A Histomorphometric Analysis of the Effects of Various Surface Treatment Methods on Osseointegration

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Purpose: *One major factor in the success and biocompatibility of an implant is its surface properties. The purposes of this study were to analyze the surface characteristics of implants after blasting and thermal oxidation and to evaluate the bone response around these implants with histomorphometric analysis.* ***Materials and Methods:*** *Threaded implants (3.75 mm in diameter, 8.0 mm in length) were manufactured by machining a commercially pure titanium (grade 2). A total of 48 implants were evaluated with histomorphometric methods and included in the statistical analyses. Two different groups of samples were prepared according to the following procedures: Group 1 samples were blasted with 50-μm aluminum oxide (Al_2O_3) particles, and group 2 samples were blasted with 50-μm Al_2O_3, then thermally oxidized at 800°C for 2 hours in a pure oxygen atmosphere. A noncontacting optical profilometer was used to measure the surface topography. The surface composition of the implants used and the oxide thickness were investigated with Rutherford backscattering spectrometry.* ***Results:*** *The different preparations produced implant surfaces with essentially similar chemical composition, but with different oxide thickness and roughness. The morphologic evaluation of the bone formation revealed that: (1) the percentage of bone-to-implant contact of the oxidized implants (33.3%) after 4 weeks was greater than that of the blasted group (23.1%); (2) the percentages of bone-to-implant contact after 12 weeks were not statistically significantly different between the groups; (3) the percentages of bone area inside the thread after 4 weeks and 12 weeks were not statistically significantly different between groups.* ***Discussion and Conclusion:*** *This investigation demonstrated the possibility that different surface treatments, such as blasting and oxidation, have an effect on the ingrowth of bone into the thread. However, the clinical implications of surface treatments on implants, and the exact mechanisms by which the surface properties of the implant affect the process of osseointegration, remain subjects for further study.* (INT J ORAL MAXILLOFAC IMPLANTS 2003;18:349–356)

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An increasing number of dental implants of different materials, designs, and surface topography are placed in humans each year. Albrektsson and coworkers[1] reported that only some dental implant systems (such as the Brånemark System [Nobel Biocare, Göteborg, Sweden]) have had a high degree of clinical success, but the reasons for such a range of effectiveness are not well understood. The properties of the biomaterials used, the host tissue, and the surgical technique are among the most important factors for successful incorporation of implants in living tissue. Further, Albrektsson and associates[2] proposed 6 factors that have been generally accepted as especially important for the establishment of reliable osseointegration: implant material, implant design, surface quality, status of the bone, surgical technique, and implant loading conditions. This study focused on 1 of these: the relationship between implant surfaces and biocompatibility.

The surface quality of the implant depends on the chemical, physical, mechanical, and topographic properties of the surface. The different properties will interact with each other, supporting the expectations of Larsson and colleagues[3] that the functional activity of the cells close to the implant surface is influenced by the properties of the implant surface. For example, a change in surface topography may also result in a change in surface energy, thickness of the oxide layer, and surface chemical composition.

The surface topography relates to the degree of roughness of the surface and orientation of the surface irregularities. In a histomorphometric study, Buser and coworkers[4] reported that increased bone-to-metal contact was found to be positively correlated to increased surface roughness. Some of the methods used to alter the surface topography of implants include electropolishing, grinding, abrasive blasting, plasma spraying, photolithography, and laser preparation.

Gotfredsen and coworkers[5] found that more bone came into contact with the implant surface when using titanium dioxide (TiO_2) –blasted implants rather than as-machined, turned ones. Currently, commercially pure titanium (cpTi) is the material of choice for dental implants because of its biologic acceptance in bone, high corrosion resistance, and weight compared to steel; in addition, it can be easily prepared in any required form without inducing any overt adverse reactions. Ti implants are covered by a surface oxide that is approximately 2 to 5 nm thick.[6] This oxide is responsible, in part, for the high corrosion resistance and biocompatibility of Ti.[7,8]

Larsson and associates[3] reported that a higher bone-to-implant contact percentage was found for the implants with a rougher surface, as well as a thicker oxide layer. During implantation, Ti releases corrosion products into the surrounding tissue and fluids, even though it is covered by a thermodynamically stable oxide film.[9] Moreover, Healey and Ducheyne[10] stated that the passive dissolution rate of the Ti decreased as the oxide film thickness increased. Studies of retrieved metal implants have indicated that thickness of the surface oxide layer may increase with time.[11] This may support reports by Taylor and coworkers[12] that Ti reduces the harmful effects of the hydroxyl radicals on the breakdown of hyaluronan (presumably acting as a scavenger for the reactive species), possibly by absorbing them into its surface oxide layer. Choi and colleagues[13] also noted the improved effectiveness on bone formation of the oxidized, blasted Ti surface over the etched, machined surface.

The purposes of this study were to analyze the surface characteristics after blasting and thermal oxidation and to evaluate the bone response around these implants with histomorphometric analysis.

MATERIALS AND METHODS

Implant Preparation

Threaded implants (3.75 mm in diameter, 8.0 mm in length) were manufactured by machining grade 2 cpTi. A total of 48 screw-type implants were evaluated with histomorphometric methods and subjected to statistical analyses. Two different groups of samples were prepared, each with a different surface preparation. Group 1 implants were blasted with 50-µm aluminum oxide (Al_2O_3) and group 2 implants were blasted with 50-µm Al_2O_3 and then thermally oxidized at 800°C for 2 hours in a pure oxygen atmosphere. Ethylene oxide gas sterilization was used to prevent changes of surface characteristics after the thermal oxidation.

Implant Surface Characterization

Surface Topographic Analysis. A noncontacting optical profilometer, TopScan 3D (Heidelberg Instruments, Heidelberg, Germany), was used to measure the surface topography. This system provides visual images as well as numeric values for different surface roughness parameters. Three screws were randomly chosen from each group and were measured 3 times each on the side, top, and bottom. The measuring area for all measurements was 245×245 µm. Numeric descriptors were denoted as Sa, Sz, Scx, and Sdr, where Sa is the arithmetic mean of the absolute values of the surface departures from the mean plane within the sampling area, Sz is the average value of the absolute heights of the 5 highest peaks and the absolute value of the 5 deepest valleys within the sampling area, Scx is the arithmetic mean spacing of the local irregularity, and Sdr is the increased surface area ratio.

Surface Chemical Composition Analysis. The surface composition and the oxide thickness of the implants were investigated with Rutherford backscattering spectrometry. The blasted implants, along with the implants that were oxidized under 400°C for 1 hour, 400°C for 2 hours, 800°C for 1 hour, and 800°C for 2 hours in a pure oxygen atmosphere, were measured.

Animals and Anesthesia

A total of 12 New Zealand White rabbits were used in the experiments. All the animals were adult females weighing 2.5 to 3 kg and age 9 to 11 months. Prior to surgery, the animals were acclimated to the vivarium for 3 months of observation to ensure that they were healthy and stable.

The rabbits were anesthetized with a combination of ketamine 10 mg/kg (Yu-han, Gunpo, South Korea) and Rompun 0.15 mL/kg (Bayer Korea, Ansan, South Korea) intramuscularly. The legs were shaved, washed, and decontaminated with Betadine (Sung Kwang, Buchun, South Korea) prior to surgical draping. One milliliter of 2% lidocaine (Yu-han; 1:100,000) was administered local to the implant sites.

Surgical Technique and Implant Placement

A controlled surgical technique was used to place 4 implants in each animal. Using sterile surgical techniques, the surgeon made an incision in the skin to expose the proximal aspect of each tibia, and the muscles were dissected to allow elevation of the periosteum. The flat surface on the lateral aspect of the proximal tibia was selected for implant placement. The implant site was drilled in the usual manner, using drills with increasing diameters under constant irrigation with sterile saline.

Two oxidized implants (group 2) were placed in every left tibia, and 2 implants blasted with 50-µm Al_2O_3 (ie, control/group 1) were placed in every right tibia. Thus, each rabbit served as its own control. After the implants were seated and stable, the cover screws were securely fastened. Surgical sites were closed in layers. Muscle, fascia, and internal dermal layers were sutured with Vicryl resorbable sutures (Woori Medical, Namyangju, South Korea), while the outer dermis was sutured to primary closure with black silks. All animals received Kanamycin 50 mg/kg (Dong-A, Pochun, South Korea) intramuscularly. After 4 weeks, 6 animals were sacrificed with intravenous injections of air. The remaining 6 animals were sacrificed after 12 weeks of healing.

Preparation of Specimens and Histomorphometric Analysis

All of the implants (n = 48) were prepared for histomorphometric analysis. The implants and surrounding bone were fixed in neutral buffered formalin, dehydrated in 70%, 90%, 95%, and 100% alcohol, and embedded in a light-curing resin (Technovit 7200 VLC; Kulzer, Wehrheim, Germany). The cutting and grinding were performed with an Exakt sawing machine and grinding equipment (Exakt Apparatebau, Norderstedt, Germany). The sections were approximately 10 µm thick and were stained with toluidine blue.

Table 1 Surface Properties of Implants

Surface	Sa (µm)	Sz (µm)	Scx (µm)	Sdr (ratio)
Group 1				
Mean	1.25[a]	16.14[a]	11.54	1.32[a]
SD	0.36	3.84	0.98	0.13
Group 2				
Mean	0.94[b]	10.96[b]	12.53	1.16[b]
SD	0.33	2.35	2.67	0.12

Group 1 = blasted; group 2 = blasted and oxidized.
a > b at $P < .05$ (ANOVA and LSD test).

The histomorphometric analysis was performed with the help of an Olympus BX microscope (Olympus, Tokyo, Japan) connected to a computer. The software used was Image Analysis (Bildanalysis, Stockholm, Sweden). All measurements were calculated with a 10× magnification objective and with eyepieces of 10× magnification. The percentage of bone-to-implant contact in the 3 best consecutive threads and the percentage of bone inside the same threads were calculated. A higher magnification objective and zoom were used to help decide whether or not the bone was in contact with the implant surface.

Statistics

To evaluate the topographic analysis, analysis of variance (ANOVA) ($P < .05$) and the LSD (least significant difference) test were used. The *t* test ($P < .05$) was used for evaluation of the histomorphometric analysis.

RESULTS

Surface Characteristics

A summary of the surface roughness of the implants is presented in Table 1. The blasted implants had higher Sa, Sz, and Sdr values than the oxidized implants (ANOVA, LSD; $P < .05$). The scanning electron microscopic investigation of the implants demonstrated that the Al_2O_3-blasted implants were rougher than the oxidized implants (Figs 1 and 2).

The oxide stoichiometry of the samples (blasted, and thermal oxidation at 400ºC for 1 hour, 400ºC for 2 hours, 800ºC for 1 hour, and 800ºC for 2 hours) was determined. As expected, the oxide thicknesses were significantly different for the different groups. The blasted implants (controls) had a thin oxide layer (2 to 5 nm), while the 4 groups of oxidized implants had much thicker oxides (Table 2). The results for the oxidized implants were in

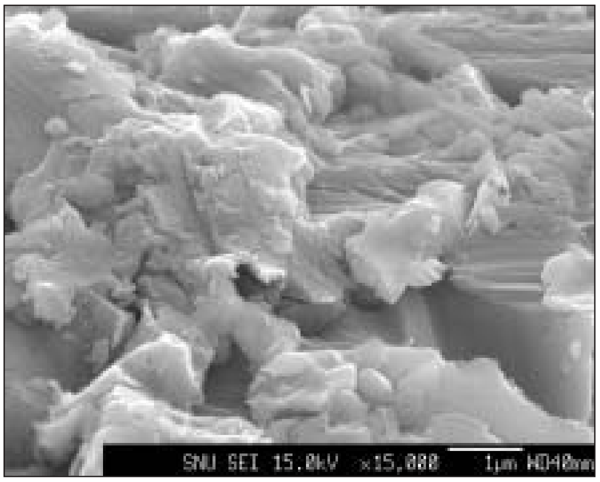

Fig 1 Scanning electron microscopic view of a blasted implant (×15,000).

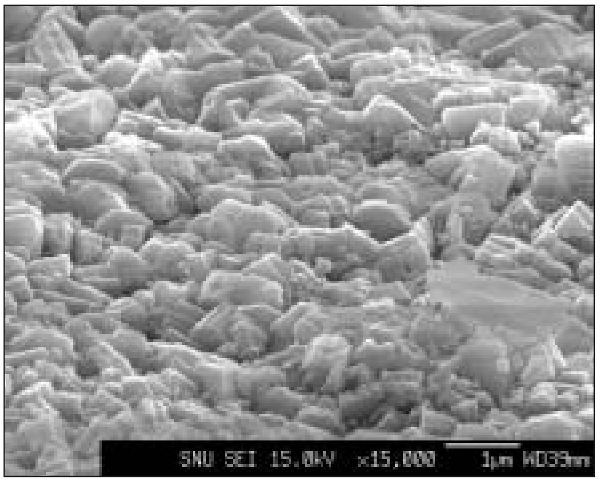

Fig 2 Scanning electron microscopic view of a blasted and oxidized implant (×15,000).

Table 2 Surface Oxide Thickness

Oxidation temperature and time	Oxide layer thickness	Ti/O ratio
400°C, 1 h	1,300 Å	1/0.3
400°C, 2 h	1,500 Å	1/0.45
800° C, 1 h	2,500 Å	1/2
800°C, 2 h	3,000 Å	1/2.3

approximate agreement with the linear relationship between oxide thickness and oxidizing temperature/time.

Histomorphometric Analysis

After 4 weeks, the best 3 consecutive threads were calculated for a percentage of bone-to-metal contact. Histomorphometric analysis showed that the oxidized implants had a statistically significantly higher percentage than the blasted implants ($P < .05$). The mean value for the oxidized implants (left tibia) was 33.3% and the mean value for the blasted implants (right tibia) was 23.1% (Table 3; Figs 3 to 5). In contrast, there was no statistical significance to the values for the percentage of bone area inside the threads, but the screws blasted with Al_2O_3 tended to have higher values (Table 4; Figs 4 to 6). There was 53.1% bone in the threads of the blasted implants and 44.9% bone in the threads of the oxidized implants ($P > .05$).

After 12 weeks, there was no significant difference in either the percentage of bone-to-implant contact or the percentage of bone inside the threads between the control and experimental groups (Tables 3 and 4; Figs 3, 6, 7, and 8).

DISCUSSION

In the present study, implants with different surface properties, and the bone response to these implants, were histomorphometrically analyzed in rabbits. The surface topography in this study was examined with TopScan 3D. This measuring equipment is based on the confocal principle. A laser beam is situated below the surface that is to be measured, thereby allowing measurements of arbitrarily shaped objects. During scanning the objective is moved in 3 directions: x, y, and z. TopScan 3D identified significant differences in the surface topography and roughness of the different groups of implants. The blasted groups had a clearly rougher surface, while the oxidized implants were smoother at the resolution examined by TopScan 3D.

Williams[14] stated that the ultrastructure, microstructure, and macrolevels of the surface topography are known to influence the behavior of the adjacent tissue. Williams indicated that the surface measurements on different scales were important for understanding how the incorporation of implants is influenced by surface topography. The studies by Larsson and coworkers[3] and Webster and associates[15] pointed out the importance of surface roughness in the nanometer range. In contrast to some investigations, which reported a strong correlation between a greater degree of roughness and greater connectivity to bone, the results of a study by Wennerberg[16] indicated that there was an optimal range of surface roughness. Implants blasted with 250-μm particles seemed to have passed beyond this range and appeared to be too rough. This might be the result of a deterioration in stability and an increased

Table 3 Measured Percentages of Bone-to-Implant Contact				
	4 weeks		12 weeks	
Implant no.	Right tibia (group 1)	Left tibia (group 2)	Right tibia (group 1)	Left tibia (group 2)
1	32.56	37.41	46.04	44.59
2	38.87	27.57	60.49	61.36
3	9.36	28.31	60.62	47.05
4	26.32	32.05	69.53	70.49
5	19.34	35.03	26.90	44.39
6	18.83	31.22	62.19	54.12
7	27.96	44.95	68.03	59.60
8	30.38	16.91	66.61	78.32
9	21.81	23.06	67.58	59.27
10	10.40	18.65	71.44	67.38
11	22.79	52.92	44.83	38.44
12	17.99	52.06	47.38	73.39
Mean	23.10	33.30	57.60	58.20
SD	8.71	11.85	13.50	12.80

Group 1 = blasted; group 2 = blasted and oxidized.
At 4 weeks: blasting < oxidation at $P < .05$ (t test). At 12 weeks: not significantly different at $P < .05$ (t test).

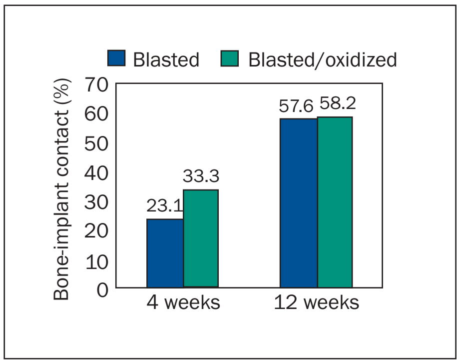

Fig 3 Percentage of bone-to-implant contact.

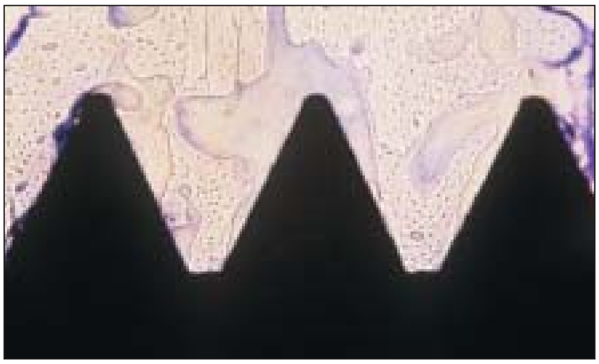

Fig 4 Light microscopic view of a blasted implant after 4 weeks (×100).

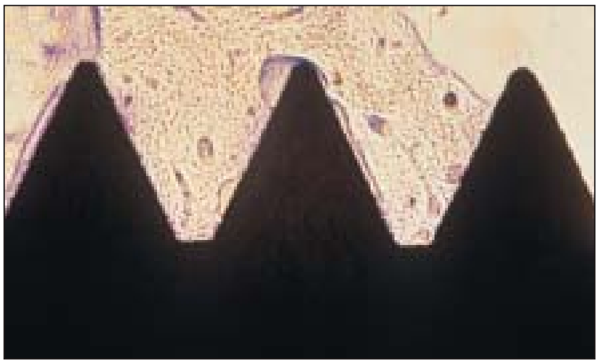

Fig 5 Light microscopic view of an oxidized implant after 4 weeks (×100).

release of Ti ions. Furthermore, the capacity for load transmission may have been reduced because the surface structure of the 250-µm–blasted implants was less homogeneous than the 25-µm and 75-µm blasted surfaces.

In addition to increasing surface roughness, blasting with 25-µm or 75-µm particles resulted in an isotropic surface with evenly spaced irregularities. One reason for the better bone fixation of these surfaces might be that the structure provided improved mechanical interlocking. Another explanation may be that the surface was rough enough for mechanical interlocking, but not so rough that the ion release was significantly increased. Although the results of the study by Wennerberg[16] seem to indicate that surface changes at the micron level will influence implant incorporation, one cannot exclude the possibility that the observed results originate from structural differences related to material inhomogeneities on the nanometer scale. Such structural changes cannot be detected with TopScan 3D, so scanning tunneling microscopy was introduced.[17–19]

Structural changes on the nanometer scale (achieved in this study by thermal oxidation) may influence the bone ground substance to aid bone induction, and structural changes at the micrometer level may stimulate mesenchymal cells to become osteoblasts.[16] The Rutherford backscattering spectroscopic analyses confirmed the authors' expectations that the oxide thicknesses of the samples were significantly different for the different groups. The

Table 4 Measured Percentages of Bone Area Inside Threads

	4 weeks		12 weeks	
Implant no.	Right tibia (group 1)	Left tibia (group 2)	Right tibia (group 1)	Left tibia (group 2)
1	21.02	24.67	80.74	80.13
2	35.51	30.11	52.26	87.67
3	49.37	49.56	57.36	59.97
4	73.87	44.64	73.41	56.28
5	45.59	63.20	74.89	63.50
6	72.34	30.26	50.42	65.72
7	52.13	23.09	77.57	85.90
8	63.70	40.26	62.52	66.64
9	35.25	45.31	61.63	61.58
10	52.87	43.92	58.09	76.34
11	61.88	71.03	68.68	54.65
12	73.72	72.71	38.75	80.43
Mean	53.10	44.90	63.00	69.90
SD	16.90	16.90	12.50	11.60

Grou 1 = blasted; group 2 = blasted and oxidized.
Not significantly different at $P < .05$ (*t* test) for both 4 and 12 weeks.

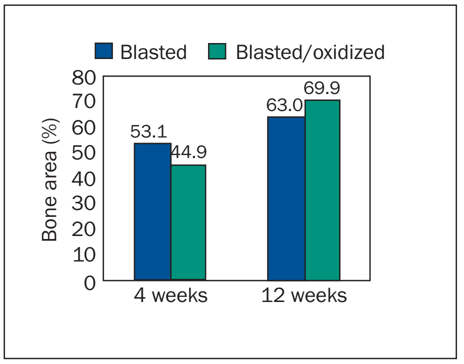

Fig 6 Percentage of bone area inside the threads.

Fig 7 Light microscopic view of a blasted implant after 12 weeks (×100).

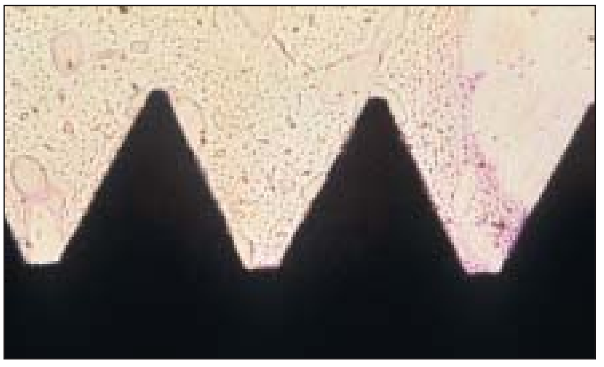

Fig 8 Light microscopic view of an oxidized implant after 12 weeks (×100).

results for the thermally oxidized implants were in approximate agreement with the linear relationship between the oxide thickness and the oxidizing temperature and time. However, Cook and coworkers[20] indicated that heat treatment in the range of 1,200°C to 1,300°C decreased the fatigue properties of titanium-aluminum-vanadium alloy (Ti-6Al-4V), so the implants in the present study were thermally oxidized at 800°C.

Previous studies[21–23] have shown that the implantation site in the proximal tibia consists almost exclusively of cortical bone, and that the formation of new bone around implants in this location could be divided into 2 major different events.[4] The first event takes place around the cortical portion of the screw (the proximal 1 to 2 threads), and the second is around the intramedullary portion of the implants (the distal 3 to 4 threads). Initially, the cortical portion made only patch contacts with the bone, but the formation of new bone that filled the gap between the implant and the bone was related to the remodeling of cortical bone. The second event was the formation of new bone around the intramedullary portion. Bone trabeculae extending toward the implants were initially formed from the cortical endosteum.

The histomorphometric analysis showed a greater degree of bone contact with the oxidized implants after 4 weeks, but after 12 weeks, there was no significant difference between the blasted and oxidized groups. It may be postulated that the thermal oxidation enhanced early bone formation around the implants. Yan and associates[24] stated that, in their study of rabbits, the heat-treated titanium implants bonded directly to the bone tissue during the early postimplantation period, but the untreated titanium implants did not form direct contact with the bone until 16 weeks. Also, Hazan and Oron[25] reported that bone formation was more advanced around heat-treated screws than around control screws.

The mechanism by which thermal oxidation of the screws induces the enhancement of osseous ingrowth is not yet clearly understood. The process of tissue reacting to the implanted screws is a complex sequence of events that may be mediated by a variety of biochemical substances. The substances are affected, each in turn, by the physicochemical interaction between the outermost layer of the metal and the molecules and cells in the adjacent area.[24]

It is thought that thermal oxidation of the implants may alter the characteristics of the oxide layer. Sundgren and colleagues[26] found that calcium and phosphate were embedded in the oxide layer and that oxidation continued for as many as several years in titanium implants embedded in the bone marrow of humans. It may also be that the heat treatment changes the corrosion resistance, thus modifying the rate at which metal ions are shed into the surrounding tissue.[27] Thus, it cannot be ruled out that this phenomenon could affect the processes associated with differentiation between the osteoblast and osteoprogenitor cells, or with the growth and maturation of bone next to the implanted screw.[24]

It is well known that rapid ingrowth of bone into the thread during the initial healing period ensures good stability of the implants after the first surgery and also contributes to better long-term success.[28–30] The present study demonstrated the possibility that different surface treatments, such as blasting and oxidation, have an effect on the ingrowth of bone into the thread. However, the clinical implications of surface treatments on implants, and the exact mechanisms by which the surface properties of the implant affect the process of osseointegration, remain subjects for further study.

CONCLUSION

The objective of this study was to evaluate the surface characteristics of screw-type implants after certain surface treatments (blasting and oxidation) and to study the response of bone to implants with those surface treatments. The different preparations produced implant surfaces with essentially similar chemical composition but with different oxide thickness and roughness. The morphologic evaluation of the bone formation revealed that:

1. After 4 weeks, the percentage of bone-to-implant contact of the oxidized implants (33.3%) was greater than that of blasted implants (23.1%) ($P < .05$).
2. The percentages of bone-to-implant contact after 12 weeks were not significantly different between the 2 groups ($P > .05$).
3. The percentages of bone area inside the threads after 4 and 12 weeks were not significantly different between the 2 groups ($P > .05$).

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