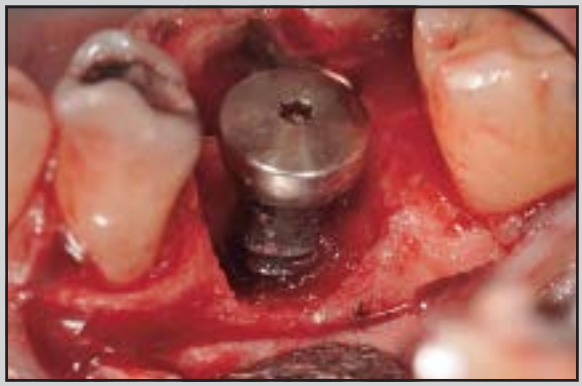
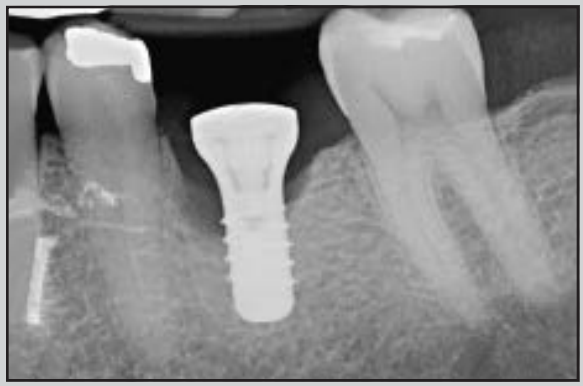
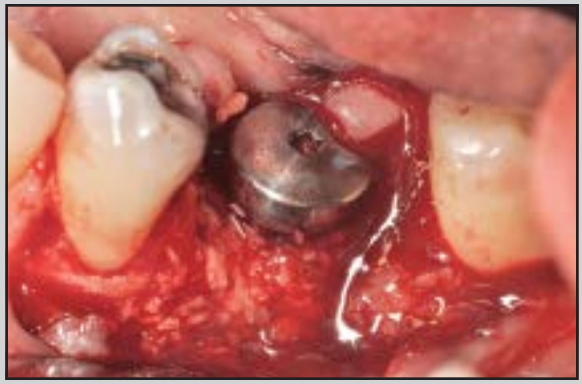
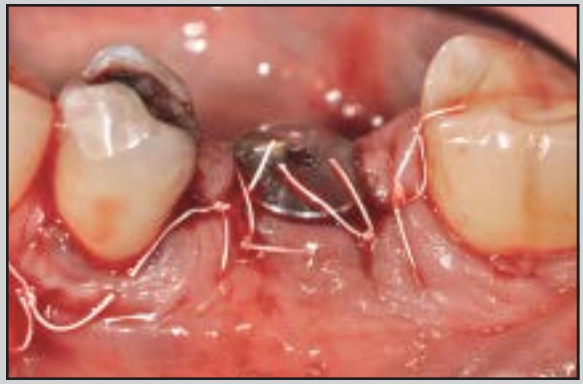
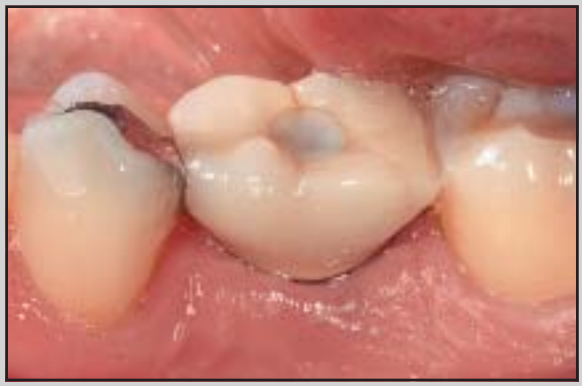
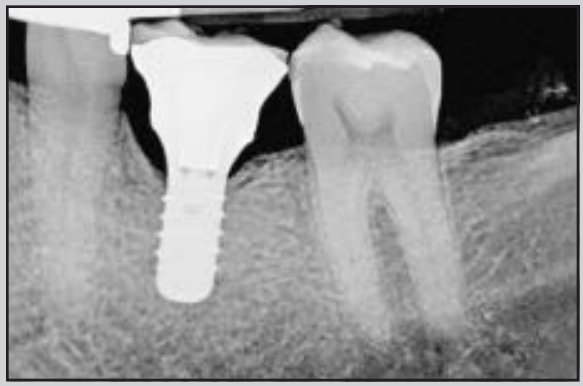

A Regenerative Approach to the Successful Treatment of Peri-implantitis: A Consecutive Series of 170 Implants in 100 Patients with 2- to 10-Year Follow-up

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This article presents the results of a consecutive case series of 170 treated peri-implantitis–affected implants in 100 patients with follow-up measurements from 2 to 10 years. A total of 51 implants in 38 patients previously reported on were followed for an additional 2.5 years, and 119 additional implants in 62 additional patients were treated with the same protocol and monitored for at least 2 years posttreatment. The treatment consisted of flap reflection, surface decontamination, use of enamel matrix derivative (EMD) or platelet-derived growth factor (PDGF), and guided bone regeneration with mineralized freeze-dried bone and/or anorganic bovine bone combined with PDGF or EMD and covered with an absorbable membrane and/or subepithelial connective tissue graft. Maintenance and monitoring followed every 2 to 3 months. Two implants were lost 6 months posttreatment, for a 98.8% survival rate. Bleeding on probing was eliminated in 91% of the treated implants. Probing depth reduction averaged 5.10 mm, bone level gain averaged 1.77 mm, and soft tissue marginal gain averaged 0.52 mm. These outcomes were obtained with one surgical procedure on 140 implants, with two procedures on 18 implants, and with three procedures on 10 implants. The results to date with this layered/combined regenerative approach for the treatment of peri-implantitis appear to be encouraging. (Int J Periodontics Restorative Dent 2015;35:857–863. doi: 10.11607/prd.2571)

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Peri-implantitis, defined as an inflammatory condition affecting the tissues surrounding an implant and resulting in bleeding on probing (BoP) and loss of supporting bone,[1] has been reported to have a prevalence of between 6% and 36% of implants in function for more than 5 years.[2] One consensus report, in fact, stated that peri-implantitis was identified in 56% of subjects and 43% of implant sites.[3] The varying prevalence of the condition reflects the differing thresholds of bone loss used in the various studies to define its existence.[4] Two recent systematic reviews and a meta-analysis reported that peri-implantitis affected approximately 10% of implants and 20% of patients 8 to 10 years after implant placement.[5,6] By 2020, it is estimated, 2 to 4 million implants will be placed annually in North America.[7] Considering the number of implants placed or projected to be placed from 2013 to 2017 in the United States alone, this estimate would predict that over 1.2 million implants will require therapy for this disease.[8]

However, treatment strategies reported on vary significantly, and this is reflected in the comments made in recent systematic reviews.[3,9–15] One systematic review concluded that the evidence available is insufficient to allow specific recommendations for peri-implantitis

treatment.[14] Issue might be taken not only with the treatment protocols, but with the great heterogeneity these reviews cite in the design of their evaluated studies, as well as variations in their definitions of peri-implantitis and the length of time for follow-up.

A case series of 51 consecutively treated implants in 38 patients with 3- to 7.5-year follow-up was previously published that documented a successful regenerative approach for the treatment of implants with peri-implantitis.[16] These patients have continued on a strict schedule of maintenance every 8 to 12 weeks. Two recent publications reported that patients who had a high standard of oral hygiene and were enrolled in a recall system every 3 or 6 months showed stable treatment outcomes following a 5-year monitoring period.[17,18]

It is the purpose of the present study to not only follow the original 51 treated implants for an additional 2.5 years but also to document an additional 119 implants consecutively treated with the same regenerative approach and monitored for at least 2 years posttreatment.

Method and materials

A total of 170 implants were consecutively treated in 100 patients using a protocol described in a previous study.[16] This included the original 51 consecutively treated implants in 38 patients previously reported on, along with an additional 62 patients with 119 implants. Patients were assigned to a maintenance interval of 8 to 12 weeks. The inclusion criteria for the additionally treated implants included demonstration of bleeding on probing (BoP), probing depths (PDs) ≥ 5 mm, and peri-implant bone loss ≥ 3 mm as measured from the implant platform. Postsurgical follow-up and measurements were required to be taken at least 2 years following surgical treatment. BoP was recorded dichotomously as either present or not present following probing. Bone loss was determined on radiographs on the mesial and distal aspects of the implant to determine the presurgical bone level. Patients were classified as nonsmokers if they did not smoke or smoked fewer than 10 cigarettes per day. All others were recorded as smokers. The patients were all consecutively treated following diagnostic screening to eliminate patients with systemic diseases or who were taking medications that would cause a poor healing response (ie, intravenous bisphosphonates, chemotherapy, recent radiation therapy). Implants eliminated from treatment included those that were mobile or that in the authors' judgment were not amenable to complete surface decontamination because of inadequate access or proximity to a vital structure (ie, the alveolar inferior nerve). Presurgical and all necessary periodontal treatment was completed at least 1 month prior to surgery, including full-mouth debridement if necessary, and all patients had to demonstrate adequate plaque control to continue with therapy. Prior to surgery, informed consent was obtained and all implants were examined for PD, BoP, and radiographic evidence of bone loss. All three of the authors were calibrated at three separate times prior to measurements to ensure similar PD and marginal soft tissue level readings were recorded. All measurements were made using a UNC periodontal probe that measured up to 15 mm (Hu-Freidy) around six aspects of the implant. Probing pressure was standardized by way of calibration, whereby similar PD measurements were recorded by the three authors on several test pockets. The deepest PD was recorded and photographs taken to reproduce the probe location at each of the reevaluation visits. Facial marginal bone levels were recorded to the nearest 1 mm on the midfacial aspect of the implant from the platform to the coronal level of mucosa. All initial radiographs as well as the most recently available were sent to an independent evaluator to measure bone gain or loss. All radiographs were kept consistent in terms of the type of radiographic film (Kodak Insight, Kodak) or digital software (DEXIS, DEXIS LLC, and ScanX, Air Techniques) employed.

Bone level measurement determination

To establish the loss or gain of alveolar bone support around implants during the study, the bone levels were measured by an independent evaluator using baseline and follow-up radiographic images of the implants. The bone level was measured from the implant shoulder to the first bone-to-implant

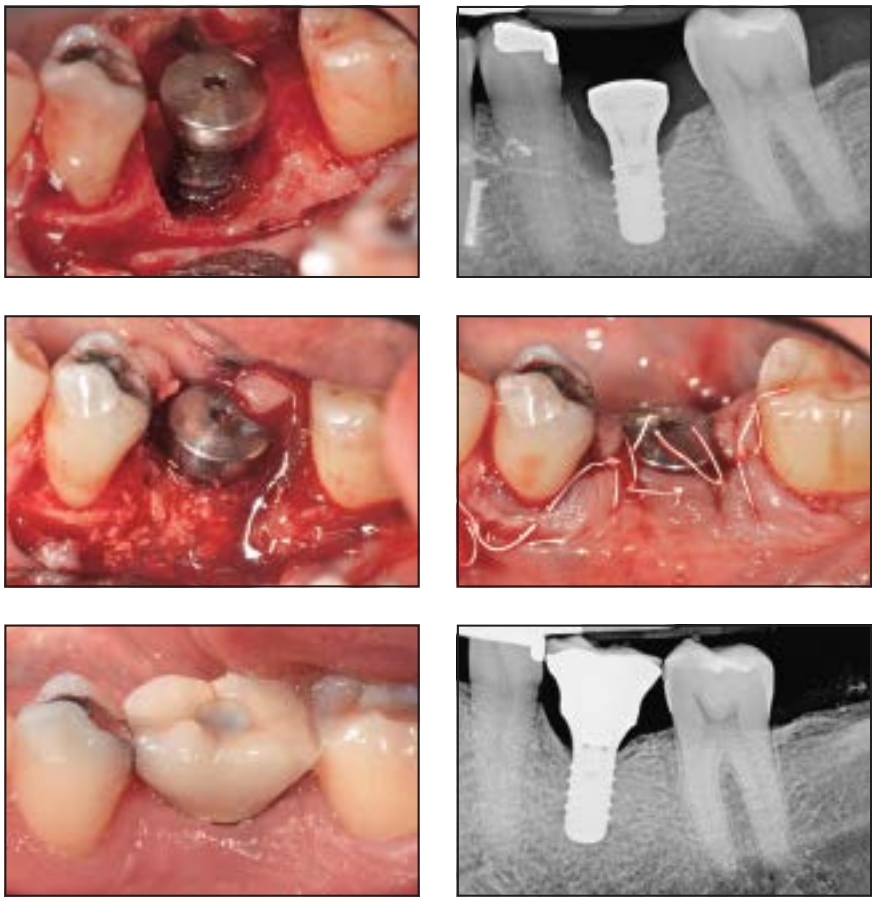

Fig 1 (left) *A 56-year-old man presented with an implant with a healing abutment in the mandibular left first molar area (36) placed 3 years prior to presenting. The crown was removed due to a peri-implantitis lesion, and probing depth and clinical attachment loss were both recorded as 8 mm.*

Fig 2 (right) *A radiograph of the implant reveals 4.58 mm of bone loss.*

Fig 3 (left) *The implant was treated with the regenerative protocol, including surface decontamination, followed by a composite graft of mineralized freeze-dried bone allograft biologics. The graft was contained by a resorbable barrier placed over it.*

Fig 4 (right) *The flap was coronally positioned and sutured with expanded polytetrafluoroethylene sutures (GoreTex, W.L. Gore & Associates).*

Fig 5a (left) *Clinical photo 2.5 years following treatment of the restored implant. Probing depth and clinical attachment levels were both 3 mm.*

Fig 5b (right) *Radiograph showing resolution of the defect with bone fill of 3.86 mm (taken 2 years postsurgery).*

contact on mesial and distal surfaces. For analysis of the data, the mesial and distal measurement values were averaged. The images were standardized for contrast and density prior to measurements. The dimensions in the images were calibrated into millimeters by using the implant length or thread distance as a known reference length to transform the length described in pixels into true millimeter values. Because the vertical calibration direction is the same direction as the bone height measurement, image distortions such as foreshortening or elongation are automatically corrected. The image calibration and measurements were performed using the Image-Pro Insight 9 image analysis software package (Media-Cyberbetics) on computers operating on Windows 7.

Treatment protocol

Local anesthesia was administered and full thickness flaps were elevated with periosteal release to allow for adequate flap mobilization for visualization, implant surface access, and coronal advancement at time of closure. Surface debridement was performed as previously described except for substitution of minocycline (50mg/ml) (for tetracycline) and included 0.12% chlorhexidine gluconate, which were applied separately for 45 seconds each with cotton pellets or a dedicated brush and washed for 60 seconds each with sterile saline. Use of the air powder abrasive preceded the chemotherapeutic treatment and was followed by a saline spray that was as described previously. The decontaminated surface was dried, and enamel matrix derivative (Emdogain, Straumann) or platelet-derived growth factor (PDGF) (Gem 21, Osteohealth) (based on availability) was then placed on the surface. The remaining guided bone regeneration (GBR) procedures and the postsurgical follow-ups were as described previously (Figs 1 to 5).

Table 1 Mean soft tissue changes from baseline to time of follow-up

No. of subjects	100
No. of implants	168
Pretreatment MR (mm)	1.14 ± 1.78 (range: 0–7)
Soft tissue gain (mm)	0.52 ± 1.44 (range: 0–5)
Pretreatment PD (mm)	8.10 ± 2.53 (range: 5–15)
PD reduction (mm)	5.10 ± 2.20 (range: 2–12)
Time of final postoperative measurement (y)	3.60 ± 1.86 (range: 2–10)
No. of sites with preoperative BoP	168
No. of sites with postoperative BoP	15

MR = mucosal recession; PD = probing depth; BoP = bleeding on probing.

Table 2 Bone level changes

	n	Mean (mm)	SD (mm)
Preoperative	167	3.8	2.28
Postoperative	167	2.03	1.49
Difference	166	1.77	1.99

SD = standard deviation.

In a number of cases, more than one surgical procedure following the previously described protocol was required to achieve the resolution of BoP and decrease in PD required for successful home care and professional maintenance. If additional surgery was performed, it was performed at least 6 months after the initial surgery and at least 2 years prior to final evaluation and recording.

Results

A total of 170 consecutively treated implants in 100 patients were included in the present study. Average patient age was 58.08 years with a range of 20 to 83 years. The population consisted of 47 men and 53 women. Of the implants, 19 were placed in smokers and 151 in nonsmokers. The mean time of postsurgical measurements was 3.60 years with a range of 2 to 10 years. Of the 170 implants treated, 2 were lost, both at 6 months postsurgery, yielding a 98.8% survival rate. The mean soft tissue changes and study times are shown in Table 1. The mean probing depth reduction of the 168 implants was 5.10 mm, with a range of 2 to 12 mm. Similar to the first study, no implant exhibited postsurgical marginal recession. In fact, there was an average gain in marginal soft tissue levels of 0.5 mm, with a range of 0 to 5 mm. BoP was reduced from 168 to 15 when assessed preoperatively and compared to the final evaluation, representing a 91.1% reduction. Mean bone level changes are reflected in Table 2, where the mean preoperative bone level was 3.80 mm (with a range of 3.01 to 9.56 mm) and the average bone gain was 1.77 mm (with a range of 0.4 to 9.0 mm).

A total of 140 implants had 1 surgical procedure, 18 implants required 1 additional surgery, and 10 implants required 2 additional surgical procedures to reach the desired outcomes.

Discussion

The results of the present case series confirm and add to the success of the protocol used in a previous publication that used the same regenerative approach for the treatment of peri-implantitis.[16] The present study documents failure of the technique in 2 of the 170 implants treated. This overall survival rate of 98.8% with 2 to 10 years follow-up suggests that the technique is predictable and outcomes can be maintained when patients are kept on a strict schedule of 2- to 3-month professional maintenance and monitoring. The importance of the latter has been discussed in a comparison study of subjects with and without preventive maintenance over a 5-year period.[19] Although the cases in the present series were consecutively treated, the fact that treatment was not attempted on a number of implants with peri-implantitis underscores case selection as an important criteria for predictable success. The authors did not attempt treatment at sites where, in their judgment, complete surface decontamination of the implant(s) was not possible because of inadequate access.

This emphasizes the importance of surface decontamination in the technique used. In publications reporting on microbial infection causing implant failure and factors affecting biofilm adhesion on osseointegrated implants, it becomes apparent that any technique used to treat peri-implantitis should include a method or a combination of methods leading to complete removal of the surface pathogens (ie, biofilm).[20] Moreover, in the 2 cases where implants were lost, surface access was limited and complete decontamination was not achieved. Both of these implants that had to be removed were mandibular left second molars that were part of fixed prostheses and exhibited no gingiva.

Two recent literature reviews on implant surface detoxification presented the advantages and risks of the various mechanical and chemotherapeutic methods of implant surface decontamination.[21,22] The conclusion of those reviews were *(1)* that comparative studies were too variable to recommend only one protocol and *(2)* that all technologies/agents were shown to be equally effective. This may be true if access is available to the contaminated implant surface. However, the morphology and location of many peri-implant defects preclude the agents used from reaching and removing the biofilm.[23] The rationale for using the air powder abrasive, saline sprays, chemotherapeutic agents, minocycline 50 mg/ml, and 0.12% chlorhexidine takes into account several factors. First, they are able to reach most exposed and infected implant surfaces. The authors avoided the risk of air embolism with the air powder abrasive and chemical flow outside of the desired area by isolating and packing the area surrounding the implant surface, bone, and throat with moist gauze pads to protect the soft tissue, periosteum, oral tissues, and open spaces. The value of the air abrasive used with powder and followed by saline alone was demonstrated in a recent literature review[24] and in an animal study that concluded that re-osseointegration can occur after an implant that has been contaminated by plaque is sufficiently cleaned, and that re-osseointegration can occur even with rough surfaces.[25] However, lack of human histology to verify re-osseointegration forces clinicians to rely on clinical surrogate parameters such as decrease of BoP, PD reduction, and radiographic evidence of bone fill in evaluating a regenerative protocol for treating peri-implantitis. A recent systematic review reported that seven studies showed that treatment outcomes were successful in a majority of patients at 12 months.[14] Although this short-term success is encouraging, lack of disease resolution and progression or recurrence of disease requires longer-term follow-up. The present study evaluated the above clinical parameters 2 to 10 years postsurgery with an average time of final follow-up of 3.60 years. The findings of an average PD reduction of 5.10 mm, an average coronal soft tissue gain of 0.5 mm, an average bone level gain of 1.77 mm, and an absence of BoP in 91% of the implants treated compares very favorably with published long-term outcomes.

A number of longer-term (> 12 month) studies used various methods of SD with GBR and reported positive outcomes in reduction of BoP and PD and radiographic bone gain. Roos-Jansaker et al,[17] Deppe et al,[26] and Schwarz et al[27–29] all reported positive clinical outcomes using hydrogen peroxide and saline, implantoplasty, air powder abrasive and CO_2 laser, and cotton-soaked saline pellets with and without a CO_2 laser for SD.

Other 4- to 5-year follow-up studies are described and discussed in the systematic literature reviews.[14,15] A number of clinical points can be gleaned from an evaluation of the present and previously mentioned studies. First, it appears that positive clinical outcomes can be achieved with various effective methods of SD provided access can be obtained to the infected implant surfaces. Any method of reaching these surfaces (eg, air powder abrasive, saline spray, chemical use, lasers) may be effective in decontaminating them. The importance of SD was shown in the present study: in the two implants where complete SD could not be achieved because of limited access, treatment failed and the implants had to be removed 6 months postsurgery. It also appears that GBR is effective in treating peri-implantitis provided it is performed correctly. In evaluating studies that concluded that a membrane covering a bone graft does not improve outcomes one must also look at the graft material used and its ability to be contained relative to the defect morphology.[17] When using particulate graft material as in the present

study, noncontained defects require a membrane to prevent particle migration. In the present study, the authors treated surpracrestal (noncontained) defects as well as walled defects with intrabony components and achieved PD reduction and bone fill that compares very favorably with other treatment modalities. Moreover, implantoplasty and soft tissue resection or apical flap repositioning was not performed because it invariably results in marginal recession, which is highly undesirable for most patients besides being in some instances rather difficult to maintain. In comparison with the others cited, the present study is the only one in which no marginal recession was seen; in fact, the postsurgical gingival margin was coronal (average 0.5 mm) to the presurgical position. This is extremely important for implant maintenance as well as for postsurgical esthetic outcomes. In the present authors' opinion, the use of subepithelial connective tissue grafts (SCTGs) in areas where gingiva was lacking and the coronal advancement of the flaps contributed to this desired outcome. The use of SCTGs in the present series as published in the original protocol was tested in a recent study by Schwarz et al, who found that the addition of SCTG to their protocol increased the mean mucosal height (0.07 mm) in the 13 implants treated.[30]

The combination of mechanical, chemical, air powder, and saline sprays used in the current study were effective as evidenced by the positive long-term clinical results. In 168 out of the 170 implants, the surfaces devoid of bone and contaminated with biofilm were accessible for decontamination. In addition, since there was heterogeneity among implant types treated (eg, titanium plasma spray, electronically obtained roughening, sandblasted and acid etched surfaces) the protocol appears to be generalizable. The GBR procedure performed in the current study used two types of grafting materials, mineralized freeze-dried bone allograft and anorganic bovine bone matrix combined with recombinant platelet-derived growth factor-BB (PDGF-BB). Use of the two biologics, enamel matrix derivative and PDGF, together was shown to be advantageous in improving wound healing in periodontal defects.[31] The authors felt the improvement found in the fibroblast response in that study could work as well with peri-implantitis defects treated with the regenerative protocol used in the present study. Moreover, as mitogens, these two agents use different pathways, which may provide a synergy to their treatment effects.

One factor seldom mentioned in the previous ≥ 2 year or even shorter-term studies on peri-implantitis is that achieving stable outcomes often requires more than one surgical procedure. In the present study, 18 implants required 2 additional surgeries and 10 implants required 1 additional procedure. Similar to the treatment of periodontal osseous defects, definitive outcomes often require more than 1 surgical procedure. The clinician must evaluate whether the BoP and PD reductions following surgical healing are sufficient for patient and professional maintenance to produce a stable result. The authors also believe that the current study protocol's inclusion of maintenance and monitoring every 2 to 3 months contributed to the positive outcomes obtained 2 to 10 years posttreatment.

Conclusions

The current study demonstrated that the protocol used in treating peri-implantitis produced positive clinical outcomes in terms of reduction in BoP and PDs, bone gain, and implant survival. More clinical studies using this protocol in randomized controlled trials are needed, as are histological studies testing the correlation of the positive clinical parameters with re-osseointegration. However, in light of the positive outcomes 2 to 10 years postsurgery obtained with this protocol, the alternative option of explantation of an implant affected by moderate to advanced peri-implantitis and the subsequent reconstructive surgery, pain, and cost necessary to insert a replacement implant should be considered by all clinicians faced with treatment versus explantation.

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