Biologic Response of Immediately versus Delayed Loaded Implants Supporting Ill-Fitting Prostheses: An Animal Study

Joke Duyck, DDS, PhD;* Luc Vrielinck, DDS, MD;† Ivo Lambrichts, DDS, PhD;‡ Yasuhiko Abe, DDS, PhD;§ Serge Schepers, DDS, MD;† Constantin Politis, DDS, MD;† Ignace Naert, DDS, PhD‖

ABSTRACT

Background: Computer-assisted preoperative implant planning and transfer toward the patient allow the production of a prosthesis prior to surgery. This implies that the prosthesis can be installed immediately following implant insertion. An inherent disadvantage of this is a cumulated error, which can lead to prosthesis misfit owing to topographic deviations of the planned versus the installed implants.

Purpose: The aim of this study was to determine whether prosthesis misfit is compromising the osseointegration of immediately versus delayed loaded implants and whether freshly installed implants adapt to the prosthesis.

Materials and Methods: In each of five New Zealand White rabbits, two experimental conditions were compared. One tibia harbored the so-called test implant, which originally showed a vertical misfit of about 500 μm with the prosthesis to which it was tightened immediately after implant installation. The control implant was installed in the other tibia and was allowed to heal during 9 weeks before the prosthesis with the vertical misfit of about 500 μm was connected to it. The prostheses were left in place for 12 weeks, after which the animals were sacrificed.

Results: All implants healed uneventfully. There were no statistically significant differences between the biologic responses of test and control implants. With a three-dimensional laser scanner, significantly more displacement of the test implants toward the prostheses was observed compared with the control implants. This led to a significant decrease in prosthesis misfit for the test implants compared with the control implants.

Conclusions: This study indicates that prosthesis misfit does not per se lead to biologic failure of immediately loaded or of already osseointegrated implants. In addition, immediately loaded implants seem to topographically adapt to the prosthesis, thereby minimizing the existing misfit.

KEY WORDS: animal, bone histology, immediate implant loading, prosthesis misfit

*Associate professor, Department of Prosthetic Dentistry, BIOMAT Research Group, Katholieke Universiteit Leuven, Leuven, Belgium; †physician, Department of Oral and Maxillofacial Surgery, Ziekenhuis Oost Limburg, Genk, Belgium; ‡full professor, Department of Basic Medical Sciences, Limburgs Universitair Centrum, Diepenbeek, Belgium; §associate professor, Department of Advanced Prosthodontics, Division of Cervico-Gnathostomatology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan; ‖full professor and chairman, Department of Prosthetic Dentistry, BIOMAT Research Group, Katholieke Universiteit Leuven, Leuven, Belgium

Reprint requests: Dr. Joke Duyck, Department of Prosthetic Dentistry, BIOMAT Research Group, Katholieke Universiteit Leuven, U.Z. St. Raphaël, Kapucijnenvoer 7, B-3000 Leuven, Belgium; e-mail: Joke.Duyck@uz.kuleuven.ac.be

Together with the introduction of the principle of osseointegration[1] for the treatment of edentulism, an unloaded healing period was considered the standard protocol for oral implant therapy. Thanks to the optimization of the implant design and surface, surgical technique, and biomechanical prosthesis conditions, clinical practice is shifting more and more toward immediate implant loading.[2] This implies an important psychosocial and economic advantage for patients. Several techniques allow a prosthesis fixation on the implants the same day following the implant installation. One system uses a prefabricated drill guide and ready-made prosthesis base for this purpose.[3,4] Other systems rely on computer-assisted preoperative implant

planning (on digitized medical images), which allows guided implant installation and the production of a provisional or final prosthesis.[5–8] Wagner and colleagues, however, compared the preoperative planned implant position with the postoperative medical images and observed deviations of up to 3.5 mm (mean 1.1 mm).[9] Even with navigation systems that are used in neurosurgery—in which precision is of the utmost importance—comparable deviations are observed.[10,11] Using stereolithographic drill guides for implant placement, entry point deviations could be limited to a mean of 1.51 mm.[12] This inaccuracy implies that considerable misfit can occur with prefabricated prostheses. It was therefore the aim of this study to find out whether this prosthesis misfit is compromising the osseointegration of the immediately loaded implants and to assess whether the implants adapt topographically to close the gaps of the ill-fitting prosthesis.

MATERIALS AND METHODS

Animal Information

Five mature female New Zealand White rabbits were selected for this study. They had an average weight of 3.3 kg (SD 0.3 kg) at baseline and 3.6 kg (SD 0.5 kg) at the end of the study. The rabbits were fed a standard diet ad libitum. During the surgery, the animals were preanesthetized with ketamine (Ketamine 1000 CEVA®, 0.12 mL/kg body weight, Ceva Sante Animale, Mechelen, Belgium) and xylazine (Vexylan®, 0.12 mL/kg body weight, Sanofi, Brussels, Belgium) and were given propofol (Diprivan® 1%, 8 mL/h, AstraZeneca, Brussels, Belgium) as intravenous anesthetic. Postoperatively, the animals were given buprenorphine as an analgesic (Temgesic®, 0.05 mg/kg body weight intramuscularly, Reckit & Coleman, Hull, USA), and antibiotics (300,000 IU/injection intramuscularly/benzylpenicillum natricum 600 mg/Continental Pharma, Brussels, Belgium) were administered peroperatively and until 4 days postoperatively.

This study was approved by the local ethical committee for laboratory animal science and was performed according to Belgian animal welfare regulations and guidelines.

Study Design

Two experimental conditions were compared:

1. Prostheses with a misfit of about 500 μm were connected to implants immediately after their installation (test). The prostheses were left in place for 12 weeks.
2. Prostheses with a misfit of about 500 μm were connected to osseointegrated implants 9 weeks after implant installation (control). The prostheses were left in place for 12 weeks.

For each rabbit, one tibia (test tibia) harbored the test implant, whereas the other (control) tibia harbored the control implant. Figure 1 represents the course of the experiment.

Nine weeks prior to prosthesis installation, two implants were placed in the test tibia. These implants were referred to as pillar implants because they were going to support the prosthesis. An elastomer impression was taken at the implant level (pick-up technique). After this, the skin was closed and the implants were left to heal subcutaneously for 9 weeks. A stone model (test model 1) was made based on the impression, and a third implant replica — representing the test implant — was added in this model between the two pillar implants. On this model, a drill guide for the installation of the test implant was produced, together with the final Cr-Co prosthesis. The prosthesis was made in such a way that there was an optimal fit with the pillar implants and a vertical misfit of about 500 μm with the test implant. After the 9-week healing period, the pillar implants were uncovered, the drill guide was installed on these, and the test implant was placed. The drill guide aimed to install the implant in such a way that the vertical and horizontal positions, as well as the inclination, of the implant replicated the positions on the model. After test implant installation, another elastomer impression was taken of all three implants (test model 2). The prostheses were tightened directly (no abutment interposition) to the pillar and test implants with a torque of 35 Ncm (Manual Torque Controller®, Nobel Biocare AB, Göteborg, Sweden) immediately following test implant installation. The skin was closed, leaving the prostheses supracutaneous. The animals were sacrificed 12 weeks after prosthesis installation. Attention was paid for any screw loosening before removing the prosthesis. At that time, a final elastomer impression (test model 3) of all three implants was taken.

On the control side, all three implants were placed simultaneously. The lateral implants were the pillar implants, and the middle implant served as the control. A first elastomer impression was taken (control

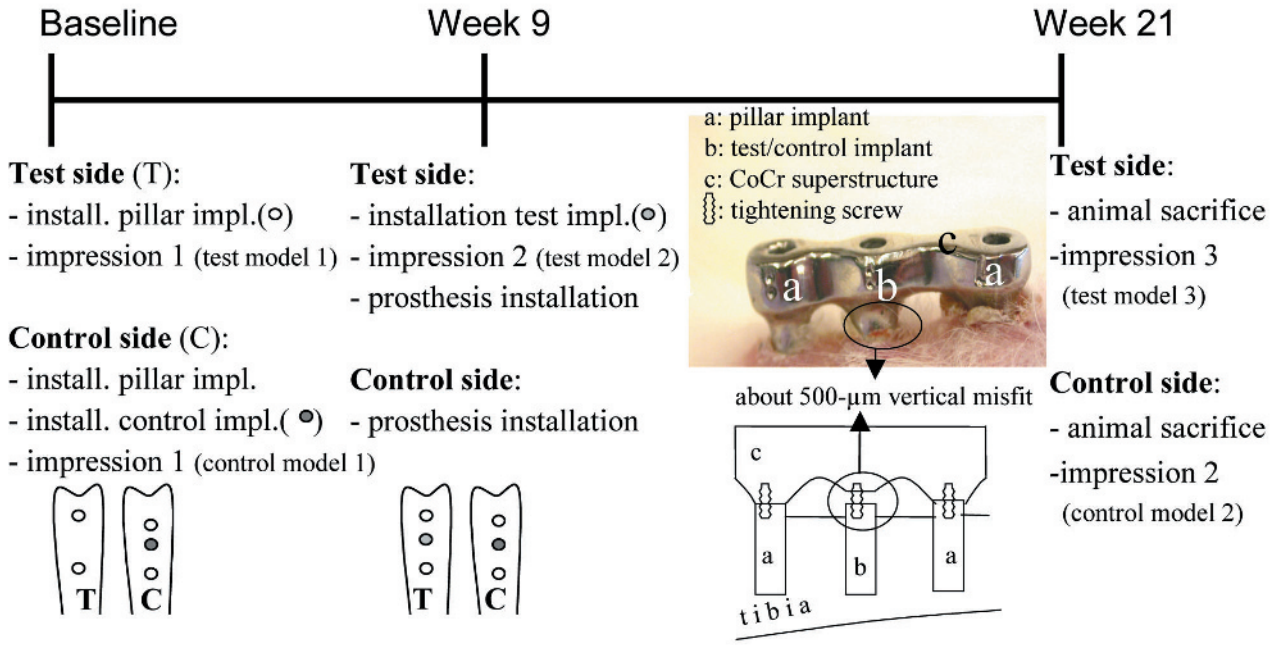

Figure 1 Schematic overview of the study.

model 1) after implant installation, the skin was closed, and all implants were left to heal for 9 weeks. On each of these control models, a Cr-Co prosthesis was prepared with a clinical optimal fit to the pillar implants and a vertical misfit of about 500 µm to the control implants. After the 9-week healing period, the implants were uncovered and the prostheses were installed and screw-tightened with a torque of 35 Ncm. The skin was closed again, leaving the prostheses supracutaneous. The animals were sacrificed 12 weeks after prosthesis installation. Again, attention was paid to any screw loosening before removing the prosthesis, and a final elastomer impression (control model 2) of all three implants was made. All implants were screw-threaded anodized-surfaced implants (Ti-Unite™, Brånemark System®, Nobel Biocare) with a 10 mm length and a 3.75 mm diameter.

Histology and Histomorphometry

After sacrificing the animals, all test and control implants with their surrounding bone were separated and fixed in a $CaCO_3^-$-buffered formalin solution. In preparation for the ground sections (SP 1600, Ernst Leitz GmbH, Wetzlar, Germany), the bone segments were dehydrated in a graded series of ethanol and embedded in methylmethacrylate and polymerized. All sections were cut parallel to the long axis of the tibia. On average, eight sections were made along the long axis of each implant, but only three were analyzed. The section closest to the middle of the implants was selected, as well as the most medial and lateral sections. These sections were about 100 µm thick and were ground to about 25 µm and finally stained with Stevenel's blue and picrofushin red.

Histologic analyses were performed to generally describe the tissues surrounding the implants. Histomorphometric analyses were done by means of a light microscope (Laborlux S, Ernst Leitz GmbH, Troisdorf, Germany) connected to a personal computer equipped with a video and image analysis system (Image Pro Plus®, 3.0.01.00, Media Cybernetics L.P., San Diego, CA, USA).

The following parameters were defined (Figure 2):

1. *Crater depth/surface (×9 magnification)*. The crater depth (µm) is measured as the distance between the deepest point of the crater and a reference line perpendicular on the implant axis, which connects the upper part of the cortical bone with the implant. If the upper part of the cortical bone is located above the level of the implant shoulder, the latter is taken as the reference point. The reason behind this is that the formation of a crater-shaped defect is evident when the implant-prosthesis interface is placed below the level of the cortical bone.

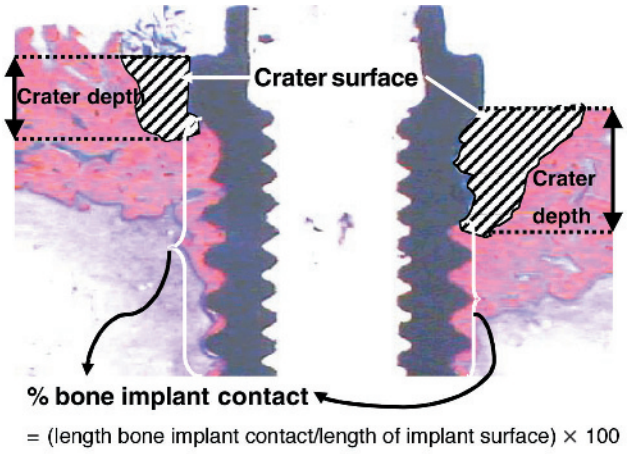

Figure 2 Illustration of the histomorphometric measurements.

The crater surface (μm^2) is measured relative to the above-mentioned reference line as the surface of the crater-shaped bony defect as observed on the two-dimensional histologic section.

2. *Bone-implant contact (×40 magnification)*. Bone-implant contact (%) is defined as the proportion of the length of the implant surface that is in direct contact with the bone and the total length of the implant surface as measured on a two-dimensional histologic section. Bone-implant contact measurements start from the first bone contact until the region where bone contact ceases (marrow space).

Resonance Frequency Analysis

In addition to the histologic analyses, implant stability was evaluated using resonance frequency analysis (Osstell®, Integration Diagnostics Ltd, Göteborg, Sweden) and expressed as implant stability quotient (ISQ) values. Resonance frequency measurements were done just before and 12 weeks after prosthesis installation. For the control implants, additional measurements were done immediately after implant installation. During the measurements, the transducer of the Ostell device was mounted directly on the implant and oriented perpendicular to the long axis of the tibia, with the elevated part of the transducer on the lateral side.

Evaluation of the Implant Position

Both the pillar implants and the prostheses were used as a reference to measure the changes in position of the test versus control implants.

The effect of implant displacement was evaluated by measuring the remaining gap between the prosthesis and the test and control implants under the light microscope (×12 magnification). The distance between the implant and the prosthesis was measured starting on six predetermined points on the implant and going perpendicular from the implant to the prosthesis (Figure 3). Each gap value is therefore the mean of six measurements. During the measurements, the prosthesis was screw-tightened only on the pillar implants, not on the test and control implants. To evaluate the influence of the fixation of the ill-fitting prosthesis on the prosthesis misfit as such, the gap was measured on test models 2 and 3 and control models 1 and 2.

Displacement of the test and control implants was evaluated by determining the relative change in topographic position between one of the pillar implants and the respective test or control implant by use of a three-dimensional laser scanner (Laserscan 3D PRO, Willytec GmbH, München, Germany). Before scanning, the first pillar implants of two models were connected by means of a metal bar (22 × 9 × 3 mm), and the test or control implant was covered with a flat surface cover screw, which was modified for the measurements. Pairs of connected models were coated with a laser-light reflecting coating (Developer D70, Helling, Heidgraben, Germany), which was sprayed onto the models from a constant distance. Figure 4 shows a schematic drawing of a scanning image acquired from the Laserscan 3D PRO device. The surface of the test or the control implant was divided into four measurement areas: a, b, c, and d. The vertical distances between five arbitrary measuring points on each area and the top surface of the metal bar (serving as reference surface) were measured. The mean value of these five measured distances was calculated as representative for each area. The differences between test models 2 and 3 were calculated and represent the displacement of the test implant. This was also calculated for control models 1 and 2. Repeated measurements of the same models revealed a deviation of maximally 14 microns.

Statistical Analyses

The histomorphometric data, the resonance frequency analyses (ISQ values), and the prostheses' misfit measurements of the test versus control implants were compared using a two-tailed paired Student's *t*-test. The three-dimensional laser scanning data were compared

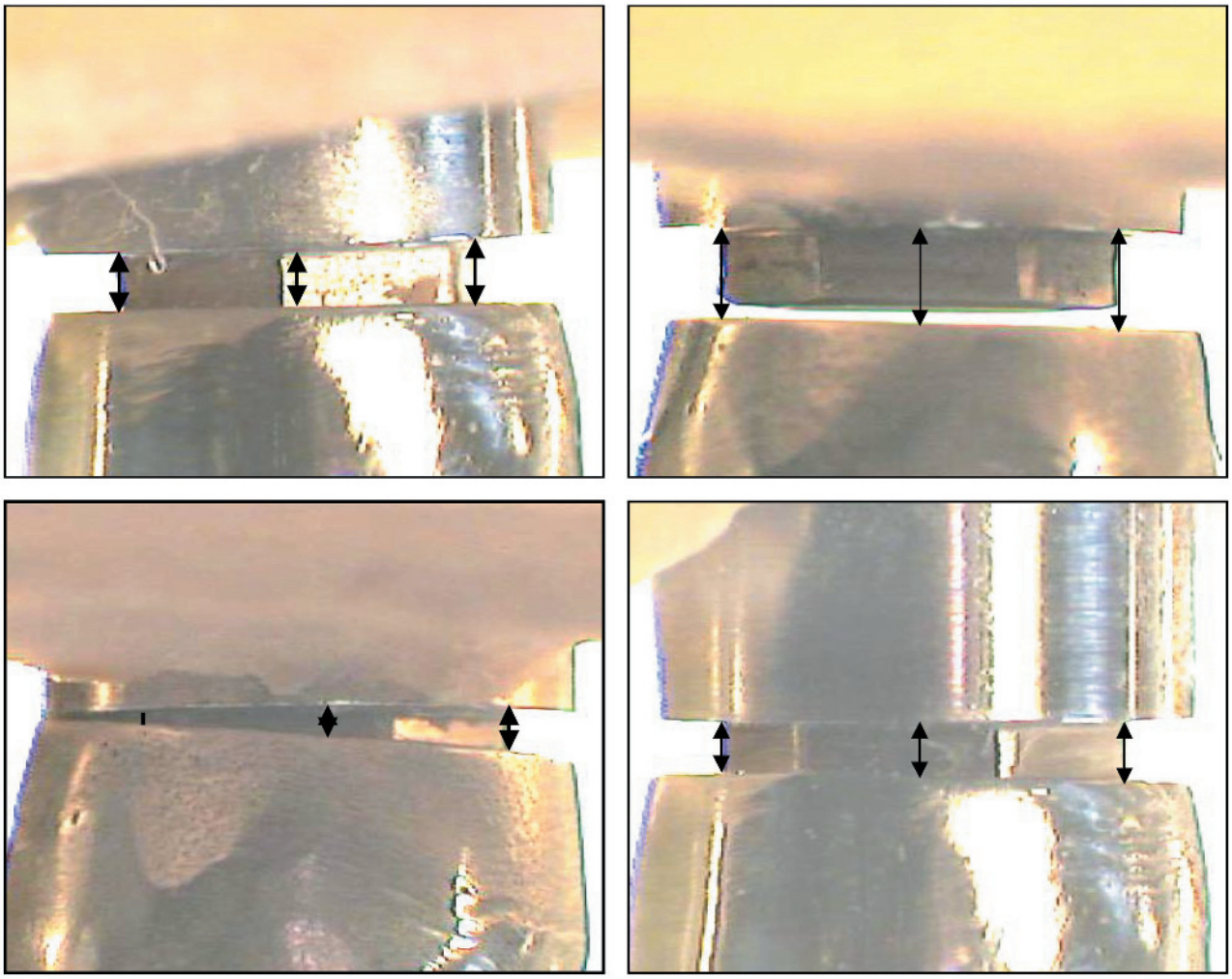

Figure 3 Light microscopic image (×12 magnification) of the gap between the test and the control implant before (*top*) and 12 weeks after (*below*) prosthesis installation. The distance between the implant and the prosthesis was measured starting on six positions on the implant and going perpendicular from the implant to the prosthesis (↔). These positions were the left and right borders of the external hexagon of the implant and exactly in the middle. These measurements were done on a front view and a back view. Note the inclination discrepancy between the test implant and the prosthesis, which prevents complete gap closure.

using a two-way analysis of variance. The level of significance was set at 5%.

RESULTS

Both test and control implants osseointegrated well. Nevertheless, they all showed some crestal bone loss. Figure 5 presents the average (standard error of measurement) crater depths, crater surfaces, and bone-implant contacts of test versus control implants. The differences in biologic response between test versus control implants were not statistically significant.

The mean (standard deviation) resonance frequency analysis (ISQ) values for test and control implants were 59 (11) and 65 (5), respectively, at baseline and 80 (10) and 75 (14), respectively, after 12 weeks. There were no significant differences between the test and control implants. The increased ISQ values after 12 weeks differed significantly from the baseline.

Table 1 depicts the gap sizes between the prostheses and the test and control implants for each individual animal before (test model 2, control model 1) and 12 weeks after prosthesis connection (test model 3, control model 2). An example of the misfit measurements is shown in Figure 3.

At baseline, the vertical misfit between the prostheses and the test implants as measured on test model 2 was, on average, 582.9 ± 204.4 μm. The control implants demonstrated an average vertical misfit of 494.6 ± 50.6 μm as measured on control model 1. There was a statistically significant decrease ($p < .05$) in

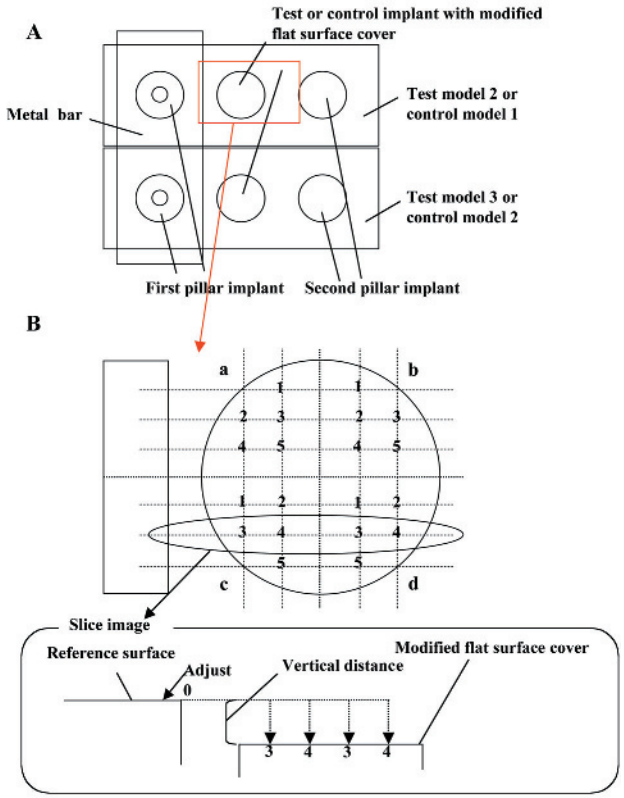

Figure 4 *A*, Scanning image acquired from the Laserscan 3D PRO device. *B*, Four measurement areas (a, b, c, d). As for five arbitrary measuring points of each area, the vertical distances from the top surface of the metal bar as a reference surface were measured. The mean value of five measuring points was calculated as a representative one of each area.

gap size between baseline and the end of the study for the test implants. The average (± SD) change in misfit amounted to 413.2 ± 232.3 μm. There was also a decrease in misfit (195.1 ± 216.3 μm) for the control implants, but this difference was not statistically significant.

Table 2 represents the displacements of the test and control implants as registered by the three-dimensional laser scanner. These measurements revealed that the displacement (510.6 ± 305.1 μm) of the test implants was significantly larger than that of the control implants (186.6 ± 239.5 μm) ($p < .01$). The values among the four measurement areas (a, b, c, and d) did not differ significantly.

DISCUSSION

The prosthesis misfit does not seem to compromise implant osseointegration for the immediately or for the delayed loaded implants. The term *immediately* or *delayed loaded implants* was used in this context despite the absence of occlusal loading of the prostheses because the prosthesis misfit induced a tensile load on the involved implants. Additional occlusal implant loading was avoided to be able to assess the influence of the static loads resulting from screw tightening the ill-fitting prosthesis only, thereby excluding the effect of any other additional loading.

Although all implants integrated, some crestal bone loss was observed around all of them. No active signs of bone resorption were seen histologically, indicating that the bone remodeling reached an equilibrium. The static tensile loads on the implants—caused by the prosthesis misfit—could be responsible for this bone loss. For the control implants, higher tensile loads are supposed to remain owing to the larger remaining gaps. Since all test implants eventually got in contact with their prostheses at some point, it is likely that the main part of the tensile loads was not further distributed to the implant surroundings. Nevertheless, a comparable bone loss was observed in test and control implants, indicating that other factors were also affecting the bone.

The observed crestal bone loss could also be the result of the percutaneous connection between the implants and the prostheses. This skin perforation allows epithelial downgrowth and access of microorganisms to the implant site. Many authors report on the importance of the microgap between the implant and abutment prosthesis for microbial leakage, eventually resulting in crestal bone loss.[13,14] It is obvious that a prosthesis misfit as large as 500 μm harbors large quantities of microorganisms, threatening crestal bone integrity. Also, the fact that a periostal flap was made

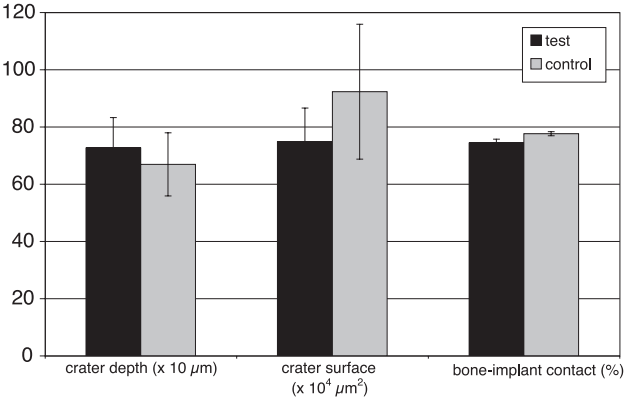

Figure 5 Graph representing the results of the histomorphometric analyses: average (standard error of measurement) crater depth (× 10 μm), crater surface (× 10^4 μm^2), and bone-implant contact (%). No significant differences were observed.

TABLE 1 Gap Size (μm) between Prosthesis and Test and Control Implant before and 12 Weeks after Prosthesis Fixation, as Measured under the Light Microscope

	Test			Control		
Animal	Before Prosthesis Fixation	12 Weeks after Prosthesis Fixation	Difference before-after	Before Prosthesis Fixation	12 Weeks after Prosthesis Fixation	Difference before-after
1	388.6	7.6	381.01	527.63	97.14	430.49
2	689.5	219.1	470.4	523.8	466.64	57.159
3	358.4	320.1	38.32	503.04	74.28	428.76
4	642.0	123.8	518.19	405.71	417.20	−11.49
5	836.2	178.0	658.23	512.63	441.93	70.7
Mean (SD)	582.9 (204.4)	169.7 (115.6)	413.2 (232.3)	494.6 (50.6)	299.4 (196.1)	195.1 (216.3)

prior to implant installation can explain some crestal bone loss as well.[15]

The screw tightening of the prostheses on the test implants resulted in a significant decrease in the gap size. Although the implants were installed bicortically in the tibia, the tightening torque (35 Ncm) seemed to be sufficient to pull the nonintegrated test implant toward the prosthesis. This movement occurred most probably during the fixation of the prosthesis, thereby possibly inducing microfractures of the bone between and outside the implant screw threads. The fact that the prostheses were as firmly connected to the implants at the time of prosthesis connection compared with 12 weeks afterward (no screw loosening was observed) makes it very unlikely that the implant moved after prosthesis fixation. In all cases, the prostheses were in contact with the test implants at some point, although not always along the entire implant neck surface. In some cases, the gaps could not close completely because there were additional horizontal prosthesis misfits and discrepancies between implant and prosthesis cylinder inclination (see Figure 3).

Although the prosthesis misfit in the case of the control implants did not decrease significantly, some implant movement toward the prosthesis occurred. The high biologic tolerance against these considerable static loads was already reported many times,[16–20] which is not the case for the present observation of displacement of osseointegrated implants. In an experiment by Gotfredsen and colleagues on three dogs, osseointegrated implants were statically loaded by means of an expansion screw that was activated every 2 weeks during a period of 10 or 46 weeks.[21] Implant posts in the models—made from impressions taken during the course of the experiment—revealed a displacement of the implant posts as well. The authors interpreted this displacement as being the result of a plastic deformation of the implant posts because no corresponding displacement of the implants could be identified on radiographs. It is unlikely that the observed implant displacement in our study is due to deformation of the implant itself or the prostheses, which were taken as a reference to measure the misfit. No deformation of the implants was seen on the histologic sections, and the fit of the prostheses on the primary models remained the same during the experiment, which confirms the lack of deformation. Taking the mechanical properties into account, cortical bone is at least 10 times more likely to deform than titanium.[22] The observed implant movement caused by bone deformation—owing to strain and microfractures—most likely occurred at the time of prosthesis connection because, also for the control implants, the prostheses were as firmly connected to the implants at the time

TABLE 2 Displacements (μm) of the Test and Control Implants, Registered by the Three-Dimensional Laser Scanner

Animal	Test Implant Displacement	Control Implant Displacement
1	607.4	485.0
2	491.3	15.2
3	267.1	409.2
4	213.2	−1.0
5	974.2	24.5
Mean (SD)	510.6 (305.1)	186.6 (239.5)

of prosthesis connection compared with 12 weeks afterward. Implant displacement after prosthesis fixation would have resulted in clinically evident relaxation of the implant-prosthesis connection. However, because the current observation is not statistically significant, more research is mandatory to support or reject the possibility of osseointegrated implant displacement.

This animal study reveals that prosthesis misfit does not lead to biologic failure of immediately loaded or already osseointegrated implants and that an immediately loaded implant is topographically forced to fit an ill-fitting prosthesis. However, these findings are not an excuse not to reach an optimal fit in clinical conditions, especially in healed implant sites. It has been well documented that a compromised fit leads to mechanical failures (eg, screw and abutment fracture) and screw loosening.[23,24]

ACKNOWLEDGMENT

Joke Duyck is a postdoctoral fellow of the Fund for Scientific Research Flanders.

REFERENCES

1. Brånemark PI, Adell R, Breine U, Hansson BO, Lindstrom J, Ohlsson A. Intra-osseous anchorage of dental prostheses. I. Experimental studies. Scand J Plast Reconstr Surg 1969; 3:81–100.
2. Gapski R, Wang H-L, Mascarenha P, Lang NP. Critical review of immediate implant loading. Clin Oral Implants Res 2003; 14:515–527.
3. Brånemark PI, Engstrand P, Ohrnell LO, et al. Brånemark Novum: a new treatment concept for rehabilitation of the edentulous mandible. Preliminary results from a prospective clinical follow-up study. Clin Implant Dent Relat Res 1999; 1:2–16.
4. Engstrand P, Nannmark U, Martensson L, Galeus I, Brånemark PI. Brånemark Novum: prosthodontic and dental laboratory procedure for fabrication of a fixed prosthesis on the day of surgery. Int J Prosthodont 2001; 14: 303–309.
5. van Steenberghe D, Naert I, Andersson M, Brajnovic I, Van Cleynenbreugel J, Suetens P. A custom template and definitive prosthesis allowing immediate implant loading in the maxilla: a clinical report. Int J Oral Maxillofac Implants 2002; 17:663–670.
6. Ganz SD. Use of stereolithographic models as diagnostic and restorative aids for predictable immediate loading of implants. Pract Proc Aesthet Dent 2003; 15:763–771.
7. Rocci A, Martignoni M, Gottlow J. Immediate loading in the maxilla using flapless surgery, implants placed in predetermined positions, and prefabricated provisional restorations: a retrospective 3-year clinical study. Clin Implant Dent Relat Res 2003; 5(Suppl 1):29–36.
8. Tardieu PB, Vrielinck L, Escolano E. Computer-assisted implant placement. A case report: treatment of the mandible. Int J Oral Maxillofac Implants 2003; 18:599–604.
9. Wagner A, Wanschitz F, Birkfellner W, et al. Computer-aided placement of endosseous oral implants in patients after ablative tumour surgery: assessment of accuracy. Clin Oral Implants Res 2003; 14:340–348.
10. Muacevic A, Uhl E, Steiger HJ, Reulen HJ. Accuracy and clinical applicability of a passive marker based frameless neuronavigation system. J Clin Neurosci 2000; 7:414–418.
11. Poggi S, Pallotta S, Russo S, Gallina P, Torresin A, Bucciolini M. Neuronavigation accuracy dependence on CT and MR imaging parameters: a phantom-based study. Phys Med Biol 2003; 48:2199–2216.
12. Vrielinck L, Politis C, Schepers S, Pauwels M, Naert I. Image-based planning and clinical validation of zygoma and pterygoid implant placement in patients with severe bone atrophy using customized drill guides. Preliminary results from a prospective clinical follow-up study. Int J Oral Maxillofac Surg 2003; 32:7–14.
13. Broggini N, McManus LM, Hermann JS, et al. Persistent acute inflammation at the implant-abutment interface. J Dent Res 2003; 82:232–237.
14. Piattelli A, Vrespa G, Petrone G, Iezzi G, Annibali S, Scarano A. Role of the micro gap between implant and abutment: a retrospective histologic evaluation in monkeys. J Periodontol 2003; 74:346–352.
15. Gomez-Roman G. Influence of flap design on peri-implant interproximal crestal bone loss around single-tooth implants. Int J Oral Maxillofac Implants 2001; 16:61–67.
16. Carr AB, Gerard DA, Larsen PE. The response of bone in primates around unloaded dental implants supporting prostheses with different levels of fit. J Prosthet Dent 1996; 76: 500–509.
17. Jemt T, Book K. Prosthesis misfit and marginal bone loss in edentulous implant patients. Int J Oral Maxillofac Implants 1996; 11:620–625.
18. Jemt T, Lekholm U. Measurements of bone and framework deformations induced by misfit of implant superstructures. A pilot study in rabbits. Clin Oral Implants Res 1998; 9:272–280.
19. Duyck J, Rønold HJ, Van Oosterwyck H, Naert I, Vander Sloten J, Ellingsen JE. The influence of static and dynamic loading on the marginal bone behaviour around implants: an animal experimental study. Clin Oral Implants Res 2001; 12:207–218.
20. Duyck J, Van Oosterwyck H, De Cooman M, Vander Sloten J, Puers R, Naert I. Preload on oral implants after screw tightening fixed full prostheses: an in vivo study. J Oral Rehabil 2001; 28:226–233.

21. Gotfredsen K, Berglundh T, Lindhe J. Bone reactions adjacent to titanium implants subjected to static load of different duration. A study in the dog (III). Clin Oral Implants Res 2001; 12:552–558.
22. Borchers L, Reichart P. Three-dimensional stress distribution around a dental implant at different stages of interface development. J Dent Res 1983; 62:155–159.
23. Taylor TD. Prosthodontic problems and limitations associated with osseointegration. J Prosthet Dent 1998; 79: 74–78.
24. Kallus T, Bessing C. Loose gold screws frequently occur in full-arch fixed prostheses supported by osseointegrated implants after 5 years. Int J Oral Maxillofac Implants 1994; 9:169–178.