Influence of Static Overload on the Bony Interface Around Implants in Dogs

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***Purpose*:** The aim of this study was to investigate bony changes around selectively overloaded implants in dogs. ***Materials and Methods*:** Twelve adult male beagles were used: 4 animals each for control, 4-week-load, and 12-week-load groups. Three implants were placed on the right side of each of the 12 animals and the time point designated as the study's baseline. Superstructures were then fabricated and attached only in the 2 implant-loaded groups 12 and 20 weeks following implant placement. Each lower distal implant was then fit with a cantilever-type superstructure extending in a mesial direction so as to be able to generate a controlled overload. The mesial and central implants were attached via superstructures equipped with a stainless steel screw, which could be tightened to create a controlled overload force. The force was induced by a controlled static 250-μm submerging of the cantilever of the distal implant. After 24 weeks, tissue specimens including implants were evaluated histologically and histomorphometrically. ***Results*:** Numerous fluorescence-labeled bone areas were noted in the 4-week-load group, showing a high remodeling activity. Marginal bone loss was significantly greater in the 12-week-load group than in the 4-week-load group. The ratio of fluorescence-labeled bone area in the inner thread region was significantly higher in the 4-week-load group than in the 12-week-load group. ***Conclusions*:** These findings demonstrate that static overload-induced forces can elicit changes in peri-implant bone in experimental animals. *Int J Prosthodont 2008;21:437–444.*

The acquisition and maintenance of osseointegration are essential for the long-term success of implant treatment.[1–3] Albrektsson et al[4] identified 6 key factors that are involved in the establishment of osseointegration. One of those 6 factors, load condition, has been reported to be the most important factor in the long-term maintenance of osseointegration.[5,6] Overload is considered to cause microinjury of peri-implant bone and eventually induce bone resorption, which may in turn result in the loss of osseointegration.[5–12]

Clinical occlusal loads in all prostheses-wearing patients may be static or dynamic[6]. If the frequency, magnitude, and duration of these loads exceed a certain force, they are regarded as overload forces and more likely to compromise the osseointegrated interface of an implant, if mechanical disparities occur in the fabrication of the prostheses. The causes of dynamic overloads are likely to be identified by the clinician or the patient and can frequently be corrected. However, identification of the causes of static overloads, such as loosening and damage of the superstructure, may be difficult before clinical problems ensue. In previous

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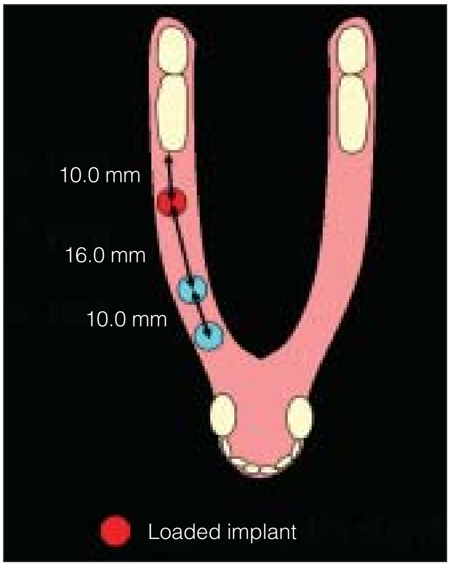
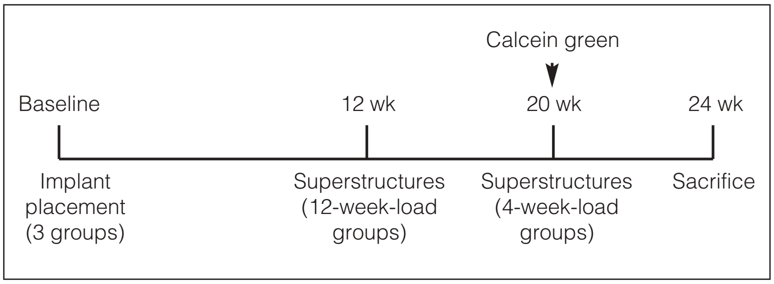


Fig 1 *(left)* The implants were placed with distances between the centers of the implants of 16 and 10 mm, starting at the 10-mm mesial site from the mesial adjacent surface of the mandibular first molar.

Fig 2 *(below)* Outline of the study.



studies on the influence of static loads on peri-implant bone, Carr et al[13] reported that a static load causing upward movement of the implant by a mean of 345 μm did not affect the peri-implant bone. On the other hand, Gotfredsen et al[14] reported that a mesiodistal static load on the implant increased remodeling activity of the peri-implant bone. Although static loads produced by misfit of the superstructure are likely to cause impalnt overload and compromise the integrity of its bony attachment, details of peri-implant bone bearing a static overload have not yet been clarified. Moreover, the biomechanical risks inherent in the design of cantilever-type superstructure have also been frequently reported,[15–19] suggesting that static overloads may indeed be involved in loss of osseointegration.

In the present study, the authors histologically and histomorphometrically investigated changes of cortical and trabecular bones around implants that were statically overloaded.

Materials and Methods

This study was performed in accordance with the Animal Experiment Guidelines of Hiroshima University and the internal experiment regulations of the Animal Experiment Institution of the Medical School, Hiroshima University, Japan.

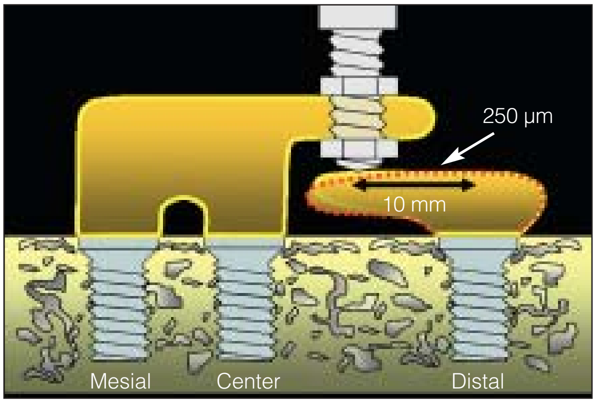
Commercially pure titanium machine-turned screw implants (Brånemark MK III, diameter: 3.75 mm, length: 7.00 mm; Nobel Biocare) were used.

Twelve adult male beagles were used: 4 animals each for control, 4-week-load, and 12-week-load groups.

The maxillary and mandibular premolars were extracted. After a 12-week healing period, implants were placed following the protocol of the Brånemark system. The implants were placed with distances between the centers of the implants being 16 and 10 mm, starting at the 10-mm mesial site from the mesial adjacent surface of the first mandibular molar (Fig 1). Using a surgical guide prepared for each animal, 3 implants each were placed parallel on the right side, and this time point was designated as the baseline.

The superstructures were attached 20 and 12 weeks after implant placement in the 4-week and 12-week-load groups, respectively. In the control groups, the superstructures were not attached. To observe the condition of unloaded bone and in early and delayed loading phases using fluorescent dye–labeled remodeling activity as an index, a fluorescent dye (Calcein green, Sigma Chemical)[14] was intravenously injected at 25 mg/kg 20 weeks after implant placement in all 3 groups (Fig 2).

The superstructures of the load groups were prepared with gold-silver-palladium alloy (Castwel MC, GC). The mandibular distal implant was attached with a cantilever-type superstructure extending in the mesial direction to add a static overload. The mesial and central implants were attached with superstructures equipped with a loading instrument composed of a stainless steel screw and 2 hexagonal screws. As a static load, the stainless steel screw was submerged to induce a 250-μm submerging of the cantilever at a 10-mm mesial site from the center of the distal implant. The same 250-μm movement was loaded by a specified number of turnings of the screw. The hexagonal screws were tightened at the same time to avoid loosening of the stainless steel screw (Fig 3). The animals were fed a soft diet after implant placement, and the peri-implant soft tissue and residual teeth were brushed 3 times a week. Bone blocks containing the implants were prepared 24 weeks after implant placement.



Figs 3a and 3b The experimental design of the study.

The blocks were kept in 10% neutral formalin for 48 hours, dehydrated with a series of alcohol, and embedded with photopolymerized methacrylate resin (Technovit 7200VLC, Exakt Apparatebau) under reduced pressure. The prepared resin blocks were processed using a hard tissue cutting machine (BS-5000, Exakt Apparatebau) and ultraprecision hard tissue grinder (Microgrinding Machine MG-4000, Exakt Apparatebau), and nondecalcified ground mesiodistal cross sections with an approximate 70-µm thickness at the center of the implant were prepared. The fluorescent remodeling activity of each preparation was observed under a fluorescence microscope (AX-70-Macro, Olympus). The preparations were then stained with toluidine-blue, and the histology was observed under a light microscope (AX70-Macro, Olympus). These microscopic views were input into a personal computer (Dimension 5150C, Dell) using a microscope equipped with a digital camera (DP71, Olympus), and histomorphometry was performed using imaging analysis software (Image J, National Institutes of Health).

The marginal bone loss was defined as the distance between the shoulder of the implant and the highest margin of the bone contacting the implant surface. The bone contact rate was defined as the value calculated by dividing the implant length contacted with the bone tissue by the length between the first thread and bottom of the implant.

Remodeling activity was investigated in the following 2 areas: *(1)* the region on the implant side of the line connecting the tips of the threads of the implant, designated as the inner thread region, and *(2)* the region 1 mm lateral to the tips of the threads, designated as the lateral region (Fig 4). In each region, the fluorescence-labeled bone area was determined by binary conversion in the fluorescence-stained preparation, the bone area was calculated in the histology preparation, and their ratio was determined as a quantitative evaluation of remodeling activity. In the binary conversion of fluorescent dye–stained areas to calculate the ratio of fluorescence-labeled bone, 3 examiners determined the optimum gray value in each preparation, and the mean was regarded as the threshold.

These values were statistically analyzed by 1-way layout analysis of variance and multiple comparisons, with a significance level of 5%.

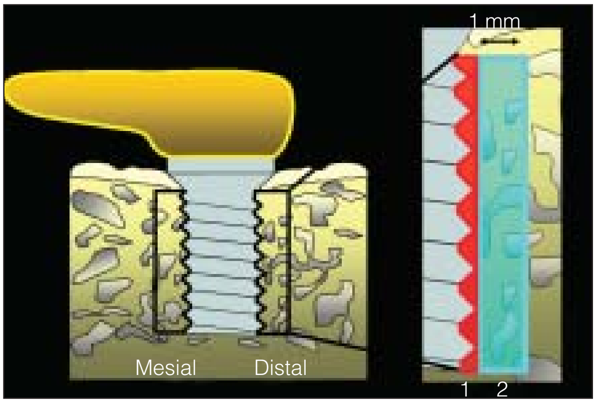


Fig 4 Remodeling activity was investigated in 2 regions. The region on the implant side of the line connecting the tips of the threads of the implant was designated as the inner thread region (1), and the region 1 mm lateral to the tips of the threads was designated as the lateral region (2).

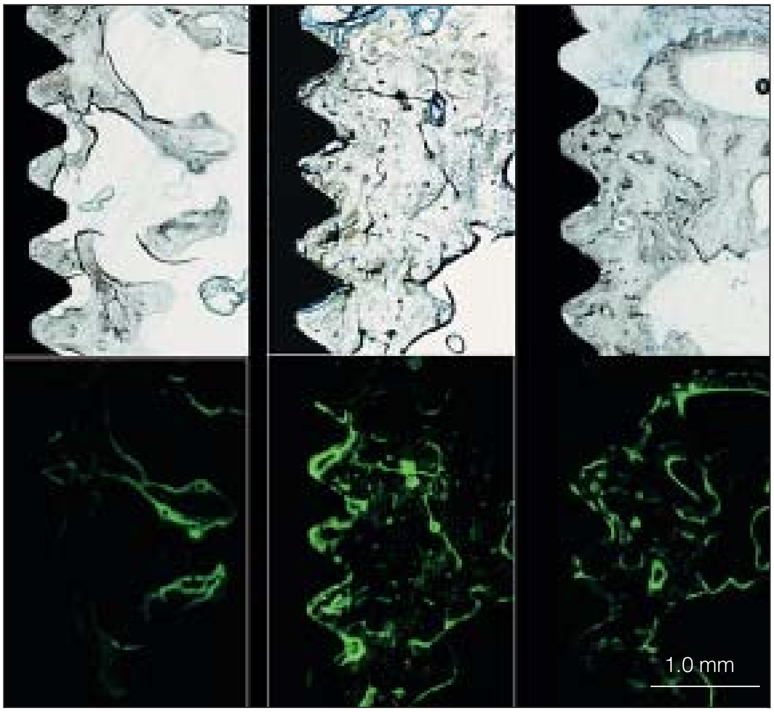


Fig 5 No fluorescence-labeled bone was present around the implant in the control group *(left)*, whereas many fluorescence-labeled bone areas were noted in the 4-week-load group *(center)*, showing a high remodeling activity. Many of these areas were detected near the boundary between the implant and bone. In the 12-week-load group *(right)*, fewer fluorescence-labeled areas were detected.

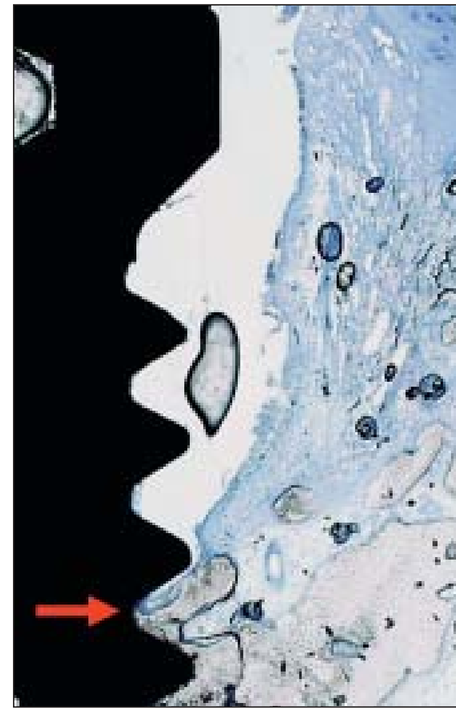


Fig 6 Light microscopic image showing marked marginal bone loss in the 12-week-load group. The loss had progressed close to the third thread in some animals.

Results

No mobility or falling out of any implant occurred. No mucosal inflammation was noted around the implants throughout the observation period. The distance between the implants was measured at the time of implant placement and sacrifice, and no horizontal change in the position was noted in any implant.

Histologic evaluation

No fluorescence-labeled bone was present around the implants in the control group, whereas many fluorescence-labeled bone areas were noted in the 4-week-load group, showing a high remodeling activity. Many of these areas were detected near the boundary between the implant and bone. In the 12-week-load group, fewer fluorescence-labeled areas were detected, and the remodeling activity was not as high as that in the 4-week-load group (Fig 5). On light microscopic observation, marked marginal bone loss was noted in the 12-week-load group, and the loss had progressed close to the third thread in some animals (Fig 6). Osseointegration was established in all groups.

The marginal bone loss was significantly greater in the 12-week-load group than in the 4-week-load group ($P < .05$). The bone contact rate was significantly lower in the 12-week-load group than in the 4-week-load group on both the mesial and distal sides ($P < .05$) (Fig 7). The ratio of fluorescence-labeled bone area in the inner thread region was significantly higher in the 4-week-load group than in the 12-week-load group on both the mesial and distal sides ($P < .05$). No significant difference was noted in the ratio of the fluorescence-labeled area in the lateral region between the 2 load duration groups (Fig 8).

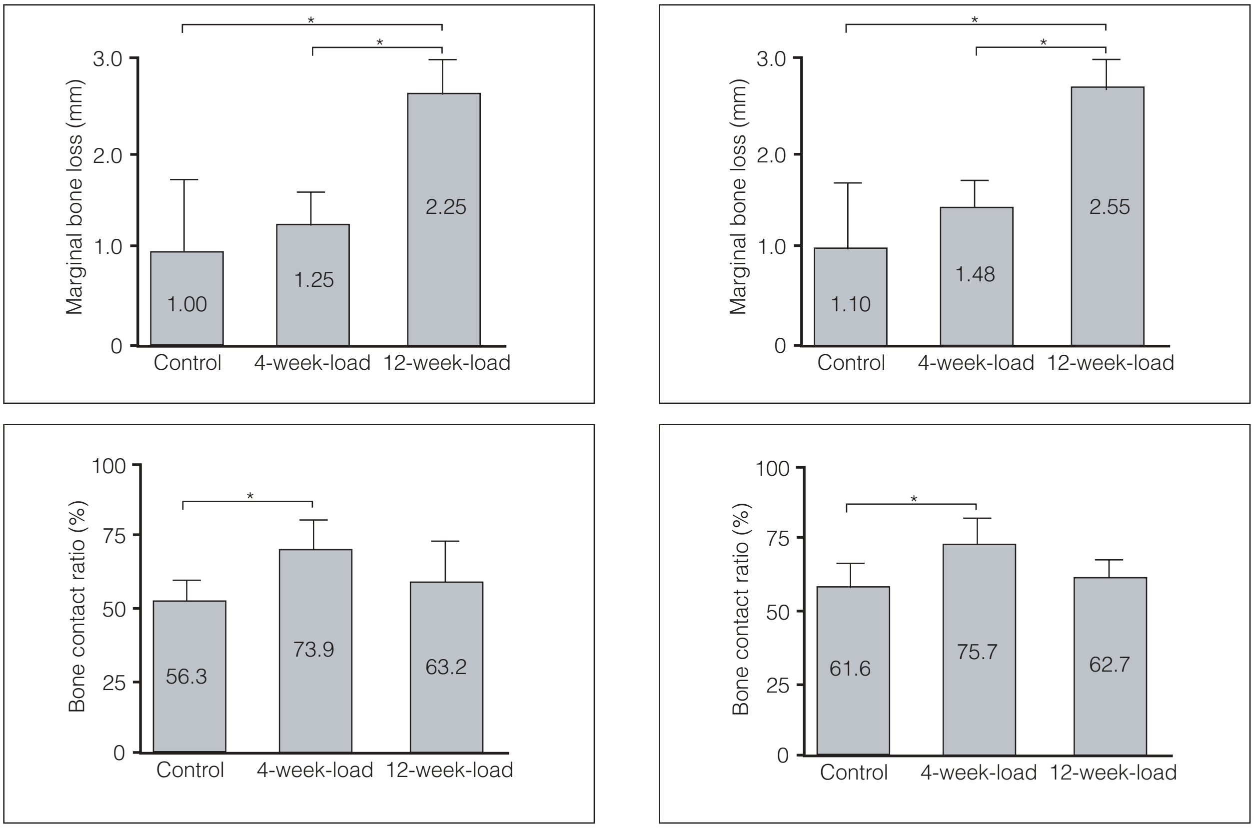


Fig 7 Marginal bone loss and bone contact ratio for mesial *(left column)* and distal *(right column)* sides. *$P < .05$.

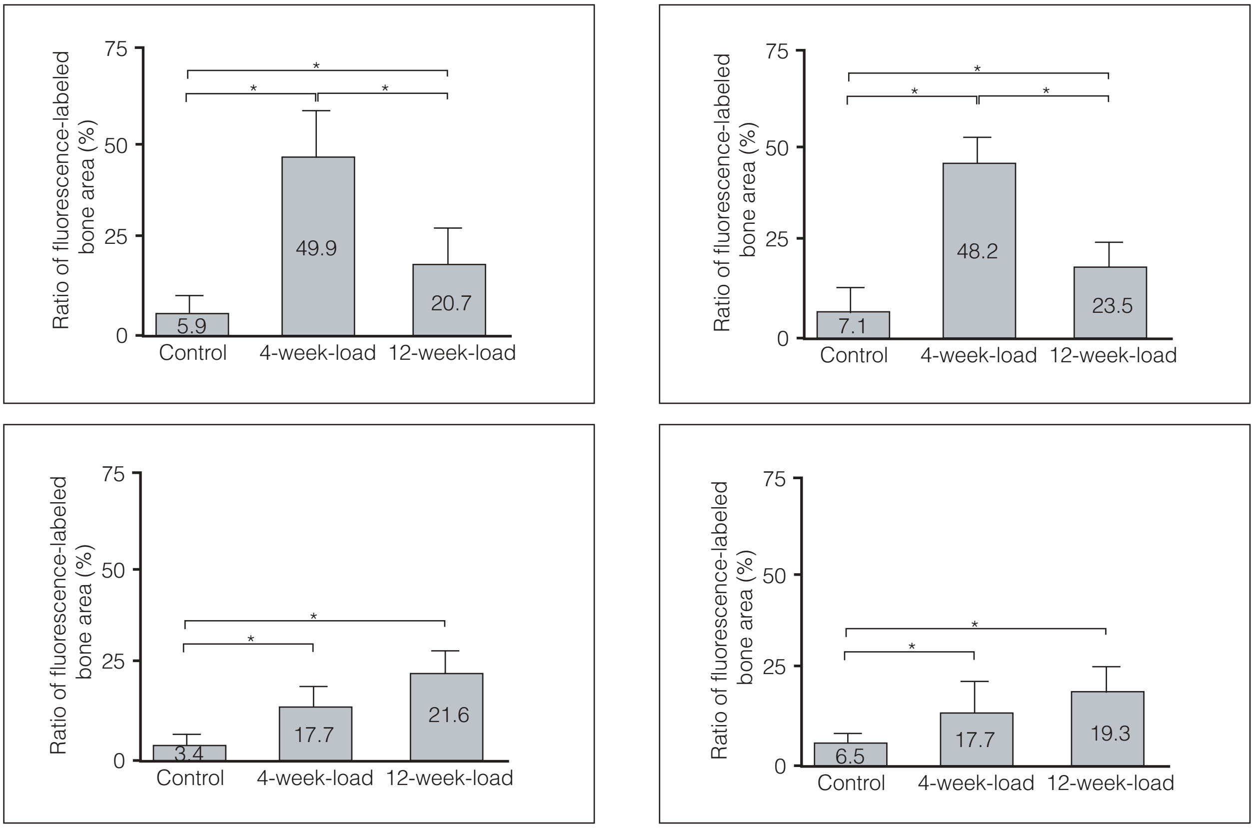


Fig 8 Ratio of fluorescence-labeled bone area in the inner thread region *(top row)* and lateral region *(bottom row)* for mesial *(left column)* and distal *(right column)* sides. *$P < .05$.

Discussion

The cantilever type was used for the load-bearing superstructure. Although many studies involving finite element analysis have reported the biomechanical risk of the cantilever-type superstructure,[15–19] fewer studies using an in vivo experimental model have been performed. Loading of a cantilevered superstructure produces the risk of an implant overload, compression and extension forces produced in the upper and lower inclined regions of the implant threads. The authors set the regions of interest as the mesial and distal regions including the upper and lower regions, and did not divide them because the ratio of compression and extension forces on the mesial side was reversed on the distal side. There has been no report on static overload inducing loss of osseointegration. As for dynamic load, Miyata et al[12] applied 250-μm occlusal interference to implants in monkeys, and found inhibition of osseointegration. Thus, the load amount in the present study was set to 250 μm. Regarding the type of load, all maxillary premolars were extracted to avoid occlusion between the screw and the maxillary teeth, and the animals were fed a soft diet to minimize dynamic load on the implants, suggesting that only static force was loaded on the implants.

The length of the implants used was 7 mm so as to maximize bony support but not penetrate the mandibular canal. This condition was necessary to standardize other factors for the evaluation of load-induced changes in bone. Longer implants may induce reactions different from those observed in this study.

To observe changes in bone remodeling induced by the load, remodeling activity was evaluated using a fluorescent dye. In addition to clarifying the remodeling state of the surrounding bone, this method easily differentiates the remodeled area from the existing bone and quantifies the area.[14] Calcein green was selected for the fluorescent dye because it does not affect the calcification ability of fibroblasts.[20] The duration of the resting period before acquisition of osseointegration differed between the 4-week-load and 12-week-load groups. However, 12 weeks after implant placement is considered to be the osseointegration acquisition period,[1] and the absence of a significant difference in the bone contact rate after this period[21] suggests that the degree of osseointegration was not markedly different between the 4-week- and 12-week-load groups.

The regions of interest for calculation of the ratio of fluorescence-labeled bone were considered the inner thread region mesiodistal to the implant and the lateral region 1 mm lateral to the thread tip. Gotfredsen et al[22] set the evaluation regions of the bone at 1 mm and 2 mm lateral to the implant when lateral static load was applied. They measured the fluorescence-labeled bone in each region and detected more fluorescence-labeled bone areas in the 1-mm region than in the 2-mm region, showing that remodeling activity was higher in the region closer to the implant in the presence of the load. Based on this report, the authors of the present study selected the inner thread and 1-mm lateral regions for evaluation of the load-induced remodeling activity.

There were no marked differences in the remodeling activity or bone contact rate between the mesial and distal sides, which is consistent with the findings of Gotfredsen et al[14] in which there were no differences in the bone density or remodeling activity between the compressed and distracted regions when a mesiodistal static load was applied to the implant.

No horizontal shift was noted in any loaded implant. The distances between the implants were measured at the times of implant placement and sacrifice, but no change was detected, showing that the horizontal positions were also maintained. In the 12-week-load group, in which marginal bone loss occurred, submerging of the implant itself was considered, but it was concluded that vertical shift did not occur because the occlusal surface of the superstructure and the bottom of the screw were contacted when the screw was loosened to the level at the time of loading on sacrifice of the animal. The 250-μm submerged loading may have been compensated for by: *(1)* loosening among the components and their extension, *(2)* flexure of the superstructure, and *(3)* flexure of bone. Regarding possible loosening among the components, the absence of a space between the superstructure and abutment was macroscopically confirmed after setting the upper surface of the abutment on the gingival margin. Neither a space between the abutment and implant nor extension of the gold screw was noted in the preparations, showing a low possibility of this condition. Thus, the submerging was more likely compensated for by flexure of the superstructure and/or bone.

Marginal bone loss in the 12-week-load group was significantly higher than that in the 4-week-load group, but no fibrous connective tissue was formed around any implant, and osseointegration was not lost during the observation period. Isidor[5] reported that when implants were placed in monkeys and given a strong occlusion, such as a dynamic load, marginal bone and osseointegration were lost within 4.5 to 15.5 months of loading. However, direct comparison with the present study is not possible because the height of occlusion was not specified in Isidor's study. Isidor[5] applied dynamic load, which caused a loss of osseointegration with implant mobility. When an implant acquires micromotion, a dynamic load may increase such mobility.[23] In the group given a static load for 14 weeks, bone microinjury may have been caused due to marginal bone loss,[5–12] which may also have induced micromotion. However, the static load did not increase the micromotion because it was a continuous force, suggesting that it did not advance to the loss of osseointegration.

The bone contact rate was reduced in the 12-week-load group, and this was associated with bone loss near the top thread of the implant due to cortical bone resorption. Based on these findings, it was very likely that the static load exceeded the biologically acceptable range over time.

In an analysis using a finite element model reconstructing the trabecular structure,[24] stress was concentrated not only in the boundary between the implant and bone, but also in the trabecular bone region. However, the stress value obtained by the finite element analysis cannot be directly connected with the remodeling activity because the stress threshold affecting remodeling is not clear at present.[25] Nevertheless, considering bone dynamics against loads, loads transmitted to bone should reach the bone reaction threshold to induce the transition of the equilibrium to bone resorption and formation.[26] The remodeling activity evaluation used bone formation–associated deposition of Calcein green as an index, which may have reflected the stress threshold produced by bone formation. Threshold stress produced near the boundary between the implant and bone may have promoted bone formation, increasing remodeling activity. Consideration of the intercellular response is also necessary for bone formation. In a previous in vitro study, c-fos and insulin-like growth factor expression were increased when a periodic extension/compression force was loaded on osteocytes, and osteopontin expression was increased when a continuous compression force was loaded.[27,28] Differences among the forces have certain intercellular influences; however, no cell-level responses were clarified in this study. It is necessary to investigate the influences of the pattern and degree of loading on cell sensitivity in vitro.

The remodeling activity after 12-week-loading was lower than that after 4-week-loading. No hexagonal screw of the loading device was loosened during the observation period, showing that the load was applied to the implant throughout the observation period. It has been reported that a force larger than the normal load within the biologically acceptable range promoted bone formation and stabilized at a high bone mass level.[29,30] It may be appropriate to consider that the low remodeling activity of the peri-implant bone in the 12-week-load group resulted from changes in the bone structure corresponding to the load.

Stress is expected to concentrate on the upper margin of the mesial peri-implant bone in the mesial cantilever-type superstructure, but the load may have been borne by a lower region of bone at 12 weeks than at 4 weeks due to marginal bone loss. This suggests that the load more strongly affected the bone at 12 weeks than at 4 weeks due to a reduction of the load-bearing strength of the implant and produced the difference in remodeling activity between the mesial and distal sides.

In the current implant treatment, 2 implants were placed in a 3-tooth defective region because of the bone width, and the cantilever-type superstructure was attached in many cases. This study suggests that overloading cantilevered superstructures may indeed damage the bone, for which mechanical investigation is essential before attachment. Treatment to support the superstructure with a minimum number of implants for edentulous patients[31] has recently been performed in clinical practice. However, since the span of the connected superstructure is extended, an incompatible superstructure may be prepared due to failure in making an adequate impression by operators or distortion of casting in the technical process, increasing the possibility of inadequate static loading on implants. This study suggested the need for reducing these technical errors and careful testing of compatibility at the time of superstructure attachment.

Regarding inappropriate load-induced changes of the peri-implant bone, the static load increased trabecular bone remodeling activity in the implant threads in the early loading phase, and the bone contact rate increased, followed by marginal bone loss over time. This reduced the bone contact rate. Osseointegration was not lost in any implant throughout the observation period.

Based on these findings, the mechanism of osseointegration loss was hypothesized as follows: When static overload larger than the biologically acceptable range is applied to an implant, rapid remodeling activity is induced near the boundary between the implant and bone to increase the load-bearing force, which increases the bone contact ratio by adding new bone. However, the overload causes marginal bone loss over time because it exceeds the biologically acceptable range and reduces the load-bearing force of the implant. This increases the micromotion of the implant, resulting in the loss of osseointegration.

Conclusions

To clarify changes in the peri-implant bone when static overload is applied to an implant, morphologic changes of cortical and trabecular bones caused by static overload placed on an implant were investigated. The remodeling activity was significantly higher in the inner thread region at 4 weeks of loading ($P < .05$). Marginal bone loss was noted at 12 weeks of loading. These findings clarify some static load–induced changes of the peri-implant bone and provide useful information for the elucidation of the mechanism of loss of osseointegration.

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