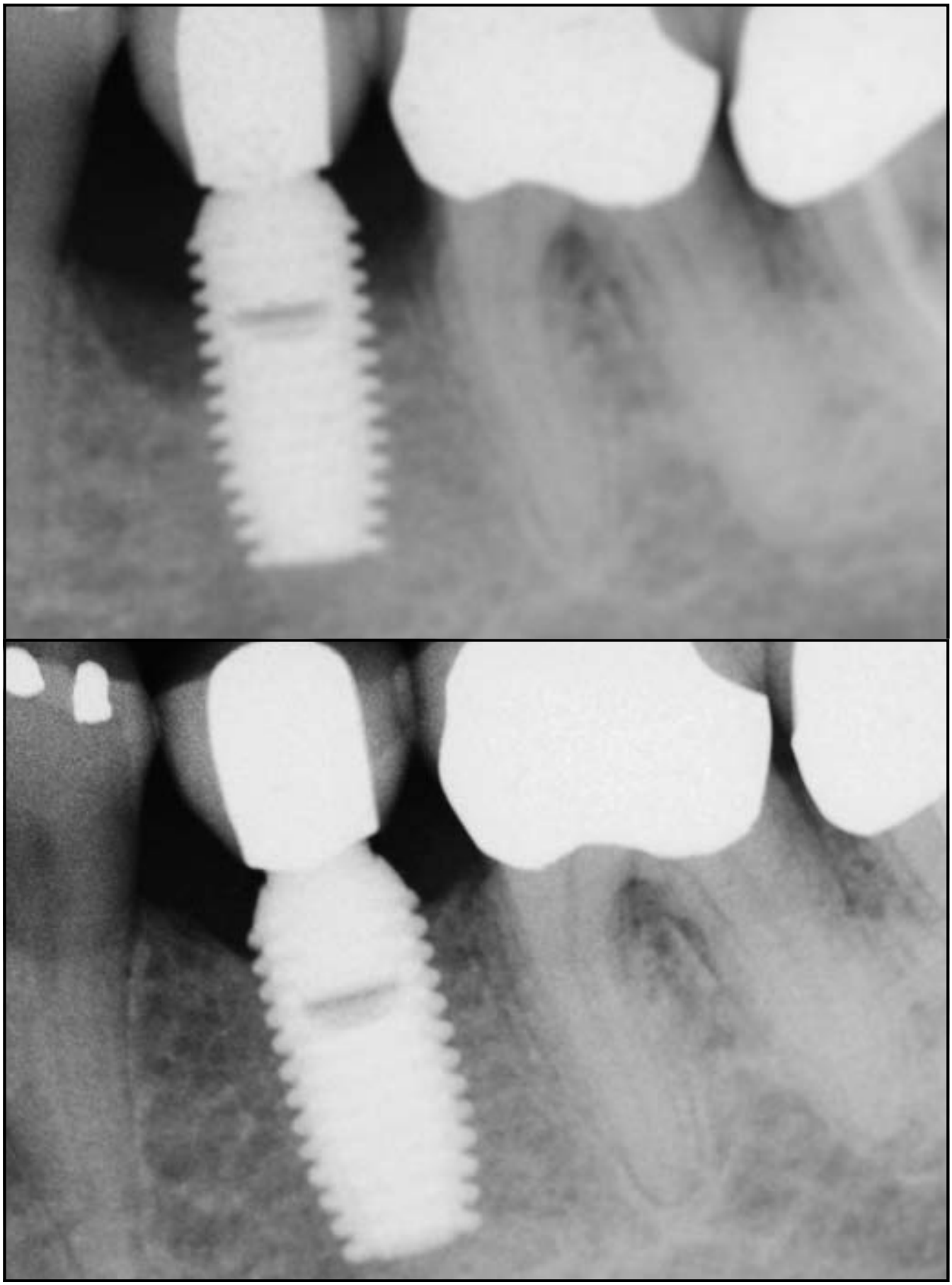
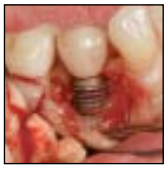


Successful Management of Peri-Implantitis with a Regenerative Approach: A Consecutive Series of 51 Treated Implants with 3- to 7.5-Year Follow-up



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The results of a case series of 51 consecutively treated, peri-implantitis–affected implants in 38 patients with follow-up measurements from 3 to 7.5 years are presented. Each implant displayed bleeding on probing, probing depths ≥ 6 mm, and bone loss ≥ 4 mm prior to surgery. A successful regenerative approach including surface decontamination, use of enamel matrix derivative, a combination of platelet-derived growth factor with anorganic bovine bone or mineralized freeze-dried bone, and coverage with a collagen membrane or a subepithelial connective tissue graft was employed in all cases. Patients were divided into two groups. Group 1 included patients in which the greatest defect depth was visible on radiographs; group 2 included patients in which the greatest loss of bone was on the facial or oral aspect of the implant. Bone level changes in patients in group 2 were determined by probe sounding under local anesthesia. Probing depth reductions at 3 to 7.5 years of follow-up were 5.4 and 5.1 mm in groups 1 and 2, respectively. Concomitant bone level gain was 3.75 mm in group 1 and 3.0 mm in group 2. No implant in either group lost bone throughout the duration of the study. The results to date with this regenerative approach for the treatment of peri-implantitis appear to be encouraging. (Int J Periodontics Restorative Dent 2012;32:11–20.)

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Peri-implantitis has been defined as an inflammatory process affecting the hard and soft tissues surrounding an implant in function.[1] This term was first introduced in the late 1980s,[2] and since, there have been a number of articles discussing its diagnosis and etiology. More recently, there have been six systematic reviews regarding the treatment of peri-implantitis.[3–8] The authors concluded that while many different treatment algorithms have been offered, including nonsurgical mechanical debridement[9,10] with or without the use of local or systemic antibiotics,[11–13] the addition of lasers to these treatments,[14,15] the use of access flaps combined with antimicrobial therapy, and regenerative procedures,[16–23] none of these approaches have evidence corroborating their long-term predictability. At best, a 5-year clinical follow-up study using systemic antibiotics and access surgery demonstrated a 58% success rate in resolution of the peri-implant disease.[18]

Bacterial plaque typically has been implicated as the cause of peri-implantitis, and as such, treatment

must include anti-infective measures. Hence, the primary objective of surgical treatment is to gain access to the affected implant surface for debridement and decontamination. Moreover, the ideal management of peri-implant disease includes not only control of the infection and detoxification of the implant surface, but also halting further loss of tissue(s), regeneration of lost soft and hard tissues, and reosseointegration of the exposed implant surfaces. This option of therapy would appear to be preferential for both the patient and clinician over an approach where removal of the integrated but ailing peri-implantitis–affected implant is performed. By maintaining the implant, there is a significant reduction in morbidity, time and cost of restoring the explanted site, and if possible, placing a replacement implant. Furthermore, replacement implants have been documented to have lower survival rates than the initial failed implant.[24]

Repair of peri-implantitis–related defects using surgical debridement together with guided bone regeneration has demonstrated feasibility in animal models where histologic proof has been offered and, more recently, in a human prospective case series where clinical measures were used as evidence of treatment success.[20,21] The latter report documented the management of 36 cases of peri-implantitis–associated bone loss in 22 patients followed for 1 year and concluded that the method used was effective in reducing probing depths by an average of 4 mm and bone defects by an average of 3.5 mm.[20] To date, however, there has been no long-term documentation in humans of soft tissue probing reduction and clinical repair of lost bone around a peri-implantitis–affected implant. The purpose of this case series conducted in a clinical private practice is to chronicle a successful regenerative treatment approach that also demonstrates long-term efficacy in the management of peri-implantitis.

Method and materials

This consecutive case series reports on 38 patients (age range, 29 to 81 years) with 51 implants diagnosed with peri-implantitis that were treated and followed for a minimum of 3 years and up to 7.5 years (mean, 3.7 years). All 51 implants had been restored for at least 3 years. The implants consisted of various types and numbers from the following manufacturers: Biomet 3i (n = 21), Nobel Biocare (n = 12), IMZ (n = 4), Zimmer (n = 3), BioHorizons (n = 2), Frialit (n = 2), Straumann (n = 2), AstraTech (n = 2), Bicon (n = 2), and Innova (n = 1). None of the peri-implantitis–affected implants demonstrated mobility or peri-implant radiolucency around the implant surfaces that were still surrounded by bone. The implants were examined for probing depth (PD), bleeding on probing (BoP), and radiographic evidence of bone loss. All measurements were made using a UNC periodontal probe that measured up to 15 mm (Hu-Friedy) around six aspects of the implant. The deepest PD was recorded for each implant. Measurements were also recorded from the buccal gingival margin to the implant-abutment junction (IAJ) to determine mucosal recession (MR). The authors were calibrated for reproducibility prior to and during the case series. BoP was recorded using a dichotomous index for its presence or absence by waiting a period of 15 seconds following light probing and reporting a positive result if bleeding occurred.[25] At each postsurgical visit, BoP, PD, and MR were again recorded.

Implants reported on had to demonstrate BoP, PDs ≥ 6 mm, and peri-implant bone loss ≥ 4 mm, as measured from the implant platform. Bone loss was determined by radiographic evidence (group 1). However, when the greatest bone loss could not be discerned from the periapical radiographs (ie, on the facial or oral aspect of the implant), bone sounding of the crestal bone was used under local anesthesia. This was performed at the time of surgery and at postrestoration recall visits. To measure this, the IAJ was used as the fixed reference point (group 2). For all group 1 defects, radiographic measurements were made by an independent examiner who used a previously described method to digitize and standardize all measurements.[26] Periapical radiographs were taken prior to and immediately following restoration and at 3- to 6-month intervals at the patients' recall visits. All radiographs were standardized in their exposure and

kept consistent with the type of radiographic film (Kodak Insight, Kodak) or digital software (Dexis, Dexis LLC) employed. Comparisons of the presurgical and most recent postsurgical radiographs were made to calculate bone changes for the defects. For implants where the deepest bone loss was probed and sounded on the facial or oral aspects (group 2), measurements were made clinically using a periodontal probe at the time of flap surgery, and postrestoration sounding was performed under local anesthesia to the deepest part of the osseous defect on the same aspect of the implant. Photographs were taken of the probe's position at the time of flap surgery to serve as a reference to facilitate future positioning with bone sounding. These measurements were made by an examiner who did not perform the patient's surgery and were rounded to the nearest 1 mm.

Patients received all necessary periodontal treatment prior to the initiation of surgical care for periimplantitis. At least 1 month prior to surgery, full-mouth debridement was performed, and all patients had to demonstrate adequate plaque control to continue with therapy.

Treatment protocol

Anesthesia was obtained, and full-thickness flaps were elevated with a periosteal release to allow for adequate flap mobilization for both visualization and coronal advancement at the time of closure. Implants were not treated (ie, excluded) if there was incomplete access to all exposed surfaces at the time of flap reflection or if an implant was deemed hopeless (≥ 80% bone loss, pain, or mobility). In either situation, the implant was explanted. Surface decontamination was performed in conjunction with thorough debridement of the osseous defects and implant surfaces using special graphite curettes (Gracey 13/14 graphite curette, Hu-Friedy) or titanium tips (H6/H7 and 204 SD curettes, Salvin Dental). Following mechanical debridement, surface decontamination in all cases consisted of a six-step protocol: *(1)* application of fine bicarbonate powder for 60 seconds using an air-abrasive device (Prophy-Jet, Dentsply) with a special contra-angled tip to reach all areas of the exposed implant surfaces; *(2)* 60-second irrigation with sterile saline delivered by an irrigation device (Infinity Irrigator, Ace Surgical); *(3)* application of tetracycline (50 mg/mL) with cotton pellets or a brush (30 seconds); *(4)* a second exposure of the implant's surface to bicarbonate air abrasion (60 seconds); *(5)* application of 0.12% chlorhexidine gluconate (Peridex Oral Rinse, 3M ESPE), applied to the implant surfaces with cotton pellets soaked in the solution (30 seconds); and *(6)* 60- to 90-second re-irrigation with sterile saline using the same device from step 2. Enamel matrix derivative (Straumann) was applied to the decontaminated implant surface, with care taken to isolate the area and avoid contamination with either saliva or blood. The defects were then filled by either anorganic bovine bone mineral (Bio-Oss, Geistlich) or mineralized bone allograft (Puros, Zimmer), which had been hydrated with platelet-derived growth factor (Gem 21, Osteohealth) at least 5 minutes prior to graft placement.

In cases where limited (< 2 mm) height of keratinized tissue was present, a subepithelial connective tissue graft (SCTG) was harvested from the palate and used as a barrier to contain the biologic material. In cases where there was sufficient keratinized tissue (≥ 2 mm), an absorbable collagen membrane (Bio-Gide, Geistlich; Ossix, OraPharma; or Mucograft, Osteohealth) was substituted for the SCTG to contain the biologic material and provide a barrier function. Suturing was accomplished with one of the following: expanded polytetrafluorotheylene (Gore-Tex, WL Gore), 4-0 silk (Ethicon), 4-0 Vicryl (Ethicon), or 4-0 chromic gut (Ethicon) sutures. Vertical incisions, when needed, were closed with 4-0 or 5-0 chromic gut (Ethicon) or 4-0 or 5-0 Vicryl (Ethicon) sutures using an interrupted technique (Figs 1a to 1i and 2a to 2e).

All patients were placed on systemic antibiotics for postoperative infection control. Antibiotics were started as a loading dose 1 hour prior to surgery by oral administration. Patients were given amoxicillin 2,000 mg (Novopharm) or, if the patient was allergic to amoxicillin, clindamycin 600 mg (Ohm Laboratories). Patients continued on

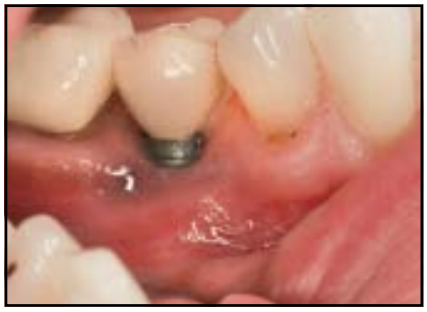


Fig 1a *Pretreatment photograph of an implant at the mandibular left second premolar implant site. There was no keratinized tissue and 3 mm of buccal recession.*

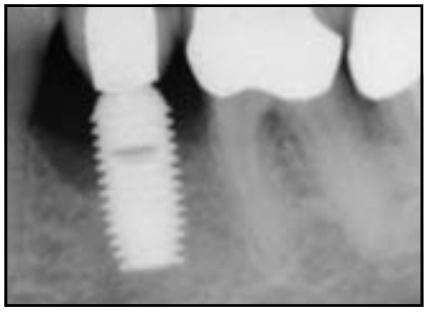


Fig 1b *Radiograph depicting a measured 5.47-mm bone loss.*

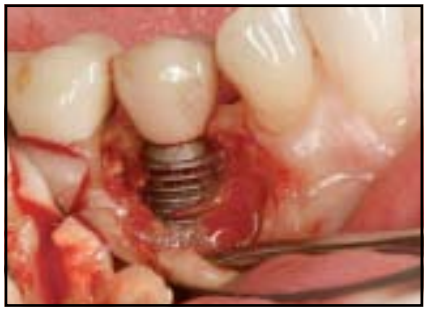


Fig 1c *Flap reflection revealed implant surface contamination and biofilm.*

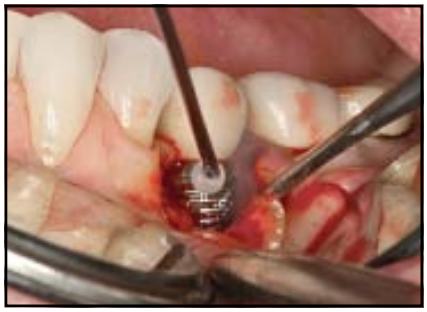


Fig 1d *Following surface decontamination of the implant and defect debridement, enamel matrix derivative was applied to the implant surface.*

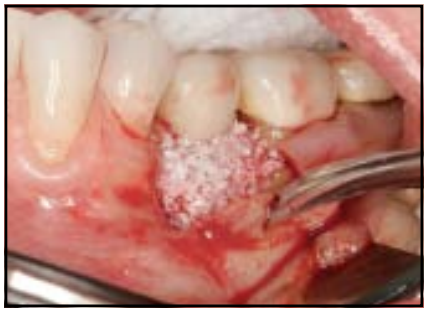


Fig 1e *A bone substitute graft of anorganic bovine bone and platelet-derived growth factor was placed over the exposed implant surface.*

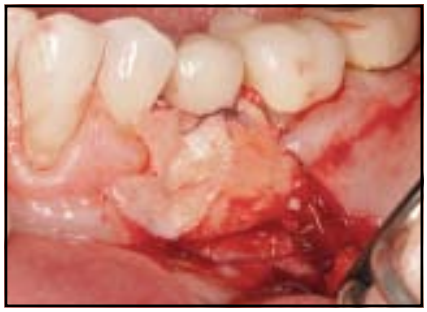


Fig 1f *A subepithelial connective tissue graft obtained from the palate was sutured over the anorganic bovine bone and platelet-derived growth factor.*

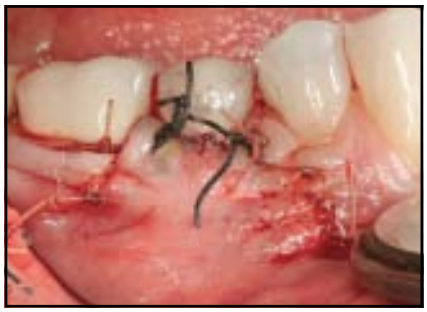


Fig 1g *The flap was advanced by means of periosteal and vertical releasing incisions and then sutured coronally.*

Fig 1h *At 6 years postsurgery, PD was reduced from 8 to 3 mm, representing a 5-mm reduction. Note the 3-mm coverage of the previously exposed implant surface.*

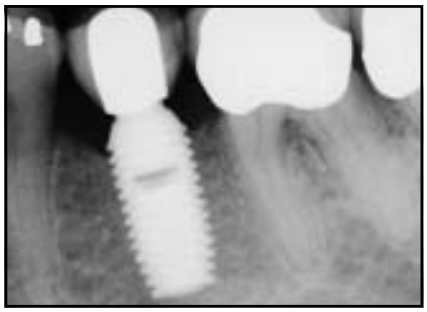


Fig 1i *Six-year postsurgical radiograph demonstrating 4.48 mm of bone growth.*

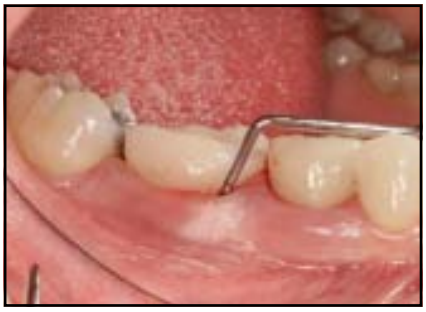


Fig 2a *Peri-implantitis–affected implant at the mandibular left first molar with BoP and pretreatment PD of 9 mm.*

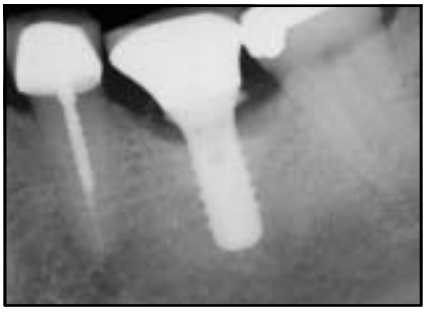


Fig 2b *Radiograph revealing 4 mm of bone loss and evidence of retained subgingival cement.*

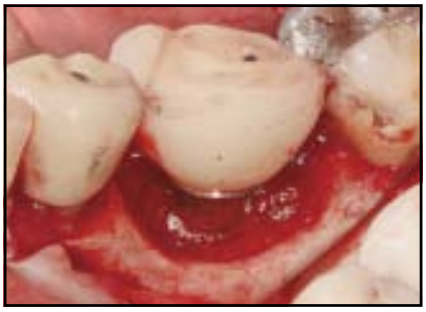


Fig 2c *The defect was debrided, cement was removed from the implant surface, and surface decontamination was performed.*

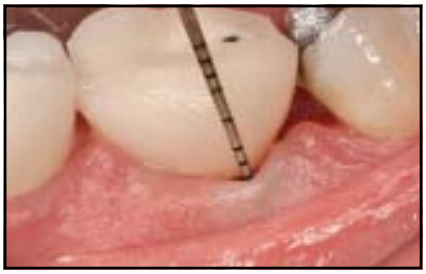
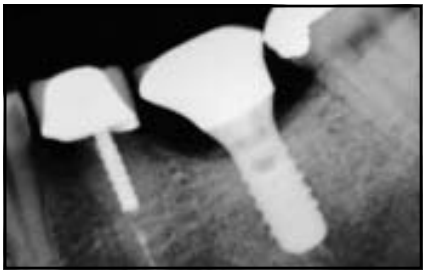


Fig 2d (left) *Three-year postsurgery PD measurement was 1.0 mm, which represents an 8-mm reduction.*

Fig 2e (right) *Radiographs and sounding of the implant revealed a bone defect depth reduction from a presurgical 4 mm to 2 mm at 3 years postsurgery.*



amoxicillin 500 mg tid or clindamycin 150 mg qid for an additional 10 days. Patients rinsed 4 to 5 times daily with isotonic saline or magnesium sulfate (Epsom salt, San Francisco Salt Company) for those with high blood pressure. Solutions were made by diluting half a teaspoon of the salt into 8 ounces of warm water. Patients also rinsed with 0.12% chlorhexidine twice a day for 2 weeks immediately following the surgery.

Patients were seen 10 to 14 days postsurgery for observation and suture removal and then weekly for the next 6 weeks. At each visit, the surgical area was debrided, and oral hygiene homecare procedures were reinforced. These consisted of saline rinses and light brushing with a soft toothbrush (Ultra Suave, PHB) using a 1:1 mixture of 3% hydrogen peroxide and water. All patients were then placed on a 6- to 8-week recall schedule following completion of treatment. At each recall visit, surface debridement was performed with rubber cups and brushes using 3% hydrogen peroxide diluted 1:1 with sterile saline. All subgingival biofilm and staining were removed using a rubber cup and pumice. Two months postsurgery, patients were instructed to begin using an interproximal brush (Proxabrush, Butler) soaked for 1 minute in 0.12% chlorhexidine three times a day at the surgical site. Six patients required multiple surgical procedures (two to three) to obtain the desired outcome. At the first recall visit and every 3 months thereafter, periapical radiographs were taken. Sites were not

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

	Group 1	Group 2
No. of subjects	15	23
No. of implants	19	32
Pretreatment MR (mm)	2.2 ± 2.1 (range, 0–7)	1.6 ± 1.9 (range, 0–6)
Soft tissue gain (mm)	1.3 ± 1.4 (range, 0–4)	1.0 ± 1.2 (range, 0–4)
Pretreatment PD (mm)	8.8 ± 1.9 (range, 5–12)	7.9 ± 1.8 (range, 5–13)
PD reduction (mm)	5.4 ± 1.5 (range, 3–8)	5.1 ± 1.9 (range, 3–10)
Time of final postoperative measurement (y)	4.2 ± 1.6 (range, 3–7)	3.5 ± 1.1 (range, 3–7.5)
No. of sites with postoperative BoP	4	5

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

probed until 6 months postsurgery, and then at every recall appointment thereafter. Radiographs of the treated implants were taken at 6-month intervals.

Results

Group 1, where the deepest bone loss was proximal and could be viewed by periapical radiographs, consisted of 15 patients (6 men, 9 women) with 19 implants, while group 2, where bone loss was greatest at the facial or oral aspect and bone sounding was needed, included 23 patients (12 men, 11 women) contributing 32 implants. The mean age for both groups was approximately 58 years (range, 27 to 81 years). Table 1 summarizes the soft tissue changes pre- and posttreatment for groups 1 and 2. Favorable improvements were recorded in soft tissue parameters, with BoP decreased to 4 of 19 and 5 of 32 sites, respectively, at

Table 2 **Bone level changes (mm)**

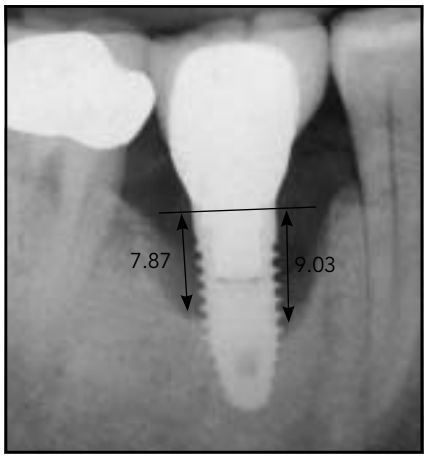
	Group 1 (radiographic)			Group 2 (bone sounding)		
	n	Mean	SD	n	Mean	SD
Preoperative	19	6.44	1.849	32	4.30	1.004
Postoperative	19	2.69	1.495	32	1.30	0.609
Difference	19	3.75	1.537	32	3.00	0.822

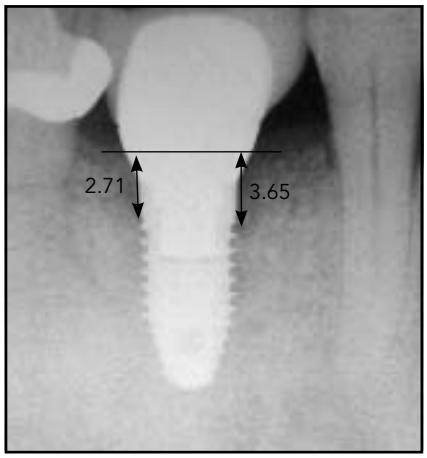
SD = standard deviation.

the time of final evaluation. Group 1 had a mean PD reduction of 5.4 mm (range, 3 to 8 mm) following a mean time to final evaluation of 4.2 years, while group 2 had a PD reduction of 5.1 mm (range, 3 to 10 mm) with a mean time to final evaluation of 3.5 years. Hard tissue improvements were consistent with those seen for the soft tissue (Table 2). For group 1, hard tissue improvement was 3.75 mm, as measured from radiographs, while in group 2, where bone sounding was used, 3.00 mm of improvement on average was achieved. No implant in either group lost bone over the course of the study. Moreover, no implant recorded an increase in mucosal buccal recession, as measured at the final evaluation following surgery. In fact, in both groups 1 and 2, there was a mean soft tissue coverage of the presurgical exposed facial implant surface of 1.3 and 1.0 mm, respectively.

Discussion

The treatment protocol described in this case series for peri-implantitis has demonstrated encouraging results to date. Reviews of nonsurgical approaches have concluded that outcomes with this particular method of care are not predictable. Moreover, surgical access, surface decontamination, and defect debridement have limited long-term reports of success.[4–7,23] Although the follow-up period for the 51 implants





Figs 3a and 3b *Radiographic measurement of the* (left) *pre- and* (right) *postoperative bone level changes of a patient in group 1 showing a reduction of the bone defect of 5.38 mm on the mesial aspect and 5.16 mm on the distal aspect 7 years following treatment.*

included in the current case series extends from a minimum of 3 years to 7.5 years, the outcomes to date appear to be better than previous reports.[18,20] Bone level improvement in the current case series averaged 3.75 mm based on radiographs and 3.00 mm based on sounding, with ranges of 1.94 to 6.89 mm and 1.30 to 4.30 mm, respectively. These gains have remained stable for an average of 4.1 years (Figs 3a and 3b).

The surface decontamination protocol used in the present consecutive case series study was empirically derived and based solely on the experience of the authors. However, a recent publication reported on a similar air-abrasive decontamination method that employed sterile saline on implants with experimentally induced peri-implantitis in dogs. They concluded that, "Cleansing of a previously plaque-contaminated implant is sufficient for re-osseointegration to occur, and rough surfaces can allow re-osseointegration."[27] The concept that surface decontamination can be performed in the mouth as part of therapy was encouraging in that the method of surface decontamination in the present study relies heavily on air-abrasive and saline irrigation procedures as part of the treatment of peri-implantitis–affected implants.

Any method of surface decontamination that does not allow for visualization of the implant surface may be compromised. A recent study testing eight different cements used for implant prostheses concluded that, "Some types of cements commonly used for the cementation of implant-supported prostheses have poor radiodensity and may not be detectable following radiographic examination."[28] This emphasizes the importance of the current management strategy being surgical in its approach to facilitate direct visualization. To date, other methods of surface decontamination have not demonstrated a significant impact on clinical outcomes in the treatment of peri-implantitis, perhaps in part because of the inability to see the surface of the implant following its treatment.[12–15]

The application of enamel matrix derivative to the thoroughly decontaminated implant surface is extremely important in the opinion of the authors. This complex of enamel proteins, derived from developing porcine tooth buds, has shown an ability to enhance hard and soft tissue wound healing and up-regulate angiogenic activity.[29,30] Enamel matrix derivative has been successfully used to regenerate intrabony defects around periodontally involved teeth.[31,32] Moreover, in two studies, when enamel matrix derivative was used in combination with an allograft or bovine porous

bone mineral, an enhanced hard tissue healing response occurred compared with the sites where enamel matrix derivative was used alone after root modification.[33,34] In the present study, the defects were filled with a highly purified protein of tissue-engineered recombinant human platelet-derived growth factor (rhPDGF-BB) combined with bovine porous bone mineral. PDGF-BB demonstrated an ability to enhance periodontal bone fill and improve attachment levels in a pivotal multicenter randomized controlled trial[35] and improve soft tissue healing in the treatment of recession defects with coronally advanced flaps.[36] This information, along with a decision tree related to the use of enamel matrix derivative with grafts and membrane barriers around periodontally involved teeth,[37] was the basis for these peri-implantitis defects being filled with either bovine porous bone mineral or mineralized freeze-dried bone allograft in combination with rhPDGF-BB.

A collagen membrane was used for graft containment in those sites where there was an adequate band of keratinized tissue. In those cases where there were limited bands (< 2 mm) of keratinized tissue, an SCTG from a palatal donor site was used as the barrier instead of the collagen membrane.[38] Corroboration for using a bone substitute with a barrier comes from a study reporting 3 years of stability for regenerated bone around peri-implantitis lesions.[23] Furthermore, the present case series also used a coronally advanced flap to further protect the healing wound.[36]

A comparison of the results obtained in this case series, which documents a 5.4- and 5.1-mm reduction in PD and bone level gains of 3.5 and 3.0 mm in the two groups, respectively, over a period of 3 to 7.5 years, compares favorably with two previous studies with 1- and 3-year follow-ups.[20,21] Moreover, at final evaluation, no implants lost bone, and the mucosal margins were more coronal than pretreatment soft tissue levels.

One limitation to any human clinical study is the lack of histology needed to determine the nature of the newly formed tissue. Past reports of reosseointegration in animal models have not been encouraging.[8,19,39] Therefore, the protocol described in the current case series needs histologic qualification of whether reosseointegration occurred. Moreover, procedures and materials used in the current protocol must be evaluated clinically in a greater number of patients, over a longer follow-up, and in randomized controlled trials.

Conclusion

The alternative of removing a failed implant that is immobile but affected with peri-implantitis exposes the patient to the risk of bone, tooth, or nerve damage. The current method of decontamination and subsequent repair warrants consideration given the downside of the former, more aggressive approach.

Acknowledgment

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