Histologic Evaluation of Bone Response to Oxidized and Turned Titanium Micro-implants in Human Jawbone

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Purpose: *To evaluate the human bone tissue response to 2 surfaces (oxidized or turned) on commercially available titanium implants.* ***Materials and Methods:*** *Screw-type turned (control) and oxidized (test) micro-implants were manufactured in the same manner as commercially available turned and oxidized (TiUnite, Brånemark System) implants. The thickness of the oxide layer of the test implants was on average 10 μm, corresponding to the oxide thickness of the apical part of the TiUnite implant. Twenty patients received 1 test and 1 control micro-implant each during implant surgery. Before placement, the surface topography of the implants was characterized with an optical confocal laser profilometer. After a mean healing period of 6.6 months in the maxilla and 3.5 months in the mandible, the micro-implants and surrounding tissue were removed with a trephine bur. Histologic sections were produced, and the specimens were analyzed histomorphometrically.* ***Results:*** *Surface roughness and enlargement were greater for the oxidized implants than for the turned implants. All micro-implants, except for 2 controls, were found to be clinically stable at the time of retrieval. Histomorphometric evaluation demonstrated significantly higher bone-to-implant contact for the oxidized implants, whether placed in the maxilla or in the mandible. Significantly more bone was found inside the threaded area for the oxidized implants placed in the mandible and maxilla, but there was no difference between implants with regard to position (maxilla or mandible).* ***Discussion:*** *The stronger bone response to the oxidized implants may have contributed to the fact that 2 control implants but no test implants were lost. The reason for these findings may depend on one or multiple differences of the surfaces between test and control implants: (1) the thicker oxide layer itself, (2) increased surface roughness, (3) different surface morphology in terms of porosity, or (4) change in crystal structure.* ***Conclusion:*** *The present histologic study in human jawbone demonstrated a significantly higher bone response for anodic oxidized titanium implants than for implants with a turned surface.* (Int J Oral Maxillofac Implants 2003;18:341–348)

Key words: *bone healing, dental implants, histomorphometry, oxides, surface characterization, titanium*

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Oral implant treatment based on the original work by Brånemark and coworkers[1] has been documented extensively and proven to be a reliable treatment modality in the restoration of edentulous jaws.[2,3] However, advanced jaw resorption and poor bone quality have been linked to high rates of implant failure.[4–7] One way to circumvent this clinical problem is to change the surface characteristics of the implant so as to enhance the bone response and thus improve the clinical success rate. Numerous experimental studies focused on surface-enlarged implants (ie, plasma spraying, grit blasting, acid etching) have found an improved bone response, in terms of bone-implant contact and removal torque, as compared to a smooth surface.[8–16]

When titanium is exposed to air, a surface oxide of mainly titanium dioxide (TiO_2) is formed very rapidly.[17] The excellent biocompatibility of titanium is largely explained by the metal's good corrosion resistance, which has been ascribed to the chemical stability of TiO_2 in biologic environments.[18] Another way to alter the surface characteristics is to enhance the oxide layer of the implant. Such modification will have an influence on surface morphology, chemical composition, crystal structure, and surface topography.[19,20] Based on histomorphometric studies of commercially pure titanium implants placed in the rabbit tibia, Larsson[21] concluded that an increased oxide thickness and roughness on the sub-micrometer scale were advantageous surface properties for early bone tissue response, while no significant differences were observed after 1 year of healing. In another experimental study in the rabbit tibia by Sul and coworkers,[22] a greater bone response, as measured with biomechanical and histomorphometric techniques, was found for implants with an oxide thickness of 600 to 1,000 nm, as compared to implants with an oxide thickness of 17 to 200 nm.

Today an oxidized implant (TiUnite; Nobel Biocare, Göteborg, Sweden) is commercially available. The surface is created by anodic oxidation and has been investigated by Hall and Lausmaa.[19] The authors reported an increase in oxide thickness, from 1 to 2 µm at the coronal part to 7 to 10 µm at the apical part of the implant. The surface exhibited numerous pores of varying size, predominantly 1 to 2 µm, as measured at the apical part of the implant. Surface roughness increased continuously from the conical upper part to the apical end, with an average R_a value of 1.2 µm. Animal studies of this surface-modified implant have shown a stronger bone reaction compared to turned (machined) implants, as measured with removal torque tests and histomorphometry.[23,24] However, results from animal studies may not be relevant in clinical reality.[25] Therefore, it may be more important to evaluate the bone tissue response to implants in human jawbone. This model has previously been used in reports of studies in which surface-enlarged micro-implants have been evaluated histomorphometrically[26,27] to investigate the bone tissue reaction.

To date, little has been published concerning the oxidized surface. The purpose of the present investigation was to evaluate the human bone tissue response to 2 different surfaces on commercially available implants.

MATERIALS AND METHODS

Patient Selection

Twenty edentulous patients (12 women and 8 men) with a mean age of 67.2 years (range 53 to 80) referred to a single clinic (Department of Oral and Maxillofacial Surgery, Mölndal Hospital, Mölndal, Sweden) for endosseous dental implant treatment were included. The Ethical Committee for Human Clinical Trials at Göteborg University, Sweden, approved the study.

Micro-implants

Screw-type turned (control) and oxidized (test) micro-implants (diameter 2.3 mm, length 5 mm) were manufactured from commercially pure titanium in the same manner as the commercially available turned and oxidized (TiUnite) Brånemark System implants (Brånemark System, Nobel Biocare). The thickness of the oxide layer of the test implants was on average 10 µm, corresponding to the oxide thickness found on the apical part of the TiUnite implant.[19]

Surface Characterization

A 3-dimensional (3D) optical profilometer (TopScan 3D, Heidelberg Instruments, Heidelberg, Germany) was used to characterize the surface roughness of the test and control implants. This instrument was previously described[28] and found to be appropriate for implant measurement.[29] Three screws of each surface modification were analyzed. Each screw was measured at 9 sites: 3 tops, 3 valleys, and 3 flanks. Each measured area was 245×245 µm. In accordance with the standard,[30] a Gaussian filter was used to separate roughness from form and waviness. The filter size was 50×50 µm. To numerically describe the surface roughness, 3 different parameters were used: S_a is the absolute average height deviation calculated from a mean plane, S_{cx} describes the average wavelength of the surface irregularities crossing the mean plane, and S_{dr} is the ratio between the measured surface and a flat reference plane (3D/2D). For visual descriptions of the 2 surfaces, digital images were prepared from the measurements.

Surgical Procedures

One hour prior to surgery, the patients were given 3 g amoxycillin (Imacillin; AstraZeneca Sverige, Södertälje, Sweden) and diazepam (Stesolid; Dumex, Copenhagen, Denmark) at a dose of 0.3 mg/kg body weight. The surgical areas were locally anesthetized (2% lidocaine with epinephrine 12.5 µg/mL; Xylocain/Adrenalin; AstraZeneca Sverige).

After a crestal incision, mucoperiosteal flaps were elevated and the endosseous implants were placed. Thereafter, the micro-implants (1 control/1 test) were placed in suitable areas, which were mostly the premolar/molar regions (ie, posterior to the most distal endosseous implant). If the patient was bilaterally edentulous in the posterior regions of the jaw, a randomization depending on birthdate determined whether the test implant was placed on the right or left side. In unilaterally edentulous patients where the test and control implants were placed on the same side, birthdate determined whether the test implant was positioned anteriorly or posteriorly.

The micro-implant sites were drilled with a 1.7-mm twist drill, and in dense bone, a 2.0-mm twist drill was added. The implants were placed with a handpiece via a connector (Fig 1) and finally tightened manually with a screwdriver. Drilling procedures and implant placements were made under profuse irrigation with sterile saline. The wounds were closed with resorbable mattress and interrupted sutures. For postoperative plaque control, patients were prescribed 0.2% chlorhexidine rinses twice daily for 2 minutes over 10 days. The dentures were relined after 10 to 14 days.

A total of 40 micro-implants (20 control/20 test implants) were placed in 9 maxillae and 11 mandibles. The mean healing time was 6.6 months (range 5.5 to 7.2 months) in the maxilla and 3.5 months (range 3.0 to 3.8 months) in the mandible. At abutment connection surgery, the test and control implants were removed with a 3.3-mm-wide trephine, and the specimens (implants together with surrounding bone tissues) were fixed by immersion in formaldehyde solution.

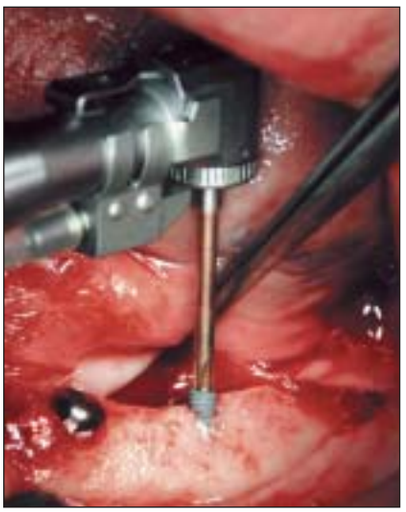


Fig 1 A test implant is placed in a posterior position of the mandible with the aid of a connector.

Histomorphometry

The specimen handling followed the internal guidelines of the Göteborg University Biomaterial/Handicap laboratories. In brief, the specimens were dehydrated in a graded series of ethanols; embedded in methylmethacrylate resin (Technovit 9100 VLC, Kulzer, Wehrheim, Germany); and polymerized. Ground sections were produced according to techniques described by Donath and Breuner[31] and Donath.[32] The implants with surrounding bone were then cut (to about 150 µm); ground (to about 10 µm) in an Exakt sawing and grinding machine (Exakt Apparatebau, Norderstedt, Germany); and finally stained with a mixture of 1% toluidine blue and pyronin G.[33]

The ground sections were examined in a Leitz Aristoplan microscope (Leitz, Wetzlar, Germany) with objectives 1.6× to 40× and with a zoom up to 2.5× when needed. The microscope was equipped with a Microvid System (Leitz) that permitted direct intraocular morphometric measurements to be made on the ground sections.[34] All measurements were performed at an objective magnification of 10×.

The mineralized bone-implant contact and the amount of bone area within the threads (from the top of the implant to the last apical thread) were calculated and expressed as percent bone contact and percent bone area, respectively. Furthermore, the bone area in an out-folded image (mirror image) was measured as described by Johansson.[34] Means and standard deviations were calculated.

Statistics

The Wilcoxon signed rank test for paired analysis was used for comparison of surface modification of the implants. For comparison between patients with treatment in maxillae and mandibles, respectively, the Mann-Whitney *U* test was used. Furthermore, a *t* test distributed variable was used to calculate 95% confidence intervals (CIs) for differences. Significance tests were 2-tailed and conducted at the 5% significance level.

RESULTS

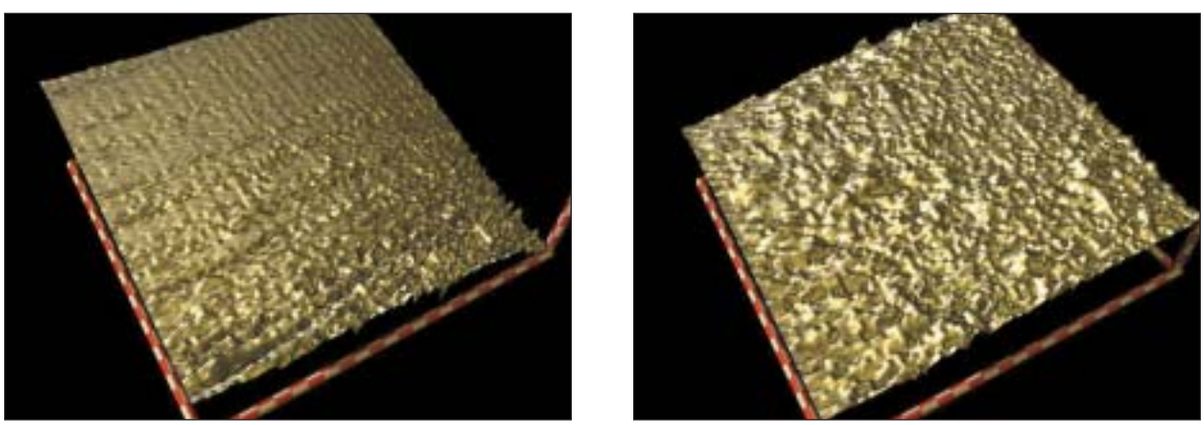
Topographic Evaluation

The average height deviation (S_a) was higher and the average wavelength (S_{cx}) was longer for the oxidized implants than for the turned ones. Thus, the turned implants had a denser surface structure. This may have resulted in a similar surface enlargement

Table 1 Roughness Measurements (Mean and SD) for Oxidized and Turned Micro-implants

Surface modification	S_a (µm)	S_{cx} (µm)	S_{dr} (%)
Turned	0.78 (0.35)	9.31 (2.68)	25.83 (15.81)
Oxidized	1.17 (0.17)	11.57 (0.98)	36.98 (6.03)

S_a = height deviation; S_{cx} = wavelength; S_{dr} = developed surface. The values are means calculated from 3 implants of each surface modification and 9 measurements (3 tops, 3 valleys, 3 flanks) per implant, ie, 27 measurements per surface modification. Measuring area 245×245 µm. A Gaussian filter sized 50×50 µm was used before roughness was calculated.



Figs 2a and 2b Visual appearance of the surface topography. Each red and white section represents a length of 10 µm. *(Left)* Image from a turned screw flank (control surface). *(Right)* Oxidized screw flank (test surface). The turned surface has a clear orientation of the surface irregularities, whereas the oxidized surface lacks such an orientation.

(S_{dr}) for the 2 investigated surfaces. However, the denser structure found on the turned implant was not enough to compensate for the much greater height deviation of the oxidized implants. Surface enlargement was 37% for the oxidized implants, versus 15% for the turned implants. The standard deviation was much higher for the turned implants, mainly the result of very rough thread tops. The numeric description of the surface roughness is presented in Table 1, and depictions of the surface topographies can be seen in Figs 2a and 2b.

Clinical Findings

All micro-implants except for 2 controls were found to be clinically stable at the time of retrieval. One of them, a maxillary control implant, was found to be situated in the maxillary sinus (but was included in the evaluation as "no bone contact or bone area"). The corresponding test implant was stable but showed marginal bone resorption of 5 threads. These 2 implants were placed in bone quality 3 according to Lekholm and Zarb[35] and achieved poor stability at placement. The other non-integrated implant, a mandibular one, was mobile and encapsulated in soft tissue, with a clinically manifest infection. The corresponding test implant was stable but showed marginal bone resorption and surrounding infection. These 2 implants were placed in bone quality 2 and achieved good stability at placement. One test and 1 control implant showed mucosal perforations and marginal bone resorption at the time of abutment surgery. In all, 2 test and 4 control implants presented with varying amounts of marginal bone resorption (1 to 5 threads) (Fig 3). Thus, 39 micro-implants were retrieved for histologic analysis, including the non-integrated mandibular implant.

Histologic and Histomorphometric Findings

Light microscopic investigations of the cut and ground sections revealed the implants to be variously integrated with respect to the quantity of bone around the implants and the remodeling rate. Samples harvested from the maxilla demonstrated a thinner bone collar around both test and control implants, compared to samples harvested from the

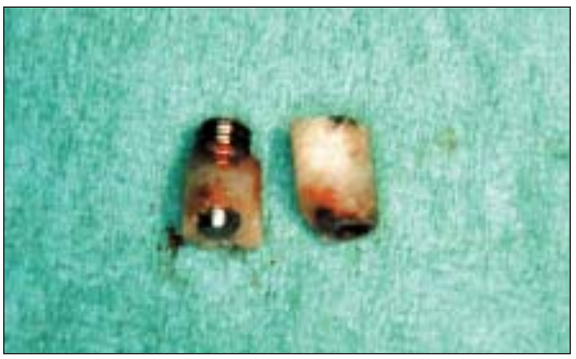


Fig 3 *(Right)* Retrieved implants demonstrating bone resorption, which is especially notable on *(left)* the turned implant modification.

Figs 4a to 4c *(Below) Representative survey pictures of undecalcified cut and ground sections (10 µm; toluidine blue). There is a distance of 600 µm between the thread peaks.*

Fig 4a Control sample from the maxilla of a male patient.

Fig 4b Test sample from the maxilla of the same male patient. Note the bone trabeculae formed along the implant surface; most likely this formation is the result of the osteoconductivity of the test samples.

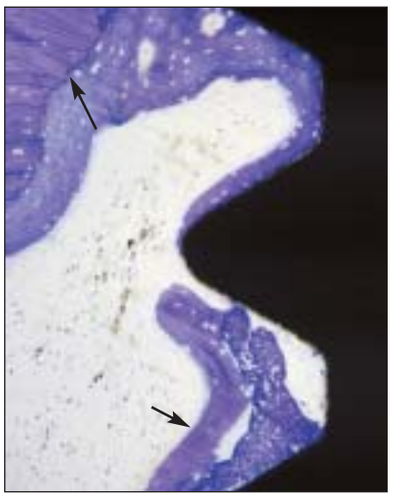
Fig 4c Test sample from a mandible. Note the bone trabeculae formed along the implant surface.

mandible. The latter samples demonstrated larger areas and more compact bone compared to the former. Irrespective of harvest site, a greater number of the test implants were surrounded by bone tissue compared to control implants (Figs 4a to 4c). All samples demonstrated a resorptive bone surface in the upper region.

In general, the control samples showed less ongoing remodeling activity, ie, they revealed a "silent impression" compared to the test samples. While the test implants seemed to be osteoconductive (ie, they often had a thin bone trabeculae formed along and in close relation to the surface), this was not observed on the controls. The bony tissue in "contact" with the implants was not fully mature; however, it was not woven bone but, compared to the original bone, was newer. A clear demarcation line (cement line) could be observed between old and newly formed bone. Some remnants of old bone (bone flakes) were observed; these were entrapped in the bone tissue and not fully resorbed (Fig 5).

In soft tissue areas as well as closer to the implant surfaces, inflammatory cells such as lymphocytes, macrophages, giant cells, some plasma cells, and occasionally granulocytes (basophils) could be seen. These cell types were observed more frequently around the test implants than the controls. In almost all test samples, soft tissue areas with cells that seemed to have particles internalized (Fig 6) were observed. These particles had a similar "light" appearance as the "coat" on the test implant surface. The coating seemed to vary in thickness between the samples.

Significantly more bone was found to be in contact with the oxidized surface than with the turned surface. This was the case regardless of whether all implants were considered in the calculation or if the calculation was performed separately for the maxillary and mandibular implants. A greater amount of bone inside the threaded area was found for the oxidized implants. However, this was statistically significant only if all implants were included in the



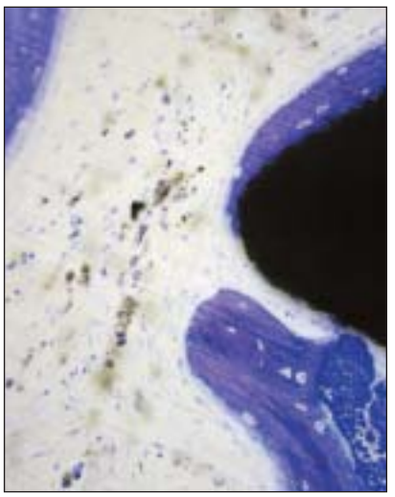


Fig 5 *(Left)* A clear demarcation (cement line) *(upper left side)* could be observed between old lamellar and newly formed bone. Some remnants of old bone (bone flakes) were observed *(inside lower thread)* as being entrapped in the bone tissue and not fully resorbed.

Fig 6 *(Right)* In almost all test samples, soft tissue areas with cells that seemed to have particles internalized could be observed.

calculation (Tables 2 and 3). The oxidized surface demonstrated no significant differences between implants placed in the maxilla or in the mandible, with respect to bone-implant contact or amount of bone in the thread area. However, significantly more bone was found in the mirror image of implants placed in the mandible compared to the maxilla (Table 4). For the turned implants, no significant difference was found between maxillary and mandibular implants concerning bone-implant contact, bone area, or bone in the mirror image area (Table 4).

DISCUSSION

In the present study, significantly more bone-implant contact and bone inside the threaded area were found for the oxidized implants than for the turned ones. These findings are consistent with those reported from animal studies comparing the bone response of turned and oxidized (TiUnite) implants. Albrektsson and associates[23] found that oxidized titanium implants showed significantly more bone-implant contact and higher removal torque values than turned implants after 6 weeks of healing, as studied in New Zealand white rabbits. In another study in the greyhound mandible,[24] significantly higher removal torque values were registered for oxidized (TiUnite) implants than for turned surfaces, implying a more stable anchorage for the oxidized implants. Histomorphometric data indicated higher values for the oxidized implants as well, but no data were presented.

In accordance with a previously published study,[27] the turned micro-implants demonstrated very rough surface (thread top) areas. Furthermore, one was isotropic (without a dominating direction of the surface topography) and the other had an anisotropic surface (with a dominating direction), which were evaluated in the above-cited study as well as in the present study, although the isotropy was achieved by blasting in the former study and with an oxidizing process in the present study. However, in the present study, 2 surfaces with quite different roughness were investigated. The rougher, isotropic, oxidized surface demonstrated better bone fixation than the turned surface, as evaluated by the amount of bone in contact with the implant surface and the amount of bone in the threaded areas. However, some small pieces resembling the oxide layer had become loose and were seen in the surrounding soft tissue areas as well as internalized in cells. Most likely this was the result of "tearing off" of the oxide coating during placement of the self-tapping implants into the bone bed. Similar findings have been observed by Sul and coworkers[20] around oxidized titanium implants placed in rabbit bone. Whether or not this could pose a risk for decreased implant stability per se cannot, however, be judged yet.

The experimental implants in the present study were subjected to a normal clinical situation (eg, chewing, load from denture, risk of infection). The stronger bone response to the oxidized implants may have contributed to the fact that 2 control implants but no test implants were lost. The reasons for the stronger bone reaction to the oxidized implants compared to the turned controls may be single or multiple. The thicker oxide layer itself may lead to a stronger bone response. The change in the morphology of the oxidized implants (size and distribution of pores) may be another reason, whereas the turned surface lacks such features. The surface enlargement and increased surface roughness for the oxidized implants may be a relevant factor for the

Table 2 Bone-to-Implant Contact, Bone Area Inside the Threads, and Bone Area in a "Mirror Image" (Means and SDs) for Turned and Oxidized Micro-implants

Measurement	Turned surface	Oxidized surface	*P* value*	Confidence interval
Bone-implant contact (%)	13 (12)	34 (13)	< .001	14 to 28
Bone area (%)	28 (17)	38 (16)	.023	2 to 20
Bone area mirror image (%)	34 (18)	36 (15)	> .300	–6 to 11

The values are calculated from 20 turned implants and 19 oxidized.
*Turned vs oxidized surface.

Table 3 Bone-to-Implant Contact, Bone Area Inside the Threads, and Bone Area in a "Mirror Image" (Means and SDs) for Turned and Oxidized Micro-implants by Jaw

Measurement	Turned surface	Oxidized surface	*P* value*	Confidence interval
Maxilla				
Bone-implant contact (%)	11 (10)	29 (15)	.021	6 to 30
Bone area (%)	23 (13)	32 (18)	.190	–7 to 25
Bone area mirror image (%)	27 (13)	27 (14)	> .300	–13 to 14
Mandible				
Bone-implant contact (%)	15 (14)	37 (11)	.003	12 to 33
Bone area (%)	31 (20)	44 (12)	.062	0 to 24
Bone area mirror image (%)	39 (19)	44 (13)	> .300	–9 to 17

The values are calculated from 9 turned implants and 8 oxidized (maxilla) and 11 turned and 11 oxidized (mandible), respectively.
*Turned vs oxidized surface.

Table 4 Comparison of Patients Treated in the Maxilla and Mandible, Respectively (Means and SDs), with Oxidized Versus Turned Surfaces

Surface	Maxilla (n = 9)	Mandible (n = 11)	*P* value	Confidence interval
Oxidized				
Bone-implant contact (%)	29 (15)	37 (11)	.15	–20 to 4
Bone area (%)	32 (18)	44 (12)	.08	–26 to 3
Bone area mirror image (%)	27 (14)	44 (13)	.02	–29 to –4
Turned				
Bone-implant contact (%)	11 (10)	15 (14)	> .30	–15 to 8
Bone area (%)	23 (13)	31 (20)	> .30	–25 to 8
Bone area mirror image (%)	27 (13)	39 (19)	.13	–28 to 4

The values are calculated from 8 oxidized implants and 9 turned.

strong bone reaction. Both animal and human studies have shown an increased bone response to surface-enlarged implants (ie, plasma spraying, grit blasting, acid etching) than for smooth ones.[8–16,26,27] With increasing oxide thickness there is a change in oxide crystallinity, in that the amorphous oxide changes to anatase and rutile forms,[19,20] which may create a stronger bone reaction. Whether the effect of the oxidized implant surface is single or synergetic has not been investigated in the present study, but Sul[36] suggested a combination of mechanical interlocking and biochemical bonding.

CONCLUSION

The present histologic study in human jawbone demonstrated a significantly higher bone response for anodic oxidized titanium implants than for implants with a turned surface. The clinical relevance of titanium implants with an increased oxide layer requires evaluation in prospective clinical long-term studies.

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