The Influence of Controlled Occlusal Overload on Peri-implant Tissue. Part 4: A Histologic Study in Monkeys

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Purpose: The purpose of this study was to observe, after removing occlusal trauma and conducting plaque control, possible macroscopic and histologic changes in peri-implant tissue that had deteriorated resulting from experimental peri-implantitis, and to investigate the necessity for treatment procedures for peri-implantitis. **Materials and Methods:** Four monkeys (Macaca fascicularis) in good general health were used in this experiment. Three months after the second premolar and the first molar were extracted from the right mandible, 2 IMZ experimental implants were placed in each monkey. After a 3-month osseointegration period, a second surgery was conducted, followed by making an impression for fabrication of the prosthesis. Excessive occlusal height of the prosthesis was adjusted to 250 μm, and the experiment was continued for 8 weeks after placement of the prosthesis. Three models were created: (1) A superstructure with an excessive occlusal height was used for 8 weeks without any brushing (positive control, model P); (2) after the first 4 weeks with a prosthesis with excessive occlusal height and no brushing, the superstructure was removed and not used for the last 4 weeks while brushing was conducted (experimental model, model E); and (3) for 8 weeks, a prosthesis with an appropriate occlusal height was used with brushing (negative control, model N). **Results:** When these 3 models were compared with each other, macroscopic findings indicated inflammation only in model P. Mobility of implants was not seen in any model. Histopathologic observations revealed a slight difference between model E and model P in terms of the degree of inflammatory cell infiltration in the connective tissue. **Discussion:** No difference was found in the degree of bone resorption. Partial tearing was observed at the contact region between epithelial tissue and implant surfaces. **Conclusions:** (1) The contact between implants and epithelial or connective tissue is fragile; (2) inflammation and occlusion must be controlled more prudently than in the case of natural teeth; and (3) once peri-implantitis has progressed, the control of occlusion and inflammation is probably not sufficient to promote the healing mechanism. (INT J ORAL MAXILLOFAC IMPLANTS 2002;17:384–390)

Key words: dental implants, histologic study, occlusal overloading, osseointegration

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It has been more than 30 years since osseointegrated implants were first used clinically.[1,2] During that time, various dental implants have been utilized and high success rates have been reported. However, as their use increased, implant failure associated with peri-implantitis has been reported.[3,4] Implant failure can be related to chronologic and etiologic aspects. Although early failure can occur because osseointegration does not materialize, late failure after successful osseointegration is commonly associated with the occurrence of peri-implantitis. Peri-implantitis is a condition involving

Table 1 Experimental Design

Model	First 4 weeks		Latter 4 weeks	
	Hygiene control	Occlusal trauma	Hygiene control	Occlusal trauma
Experimental model (model E)	—	+	+	—
Negative control model (model N)	+	—	+	—
Positive control model (model P)	—	+	—	+

+ = yes.
— = no.

the resorption of peri-implant bone and inflammation of peri-implant tissue prompted by infection by specific bacteria, occlusal overload, or a combination of these factors.[5,6] Although malocclusion is known to affect periodontal tissue directly, its effect on peri-implant tissue is poorly understood. Based on a study in which peri-implantitis was induced mechanically in experimental monkeys, Hürzeler and coworkers[7] reported no significant loss of osseointegration associated with occlusal overloading to the implant. However, Isidor[8] reported implant mobility caused by progressive peri-implant bone loss after the implants were exposed to mechanical occlusal trauma for 18 months. The present authors[9] have reported no significant peri-implant bone loss when experimental monkeys with good oral hygiene were subjected to a prosthesis with approximately 100 µm of excess occlusal height. This prosthesis was kept in place for 1 to 4 weeks so as to provide occlusal trauma, after which histopathologic examination was conducted. In an additional report,[10] experimental ligature-induced peri-implantitis was produced after second-stage surgery, followed by 100 µm excessive occlusal overloading of the implant, as in the first study. A significant increase in peri-implant bone breakdown was observed from 1 to 4 weeks. These results suggested that, in addition to the lack of inflammation in the peri-implant tissue, controlled occlusal overload of approximately 100 µm may not cause breakdown of the peri-implant bone. However, in the presence of inflammation, this occlusal overload may play a role in peri-implant bone breakdown.

In the third investigation[11] of this series, while the peri-implant tissue was maintained in an inflammation-free state, bone level changes around the implants were investigated when various levels of occlusal overload were exerted. Experimental prostheses were fabricated to be supra-occluded by 100, 180, and 250 µm. This study suggested that peri-

implant bone breakdown tended to increase with 180 µm or more extra prosthesis height. It also suggested that bone resorption around the implants could be caused by occlusal overload, even when there was no inflammation in the peri-implant tissue.

Thus, while it appears that peri-implant bone can be destroyed by the concurrence of inflammation and occlusal overload, there is still insufficient data to assess the clinical importance of these factors. As for the treatment to be administered when osseointegration has failed because of peri-implantitis, various studies have indicated that complete recovery is difficult once the peri-implant bone has been destroyed.[12] Since the contact status at the interface between bone and implant has not yet been completely elucidated, in the present study possible changes in osseointegration status after removal of causative factors (occlusal overload and inflammation) were investigated histopathologically.

MATERIALS AND METHODS

Experimental Animals

Four male monkeys *(Macaca fascicularis)* from the Japan Medical Science Animal Material Research Institute (Tokyo, Japan) were used for the experiment. They were estimated to be 4 to 5 years old with a body weight of 5.5 to 5.7 kg. As in previous studies, the experimental animals were kept in a room under constant temperature and humidity (28 ± 1°C; 50% to 60% humidity) in the experimental animal center. Until placement of the prosthesis, oral cleaning was provided weekly under general anesthesia to maintain healthy conditions of the peri-implant tissue as much as possible.

Experimental Design

The schedule of experiments is shown in Table 1. The animals were divided into 3 experimental models; 2

Fig 1 The excessive occlusal height of the prosthesis was adjusted to 250 µm by Miyata's method using an analyzer, as in previous studies.

Fig 2 Radiograph taken at 3 months, following prosthesis placement.

animals were used in model E, 1 animal was used in model N, and 1 animal was used in model P. All the models followed the same procedure up to the time of prosthesis placement. The animals were anesthetized by intramuscular injection (0.1 mL/kg droperidol, 0.2 mL/kg atropine sulfate, 0.08 mL/kg xylazine as pre-medication, and 0.2 mL/kg ketamine hydrochloride for general anesthesia), and their mandibular right second premolars and first molars were extracted. After a 3-month healing period, 2 IMZ experimental implants (diameter 2.8 mm, length 8 mm; Friatec, Mannheim, Germany) were placed according to established procedures. After another 3-month osseointegration period, a second surgery was conducted, followed by impression making and fabrication of prostheses. The excessive occlusal height of the prosthesis was adjusted to 250 µm by Miyata's method[13] using an image analyzer as in previous studies (Figs 1 and 2).

The 3 experimental models were as follows (Table 1): *(1)* the superstructure with the excessive occlusal height was used for 8 weeks without any tooth brushing (positive control, model P); *(2)* after the first 4 weeks with a superstructure with excessive occlusal height and no brushing, the superstructure was removed and not used for the last 4 weeks, when brushing was conducted (experimental model, model E); and *(3)* for 8 weeks, a superstructure with a normal occlusal height was used with brushing (negative control, model N). Comparisons were made in terms of macroscopic findings in the peri-implant tissue, bone resorption around implants, inflammatory cell infiltration, contact between implants, and epithelial tissue among the 3 groups.
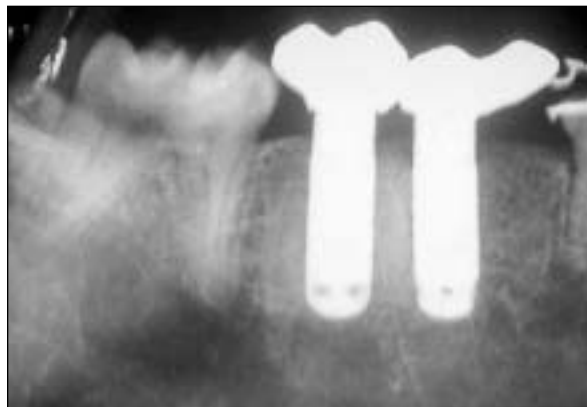
RESULTS

Macroscopic Findings

None of the models showed implant mobility or peri-implant tissue swelling (Table 2). Bleeding from the peri-implant sulcus and erubescence were seen in model P (Fig 3) but not in models E or N (Fig 4).

Histopathologic Findings

Histopathologic findings are summarized in Table 3.

Model N. Contact was confirmed between bone and implants by light microscope (Figs 5a and 5b). Epithelial tissue and implants were in contact with each other as well. Only slight infiltration by inflammatory cells was observed in the connective tissue.

Model P. Bone resorption reaching approximately the apical third of the implant body was observed (Figs 6a to 6c). Massive inflammatory cell infiltration was seen in the connective tissue. The contact region between implants and epithelial tissue was partially torn. Bone apposition or remodeling was not confirmed at the bone surfaces.
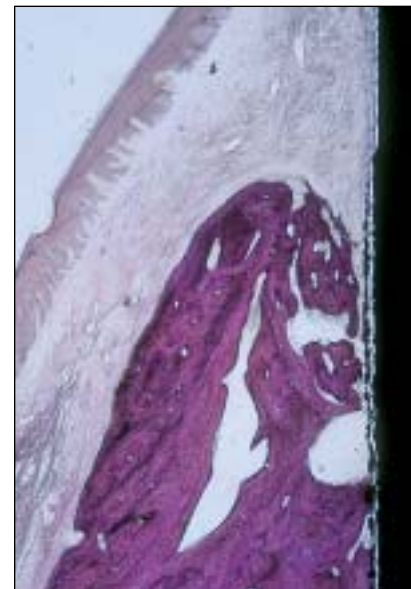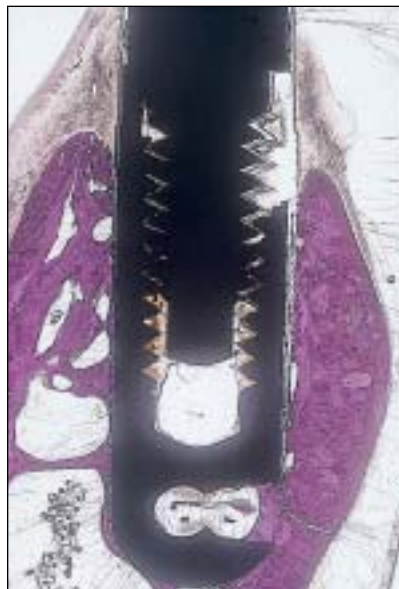
Model E. Bone resorption reaching approximately the apical third of the implant body was observed and did not indicate a clear difference from model P (Fig 7a to 7c). Although evidence of inflammatory cell infiltration was seen in the connective tissue, the amount seemed to be less than that of model N. As in model P, the contact between implants and epithelial tissue was partially torn. Also similar to model P, model E showed no bone apposition or remodeling at the bone surfaces.

Table 2 Clinical Aspects of Peri-implant Tissue 8 Weeks After Implant Placement

| Model	Pus discharge	Implant mobility	Reddening of peri-implant gingiva	Enlargement of peri-implant gingiva
Model E	None	None	None	None
Model N	None	None	None	None
Model P	Moderate	None	Moderate	None

Table 3 Histopathologic Aspects of Peri-implant Tissues

Model	Inflammatory cells within connective tissue	Destruction of peri-implant bone	Contact situation between epithelium and implant surface
Model E	Scanty	None	Contact
Model N	Mass	Severe	Poor contact
Model P	Moderate	Severe	Poor contact

Fig 3 Clinical view of model P (8 weeks after prosthesis placement). Note the redness and bleeding involving the peri-implant gingiva.

Fig 4 Clinical view of model N (8 weeks after prosthesis placement). Inflammation is not seen in the peri-implant tissue.

Figs 5a and 5b Model N demonstrated integration with bone for both implants (*left:* original magnification ×30; *right:* original magnification ×100).
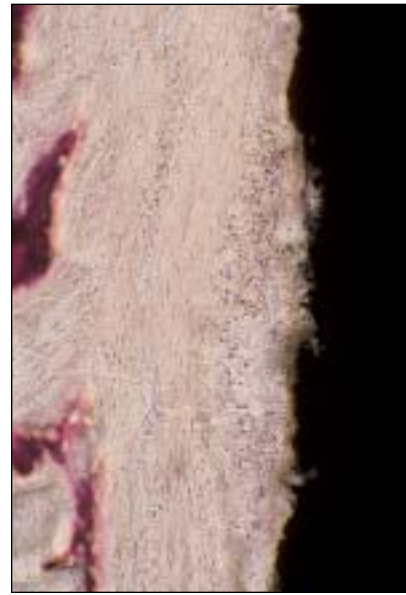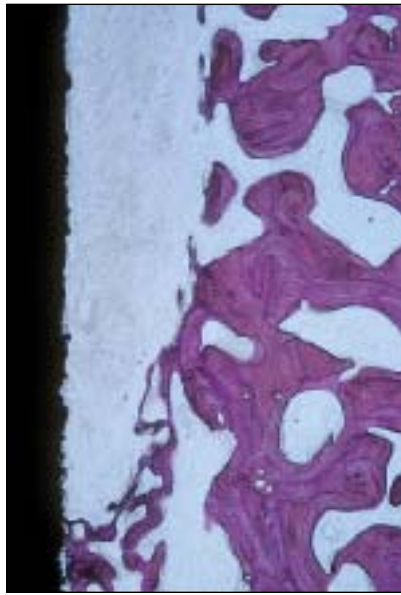
Figs 6a to 6c   Model P: Bone resorption reaching approximately the apical ⅓ of the implant body was observed. Inflammatory cell infiltration was seen in the connective tissue. The contact region between implants and epithelial tissue was partially torn (*left:* original magnification ×30; *center:* original magnification ×100; *right:* original magnification ×300).
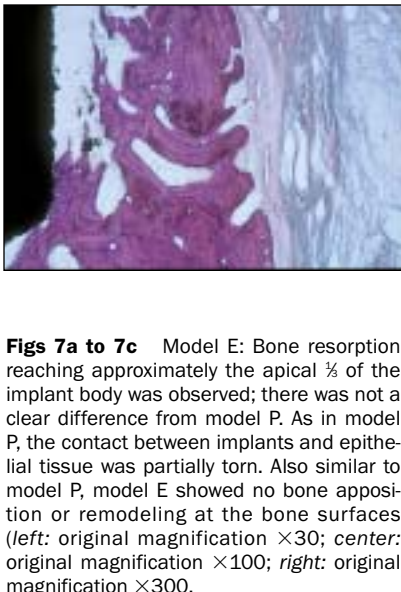
Figs 7a to 7c   Model E: Bone resorption reaching approximately the apical ⅓ of the implant body was observed; there was not a clear difference from model P. As in model P, the contact between implants and epithelial tissue was partially torn. Also similar to model P, model E showed no bone apposition or remodeling at the bone surfaces (*left:* original magnification ×30; *center:* original magnification ×100; *right:* original magnification ×300.

DISCUSSION

In the 1994 Consensus Report of Session IV of the First European Workshop on Periodontology, peri-implantitis was defined as an inflammatory process affecting the tissue around an osseointegrated implant in function, resulting in the loss of supporting bone.[14] While multiple factors can contribute to the onset of peri-implantitis, infection by bacteria and biomechanical overload are usually considered as the primary etiologic factors. Many clinical studies considering the role of bacteria in peri-implantitis have been reported.[15] Some reports have demonstrated distinct quantitative and qualitative differences in the microflora associated with successful and failing implants.[16–19] According to these articles, there was a marked difference in the composition of the associated microflora between successful and failing implants; the failing implants yielded larger amounts of gram-negative anaerobic bacteria.[5,6,15]

In studies of experimentally induced peri-implantitis, peri-implant lesions were reported to develop directly in the alveolar bone,[20] and very similar increases in clinical periodontal parameters, changes in histologic features, and shifts in the composition of microflora around implants and teeth were noted.[21] The other probable etiologic factor, biomechanical overload, has been suggested to account for the features of bone loss at the coronal aspect of the implant and microfractures at the same aspect of the bone-implant interface. Loss of osseointegration in this region results in the apical downgrowth of the epithelium and connective tissue, and this situation is conducive to bacterial invasion in the region of bone loss. van Steenberghe[22] reported significantly greater peri-implant bone loss in direct relation to the magnitude of implant loading. Most experimental studies on overload-induced peri-implantitis have used metal splints or cast crowns at the occlusal plane to induce repetitive occlusal trauma to the implant. However, these experimental studies have not been appropriately controlled with respect to the quantity of excessive height and the duration of mechanical overload. Therefore, great variation and different results were seen. Hürzeler and associates[23] found no significant loss of osseointegration by experimentally overloaded implants. On the other hand, Isidor[24] reported that implant mobility occurred, caused by progressive resorption after implants were exposed to occlusal trauma for 18 months. Then after 4.5 months, 1 implant was lost. The present authors consider such different results to be based on factors such as implant shape, duration of the overload, and magnitude of the overload not being uniform between the experiments. In the present series, the implant type and shape, the duration of overload, and the magnitude of excessive height for overload to the implant have been controlled.[9–11]

The type and shape of the experimental implants were those of an experimental cylindric implant (IMZ) 2.8 mm in diameter and 8 mm in length. This experimental implant was considered to be the proper size clinically, when the size of the mandible is compared between the experimental animals and humans. The timeline of this study series was controlled to give a period of healing after tooth extraction of 3 months, a 3-month healing-in of the implant, and a 4-week period of overloading. The excessive height of the superstructure for the overload could be controlled at any magnitude by using the image analyzer system developed by Miyata.[13]

To the authors' knowledge, this study is the first to examine changes in the damaged peri-implant tissue after removal of the occlusal factor in the deterioration of these tissues. This experimental study was based on the methods used in previous studies. It was observed that the peri-implant tissue was destroyed by the overload produced with 250 μm of excessive occlusal height, identical to the previous results. However, there was no significant difference in the level of bone destruction between the 2 experimental models. Therefore, if occlusal stress (via excessive prosthesis height) is added to a peri-implant tissue, the velocity of bone destruction becomes greater than that with plaque-induced inflammation alone. However, in model P there was more extensive inflammatory cell infiltration into the connective tissue, suggesting that toothbrushing during the last 4 weeks had suppressed the infiltration. On the other hand, even when both destructive factors were removed, the healing mechanism did not function at all with respect to bone loss. This result substantiates the previous view that regeneration and healing of the destroyed peri-implant tissue do not occur because there is no periodontal ligament around an implant.

As to the detailed macroscopic findings on the condition of the contact region between the implant surface and epithelium, laceration was observed in part of the contact region in both model P and model E. This finding suggests the possibility that micromotion related to occlusal overload can disrupt the fragile area of contact between the implant and epithelium or connective tissue. Therefore, there is a risk that the plaque-induced infection can easily reach the apical portion of the implant and destroy peri-implant tissue. The fact that model E showed less inflammation than model P indicates the importance of good oral hygiene in reducing the effects of peri-implantitis.

CONCLUSIONS

This experimental study using monkeys suggests that the contact between implants and epithelial or connective tissue is fragile, and inflammation and occlusion need to be controlled more prudently than in the case of natural teeth. Once peri-implantitis has progressed, the removal of excessive occlusion and inflammation may not be sufficient to promote the healing mechanism.

ACKNOWLEDGMENTS

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