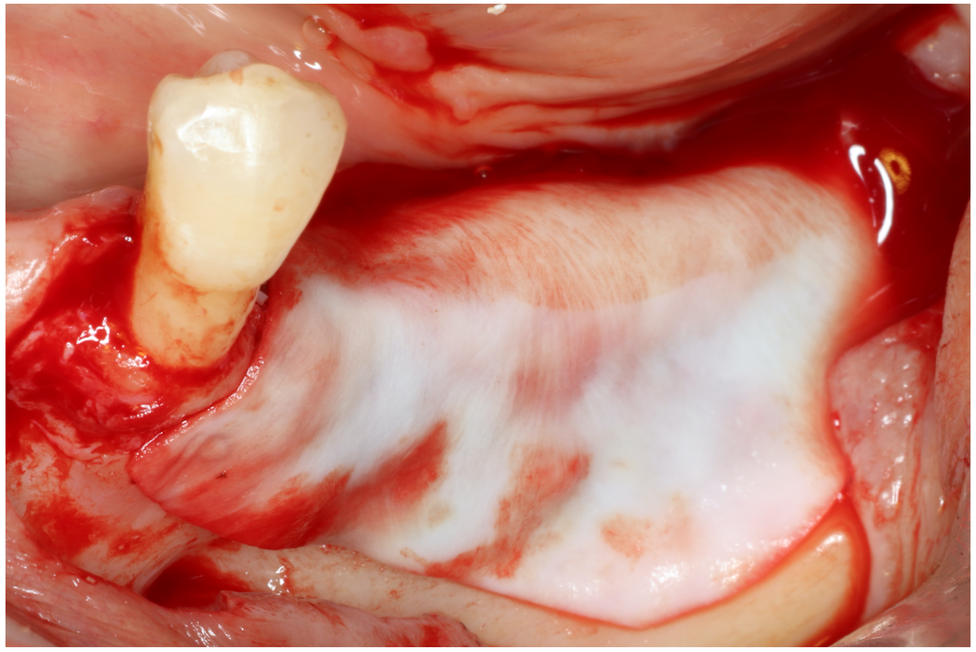

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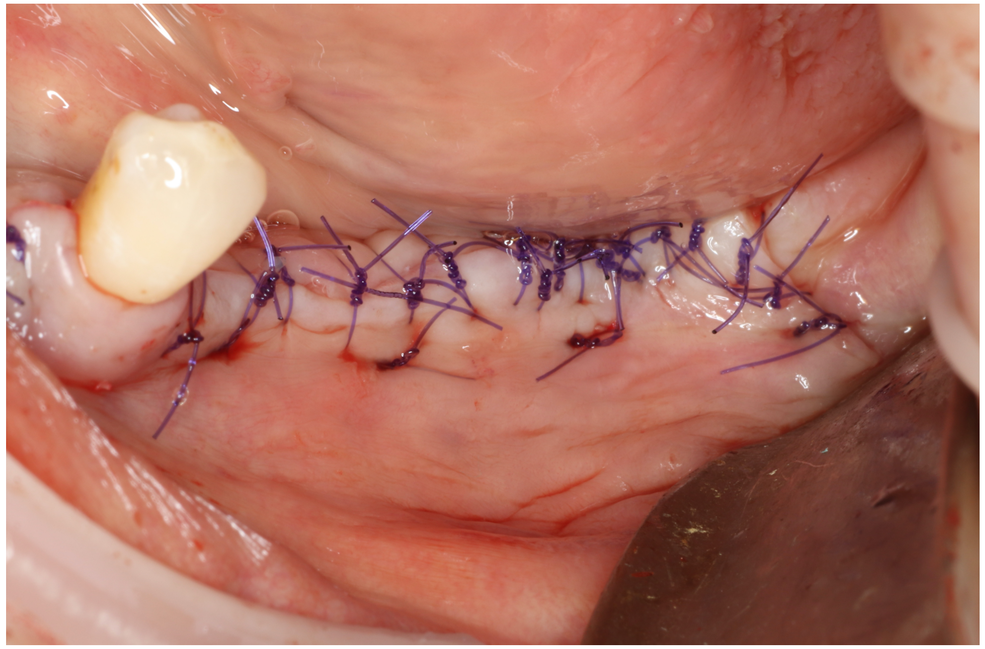

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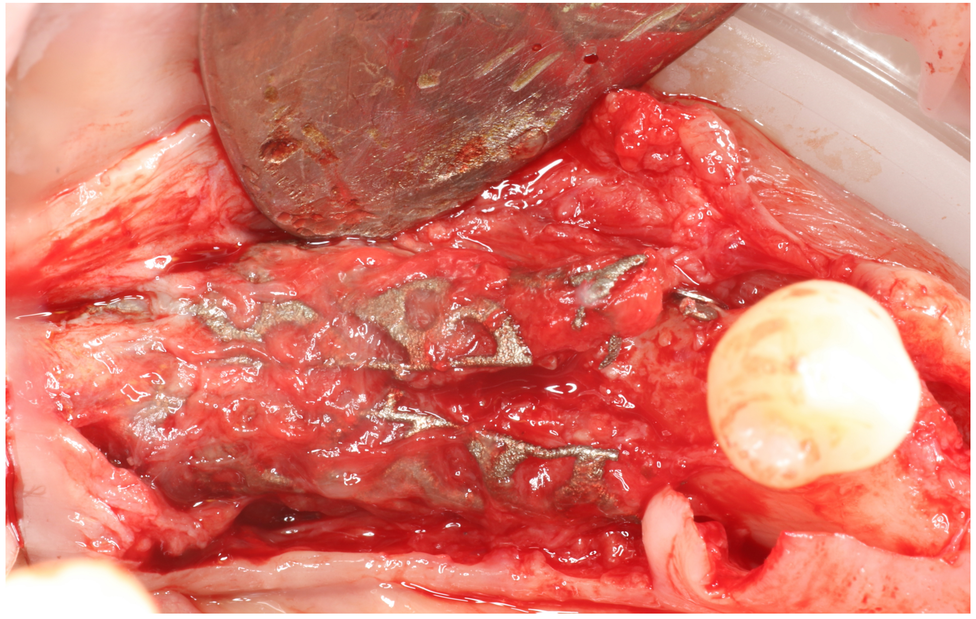

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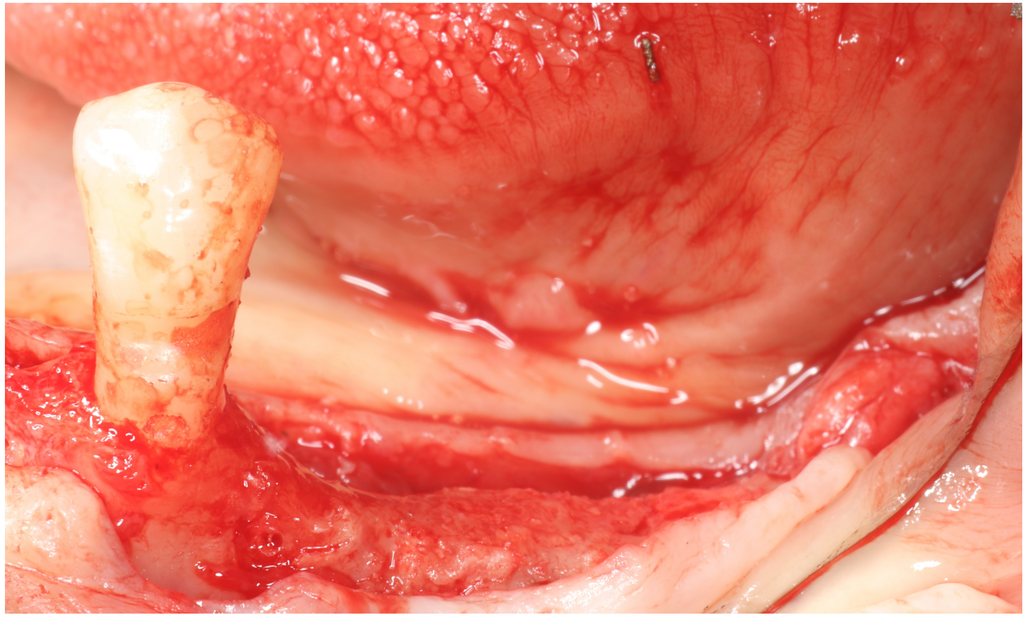

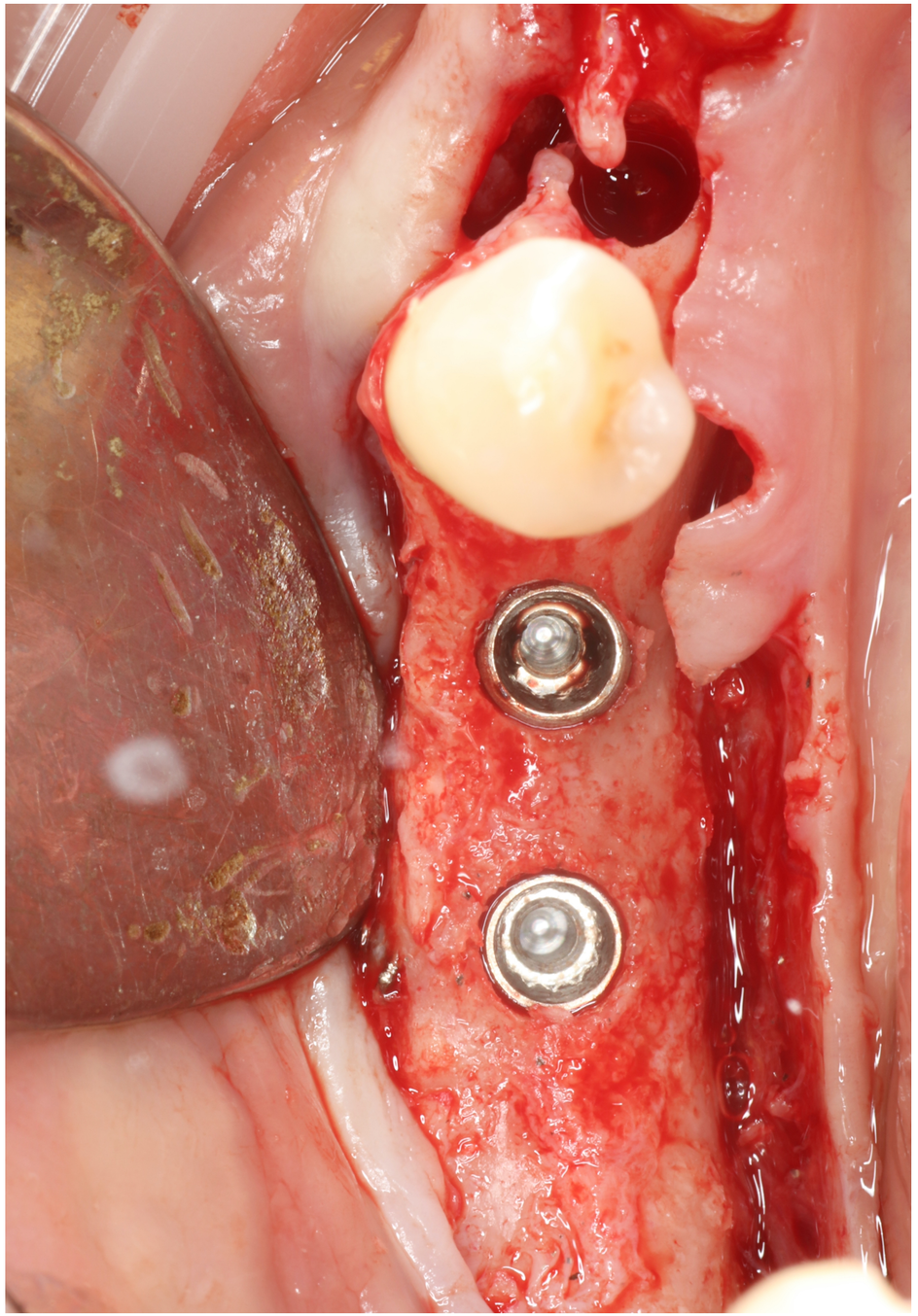

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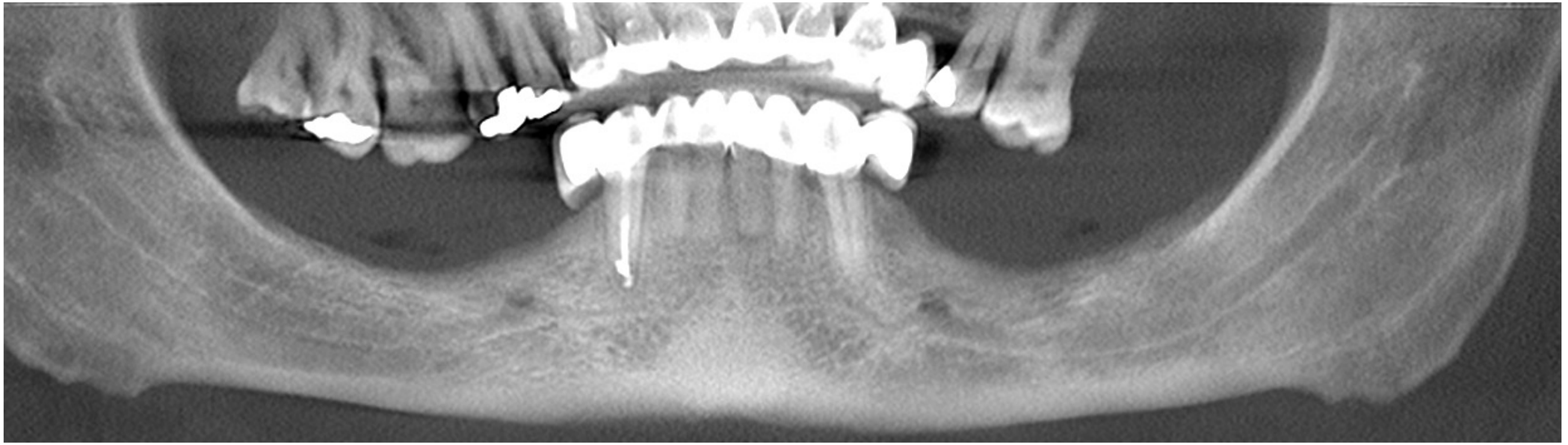

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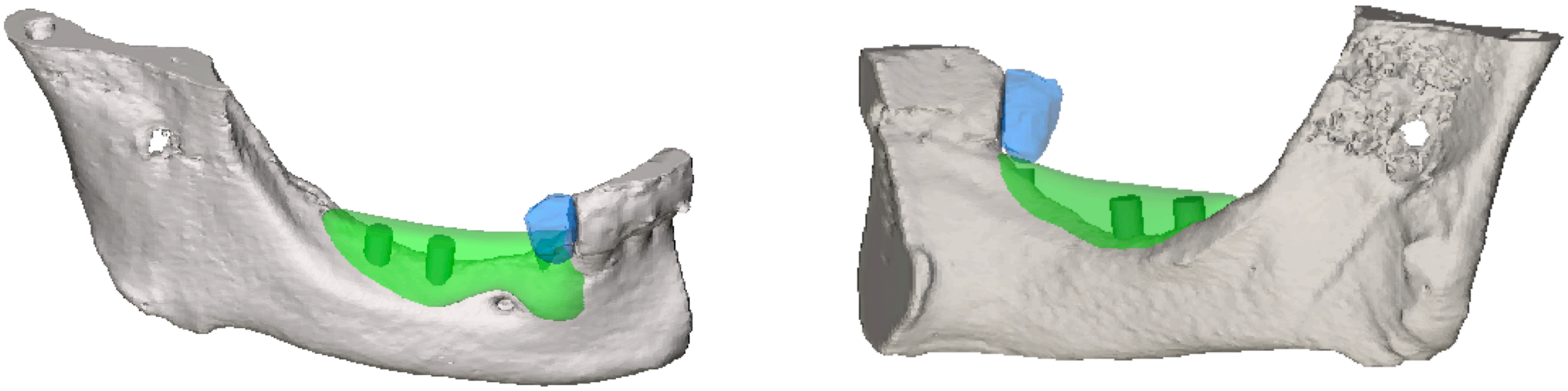

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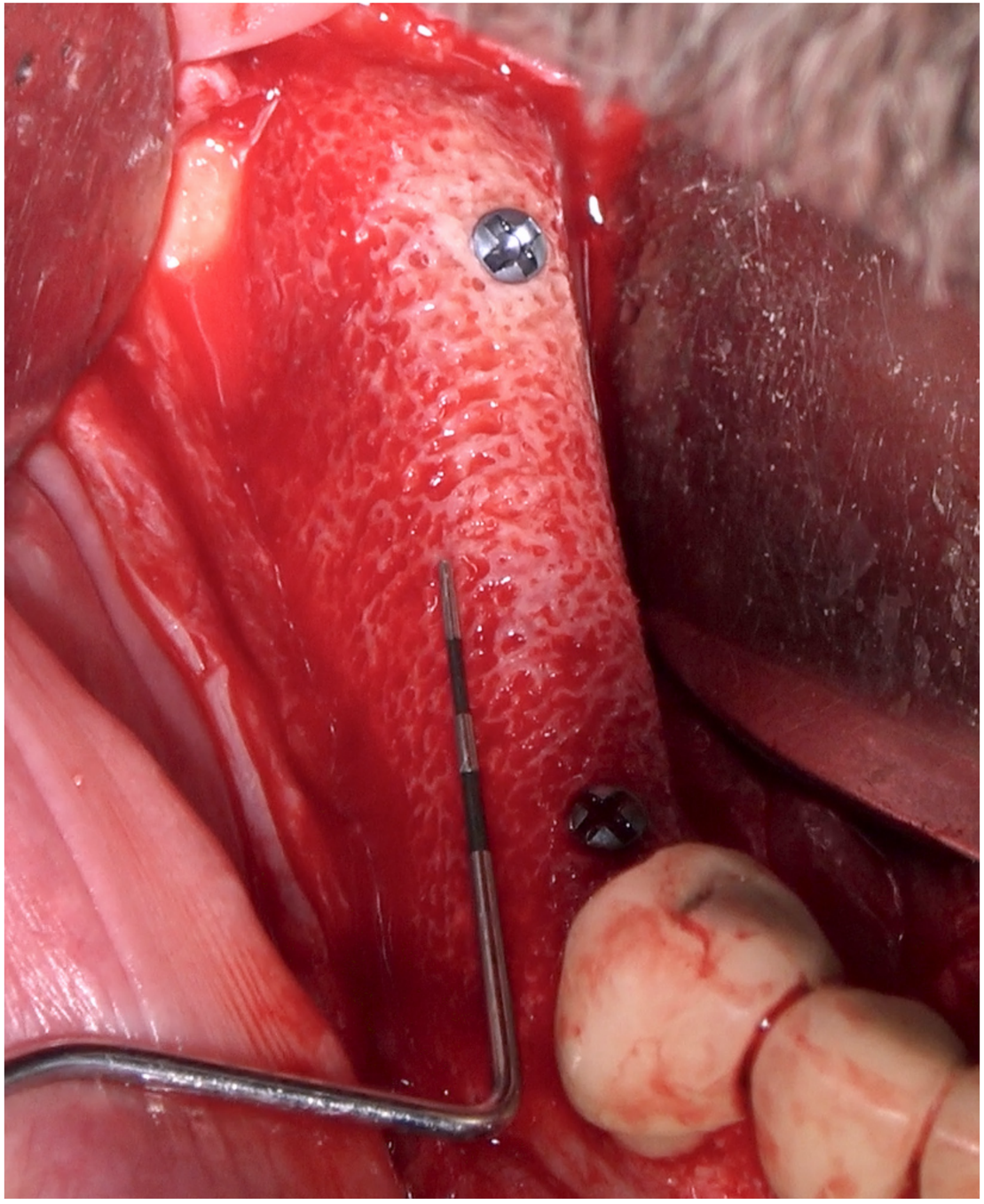

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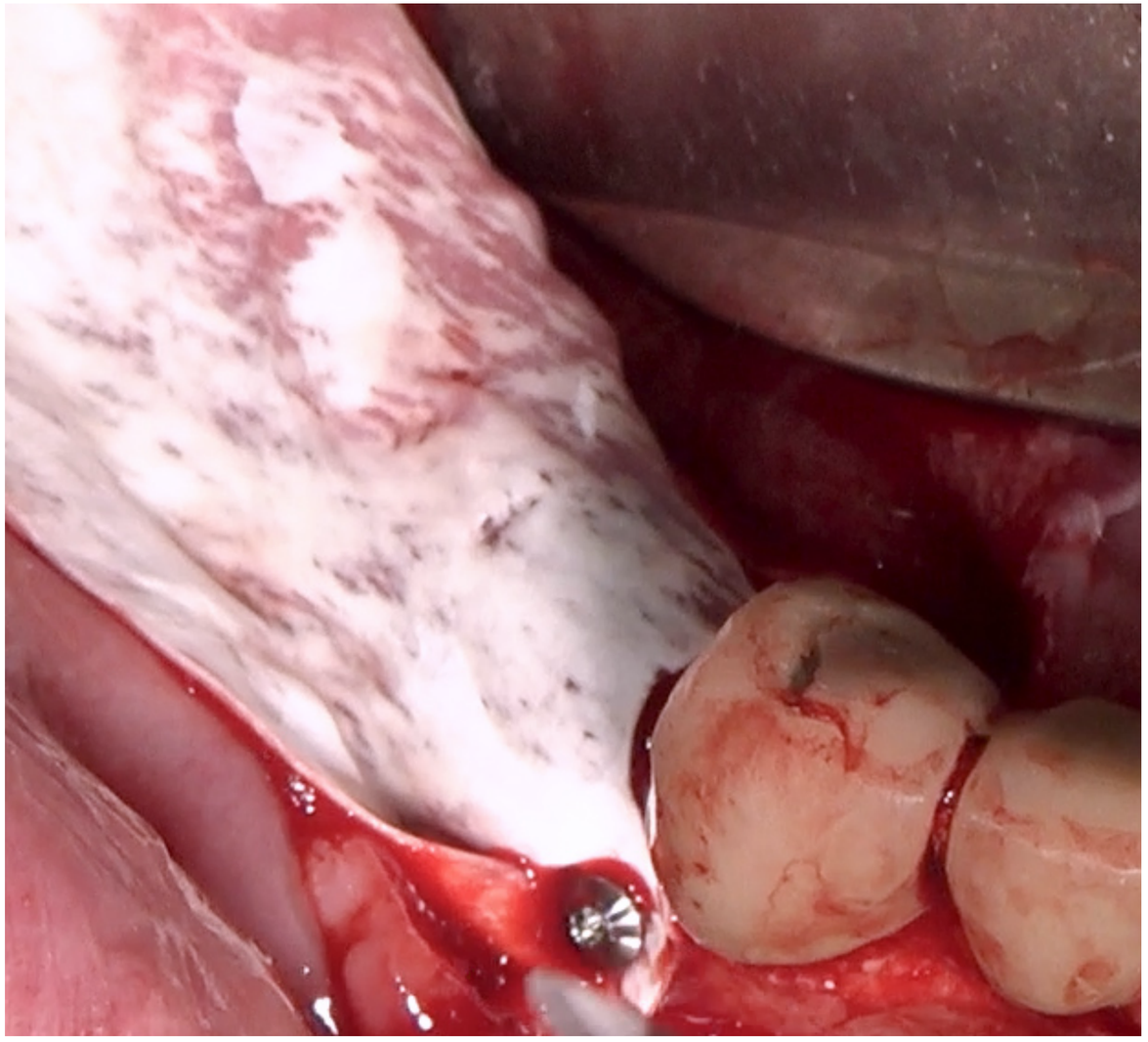

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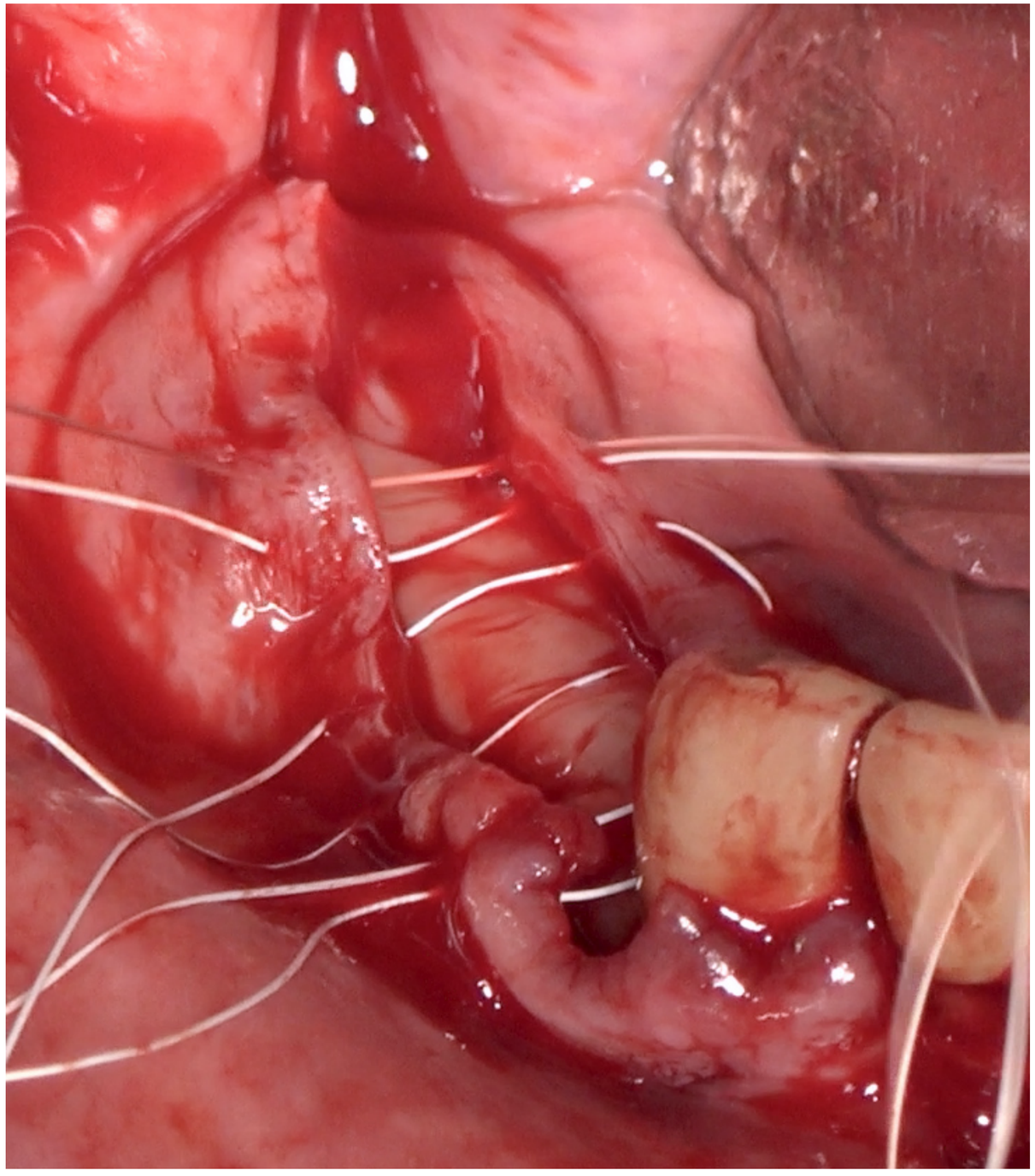

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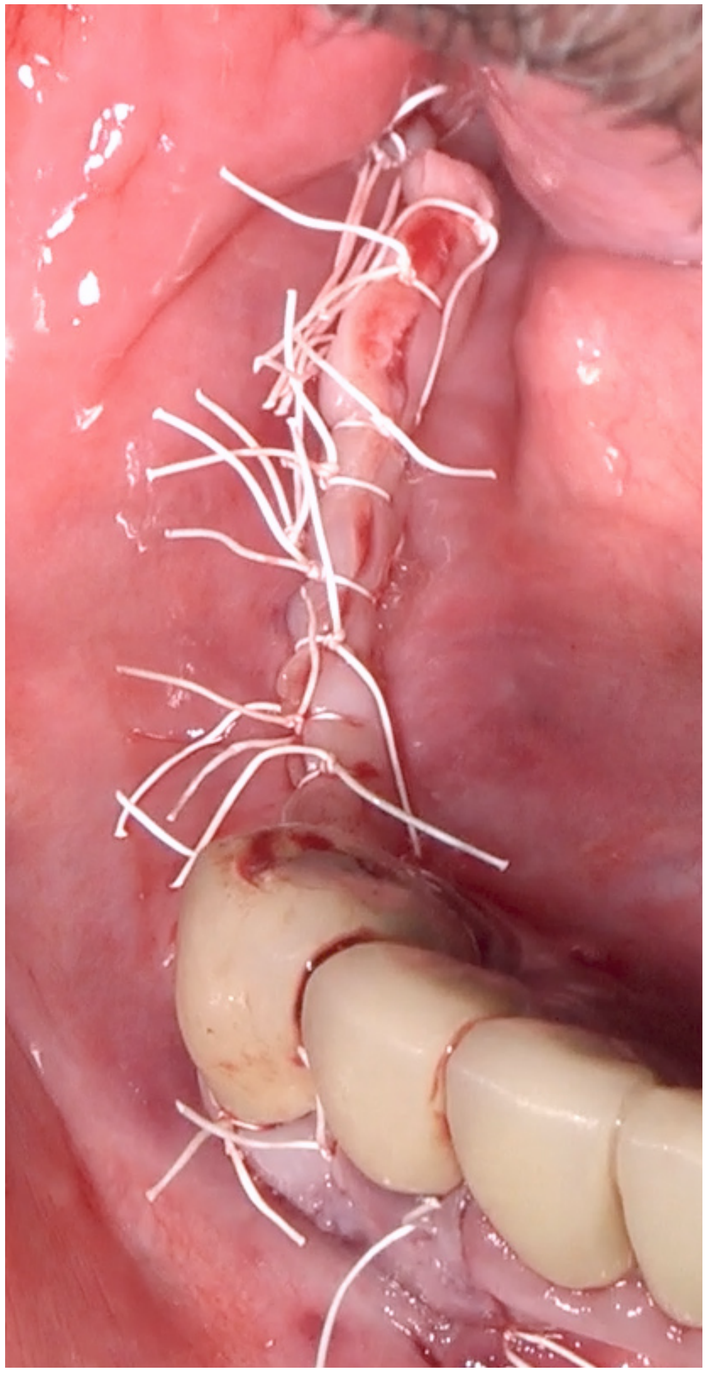

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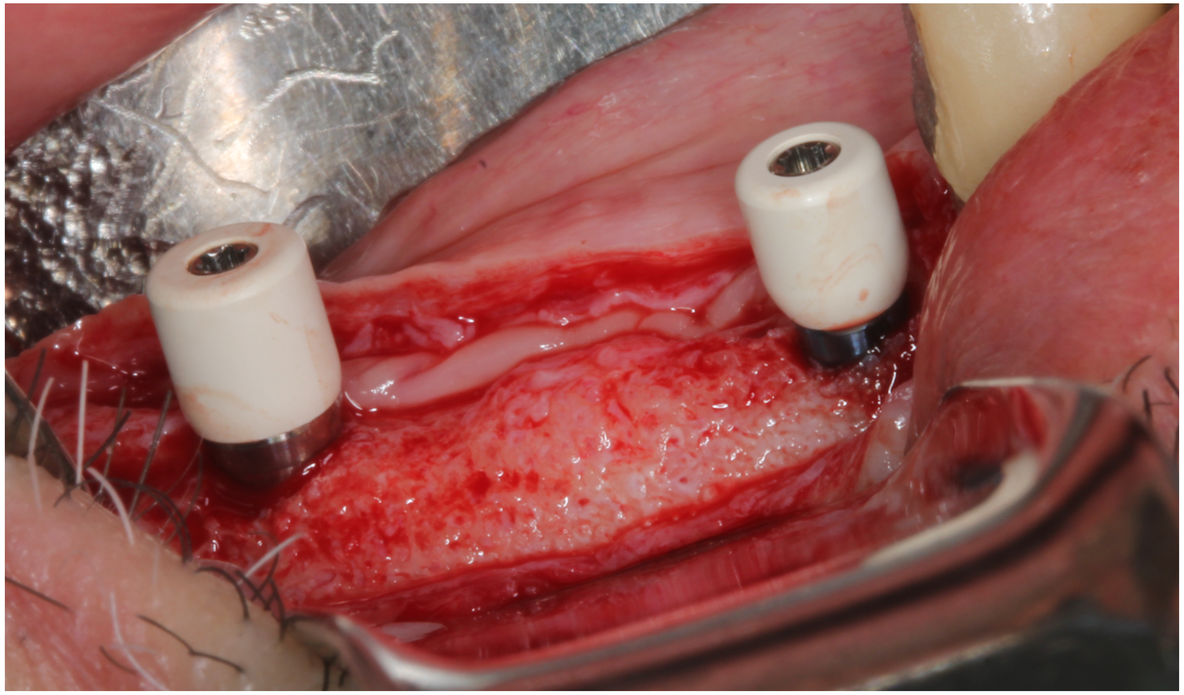

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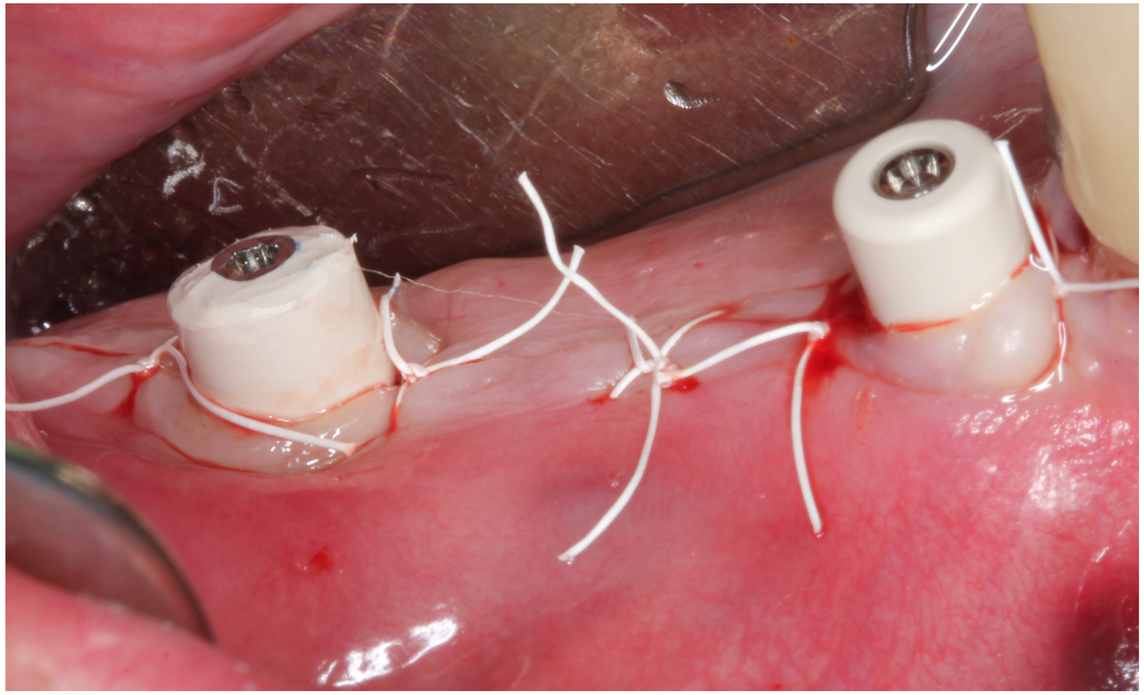

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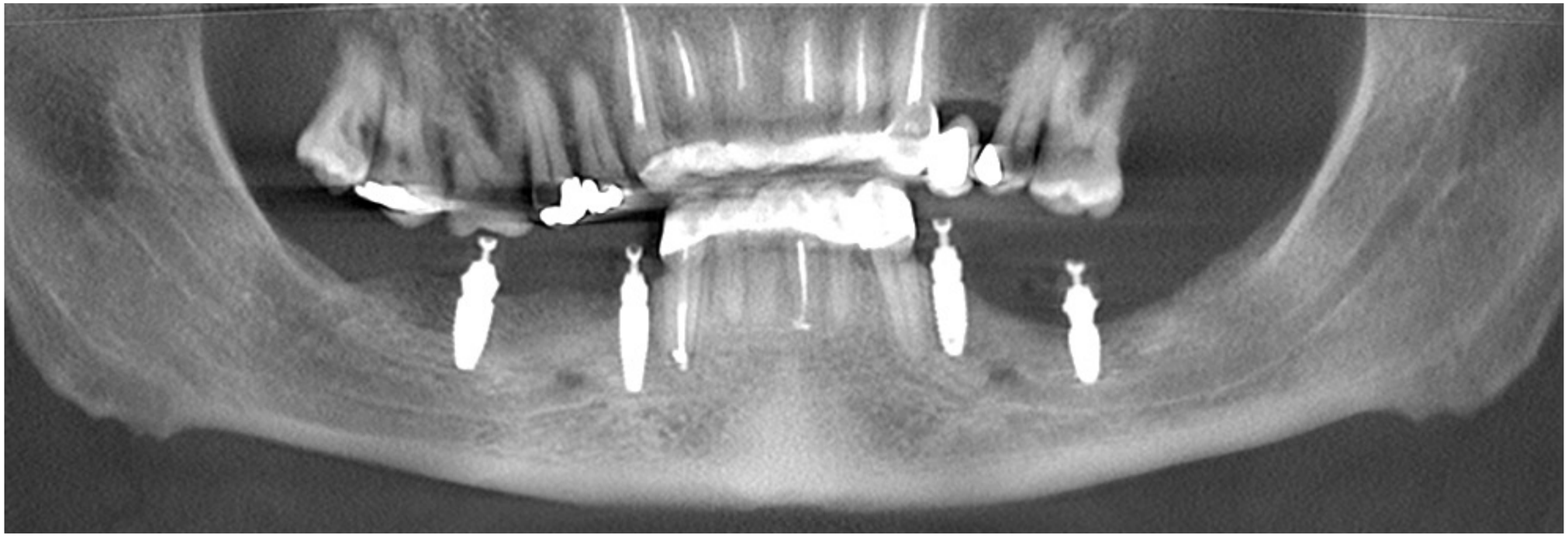

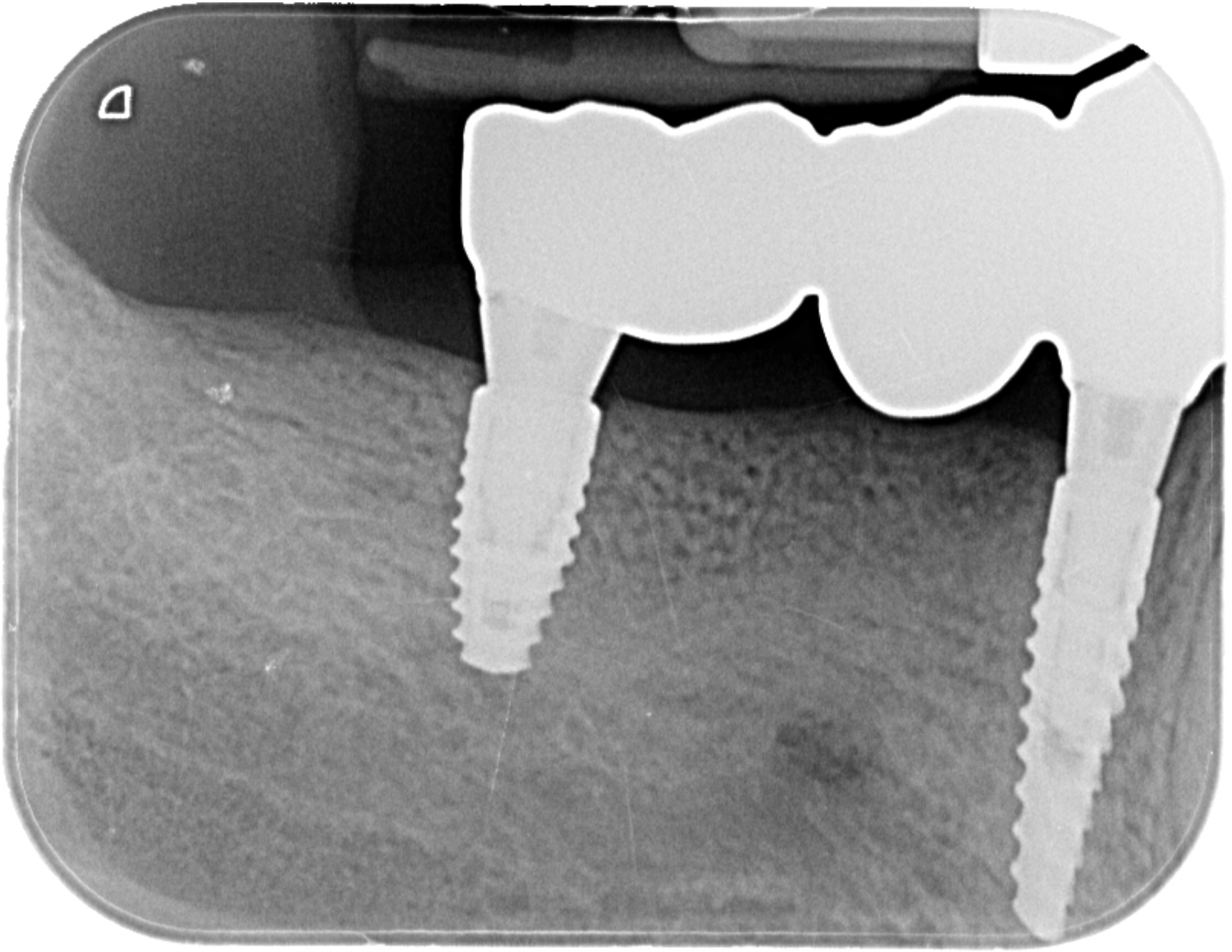

(J)

Representative case of a patient presenting an anterior maxillary vertical defect. Labial and occlusal views of an advanced vertical and horizontal defectb(A, B). Labial and occlusal views of a particulated bone graft immobilized with a perforated d-PTFE membrane. A 1:1 ratio of intraoral autogenous particulated bone graft mixed with a xenogenic bone graft (ABBM) was utilized (C-F). Labial and occlusal views of regenerated bone at membrane removal. Three implants were placed into the newly formed bone (G, H).

Vertical and horizontal ridge augmentation to handle the sequalae of peri-implantitis by means of guided bone regeneration via resorbable membrane. Patient presenting stage IV periodontitis and peri-implantitis in the anterior mandible (A). Note the severity of peri-implantitis (B). After implant removal with a trephine and reverse torque an alveolar ridge defect is identified that preclude oral rehabilitation with dental implants. Tenting screws were placed to support the long-lasting resorbable barrier membrane (C). A mixture of particulate autogenous bone harvested from the posterior mandible and anorganic bovine bone mineral together with a cross-linked collagen membrane was secured by means of a subperiosteal suture and used to fulfil the principle of compartmentalization (D, E). Four implants retain an overdenture were placed achieving adequate primary stability 5 months after guided bone regeneration (F). Two months later, free epithelialized mucosal grafts were placed at the buccal aspect at second-stage surgery (G). Peri-implant health and stability are noted at 12-month follow-up (H).

Figure legend

Representative case of the use of a customized Titanium mesh. Patient presenting a vertical bone deficiency in the posterior mandible. Buccal view of the posterior area of the third sextant in which the vertical ridge defect can be appreciated (A). Customized printed titanium mesh (B). Titanium mesh placed above the defect. A 5 mm vertical bone gain was planned (C). Titanium mesh fixed in its place using titanium pins. A mix of autologous particulated bone and xenograft was used to fill the mesh (D). A resorbable native collagen membrane was used to cover and protect the titanium mesh (E). Suture of the flaps using horizontal internal mattress sutures and single sutures (F). Re-entry at 8 months after the augmentation procedure. The titanium mesh can be broken at the middle portion to facilitate its removal (G). Buccal view of the posterior third sextant in which the vertical defect has been completely regenerated (H). Occlusal view of the ridge with 8 mm length implants inserted (I).

Figure.

Representative case of the use of a CAD-CAM (Computer-Aided Design; Computer-Aided Manufacturing) customized allogenic bone graft. Patient presenting bilateral vertical bone deficiencies in the posterior mandible (A). Computer-Aided Design of the allogenic bone blocks that will be placed in the affected areas (B). Intrasurgical view of the block in placed after its fixation and covering with a native collagen membrane (C, D). Suturing of the surgical area with a combination of internal matress sutures and single stitches (E, F). Implant placement in the ideal position 6 months later (G-I). Periapical radiograph after the placement of the implant supported restoration 5 months after implant placement (J). Case kindly provided by Dr. Juan Blanco (University of Santiago de Compostela, Spain).