BONE REMODELING IN IMMEDIATELY LOADED AND UNLOADED TITANIUM DENTAL IMPLANTS: A HISTOLOGIC AND HISTOMORPHOMETRIC STUDY IN HUMANS

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KEY WORDS

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Remodeling is thought to prevent microdamage accumulation caused by repetitive loading and to increase the fatigue life of bone. The bone remodeling rate (BRR) is the period of time needed for new bone to replace the existing bone and to allow for the adaptation of bone to its environment. BRR is expressed as a percentage or volume of new bone within a specific time period. The aim of the present study was to evaluate bone remodeling events on submerged and immediately loaded dental implants. Twelve patients with edentulous mandibles participated in this study. All patients were rehabilitated with fixed mandibular prostheses, with 10 dental implants per patient. An additional implant was inserted in the most distal posterior mandibular jaw region. In 6 patients, these additional implants were loaded with a fixed provisional prosthesis the same day of the implant surgery and loaded. In the other 6 patients, the additional implants were left submerged and not loaded. After 6 months, all the additional implants were retrieved with a trephine. The percentage of woven and lamellar bone, number of osteoclasts and osteoblasts, and percentage of bone labeled by tetracycline at 0.5 mm and 2 mm from the implant surface were evaluated. The percentage of lamellar bone, number of osteoblasts, and percentage of bone tetracycline labeling was significantly higher in the loaded implants than in the unloaded implants ($P = .0001$). Also in the loaded implants, the percentage of woven and lamellar bone, number of osteoclasts and osteoblasts, and percentage of bone tetracycline labeling was significantly higher at 0.5 mm than at 2 mm from the implant surface ($P = .0001$). No such differences were found in unloaded implants ($P = .377$). In conclusion, we found that (1) loading appeared to stimulate bone remodeling at the interface, (2) a higher percentage of lamellar bone was found in

loaded implants, (3) the percentage of bone labeling was higher at the interface of loaded implants, (4) no differences were found in the BRRs between immediately loaded and unloaded implants, and (5) immediate loading had not interfered on the lamellar bone formation at the interface and had not produced formation of woven bone at the interface.

Introduction

Few reports have been published on bone adaptation to oral implants.[1] According to the mechanostat theory of Frost, bone adapts by different biological processes within 4 mechanical usage windows: trivial, physiological, overload, and pathological.[2] The thresholds are defined by minimum effective strains for activating adaptive processes.[2] Modeling is the result of independent sites of formation and resorption[3,4] that add cortical and trabecular bone and reshape surfaces by resorption or lamellar formation drifts.[2]

Remodeling is a simultaneous process of resorption and formation that replaces previously existing bone,[3,4] tends to remove or conserve bone, and is activated by reduced mechanical usage in the trivial loading zone or microdamage in the pathological loading zone.[2,5-7] The repair process is thought to prevent microdamage accumulation caused by repetitive loading and to increase the fatigue life of the bone.[8,9] Long-term maintenance and success of osseointegrated implants involves continued remodeling activity at the periphery of the implant to avoid bone fatigue fracture[10] and to replace bone that may have sustained microfractures as a result of cyclic loading.[3,8,9] Load bearing is threatened by fatigue microdamage, and damaged bone must be promptly removed.[5] Woven bone is produced in response to extraordinary loading conditions[2] and provides a rapid, almost immediate increase in the sectional geometry of bone.[2] The amount of new, less-mineralized bone at the interface as well as the type of bone (woven vs lamellar) influence the strength of the interface.[11] The bone remodeling rate (BRR) or bone turnover is the period of time needed for new bone to replace the existing bone and to allow for the adaptation of bone to its environment.[3] BRR has also been expressed as a percentage or volume of new bone within a specific time period.[3] Lamellar bone forms at a rate of between 1 and 5 μm each day, whereas woven bone can form at rates of more than 60 μm each day; hence, a higher BRR is directly related to an increase in the amount of woven bone formation.[3] Higher risks for the bone-implant interface are related to higher turnover rates because the bone is less mineralized, less organized, and weaker at the interface, and different BRRs are most likely related to the microdamage resulting from repetitive loading.[3] A heightened remodeling of bone may occur after loading.[3]

The microstrain environment may affect the turnover rate of bone adjacent to an implant during prosthetic loading.[3] The rate of bone turnover in the regional environment of an implant has a great clinical importance for the long-term maintenance of dental implants.[11] Immediate loading of dental implants has been said to determine the formation of fibrous tissue at the interface. In reality, several histologic studies in humans and experimental animals have found that loading did not impede osseointegration and did not produce untoward effects on bone formation in a periimplant location.[12-24] Also, clinical studies have shown very high success percentages for immediately loaded implants in different clinical situations.[25-37]

The aim of the present study was to evaluate bone remodeling events around submerged and immediately loaded dental implants.

Materials and Methods

Twelve patients (8 men, 4 women; mean age 48 years, range 40–55) with an edentulous mandible participated in this study. The Ethics Committee of the University of Chieti, Chieti, Italy, approved the protocol, and all patients gave their written informed consent. The past medical history of all patients was noncontributory. No smokers were present. All patients were rehabilitated with fixed mandibular prostheses with ten 3.8- × 9.5-mm XiVE dental implants (Dentsply Friadent, Mannheim, Germany). An additional 3.8- × 9.5-mm XiVE implant was inserted in the most distal posterior mandible in sites 37 and 38. In 6 patients, these additional implants were loaded with a fixed provisional prothesis the same day of the implant surgery. All these implants were immediately put into occlusal loading mode and joined with the other implants that supported the temporary restorations. In 6 patients, the additional implants were left

submerged and were not loaded. All patients received an intramuscular injection of oxitetracycline (Reverin, Hoechst, Darmstadt, Germany; 25 mg/kg body weight) 30 and 60 days before implant retrieval to mark the newly formed bone and to evaluate the distance between the 2 fluorescent lines.[38] After 6 months, all the additional 12 implants and surrounding tissues were retrieved with a 5-mm trephine.

Specimen processing

Implants and surrounding tissues were washed in saline solution and immediately fixed in 4% paraformaldehyde and 0.1% glutaraldehyde in 0.15 M cacodylate buffer at 4°C and pH 7.4 to be processed for histologic examination. The specimens were processed to obtain thin ground sections with the Precise 1 Automated System (Assing, Rome, Italy).[39] The specimens were dehydrated in an ascending series of alcohol rinses and embedded in a glycolmethacrylate resin (Technovit 7200 VLC, Kulzer, Wehrheim, Germany). After polymerization, the specimens were sectioned along their longitudinal axis with a high-precision diamond disc at about 150 μm and were ground down to about 30 μm with a specially designed grinding machine. A total of 3 slides were obtained for each implant, stained with acid fuchsin and toluidine blue, and observed in normal transmitted light under a Leitz Laborlux microscope (Laborlux S, Leitz, Wetzlar, Germany). The microscopic images were assessed under fluorescence microscopy (Zeiss, Göttingen, Germany). Filters of wavelengths 510 to 560 nm (green filter), 450 to 490 nm (blue filter), 355 to 425 nm (violet filter), and 340 to 380 nm (ultraviolet filter) (Zeiss) were used. The green fluorescent lines, indicative of tetracycline labeling, were photographed with a sensitive photographic film (640T Chrome, Imation Spa, Segrate, Italy). The histomorphometry was carried out with a light microscope (Laborlux S) connected to a high-resolution video camera (3CCD, JVC KY-F55B) and interfaced to a monitor and personal computer (Intel Pentium III 1200 MMX). This optical system was associated with a digitizing pad (Matrix Vision GmbH) and a histometry software package with image-capturing capabilities (Image-Pro Plus 4.5, Media Cybernetics Inc, Immagini & Computer Snc, Milano, Italy). The bone surrounding the implants was divided into 2 distinct regions for histomorphometric comparisons. Bone located within 0.5 mm from the implant surface was classified as adjacent, whereas bone located more than 0.5 mm but less than 2 mm from the implant surface was classified as distant. The images were analyzed for percentage of woven and lamellar bone, number of osteoclasts and osteoblasts, and percentage of bone labeled by tetracycline at 0.5 mm and 2 mm from the implant surface. At low-power magnification (×12) the total area of peri-implant bone was calculated, and then the percentage of this area occupied by the fluorescent areas was evaluated. The osteoclasts and osteoblasts were counted in 10 high-power fields. The distance between the 2 outer fluorescent lines was measured. The birefringent organization of the bone collagen fibers under polarized-light microscopy was used to distinguish lamellar from woven bone.

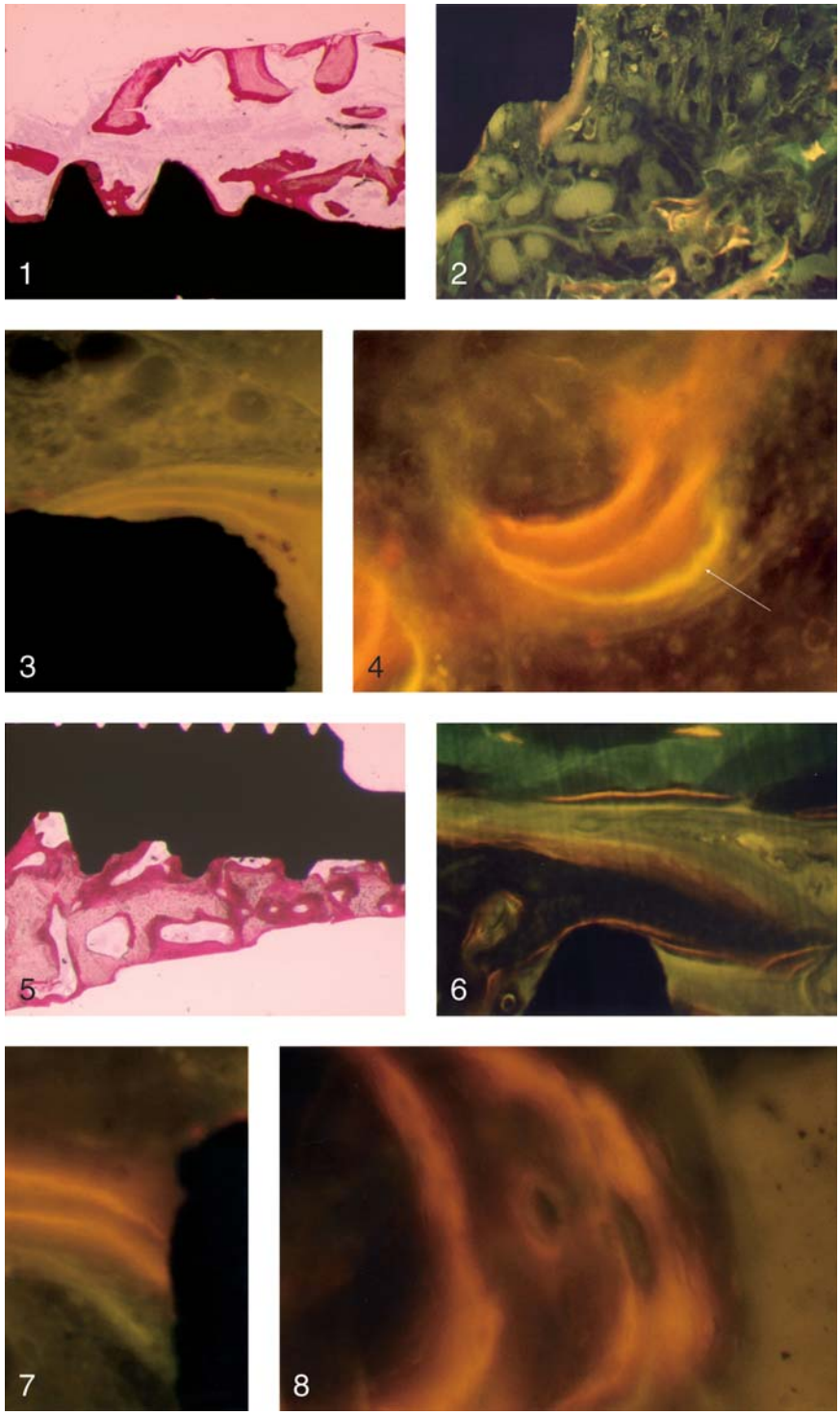
Data analysis

Analysis of variance was used to evaluate the differences in the percentage of woven and lamellar bone, number of osteoclasts and osteoblasts, and percentage of bone tetracycline labeled at 0.5 mm and 2 mm from the implant surface and the distance between the 2 fluorescent lines. All these values were expressed as a mean ± SD and SE. Statistically significant differences were set at $P < .05$.

RESULTS

Unloaded implants

Newly formed bone and bone trabeculae were found in contact with the implant surface (Figure 1). In some areas, newly formed blood vessels were observed. Some osteoblasts were actively secreting osteoid matrix directly on the implant surface. Woven bone in direct contact with the implant surface was present in some areas, and lamellar bone with a perpendicular or parallel orientation to the implant surface was observed in other areas. No lymphocytes or plasma cells were observed near the implant surface. The mean number of osteoclasts located on the bone surface per unit length of bone surface was 0.75 ± 0.02 mm, and the mean value for the osteoblasts located on bone surface per unit area was 2.4 ± 0.1 mm^2 at 0.5 mm from the implant surface. In the bone distant from the implant surface, the mean number of osteoclasts located on the bone surface per unit length was 0.77 ± 0.04 mm, and the mean value for the osteoblasts located on the bone surface per unit length was 3.2 ± 0.3 mm. The lamellar bone adjacent to the implant surface at 0.5 mm was 68% ± 5.5%, and the woven bone was 21% ± 3.2%. The trabecular bone labeling by tetracycline was 7.1% ± 0.5% at 0.5 mm and 6.8% ± 0.7% at 2 mm from the implant surface (Figure 2).



FIGURES 1–8. FIGURE 1. Unloaded implant. Bone trabeculae are in close contact with the implant surface (acid fuchsin and toluidine blue, original magnification ×18). FIGURE 2. Unloaded implant. Bone labeled by tetracycline is present in the bone around the implant (polarized light, original magnification ×40). FIGURE 3. Unloaded implant. Lines labeled by tetracycline are observed (polarized light, original magnification ×100). FIGURE 4. Unloaded implant. Lines labeled by tetracycline are present 2 mm from the implant surface (polarized light, original magnification ×200). FIGURE 5. Loaded implant. Newly formed bone is found near the implant surface. This bone is more strongly stained than preexisting bone (acid fuchsin and toluidine blue, original magnification ×20). FIGURE 6. Loaded implant. The fluorescence is observed in the newly formed bone near the implant surface (polarized light, original magnification ×40). FIGURE 7. Trabecular bone labeled by tetracycline is in direct contact with the implant surface (polarized light, original magnification ×100). FIGURE 8. Trabecular bone labeling by tetracycline 2 mm from the implant surface (polarized light, original magnification ×200).

Two lines marked by tetracycline were observed, and the distance between them was 60 ± 4 μm (Figures 3 and 4, Table).

TABLE 1
Bone remodeling in loaded and unloaded implants

	Unloaded Implants		Loaded Implants	
	Mean	SD	Mean	SD
% of woven bone at 0.5 mm	21	3.2	14	0.21
% of lamellar bone at 0.5 mm	68	5.5	86	4.5
% of lamellar bone at 2 mm	14	0.21	14	0.21
No. of osteoclasts per unit length (mm)	0.75	0.02	0.76	0.03
No. of osteoblasts per unit length (mm)	2.4	0.1	3.4	0.2
% of bone labeled by tetracycline at 0.5 mm	7.1	0.5	15.2	0.8
% of bone labeled by tetracycline at 2 mm	6.8	0.7	6.3	0.6
Distance between the 2 fluorescent lines (μm)	60 μm	4	90 μm	6

Loaded implants

Mature mineralized bone and, in only a few areas, not-yet–mineralized osteoid matrix were present at the interface in the cortical region (Figure 5). Mature bone and marrow spaces were present in other areas of the interface. Actively secreting osteoblasts were observed in marrow spaces in only a few portions of the interface. Peri-implant bone trabeculae were thick. No lymphocytes or plasma cells were observed near the implant surfaces. At 0.5 mm from the implant surface, the mean number of osteoclasts located on the bone surface per unit length was 0.72 ± 0.02 mm, and the mean number of osteoblasts located on the bone surface per unit length was 3.6 ± 0.1 mm. In the bone distant from the implant surface, the mean number of osteoclasts located on the bone surface per unit length was 0.76 ± 0.03, and the mean number of osteoblasts located on the bone surface per unit length was 3.4 ± 0.2 mm. The bone adjacent to the implant at 0.5 mm was mostly lamellar at 86% ± 4.5% whereas the woven bone was 14% ± 0.21%. The fluorescence was observed in the newly formed bone layers. At 0.5 mm from the implant surface, most of the bone trabeculae were labeled by tetracycline (Figure 6). In many areas, the trabecular bone labeling by tetracycline was in direct contact with the implant surface (Figure 7). The newly formed bone showed an extensive labeling by tetracycline, which clearly marked the level of the preexisting peri-implant bone. The bone marked by tetracycline was mostly present at 0.5 mm and was present in scarce quantities 2 mm from the implant surface (Figure 8). The percentage of trabecular bone labeling by tetracycline was 15.2% ± 0.8% at 0.5 mm and 6.3% ± 0.6% at 2 mm from the implant surface. Two lines marked by tetracycline were present, and the distance between them was 90 ± 6 μm (Table).

Statistical evaluation

The percentage of lamellar bone, number of osteoblasts, and percentage of bone tetracycline labeling was significantly higher in the loaded implants than in the unloaded implants ($P = .0001$). The percentage of woven and lamellar bone, number of osteoclasts and osteoblasts, and percentage of bone tetracycline labeling was significantly higher at 0.5 mm than at 2 mm from the implant surface in loaded implants ($P = .0001$). No statistically significant differences were found in the percentage of woven and lamellar bone, number of osteoclasts and osteoblasts, and percentage of bone tetracycline labeling at 0.5 mm and 2 mm in the unloaded implants ($P = .377$).

DISCUSSION

Bone is a dynamic tissue, and the long-term maintenance of a rigid implant requires continuous remodeling at the bone-implant interface.[40] This activity serves to renew the interfacial and supporting bone by replacing the oldest bone and repairing the foci of fatigue damage while maintaining the integrity of the implant.[40] Mechanical load plays an important role in the development, maintenance, and adaptation of the skeleton.[41] Wolff's law gives the connection between mechanical events (eg, stress, strains) and bone biological events (eg, bone remodeling, bone formation, and resorption).[42-44] Bone adaptation is dependent upon strain magnitude, duration, frequency, history, type (compression, tension, or shear), and distribution.[45] Immediate loading may have the potential to increase the density of the alveolar bone around endosseous implants.[21,46] New bone formation and active remodeling may be observed when the bone is mechanically stimulated.[21] Peri-implant mineralized bone areas showed a higher density within the threads of immediately loaded implants.[21] Also, Rocci et al[22] found that remodeling was evident and appeared to be more active near the implant surfaces. On the other hand, animal research has shown that excessively high dynamic implant loading can produce a pathologic ovderloading of bone, determining a higher

level of marginal bone loss or, sometimes, a loss of osseointegration.[9] Our results confirm those reported by Garetto et al,[11] who found a 50% to 60% greater labeled bone volume in the region immediately adjacent to the implants, with a much greater remodeling rate in the adjacent regions as compared with the distant regions. Finite element analysis studies have shown that the region within 1 mm of the implant surface has a marked change in the mechanical stress distribution, resulting in both stress levels and stress gradients.[11] Therefore, loading within physiologic limits can be speculated to stimulate bone formation as a result of the bone adaptation to loading.[22,24] Repetitive loading of bone leads to microfractures; such microdamage has been hypothesized to act as a stimulus to bone remodeling,[8] and this increased remodeling in the region adjacent to an implant is apparently necessary to repair local areas of bone microdamage or fatigue-induced microdamage.[11]

The BRR in our specimens was 2 μm (60 μm:30 days) in unloaded implants and 3 μm (90 μm:30 days) in loaded implants. These rates correspond to the rate of lamellar bone remodeling.[3,4] This condition may place the bone-implant interface at less biomechanical risk, for lamellar bone is more mineralized, more rigid, and stronger compared with woven bone.[3,4]

In conclusion, in our specimens (1) loading appeared to stimulate bone remodeling at the interface, (2) a higher percentage of lamellar bone was found in loaded implants, (3) the percentage of bone labeling was higher at the interface of loaded implants, (4) no differences were found in the BRRs between immediately loaded and unloaded implants, and (5) immediate loading had not interfered on the lamellar bone formation at the interface and had not produced formation of woven bone at the interface.[47-49] We can confirm the results of the study of Garetto et al,[11] who found that the successful long-term maintenance of endosseous implants involves a sustained increase of bone remodeling in the local region surrounding the implant and that the local biomechanical environment of the bone-implant interface may require a continuous remodeling to avoid bone fatigue fracture.

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