Reosseointegration After Regenerative Surgical Therapy Using a Synthetic Bone Substitute for Peri-implantitis: Human Autopsy Study

Sungtae Kim, DDS, PhD1
Kyung-Seok Hu, DDS, PhD2
Ui-Won Jung, DDS, PhD3

Bone regeneration and reosseointegration around a dental implant were radiographically and histologically analyzed after regenerative treatment for peri-implantitis, using a case from a human autopsy. A block specimen including the tissue around the implants was obtained from the patient, who died from cancer 20 months after regenerative surgery using a synthetic bone substitute to treat peri-implantitis. Microcomputed tomographic and histologic analyses were performed. Three-wall intrabony defects at the implant placed at the site of the mandibular left first molar and a circumferential defect at the implant at the site of the mandibular left second molar were substantially filled with newly formed bone and residual bone substitute particles, and reosseointegration on the previously exposed implant surface was histologically observed. Int J Periodontics Restorative Dent 2018;38:585–591. doi: 10.11607/prd.3046

Nonsurgical and surgical therapies have been used for the management of peri-implant disease, including peri-implant mucositis and peri-implantitis, with wide variation in clinical outcomes reported.1,2 Peri-implantitis, which involves peri-implant bone loss, usually requires surgical intervention for better access and visibility.1,3 Depending on the defect configuration, regenerative surgical therapy could be selectively applied.4,5 In addition, peri-implantitis that has been properly managed with regenerative therapy has shown favorable treatment outcomes.6–8

In a case series with reentry of the surgical site, new bone formation was found after regenerative therapy.8 Mean bone fill and mean bone gain values were 91.3% and 4.88 mm, respectively. Regenerative therapy was effective, irrespective of submergence or nonsubmergence of the implant after surgery. However, reosseointegration on the previously contaminated implant surfaces could not be evaluated because these were clinical cases. Without reosseointegration, there could be greater chance of disease relapse through the implant surface.9

To achieve ideal treatment outcomes after regenerative therapy for peri-implantitis, bony defects around dental implants should be resolved with new bone formation.

1Associate Professor, Department of Periodontology, College of Dentistry, Dental Research Institute, Seoul National University, Seoul, Korea.
2Professor, Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, Yonsei University College of Dentistry, Seoul, Korea.
3Professor, Department of Periodontology, Research Institute for Periodontal Regeneration, Yonsei University College of Dentistry, Seoul, Korea.

Dr Kim and Dr Hu contributed equally to this work.

Correspondence to: Dr Ui-Won Jung, Department of Periodontology, Yonsei University College of Dentistry, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea. Fax: +82-2-3920398. Email: drjew@yuhs.ac

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There should also be reosseointegration on the previously exposed and contaminated implant surface. In previous animal studies, a wide range (1% to 84%) of reosseointegration after regenerative therapy has been reported. Even in the study that showed the greatest reosseointegration, it was only seen on 1.2 mm of the length of the implant surface. Reosseointegration is required for ideal treatment outcomes, but it was not found on the entirety of the previously contaminated implant surface.

In this case report, the amount of reosseointegration after regenerative therapy for peri-implantitis could be measured because the patient who underwent regenerative therapy prior to his death agreed to donate his corpse for medical research. Radiographic analysis using microcomputed tomography (microCT) and histologic evaluation was thus possible in this case report using human autopsy.

Case Report

A 60-year-old man presented to the Department of Periodontology at Yonsei University Dental Hospital, with chief complaints of bleeding, swelling, and tenderness around the dental implants. Three splinted implants (Straumann) supported the fixed prosthesis, which had functioned for 6 years to, replacing the mandibular left second premolar and first and second molars. Peri-implantitis was diagnosed due to the clinical manifestation of a probing depth of > 7 mm and angular bone defects in the periapical radiograph (Figs 1a and 1b).

Surgical Procedure

Nonsurgical therapy was repeated until the soft tissue inflammation was resolved. After the nonsurgical therapy, regenerative surgical therapy was planned. Since the prosthesis was screw retained with stock abutments (SynOcta, Straumann), the entire surgical procedure was performed after the prosthesis was retrieved to obtain better surgical access and to simplify the procedure. After local anaesthesia, a horizontal crevicular incision was made around the two most distal implants and further extended distally to expose the entire contaminated implant surface. A full-thickness flap with preserved papilla was elevated, and the inflamed granulation tissue around the implant was thoroughly debrided. The dimensions of the intrabony defects were measured using a periodontal probe. A three-wall (2 × 2-mm defect depth and width) and a circumferential intrabony defect (3 × 2-mm depth and width) had formed at the distal side of the implants at the site of the first and second molars, respectively (Fig 1c). The exposed implant surface was first mechanically decontaminated via an...
ultrasonic scaler with copper alloy tip (IS-STS-5E Tip, B&L Biotech) to avoid excessive scratches on the implant surface. An adjunctive chemical decontamination procedure was performed by applying cotton balls soaked with a solution mixed with 5 mL of saline and 250 mg of a tetracycline hydrochloride solution (Chong Kun Dang) for 5 minutes. After thorough rinsing with saline, particulate biphasic calcium phosphate bone substitute (Oseon II, Genoss) was grafted to the circumferential intrabony defect on the distal side of the implant at the first molar site and on the mesial side of the second molar implant (Fig 1d). The flap was repositioned and sutured using 4-0 monofilament nylon suture (Ethilon, Ethicon). Systemic antibiotics (500 mg amoxicillin, Chong Kun Dang) were administrated for 5 days. A chlorhexidine gluconate mouth rinse (0.5% Hexamedine, Bukwang) was recommended. The suture was removed 10 days postoperatively. The surgical site was monitored every 3 months through a supportive periodontal maintenance program. At 20 months after the regenerative surgical intervention, an autopsy of the tissue around the implants was obtained because the patient had agreed to donate his corpse for medical research on his death, which eventually occurred due to cancer.

Radiographic Analysis

Before being embedded in methyl methacrylate, the block section was scanned using microCT (SkyScan 1173, Skyscan) at a resolution of 14.91 µm (130 kV, 60 µA). A two-dimensional cross-sectional view that equally divided the implant buccolingually was obtained. From the microCT scan, which was taken 20 months after the regenerative therapy, the estimated bone level was located at the first thread on the distal surface of the implant in the first molar area, and between the first and second threads on the mesial surface of the implant in the second molar position (Figs 2a to 2c). Two
previous defects, from the distal side of the first molar and the mesial side of the second molar, were separated, with the bony peak of pristine bone in between. A remnant of bone substitute was found in the soft tissue in the distal area of the first molar implant. A well-maintained bone around the implants was found on the mesial surface of the first molar implant and the distal surface of the second molar implant. This finding shows that this area was not involved in bony defects caused by peri-implantitis (Fig 2a). The buccal and lingual sides of the first molar implant formed physiologically positive architecture. Narrow angular bony defects remained on the buccal side of the second molar implant (Fig 2c). From the 3D reconstructed image, the resolution of the intrabony defects was found mostly on the distal area of the first molar implant and on the mesial area of the second molar implant. Horizontal bone loss was found on the lingual side with the configuration of noncontained bony defect. A remnant of bone substitute particles was found in the soft tissue area over the newly made bone in the bony defect. Significant defects, or scratches that occurred during mechanical decontamination, were not found on either implant (Figs 2d and 2e).

**Histologic Evaluation**

A block section that included the implants and the treated site, with hard and soft tissues, was prepared. The block was fixed in 10% neutral buffered formalin for 10 days. The specimen was trimmed and dehydrated in ethanol and then embedded in methyl methacrylate without decalcification. It was then sectioned equally, dividing the implants buccolingually. After being reduced to about 20 µm, the sections were stained with hematoxylin-eosin and Masson-Goldner trichrome stains. Reosseointegration of 1.90 mm and 1.41 mm were measured around the previously exposed distal surface of the first molar implant and the mesial surface of the second molar implant, respectively (Fig 3). Clusters of remaining bone substitute particles were embedded in the newly formed bone, and these were tightly connected with in the formation of the bone bridge. Some particles were surrounded by fibrous tissue within the mucosa, but no inflammatory reaction was found. In the higher-magnified histology, multinucleated giant cells were seen on the surface of the remaining bone substitute (Fig 4).
In the buccolingual section of the site of the first molar, no intrabony defect was observed and physiologically positive architecture was maintained (Fig 5). The surrounding bone tissue showed a high rate of contact with the implant surface. The buccolingual section of the second molar site showed a rather thick alveolar bone dimension compared to the first molar (Fig 6). Even if a slit of intrabony defect remained at the buccal side, a thin layer of new bone lining the implant surface, from the estimated defect base to the first implant thread, was evident. The percentage of bone-to-implant contact (BIC) was as high as for the rest of the implant surface. Soft tissue ingrowth was found between the pristine bone and the thin lining bone.

Discussion

The ultimate goal of regenerative therapy for the treatment of peri-implantitis is not only defect resolution with hard tissue, but also reosseointegration of the previously exposed implant surface without any soft tissue engagement. The proof of direct contact of newly formed bone on the implant’s surface was histologically confirmed in this study. In addition, most of the bone substitute particles grafted around the dental implant were embedded in newly formed bone. Between the implant surface and the newly formed bone, the connective tissue capsule reported in the previous studies was not observed. The percentage of BIC on the implant surface, which was previously contaminated and treated, was as high as on the implant surface without previous contamination at 20 months of healing. To the authors’ knowledge, this case report could be the first histologic proof of the amount of reosseointegration and BIC in human subjects after regenerative therapy for peri-implantitis.

Healing after regenerative therapy has been investigated in animal studies, where in some cases a limited amount of BIC was reported. In one study, various amounts of reosseointegration on the implant surfaces was reported. The greatest amount of reosseointegration was found in a sandblasted and acid-
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etched surface, which is the same surface used for the implant in the present case report. If the surface of the implant in this case report had been a machined surface, less reosseointegration would have been present. The favorable result of this case report could be attributed to the surface of the implant used.

Decontamination of the implant surface is one of the most important prerequisites for the success of the peri-implantitis treatment. Various devices, including air powder abrasives, metal brushes, and lasers, have been introduced for mechanical decontamination of the implant surface. In this case, since firmly attached deposits such as subgingival dental calculus were not found on the exposed implant surface, application of such devices was not considered to prevent unwanted deformation of the original surface configuration. An ultrasonic scaler with a copper alloy tip was used to minimize a prominent scratch. Rubbing with a cotton pellet soaked in a tetracycline hydrochloride solution was also performed for chemical detoxification. With this mechanical and chemical surface decontamination protocol, signs of infection or inflammation after surgery were not found around the surgical sites during the maintenance phase. A systematic review demonstrated that the regenerative procedure and the surface characteristics of implant might be more important than the decontamination method in regenerative therapy for peri-implantitis.11

In animal models, an implant surface previously contaminated by plaque was effectively decontaminated even with saline irrigation, resulting in a high level of reosseointegration in accordance with the present result.

The morphology and dimension of osseous defects should be carefully examined to determine whether the surgical approach should be regenerative or regenerative. In this case, since the osseous defects were surrounded by bone walls and were containable, the grafted bone substitute particles and blood coagulum were able to be stabilized in the defects. The number of bone walls is also an important factor for predicting regenerative potential. In the same context of healing periodontal intrabony defects, more favorable reosseointegration was found around the implant having three-wall defects without buccal or lingual bone loss than around the implant with a deep circumferential defect.

Biphasic calcium phosphate was grafted for regenerative treatment of peri-implantitis in this case report. Even if some particles were surrounded by fibrous tissue without any inflammatory reaction, a substantial quantity of particles was replaced by mature new bone and embedded in the bone network with partial resorption. Based on the multinucleated giant cell found around the particle, resorption was still occurring. Application of such osteoconductive biomaterial for peri-implant treatment was successful in defect resolution and reosseointegration in the histologic evaluation of this case report. Barrier membrane was not used, as the benefit of using it for the regenerative therapy of peri-implantitis is not clear in previous studies.15 In addition, a well-contained defect does not require barrier membrane.

On the buccal side of the buccolingual section of the second molar area (Fig 6), a thin layer of new bone was found lining the implant surface from the defect base to the first thread of the implant. However, defect fill was incomplete with soft tissue ingrowth. Considering no remnants of bone substitute were found on the estimated intrabony defect, this thin lining of bone is probably from the mesial surface, where the containable defect, a good indication for regenerative therapy, existed. Although this reosseointegration would be beneficial from the prognostic point of view, it is unclear how reosseointegration without defect fill would affect the long-term prognosis of the implant.

Conclusions

This human autopsy study provides clinically relevant and valuable information to elucidate healing after regenerative surgery for treatment of peri-implantitis.

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