Bone construction surgery. A case report using recombinant human Platelet Derived Growth Factor-BB.

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One-sentence summary describing key findings: rhPDGF-BB helped produce a viable functional matrix and successful reconstruction outcome in complex guided bone regeneration for the maxillary anterior region.

Abstract

Background: The position and condition of bone largely sets the stage for functional and esthetic implant success. In bone construction surgery, creating a sustainable functional matrix is complex, but necessary, to enable long-term mechanotransduction and maintenance of soft tissue support.

Methods: A patient with a severe peri-implantitis ridge defect in the anterior maxilla underwent bone construction surgery simultaneous with implant removal using a composite bone graft (mineralized freeze dried bone allograft + xenograft) enhanced with recombinant human platelet derived growth factor (rhPDGF-BB). Space maintenance for bone construct immobility and unimpeded wound healing was ensured via a non-resorbable titanium reinforced polytetrafluourene (PTFE) membrane and an absorbable porcine collagen membrane in the surgical management of a patient with severe peri-implantitis requiring bone construction.

Results: Primary closure was maintained throughout the 6 month healing process at which time implant diagnostics commenced for prosthetically directed implant placement using dynamic navigation and involving soft tissue augmentation. Uncovery was performed 3 months thereafter leading to provisionalization and prosthetic phase completion.

Conclusion: This case report highlights a severe maxillary anterior ridge defect secondary to advanced peri-implantitis in a systemically healthy Caucasian male patient. The surgical outcome success, both clinically and radiographically, underscores the complexities of complete regional anatomy rehabilitation after suffering catastrophic and debilitating loss from inflammatory peri-

implantitis. Further, it demonstrates the importance of incorporating optimized angiogenetic therapeutics to help establish a vascularized functional bone matrix for implant success.

Key words: Peri-implantitis, Alveolar ridge augmentation, biological products, dental implants

Introduction

Peri-implantitis is an inflammatory condition which often causes rapid, catastrophic and, in many cases, irrecoverable bone loss. [1] Its early recognition is key to offset more severe disease and consequences.[1] However, unrecognized and unintended iatrogenic clinical events (ie. too buccal implant placement, cement sepsis, or other technical surgical mistakes) often increase the risk for downstream problems.[2-3] Two foundational keys that influence implant esthetics and long-term function are the (1) volume and (2) quality of bone anatomy for which the implant is expected to survive in. In this context, marrow quality and vascular potential are paramount.[4]

The position and condition of bone largely sets the stage for functional and esthetic implant success.[4] In bone construction surgery, creating a sustainable functional matrix is complex and requires a vascularized construct to be capable of long-term mechanotransduction.[5,6] Angiogenesis derived from the periosteum or marrow is key for successful bone matrix construction and in the ability to deliver a long-term homeostatic balance of coupled osteoblastogenesis and osteoclastogenesis.[7] Factors that can help upregulate angiogenesis during wound healing would be invaluable towards improving predictable outcomes, especially in a regional anatomy environment that has been ravaged from inflammatory diseases affecting bone and connective tissue such as advanced stage peri-implantitis.

Recombinant human platelet derived growth factor (rhPDGF-BB) is a mitogen that has been shown to upregulate angiogenesis as well as promote guided tissue regeneration efforts in conditions where periodontal anatomy has been impacted by inflammatory disease, guided bone regeneration efforts (for optimizing bone fill in buccal wall defects), and in rehabilitating larger

horizontal ridge defects.[8,9,10] rhPDGF-BB is a key growth factor derived from human platelets following tissue injury.[11] Its fundamental action is mitogenesis and chemotaxis for cells of mesenchymal origin.[11] Its effects could provide distinct benefits in advanced reconstruction surgery by helping recruit key cells and encourage a more profound response to wound healing events, namely vascular ingrowth.

Materials and Methods

A 44-year-old systemically healthy Caucasian male presented to our clinic for management of advanced peri-implantitis. His past dental history was significant for trauma resulting in eventual loss of #8 and subsequent dental implant placement in 2006. The patient acknowledged persistent redness and bleeding since the delivery of the dental implant prosthesis which was cement retained. At our initial consultation (January 2018), probing depth range was 7-9mm with notable bleeding on probing and tissue distention as well as severe bone loss radiographically (Figures 1 and 2). A treatment plan was developed to provide guided bone regeneration and construct the regional anatomy at #8 simultaneous with implant removal while maintaining the patient in a fixed, bonded interim tooth replacement on adjacent natural teeth.

The patient premedicated with 2.0g amoxicillin 1 hour prior to surgery. Surgical treatment commenced following moderate intravenous conscious sedation consisting of 5mg midazolam, 40mg fentanyl, 4mg dexamethasone and 30mg ketoralac. Profound local anesthesia to the maxilla was provided via infiltration using 2% lidocaine with 1:100,000 epinephrine. Initial incisions were made sulcularly from #5-11 with vertical releases at #5MF and #11MF followed by full thickness flap reflection to expose the underlying regional anatomy. (Figure 3) The implant was observed to be placed shallow and was subsequently restored with an over-contoured ceramic restoration. No cement sepsis was found during surgery. The extent of peri-implant bone loss was severe and caused near complete buccal and palatal bone loss surrounding the implant. The regenerative potential for re-establishing bone integration to the exposed implant threads was determined to be

poor and the implant was subsequently explanted using forceps. The residual peri-implant defect was classified as an International Team for Implantology Classification 4/4 residual ridge site.[12] (Figure 4) Favorably, the alveolar bone observed on the adjacent natural teeth were not compromised by the disease affecting the implant at #8.

Following thorough degranulation, cortical perforations were made in the residual maxillary base to stimulate angiogenesis from the marrow. A titanium reinforced polytetrafluourene (PTFE) membrane** was trimmed and stabilized deep on the palatal aspect of #8 allowing the composite bone graft to be condensed until an ideal geometric form of the desired ridge morphology was achieved. (Figure 5) The construct was a composite bone graft consisting of 50% mineralized freeze dried bone allograft[§] and 50% anorganic bovine bone[‖] hydrated for > 10 minutes in rhPDGF-BB.[¶] The PTFE membrane was then rotated to the buccal, extending apically beyond the extent of the defect as well as laterally by one tooth. The membrane was stabilized on the lateral buccal margins using an additional 2 bone tacks.[#] Immobility of the bone graft was ensured as was its position so as not to encroach on the on either neighboring tooth. (Figures 6a and 6b). Next, an absorbable porcine collagen membrane[††] was placed over the PTFE membrane (Figure 7) and the flap was released through blunt dissection to ensure tension free primary wound closure using multiple figure “o” and vertical mattress design sutures via 4-o and 5-o PTFE. (Figure 8). Lastly, a post-operative radiograph was secured at the end of surgery. (Figure 9) Post-operative instructions were reviewed verbally with the patient pre-surgery and with the patient’s escort post-surgery as well as provided in writing. Post-operative antibiotics consisted of Amoxicillin 500mg q8h x 10 days, bimodal dosing of Ibuprofen 600mg + acetaminophen 650mg q6h prn and bid rinsing of 0.12% chlorhexidine digluconate. Post-operative follow-up occurred at 2 weeks, 4 weeks, 2 months, 4 months and 6 months at which time implant diagnostics began for guided implant placement. Sutures were removed at 4 weeks. Throughout the duration of healing, the patient reported minimal discomfort and no complications.

Results

Healing was uneventful and primary wound healing ensued throughout the entire post guided bone regeneration (GBR) surgery healing phase. (Figure 10) At 6 months, implant diagnostics was pursed and included cone beam computed tomography (CBCT) imaging of the maxillofacial complex as well as digital impressions.[₹ ₹] The CBCT field of view was approximately 10x10cm at 0.15 mm voxel size and the exposure factor settings were fixed at 120 kvp, 6.6 mAs and 20 seconds of acquisition time. A digital diagnostic wax up was performed (Carestream 3600 intraoral scanner) for prosthetically directed guided implant surgery using a dynamic navigation approach.[₺] (Figure 11) Implant surgery was performed under intravenous conscious sedation with infiltration local anesthesia. Flap reflection allowed removal of the titanium reinforced PTFE membrane revealing outstanding three dimensional bone gain. (Figure 12) The bone reconstruction was well consolidated and unionized. During osteotomy site preparation, the bone was notably vascularized with excellent bleeding. Implant placement was stable and firm. Insertion torque value was 20N/cm. A tapered 4 x 10mm implant fixture was placed in a two stage fashion.[₳] (Figures 13a and 13b) To optimize soft tissue dimensions, an autogenous rotated palatal pedicle connective tissue graft was placed and the field sutured for primary wound closure. (Figures 14 and 15). A post-operative radiograph was secured to confirm implant positioning two dimensionally. (Figure 16). The fixation tack placed at the GBR surgery on the palatal apical aspect was left to sleep as its was covered with osseous tissue and its existence did not influence implant placement. Uncovery/stage II implant surgery was performed at 3 months at which time a healing abutment was placed. (Figure 17) At this time, clinical and radiographic parameters confirmed that the implant fixture was ready for occlusal loading and provisionalization.

Discussion

Bone is the foundation of the face, the periodontium, and the smile.[13] While many factors participate in an implant outcome, optimal four dimension considerations of bone (height, width, volume and marrow quality) influence esthetics and function.[4] This case demonstrates a severe ridge defect secondary from inflammatory peri-implantitis and the construction of regional anatomy through advanced GBR surgery.

Embryologically, it is widely accepted that for the craniofacial skeleton to develop properly, the four "Harvold's principles" must be adhered to.[14] These principles include: a stabilized environment, a source of cells, a source of neuromuscular input, and an absence of pathology. Similarly, in bone construction efforts during GBR therapy for future implant site development purposes, the "PASS" principles (primary wound closure, angiogenesis, space maintenance, and wound stability) become paramount to follow for predictable results.[15]

Of all 4 wound healing tenants required for proper embryologic development or predictable bone regeneration purposes, the one that has the least technical control by the surgeon and is almost exclusively dependent upon the patient response is angiogenesis. Upregulating the angiogenic process to the bone construct is desirable to help ensure a vascularized network for which mesenchymal stems cells can infiltrate and convert an inert composite bone graft to one that is a functional matrix whereby coupled osteoclastogenesis and osteoblastogenesis is ensured. In designing and developing a sustainable functional matrix capable of long-term mechanotransduction, a novel fiber network system has been discovered and may be an under-appreciated or under-recognized factor for successful bone augmentation results.[16,17] The periosteal-sharpey fiber-endosteum (PSE) structural continuum has been described and may serve as a novel bone matrix regulatory system that influences regeneration. In our case presented here, the neighboring teeth were not affected by the inflammatory peri-implant disease and had an intact periodontal ligament apparatus that may have helped influence the outcome to a degree that cannot be objectively quantified or scientifically proven at this time, only theorized biologically.

What is known is that bone is a complex organ system that is regulated by an intricate and dynamic relationship of muscles-nerves-bone.[18, 19] The PSE structural continuum concepts propose a novel sensory regulatory system within the bone matrix that is important for bone maintenance, of which the periodontal ligament of neighboring teeth could play a role in the results gained here, especially the gain noted on the adjacent lateral incisor.[17] These concepts submit that bone construction surgery may be influenced and regulated, in part, by signals within the central nervous system of which the periodontal ligament is apart of. This, in addition to any mitogenic upregulation via neovascularization to the bone construct used for guided bone regeneration surgery using growth factors such as rhPDGF-BB, would seem prudent to help optimize wound healing dynamics in complex and demanding reconstruction surgery.

This case demonstrates the essential need to follow proper case selection and adherence to key surgical principles which are bedrock doctrines of predictable bone development- both from an embryologic and future implant site development standpoint.[5,6 14,15] The use of rhPDGF-BB may help further enhance wound healing predictability in the one aspect with which any surgeon has the least control, the patient-dependent response of angiogenesis infiltration and targeted chemotaxis-mitogenesis of mesenchymal cells into the bone construct. Unfortunately for implant reconstruction efforts, once the bone regeneration has been successful, the story is not over. Accurate and precise implant placement that follows a prosthetically directed template is critical to negate operator-induced errors that could trigger unwanted future peri-implant disease conditions.[2, 3] Guided surgery was employed via dynamic navigation technology to provide real-time verification and validation of position accuracy for the osteotomy site and the implant positioning within the regenerated construct.[20] In addition, soft tissue augmentation was performed to optimize the position and condition of peri-implant soft tissue dimensions.[21] Because the connective tissue augmentation was of an autogenous source, further recruitment of inherent vascular supply, innervation and cells could have conceivably helped to further establish an optimal biologic response.

In short, the wound healing dynamics and the ultimate outcome of achieving successful bone construction and osseointegration in severely compromised sites are beyond complex. The interplay of accurate diagnoses, patient selection, meticulous detail to planning and execution at every level, as well as astute re-assessment during key decision making time points in patient care are critical. The influence of growth factor therapeutics, such as rhPDGF-BB, to bone construction surgery efforts in order to achieve more optimal success is but one piece of a complex biologic puzzle in successful bone construction. The more routine use of rhPDGF-BB in highly demanding bone construction surgery may prove beneficial by enhancing the patient-dependent response of vascular ingrowth through upregulating the angiogenic intensity.

Conclusions

This case demonstrates significant bone destruction secondary to peri-implantitis with near 100% bone regeneration using a composite graft enhanced with rhPDGF-BB. In the most demanding of cases, optimizing wound healing conditions with angiogenic enhancers as well as following key principles of GBR may be important to ensure predictable and sustainable results.

Summary Table

Why is this case new information?	- this case documents the treatment of advanced peri-implantitis in the esthetic zone by complex GBR surgery and key space maintenance principles. It also highlights some novel principles of the periosteal-sharpey fiber-endosteum continuum as a contributing and influencing factor to bone regeneration outcome success.
What are the keys to successful understood, management of this case?	- Accurate diagnosis, regional anatomy careful planning and meticulous surgical execution.
What are the primary limitations to success in this case?	- limited follow up due to patient conflicts

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Author Contribution Statement

This manuscript was prepared by Dr George Mandelaris and edited by Dr Bradley DeGroot. The patient received surgical treatment by Dr Bradley DeGroot.

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Competing interests

The authors declare a lack of any financial interests in relation to this work.

Patient Consent

The authors received verbal consent from the patient to photograph and present this case for publication.

Legends

§ MinerOss® Cortical & Cancellous Chips. Medtronic Sofamor Danek USA. Memphis, TN.

‖ Bio-Oss®. Geistlich PharmaAG. Wolhusen Switzerland.

¶ GEM-21S®. Lynch Biologics. Franklin, TN.

#Meisinger master pin control membrane fixation tacks. Meisinger USA. Centennial, CO.

†† Biogide resorbable bilayer collagen membrane. Geistlich Pharma Ag. Wolhusen, Switzerland.

**Cytoplast® Titanium-reinforced. Osteogenics Biomedical Inc., Lubbock, Texas, USA

₸ Carestream 9600 cone beam computed tomography scanner. Atlanta, GA

₹ Carestream 3600 intraoral surface scanner. Atlanta, GA

ⱡ Navident. ClaroNav Technologies; Toronto, ON, Canada

₳ Straumann. Andover MA

Figure Legends

Figure 1. Clinical presentation of #8 affected by inflammatory peri-implantitis

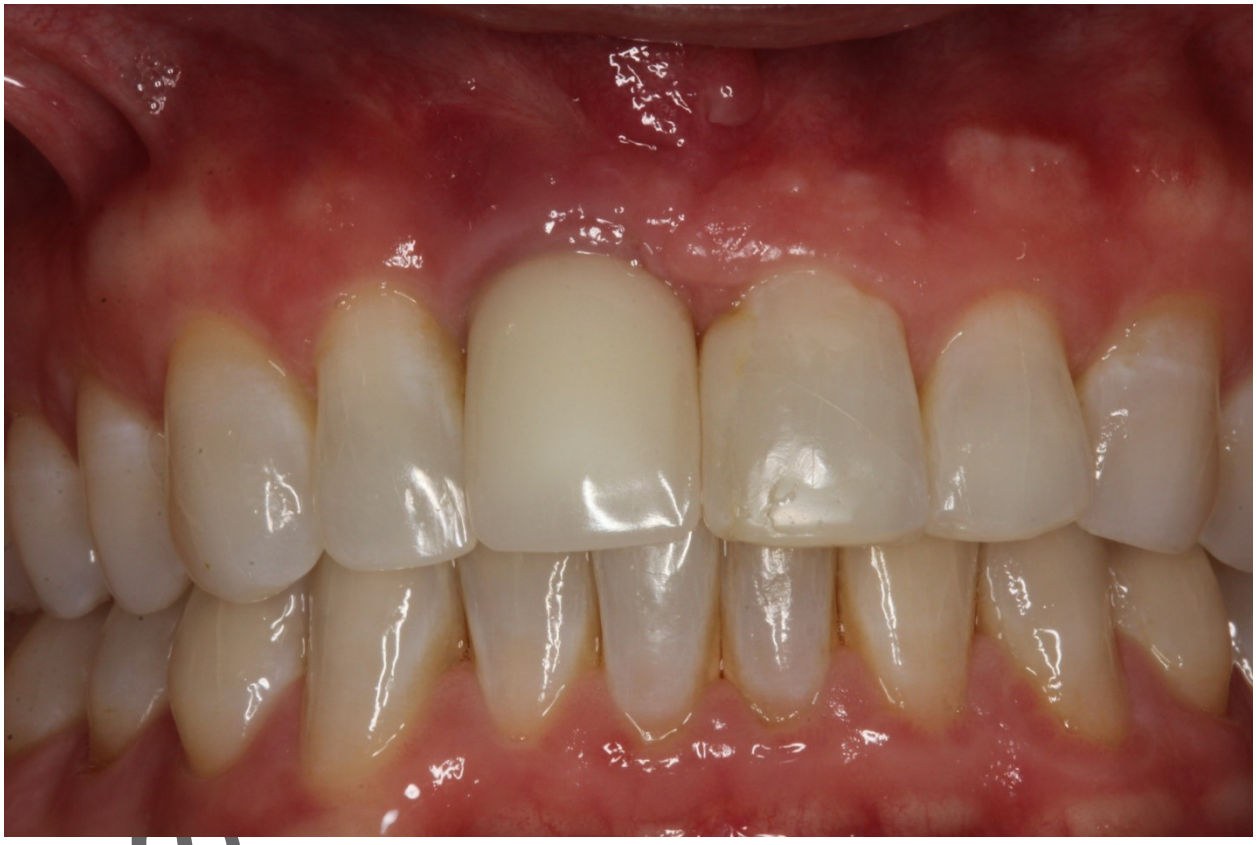


Figure 2. Radiographic documentation of severe peri-implant bone loss

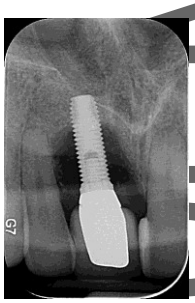


Figure 3. Full thickness flap reflection, degranulation and implant debridement demonstrating severity of peri-implant bone loss.

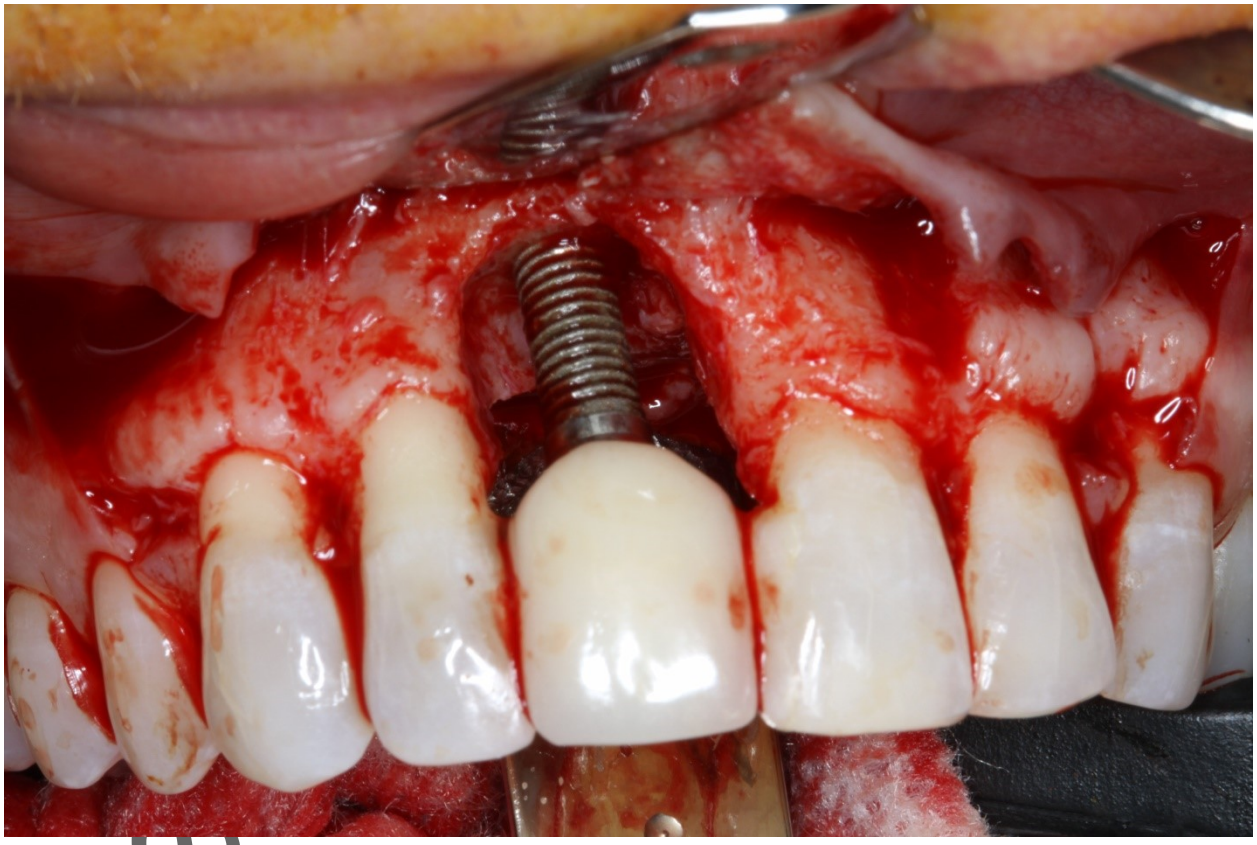


Figure 4. Implant removal and severe residual defect observed.

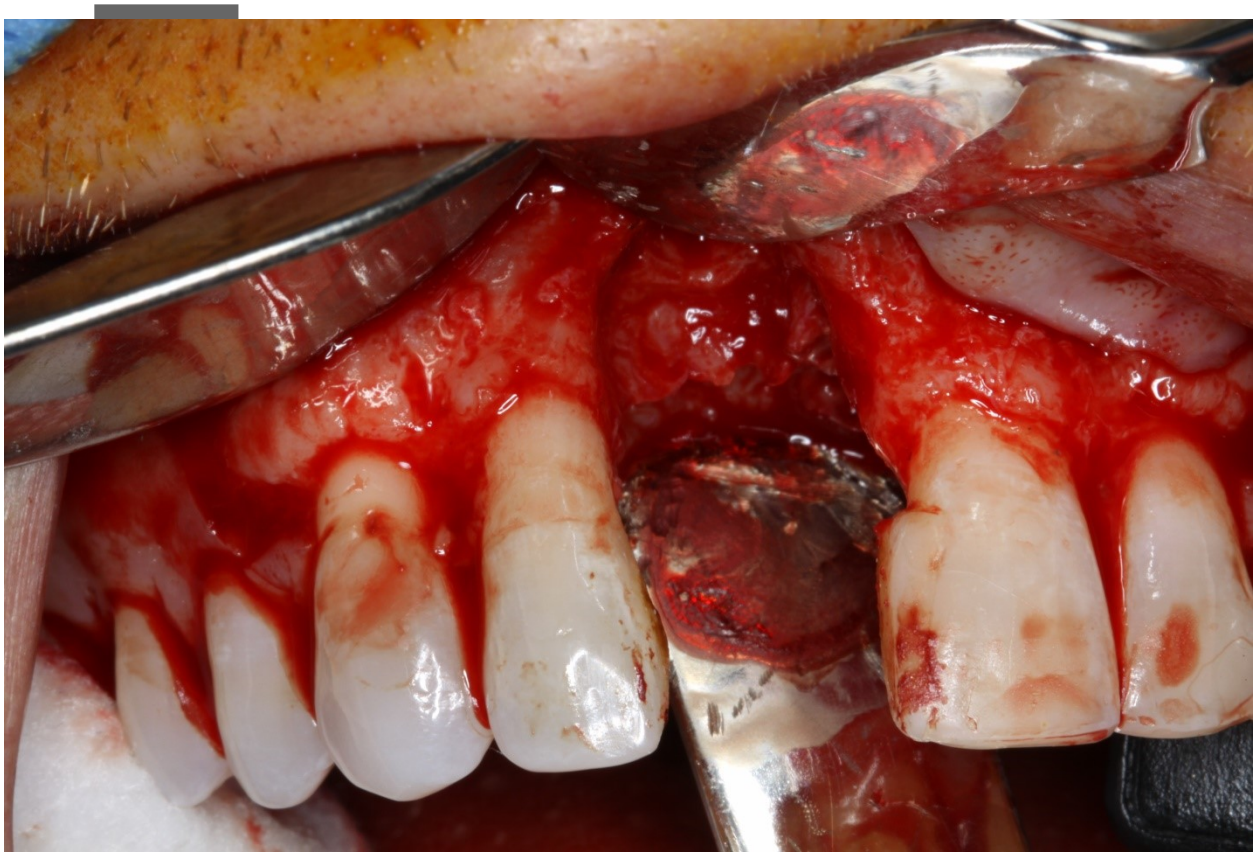


Figure 5. Titanium reinforced membrane fixated on the palatal aspect and composite bone graft condensed to re-establish ideal geometric form for future implant placement.

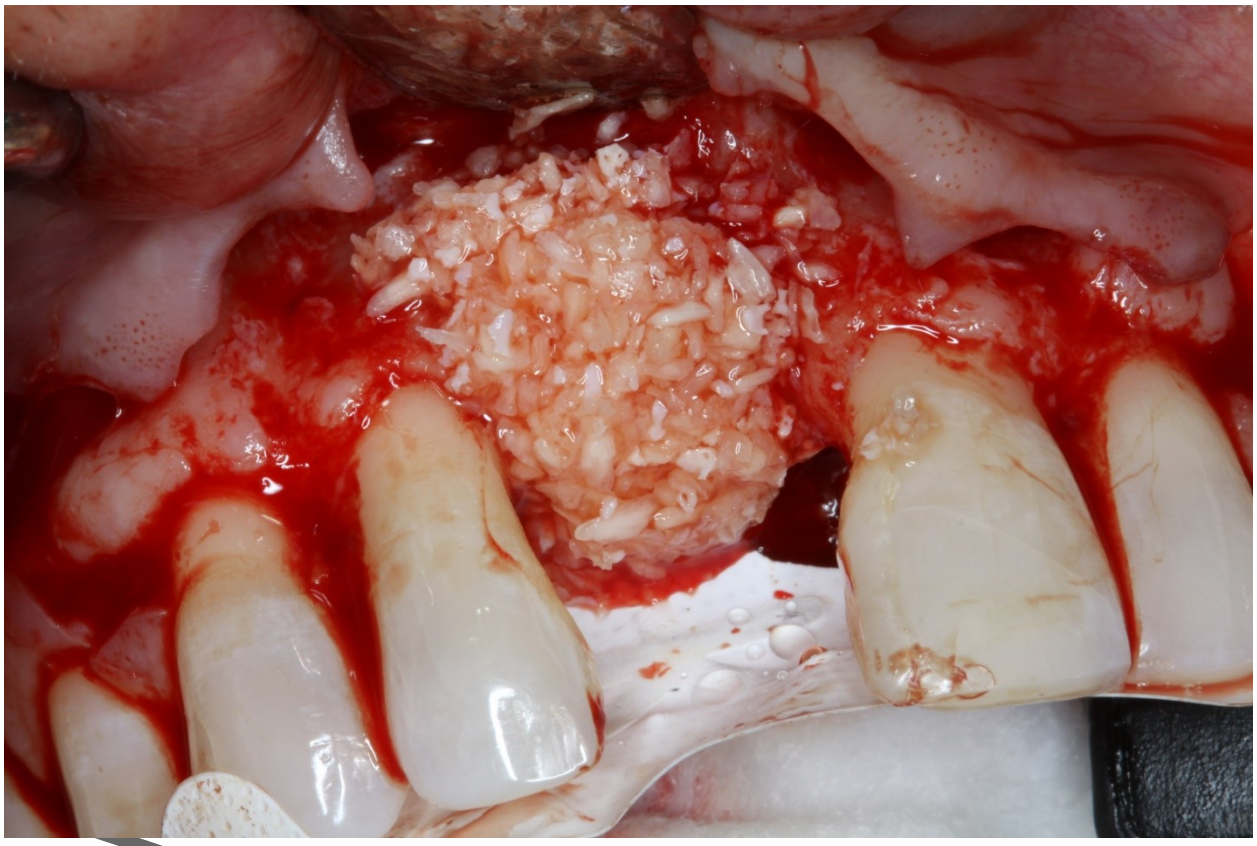


Figure 6a and 6b. Facial and occlusal views of PTFE membrane rotated to the buccal and stabilized with an additional two tacks to ensure entire bone construct immobility.

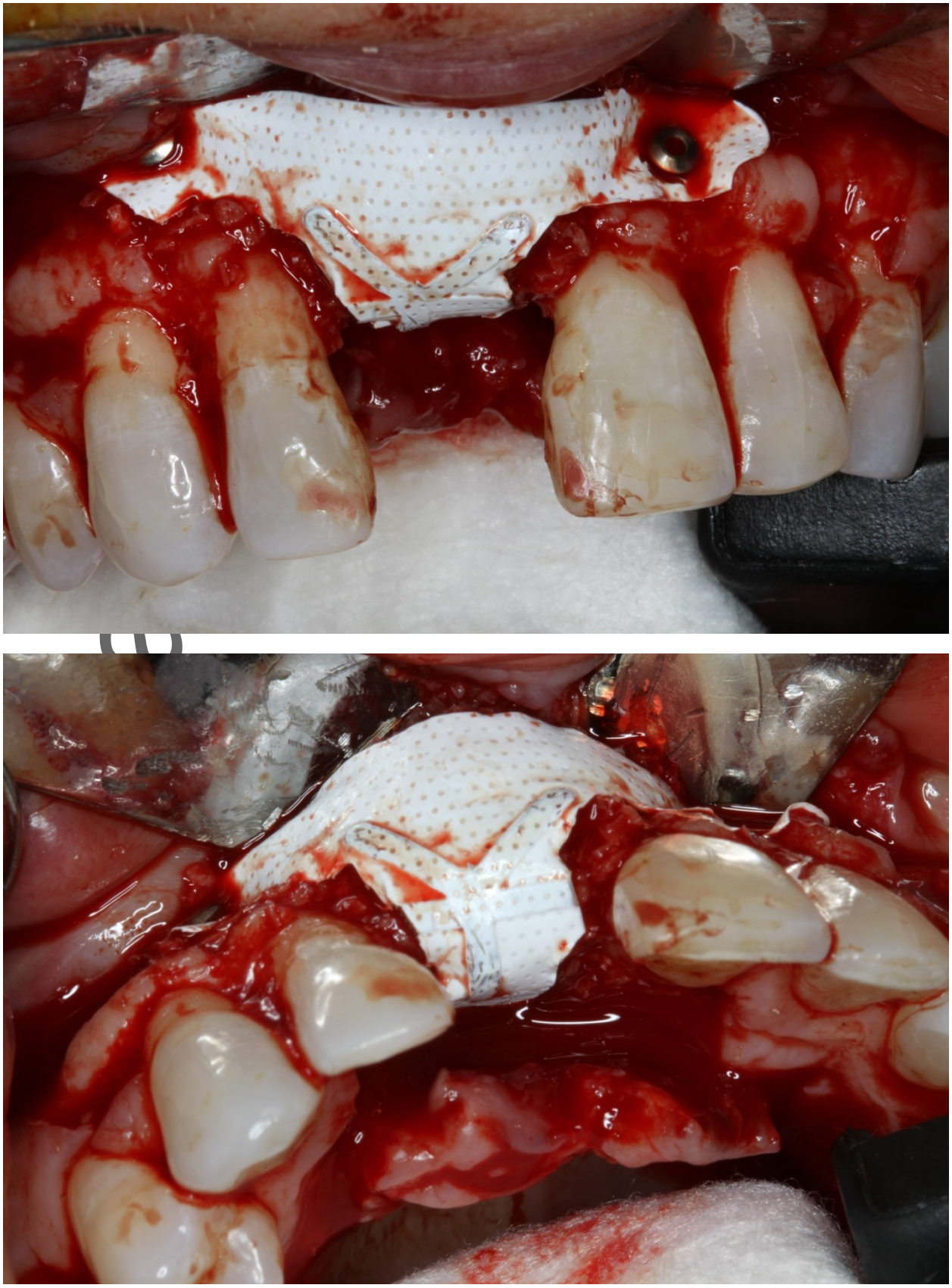


Figure 7. An absorbable porcine collagen membrane positioned over the titanium reinforced PTFE membrane.

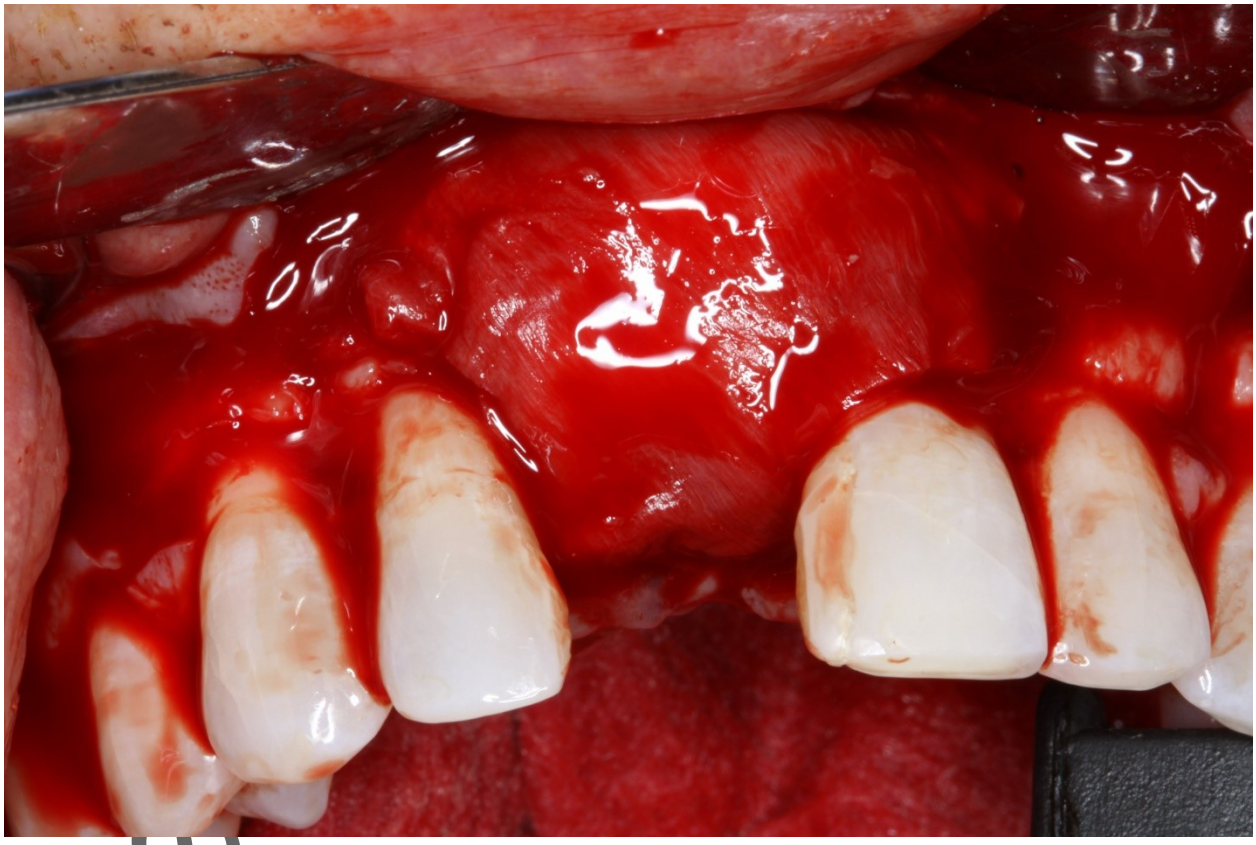


Figure 8. Sutures for primary and tension free wound closure

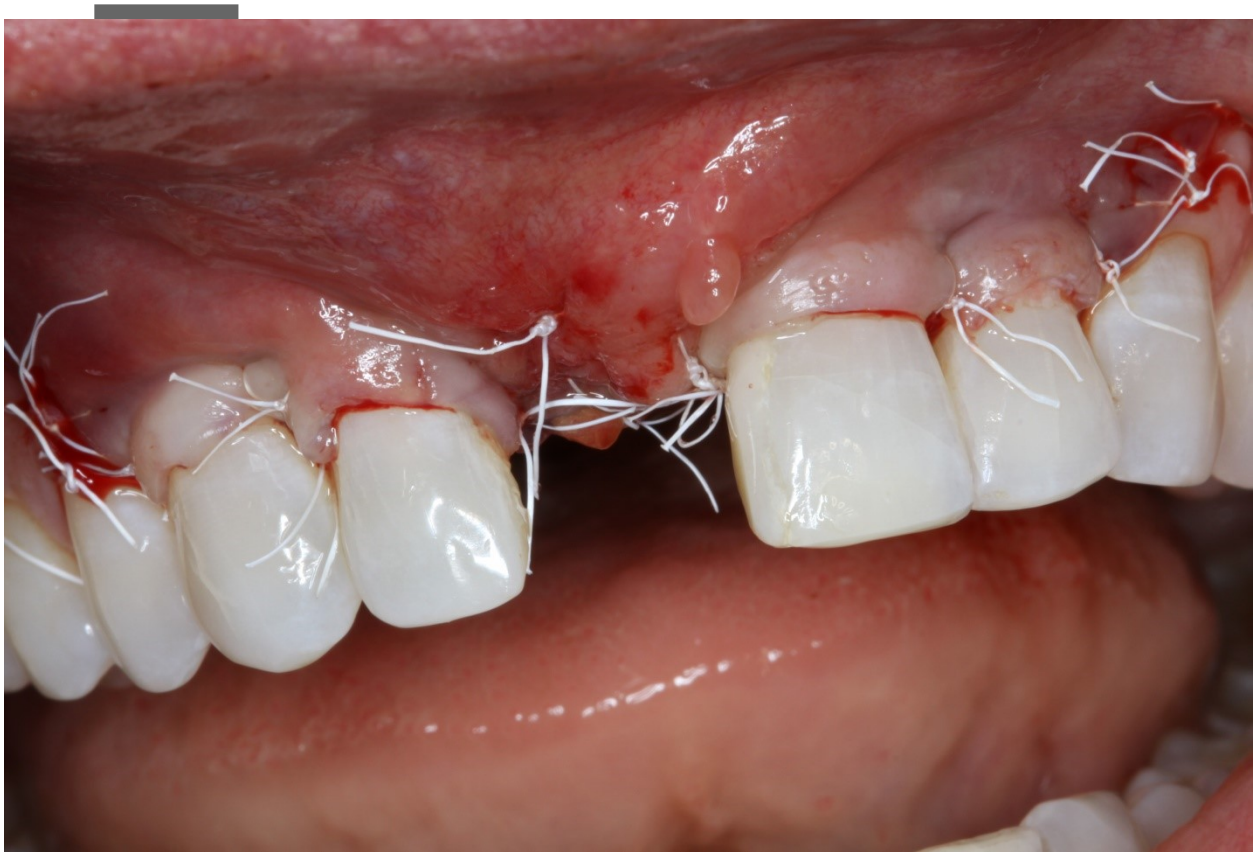


Figure 9. 6 month post-bone construction surgery radiograph

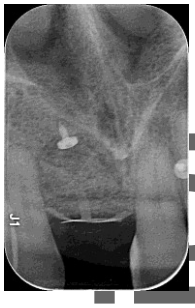


Figure 10. 6 month post bone construction surgery clinical view.

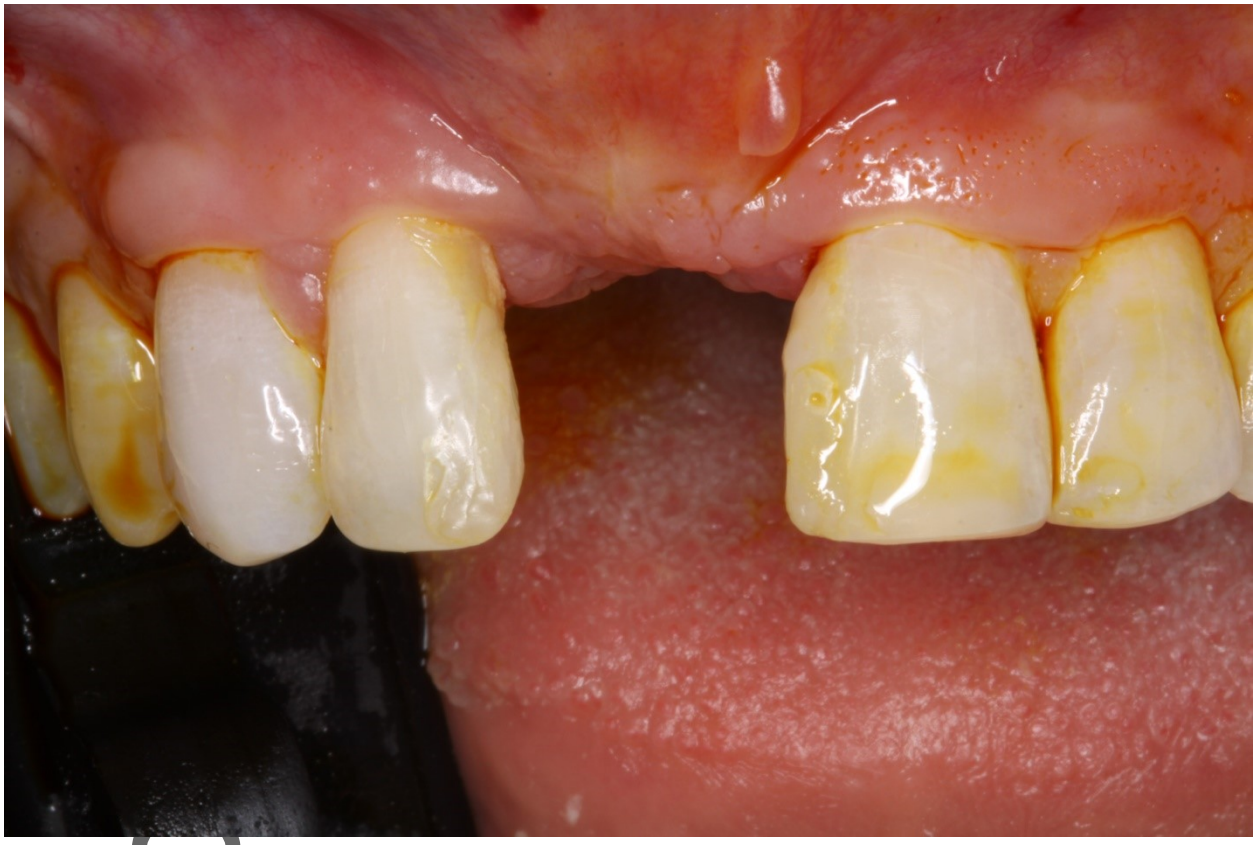


Figure 11. Post GBR prosthetically directed guided implant planning using dynamic navigation

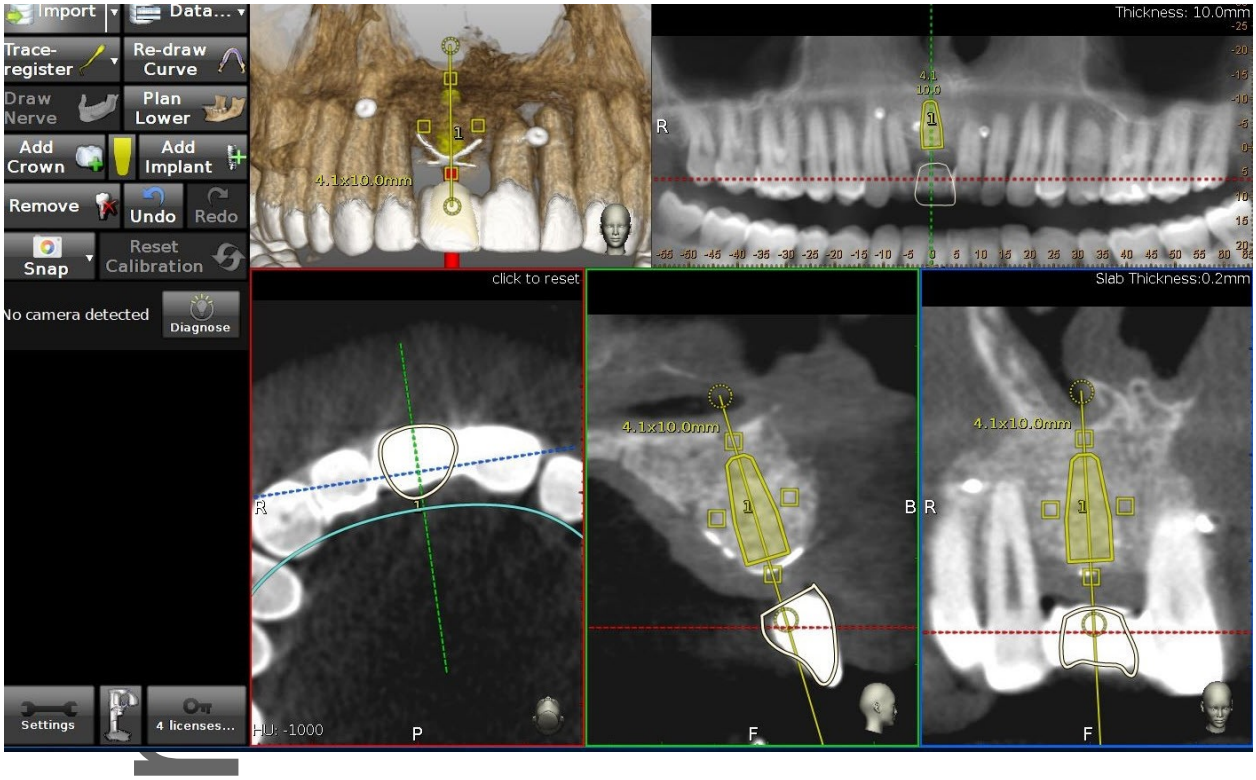


Figure 12. Flap reflection and membrane removal revealing bone gain.

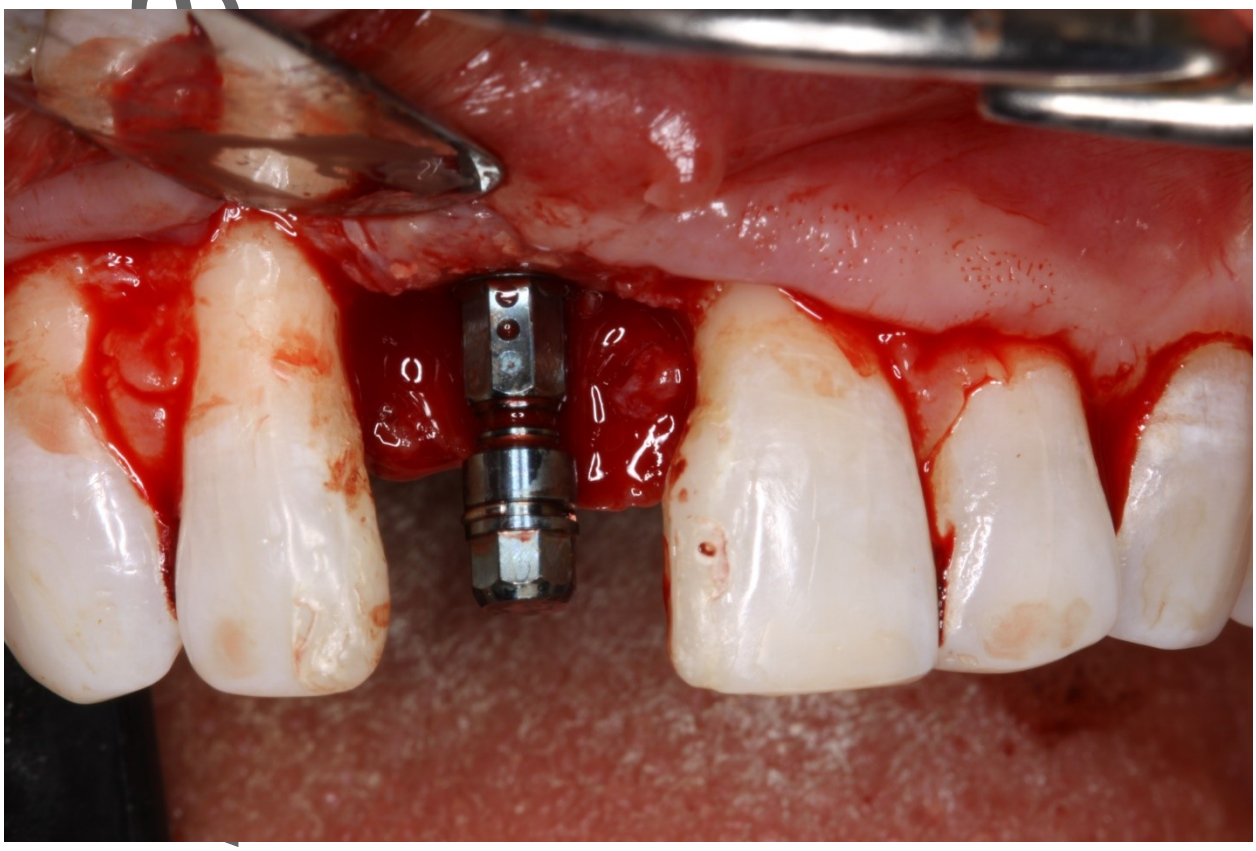


Figure 13a and 13b. Facial and occlusal views of final guided implant placement using dynamic navigation

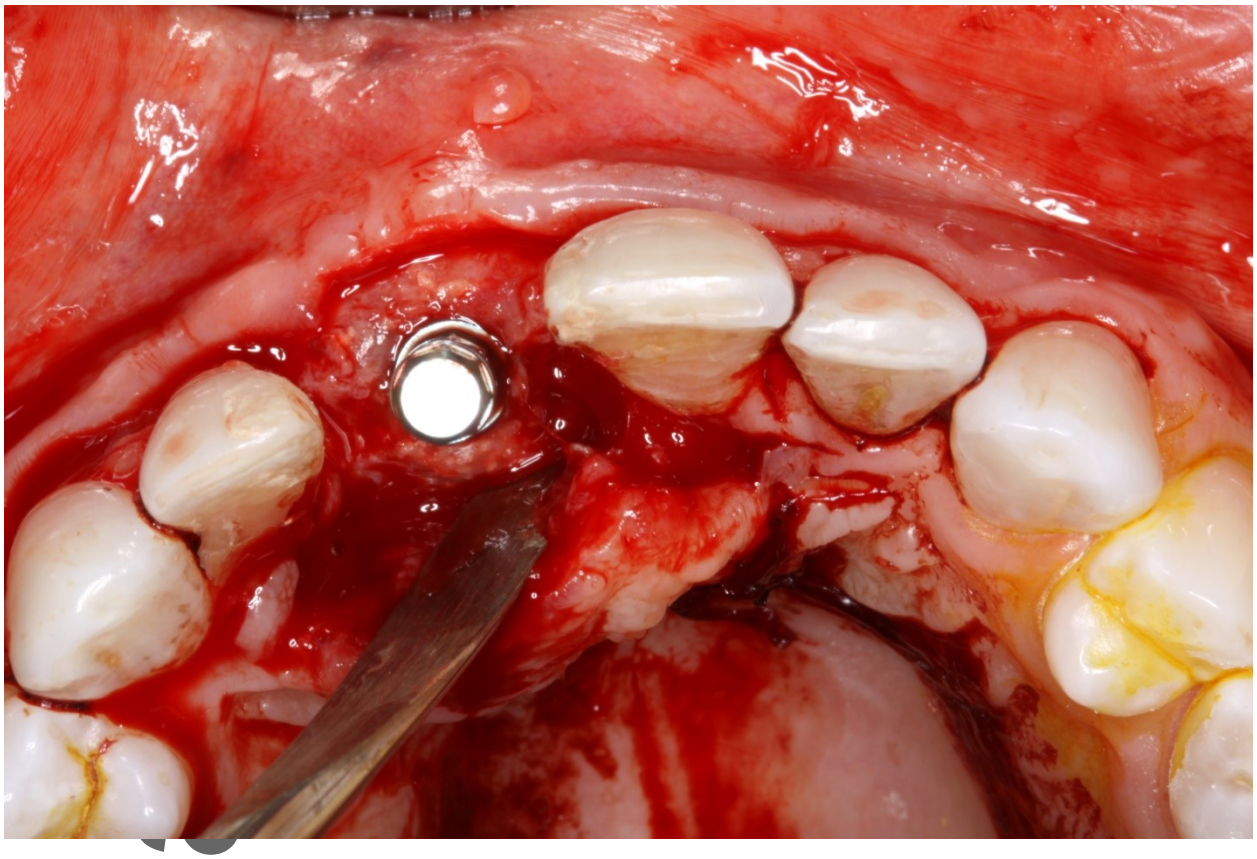


Figure 14. Rotated palatal pedicle connective tissue grafting for soft tissue augmentation.

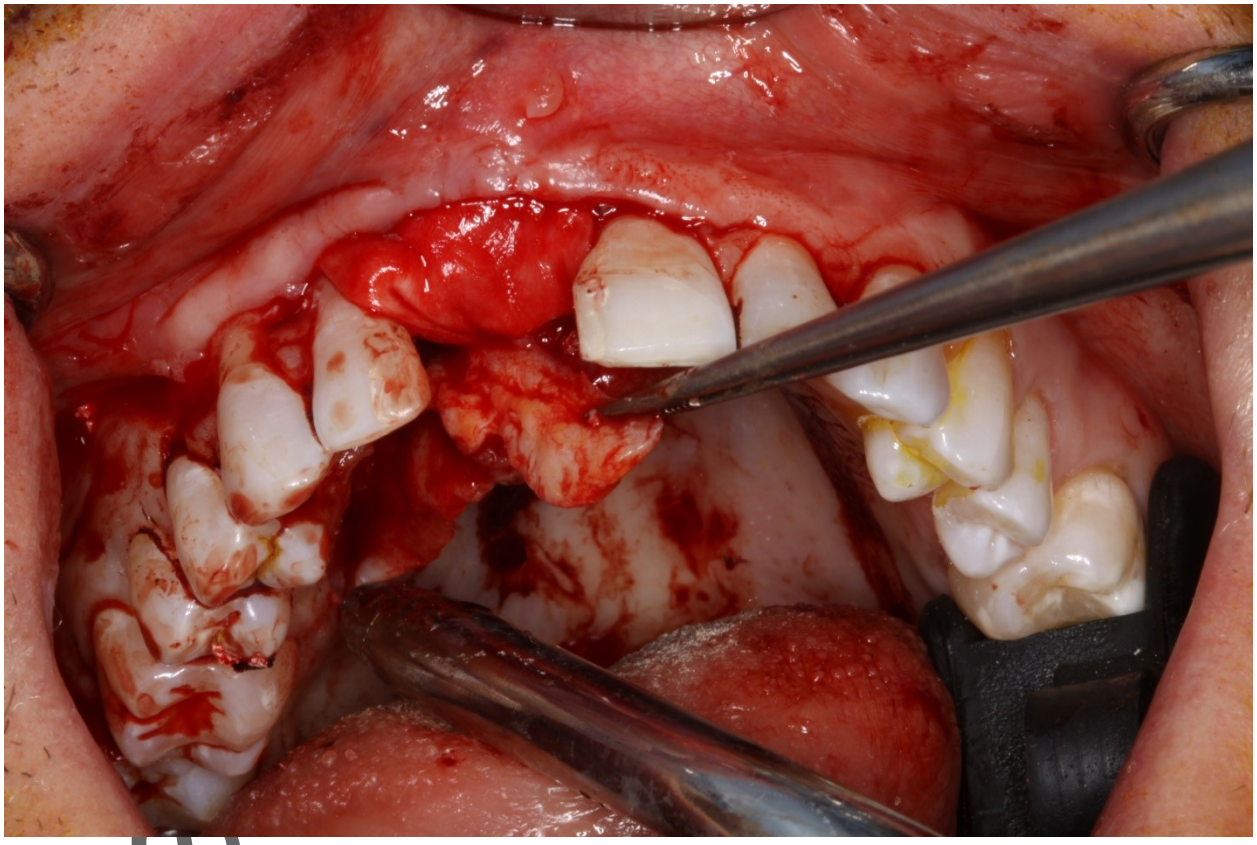


Figure 15. Sutures and provisionalization.

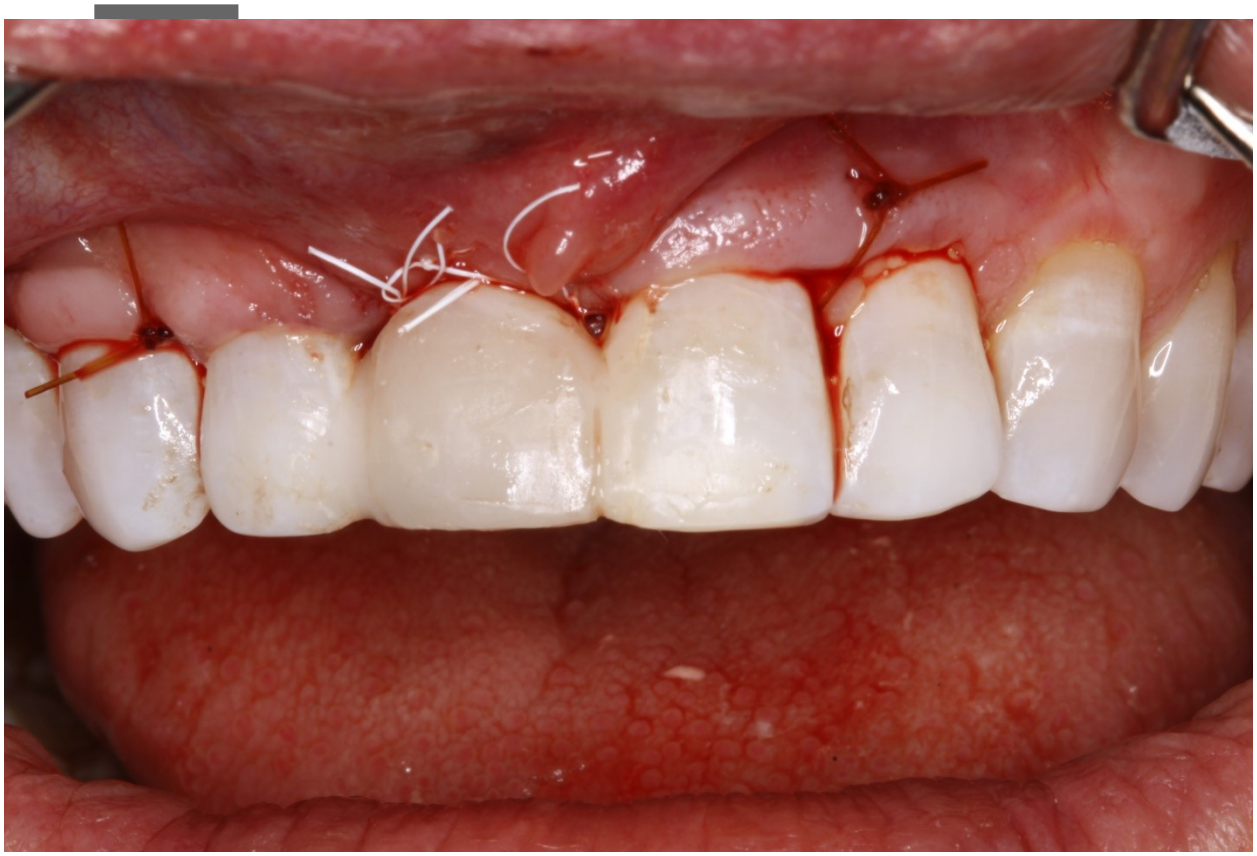


Figure 16. Radiographic confirmation of implant positioning.

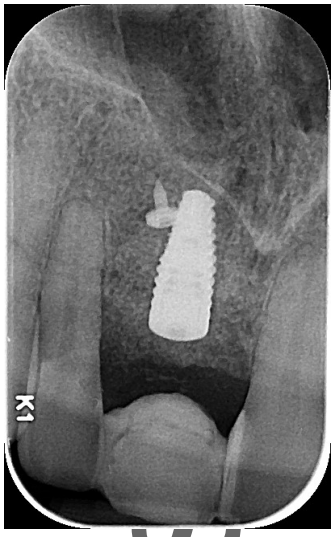
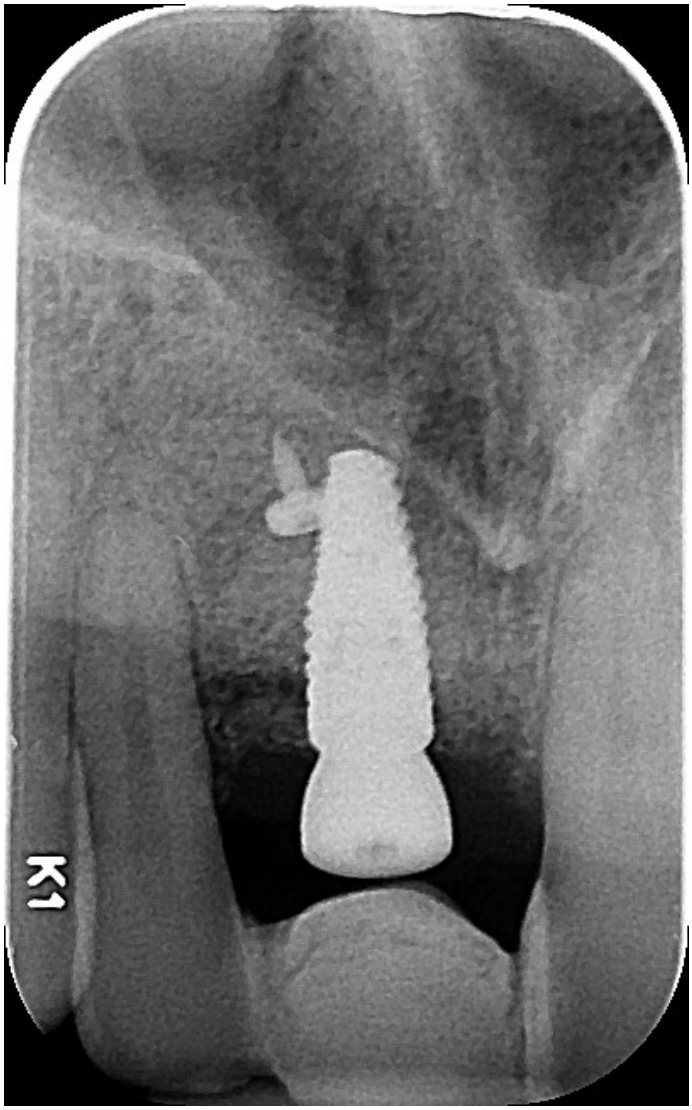


Figure 17. Radiographic outcome of uncovery and healing abutment connection.



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