

Application of biologics for ridge preservation/reconstruction after implant removal.

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Abstract

Focused clinical question: The purpose of this review was aimed at providing the rationale supported with a series of cases to apply biologics to enhance orchestrating the healing process at implant removal sites.

Summary: Implant removal is commonly applied on a daily basis, in particular, in cases that exhibit esthetic failures linked to inadequate implant position or in cases of advanced peri-implantitis. Implant removal sites differ substantially from tooth extraction sockets. Implants are ankylosed within the alveolar bone, which therefore have neither mechanoreception nor the elasticity provided by periodontal ligament fibers. As a result, the bone-to-implant contact must be disrupted by means of using a reverse-torque device to minimize trauma. It is possible that the surrounding bone provides limited vascularity, which may interfere with the healing and bone forming process within the socket. Therefore, the use of biologics may enhance this healing and accelerate bone formation in sites where implants are removed due to hopeless functional or esthetic prognoses.

Conclusion: The use of biologics, in particular autologous blood-derived products, may enhance and boost the healing process to potentiate bone availability at a later stage during implant placement.

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Introduction

In contemporary dental implantology, as the effectiveness of dental implant treatment has improved over time, patient expectations have also increased significantly. Patient-reported outcomes have become one notable criterion for assessing implant success. Satisfying esthetic outcomes in implant dentistry requires the reconstruction to mimic the natural appearance of the lost dentition and the adjacent soft tissues.¹ This is a very challenging task that demands comprehensive technical knowledge relating to implant position and how it drives the prosthetic emergence profile and the orchestration of bone/soft tissue reconstructions to achieve a harmonious profile. Unfortunately, if these above-mentioned considerations are ignored, the prosthesis design is often suboptimal leading to inadequate cleansability and/or poor esthetics. In this sense, the implants installed in an inadequate 3D position are often assigned a poorer prognosis and are advocated for removal.

Moreover, the longevity of dental implants is further compromised by the incidence of biological complications, in particular peri-implantitis. Peri-implantitis is featured by progressive bone loss that results from the inflammation evoked by the colonization of the peri-implant sulcus by pathogenic bacteria.² One key aspect to understand this disorder falls in the site-specific onset and progression as reported by epidemiological studies.³ In other words, certain local factors have been identified to be predisposing or precipitating towards peri-implantitis (e.g., malposition, inadequate oral hygiene, lack of cleansability, poor prosthetic design). These factors need to be addressed for two main reasons: 1) the efficient primary/secondary prevention of the incidence of the disease and 2) for the adequate and effective management of peri-implantitis. The therapeutic goal of peri-implantitis is to resolve soft tissue inflammation and to halt progressive bone loss. Therefore, given the shortcomings of non-surgical therapy in terms of limited visibility,⁴ surgical access is often advocated to efficiently remove the biofilm adhered to the implant surface. In fact, various surgical

modalities have been proposed according to peri-implantitis bone configuration⁵ or soft tissue characteristics,⁶ amongst others. Nevertheless, it is worth noting that the scientific evidence on the superiority of any given strategy is sparse. Regardless, long-term tissue stability after the lesions have been managed does not seem to be completely foreseeable. For instance, it was noted that implants with $\geq 50\%$ of bone loss are more prone to fail after surgical therapy.^{7, 8} Therefore, these implants should be assigned with unfavorable prognosis during initial diagnosis, where the most reasonable therapy to eradicate the disease is to remove the implant.

Indications for implant removal

The dominant factors that dictate a hopeless prognosis and where, implant removal is recommended are the following:

- Implants exhibiting peri-implantitis in patients unwilling to enroll in a professionally-administered maintenance program and inadequate motivation to perform self-performed oral hygiene measures for plaque control.
- Implants exhibiting advanced peri-implantitis. Studies have demonstrated a significantly lower likelihood to succeed in the surgical management of peri-implantitis if the lesions extend $\geq 50\%$ of the implant length (Figure 1).^{7, 8}

[Figure 1 about here]

- Inability to address local factors associated with the onset of peri-implantitis: Identifying and modifying local predisposing factors is key in preventing recurrence.

Amongst them, the three major factors to be considered include: soft tissue characteristics, the prosthesis design, and three-dimensional implant position.

- Expendable implants that present with biomechanical, functional or esthetics complications and can be removed without altering (or minimal modification of) the prosthesis. These implants can be extracted irrespectively of the extension of disease.
- Inability to obtain adequate esthetics in the facial area due to three-dimensional inadequate implant position in patients demanding an anterior harmonious profile (Figure 2).⁹

[Figure 2 about here]

Bone healing at removed implant sites

The dynamic changes and healing events occurring after tooth extraction have been exhaustively explored in preclinical and clinical trials.¹⁰⁻¹³ Cardaropoli et al. demonstrated that during the early stages of healing, a blood clot occupies most of the extraction site. Two weeks later, the tissue of the socket is dominantly comprised of woven bone. Mineralized bone occupies the vast majority of the socket volume one month after extraction. Thereafter, bone matures to consolidate a higher proportion of lamellar bone.¹¹ This may result in horizontal (3.6 in molar sites and 2.7 in non-molar sites) and vertical (1.4 in molar sites and 1.7 in non-molar sites) dimensional changes that may compromise implant placement at a later stage.¹⁴ In contrast, healing events after implant removal are yet unknown. Sparse preclinical data evidenced the presence of osteocytes within the lacunae in close contact with the bone surface where the implants were removed.¹⁵ Concerning the dimensional changes, a clinical study showed that minimal bucco-lingual alveolar changes occur at

removed implant sites (about 10%). In fact, these changes can be further minimized using implant-removal kits based on counter-torque (up to 250Ncm) and to regenerate simultaneously with implant removal.¹⁶ Nevertheless, further research is warranted for the healing process and the three-dimensional volumetric changes occurring at implant removal sites. While subtle remodeling has been reported after extraction of implants affected by peri-implantitis via minimally invasive implant-removal kits,¹⁶ the explantation of fixtures can vary significantly depending on multiple different factors, including but not limited to: atraumatic (removal kit) vs more traumatic (trephines and/or traditional measures such as elevators or forceps) protocols, characteristics and availability of the surrounding bone (adjacent bony peaks/walls) and, more specifically, the presence/thickness of the buccal bony wall, soft tissue characteristics, and remaining surface/length of implant embedded into bone.

Rationale for the use of biologics at removed implant sites

The cementum is embedded by the periodontal ligament, it provides a source of formative elements for growth and repair of the alveolus as well as itself.¹⁷ This, together with the presence of the bundle bone of the alveolus, may explain the major dimensional changes occurring at tooth in contrast to implant sites after removal. Therefore, it is hypothesized that the sparse vascularity derived from the neighboring haversian canals may limit the reparative potential to promote the formation of the clot and the subsequent healing events that may lead to bone formation within the extraction site. In this sense, biologics may provide a source of reparative mediators to boost healing and stimulate repair. In particular, in scenarios where implant placement at a previously extraction site is desired to achieve oral rehabilitation. This may be indicated specially in scenarios that exhibit inadequate implant position or that manifest advanced forms of peri-implantitis with insufficient residual bone that may demand staged regeneration.

Biologics are named for a group of mediators that exert a biological effect through various mechanisms to promote soft and hard tissue repair, in particular boosting deoxyribonucleic acid synthesis, chemotaxis, differentiation, mitogenesis and matrix biosynthesis.¹⁸ Consequently, these mediators have been widely employed in the treatment of post-extraction sites. Multiple investigations have demonstrated that the use of these biologics, alone or in combination with alternative and more conventional grafting protocols, may represent a plausible alternative.¹⁹⁻²²

The American Academy of Periodontology Best Evidence Consensus identified the potentials of biologics to promote earlier healing.²³ In particular, autologous blood-derived products (ABPs) alone proved outperformance in unassisted healing with regard to dimensional changes after ridge preservation procedures. Moreover, superior histomorphometric outcomes were shown in these interventions. This might be explained by the anti-inflammatory response in macrophages and the suppression of osteoclastogenesis elicited by ABPs (Figure 3-4).^{24, 25} In addition, the use of biologics can also elicit a favorable response in terms of patient-reported outcomes as measured by reducing pain and swelling.

[Figure 3-4 about here]

Therefore, the use of ABPs is hypothesized to be beneficial in promoting healing at removed implant sites. Indeed, platelets release a variety of growth factors listed that may assist healing²⁶ such as:

- Platelet-derived growth factor (PDGF) acts as potent mitogen in serum for mesenchymal cells. It has further demonstrated being a chemoattractant for

fibroblast, macrophages and leukocytes, and to stimulate the collagen and matrix formation.²⁷

- Transforming growth factor β (TGF- β) stimulates angiogenesis and chemoattract osteoblast precursors. Additionally, it inhibits osteoclast formation and activity.²⁸
- Vascular endothelial growth factor (VEGF) stimulates the endothelial chemotaxis while promoting angiogenesis.²⁹
- Platelet derived angiogenesis growth factor (PDAF) stimulated the mitogenesis for endothelial cells while increasing angiogenesis.³⁰
- Insulin-like growth factor-1 (IGF-1) stimulates bone matrix formation and promotes the replication of pre-osteoblasts and osteoblasts.³¹
- Platelet factor 4 (PF-4) is a chemoattractant for neutrophil and also acts as antiheparin agent.³²

Therefore, the use of ABPs to promote the healing of alveolar sockets immediately after the removal of dental implants seems to be pertinent to upregulating healing potential in surgery.

Material and Methods/Results

Case scenario of implant removal due to peri-implantitis

A 71-year-old male healthy patient (ASA I) presented to a private practice (CICOM Institute, Badajoz, Spain) demanding oral rehabilitation after prosthesis unfitting due to multiple implant failure as consequence to peri-implantitis. Based upon the severity of peri-implantitis (>50% of bone loss), remaining implants were prognosed hopeless. Accordingly, implants were removed with an implant removal kit[§] applying a reverse torque of 200N/cm.

[§] Nobel Biocare AG, Zurich, CH

Subsequently, comprehensive curettage of the sockets was performed followed by superficial corticotomies with a diamond bur within the alveolar sockets to boost bleeding. Immediately after, platelet-rich plasma and a collagen sponge were used to graft the sockets and promote the healing process. After a healing period of 8 weeks, soft tissue thickening together with the presence of woven bone were noted. Re-entry was performed to place 4 tissue level implants^{||} in the ideal position aiming at providing support for an overdenture. Given the slight buccal bone dehiscences that were exhibited the implants after placement, simultaneous contour augmentation with autogenous bone and anorganic bovine bone[¶] was carried out. A long-lasting barrier membrane[#] was used to fulfil the principle of compartmentalization. Note hard and soft tissue stability, indicating peri-implant health at 15-month follow-up (Figure 5).

[Figure 5 about here]

Scenario of implant removal due to esthetic concern

A 42-year-old female patient with hyperglycemia (ASA II) presented to a private practice (CICOM Institute, Badajoz, Spain) demanding esthetics due to a severe concern together with multiple dental mobility that impact negatively upon her quality of live. An initial inter-consult with her monitoring medical doctor was recommended to check the glycemc levels. These proved to be under control (118 mg/dl) with a daily intake of metformin. Under comprehensive examination, it was diagnosed as generalized stage IV grade C periodontitis.

^{||} TLX, Straumann, Basel, CH

[¶] Inteross, SigmaGraft, California, USA

[#] Ossix Plus®, Datum, Lod, Israel

Moreover, an implant placed in the upper centra incisor manifested signs of mucosal inflammation. The cone-beam computed tomography assessment indicated an inadequate apico-coronal position that unfavored the emergence profile. Accordingly, initial non-surgical periodontal therapy and the extraction of teeth with hopeless prognosis was carried out. At this stage, the implant was further removed with a removal kit[§]. Corticotomies were performed in the sockets. In all the sockets, platelet rich plasma combined with a collagen sponge was used to graft. After a healing period of 8 weeks, re-entry was performed to place 2 implants in the anterior maxillary area** in the ideal position aiming at providing support for a fixed prosthesis. Even though no bone dehiscence or fenestration were noted, simultaneous grafting to compensate the thin buccal bone and to enhance the esthetic contour was carried out using a sugar-based bone substitute^{††}, plasma rich fibrin to stability the grafting. A long-lasting barrier membrane[#] was used to fulfil the principle of compartmentalization and to provide stability to the graft. The membrane was suture using subperiosteal sutures. Note hard and soft tissue stability at 12-month follow-up where patient's esthetic satisfaction was further met (Figure 6).

[Figure 6 about here]

[§] Nobel Biocare AG, Zurich, CH

** BLX, Straumann, Basel, CH

†† Ossix Bone®, Datum, Lod, Israel

Discussion/Conclusion

The nature of the biological events and dimensional changes that arise following implant removal are poorly understood; nonetheless, the clinical impression is that the formation of the coagulum that would promote bone apposition within the socket is reduced. The use of biologics, in particular ABPs, seemed to promote bone formation favoring implant placement at a later stage. This treatment approach poses no harm to the post-implant-removal healing process. Further investigations to assess bone apposition compared to other treatment approaches is warranted.

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Figure 1. Advanced peri-implantitis often predicts an unfavorable therapeutic prognosis. Implants exhibiting these scenarios are often advocated to removal.

Figure 2. Esthetic concerns associated with inadequate implant position often limit the ability to achieve patient's satisfaction

Figure 3. Biologic-assisted healing by means of platelet rich plasma at a mandibular implant removal site due to advanced bone 4-month follow-up. (A-B) Note the increase in grey scale density assessed by cone beam computed tomography within the socket that may indicate the formation of woven bone.

Figure 4. Advanced peri-implantitis exhibited on a first lower molar implant. Note at 4-month post-removal how biologic-assisted healing promoted bone gain within the alveolar socket and bucco-lingual dimensional stability.

Figure 5. Implant removal due to advanced peri-implantitis. (A) Based upon the severity of peri-implantitis (>50% of bone loss), implants were removed. Implants were removed applying a reverse torque of 200N/cm.

(B) platelet-rich plasma and a collagen sponge were used to graft the sockets and promote the healing process.

(C) After a healing period of 8 weeks,

(D-E) re-entry was performed to place

(F) 4 tissue level implants in the ideal position aiming at providing support for an overdenture. Given the slight buccal bone dehiscences that were exhibited the implants after placement,

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(G-J) simultaneous contour augmentation with autogenous bone and anorganic bovine bone was carried out. A long-lasting barrier membrane was used to fulfill the principle of compartmentalization.

(K-L) Note hard and soft tissue stability, indicating peri-implant health at 15-month follow-up.

(M) Patient further manifested functional and aesthetic satisfaction with the implant-retained overdenture.

(N) An implant-retained overdenture was delivered

(O) The esthetic appearance is satisfying to the patient

Figure 6. Implant removal due to inadequate implant placement. (A-B) Unsatisfying esthetics displayed by a patient diagnosed as stage IV grade C periodontitis.

(C) The cone-beam computed tomography assessment indicated an inadequate apico-coronal position that unfavored the emergence profile.

(D) Implant was removed with a removal kit. Platelet rich plasma was used to graft the socket.(E-F) After a healing period of 8 weeks, re-entry was performed to place 2 implants in the anterior maxillary area in the ideal position aiming at providing support for a fixed prosthesis.

(G-H) Even though no bone dehiscence or fenestration were noted, simultaneous grafting to compensate the thin buccal bone and to enhance the esthetic contour was carried out using a sugar-based bone substitute, plasma rich fibrin to stability the grafting. On the top of it, a long-lasting barrier membrane was used to fulfil the principle of compartmentalization and to provide stability to the graft.

(I-J) The membrane was suture using subperiosteal sutures.

(K-L) Note soft tissue stability at 12-month follow-up where patient's esthetic satisfaction was further me