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Bone regeneration at implants with turned or rough surfaces in self-contained defects. An experimental study in the dog

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Abstract

Background: Marginal hard tissue defects present at implants with a rough surface can heal with a high degree of bone fill and osseointegration. The healing of similar defects adjacent to implants with a smooth surface appears to be less predictable. **Objective:** The aim was to compare bone healing at implants with turned or rough surface topographies placed in self-contained defects using either a submerged or non-submerged installation technique.

Material and Methods: Six dogs were used. Three months after tooth extraction four experimental sites were prepared for implant installation in both sides of the mandible. The marginal 5 mm of the canal prepared for the implant was widened. Thus, following implant placement a circumferential gap occurred between the bone tissue and the implant surface that was between 1 and 1.25 mm wide. In each side of the mandible two implants with a turned surface and two implants with a rough surface were installed. The implants in the right side were fully submerged, while a non-submerged technique was applied in the left side. The animals were sacrificed 4 months later, block biopsies of each implant site were dissected and ground as well as paraffin sections were prepared.

Results: The marginal defects around rough surface implants exhibited after 4 months of healing substantial bone fill and a high degree of osseointegration following either the submerged or the non-submerged installation technique. Healing at turned implants was characterized by incomplete bone fill and the presence of a connective tissue zone between the implant and the newly formed bone. The distance between the implant margin (M) and the most coronal level of bone-to-implant contact (B) at implants with a rough surface was 0.84 ± 0.37 mm at submerged and 0.90 ± 0.39 mm at non-submerged sites. The distance M–B at implants with a turned surface was 2.20 ± 0.52 mm at submerged between the implant.

 3.39 ± 0.52 mm at submerged and 3.23 ± 0.68 mm at non-submerged sites. The differences between the rough and turned implants regarding the length of distance M–B were statistically significant (paired *t*-test).

Conclusion: Osseointegration at implants placed in sites with marginal defects is influenced by the surface characteristics of the implant.

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In a review paper Cochran (1999) concluded that the surface characteristics of implants made of c.p. titanium may play an important role in the processes of modeling and remodeling that occur in the bone tissue of the recipient site following implant placement. This conclusion was supported by results from recent experiments in the dog (Botticelli et al. 2003, 2004a). In the studies referred to it was demonstrated that marginal bone defects of varying dimensions that occurred following placement of implants with a modified, *roughened* surface were resolved by *de novo* formation of hard tissue including optimal amounts of osseointegration, i.e., boneto-implant contact. In contrast, similar experiments in the dog in which implants with turned surface features were used, matching marginal hard tissue defects failed to heal with proper osseointegration (e.g. Akimoto et al. 1999).

Findings from clinical studies in man and experiments in various animal models documented that implants installed by the use of 1-stage (non-submerged) and 2-stage (initially submerged) techniques exhibited similar features of initial hard tissue integration and proper longterm treatment outcome (e.g. Buser et al. 1991, Ericsson et al. 1994, 1996, 1997, Abrahamsson et al. 1996, 1999, Weber et al. 1996, Cecchinato et al. 2004).

In a recent clinical study, Botticelli et al. (2004b) studied hard tissue formation in marginal bone defects that were present in fresh extraction sockets following implant installation. 21 International Team for Implantology (ITI^w) implants with a sand-blasted, large-grit, acid-etched (SLA") surface (Straumann AG, Waldenburg, Switzerland) were placed in 18 patients using a non-submerged technique. Measurements were made immediately after implant placement and at re-entry after 4 months of healing. It was demonstrated that such marginal hard tissue defects may predictably heal with new bone formation and defect resolution.

The aim of the present experiment was to study hard tissue formation in marginal bone defects present following implant installation and some associated aspects of soft tissue healing. Comparisons were made between (i) implants with varying surface characteristics and (ii) submerged and non-submerged installation techniques.

Material and Methods

The study protocol was approved by the Regional Ethics Committee for Animal Research.

Six Labrador dogs, about 1-year-old, were used. During surgical procedures the animals were given atropine (0.05 mg/kg subcutaneously) and thiopentone (2.5% solution, 20 mg/kg intravenously). An endotracheal tube was used for intubation, and a mixture of halothane (0.5–2.0%) and $N_2O:O_2$ (1:1) was administered.

The mandibular premolars and first molars were extracted. After 3 months of healing, defect preparation and im-



Fig. 1. Submerged implant sites. Clinical photographs illustrating the four recipient sites, after defect preparation and implant installation. Note the presence of circumferential defects around the implants.



Fig. 2. Submerged implant sites. Schematic diagram illustrating one implant with a sandblasted, large-grit, acid-etched (SLA) and one with a turned surface configuration. After implant installation a gap occurred between the implant surface and the bone wall that was 5 mm deep and varied between 1 and 1.25 mm in width.

plant installation were performed in both sides of the mandible. In the right side, four custom made implants (diameter = 3.3 mm; length = 10 mm Straumann AG) without a transmucosal neck portion were used (for further detail see Botticelli et al. 2003). Two implants were designed with a turned surface while two implants had a SLA surface. The roughness of the implant surfaces was examined (Sennerby et al. in press) using a technique described by Wennerberg et al. (1996). Thus, the calculated Sa-values were $0.35 \pm 0.17 \,\mu m$ (turned surface) and $2.29 \pm 0.59 \,\mu m$ (SLA surface).

The surgical site preparation was performed according to the manual of the ITI^{m} system ("Concepts and Surgical Procedure", Straumann). An incision was made at the crest of the ridge and full thickness flaps were raised. In all sites a step drill was used to widen the marginal portion (5 mm) of the intra-

osseous canal to a final diameter of 5.3 mm (for details see Botticelli et al. 2003). The rim of the implant was positioned so that it coincided with the level of the bone crest (Fig. 1). Two randomly assigned sites received implants with a SLA surface, while the two implants with a turned surface were placed in the remaining sites. Following the placement of the implants, a circumferential gap about 1-1.25 mm wide and 5 mm deep, occurred between the implant rod and the bone wall (Fig. 2). Custom-made healing caps of titanium were attached to all implants. Resorbable barrier membranes (Bio-Gide Geistlich AG, Wolhusen, Switzerland) were placed to cover the implants and the surrounding bone tissue. The mucoperiosteal flaps were replaced and sutured to fully submerge all implant sites.

In the left side of the mandible the surgical preparation of experimental sites was repeated using ITI[®] implants



Fig. 3. Non-submerged implant sites. Clinical photographs illustrating the four recipient sites. Note that the neck of the implants was kept above the bone crest.



Fig. 4. Non-submerged implant sites. After implant installation a gap occurred between the implant surface and the bone wall that was 5 mm deep and varied between 1 and 1.25 mm in width. Note that the shoulder of the implant was located about 2.8 mm coronal to the sand-blasted, large-grit, acid-etched (SLA) surface.

with a transmucosal neck-portion, that was 2.8 mm long and had a shoulder that was 4.8 mm wide. In two sites, implants with a SLA surface and in two sites implants with a turned surface were placed using the randomization protocol applied for the contralateral side. The border between the intra-osseous and the transmucosal portion of the implant coincided with the level of the bone crest after implant placement (Fig. 3).

Thus, a circumferential gap about 1-1.25 wide and 5 mm deep, occurred between the implant surface and the bone wall (Fig. 4).

Resorbable membranes (Bio-Gide^{∞}) were used to cover each defect. A standardized, circular hole was made in the center of the membrane using a punch. The membrane was adapted around the neck of the implant. The flaps were closed and sutured to ensure soft tissue adaptation to the neck of the implants. Hence, the requirements

of a non-submerged healing protocol were met.

Four months following implant installation, the animals were sacrificed with an overdose of Pentothal Sodium (Abbot Laboratories, Chicago, IL, USA) and perfused with a fixative (Karnovsky 1965) through the carotid arteries. The mandibles were removed and block biopsies of each implant site dissected using a diamond saw (Exakt[®], Apparatebau, Norderstedt, Germany) and placed in the fixative.

One unit containing one implant with a turned surface, and one unit with one implant with a SLA surface from each side of the mandible, were prepared for ground sectioning according to Donath and Breuner (1982) and Donath (1988). The biopsies were dehydrated in increasing grades of ethanol and embedded in methacrylate (Technovit[®] 7200 VLCresin, Kulzer, Friedrichsdorf, Germany). The specimens were first divided in a mesio-distal_direction using a cutting saw (Exakt[®]). From each buccal and lingual portion one mesial-distal section was prepared. The remaining buccal and lingual portions of the blocks were cut perpendicular to the mesio-distal sectioning and two additional sections of each unit were obtained (Persson et al. 2001). All sections were reduced to a thickness of about 20 µm using a cutting-grinding device (Exakt^w). The sections were stained in toluidine blue (Donath 1993). Thus, from each experimental site, six sections representing the mesial, distal, buccal and lingual aspect of the implant were prepared.

The tissue units of the remaining sites were decalcified in ethylene diamine tetra acetic acid (EDTA) and processed using the fracture technique described by Berglundh et al. (1994). Thus, before the decalcification was completed, cuts parallel to the long axis of the implant were made through the tissues until contact was made with the implant surface. The cuts were placed in such a way that mesio-buccal, mesio-lingual, distobuccal and disto-lingual portions of the tissue block could be separated from the implant. Decalcification was completed in EDTA. The soft tissue portions were dehydrated in ethanol, embedded in paraffin and sectioned with the microtome set at 5 μ m. The sections were stained in hematoxyline-eosin. Five sections, representing the central part of each of the four separated portions, were selected and used in the histological examination.

Histological examination

The examinations were made in a Leitz DM-RBE[®] microscope (Leica, Wetzlar, Germany). The following assessments were made in the ground sections (histometry: magnification \times 100, morphometry: magnification \times 200):

- (i) The distance between M and B (Fig. 5). M was in the submerged sites located at the margin of the custom made implant. In the nonsubmerged sites M was located 2.8 mm apical of the shoulder (S) of the metal unit. B was the most coronal level of contact between bone and implant.
- (ii) The degree of bone-to-implant contact (BIC %) within the zone located between B and the base of the original defect (D).



Fig. 5. Schematic drawing illustrating the landmarks used for the histological assessments. The dotted frame indicates the dimensions of the surgically prepared defect. M, margin of the implant at the submerged site or a level located 2.8 mm apical of S of the implant at the non-submerged site. S, shoulder of the implant at non-submerged sites; B, most coronal level of contact between bone and implant; D, base of the surgical created bone defect.



Fig. 6. Microphotograph illustrating the landmarks used for the histological measurements made in the paraffin sections. P, periimplant mucosa; J, apical termination of the barrier epithelium; B, most coronal level of bone to implant contact.

(iii) The composition of the newly formed tissue in the original defect region. Thus, a lattice comprising 100 light points (Schroeder & Münzel-Pedrazzoli 1973) was superimposed over the tissues and the percentage area occupied by lamellar bone, woven bone, bone marrow like-tissue and connective tissue was determined. In the paraffin sections representing the non-submerged implants additional linear measurements (magnification \times 100) were made (Fig. 6). The distance between the margin of the peri-implant mucosa (P) and the apical termination of the barrier epithelium (J); the distance between J and the most coronal level of bone to implant contact (B).

Data analysis

Mean values and standard deviation were calculated for each implant and animal. Differences between sites with different implant surfaces and between the two installation techniques were analysed using the Student's *t*-test for paired observations. *p*-values < 0.05 were considered significant.

Results

Overall histological characteristics

Submerged sites

Sites that included submerged implants are illustrated in Fig. 7. The defect adjacent to the SLA implant in Fig. 7a was filled with newly formed bone that was in contact with the implant surface. In the corresponding area around a turned implant (Fig. 7b), newly formed hard tissue was present adjacent to the lateral bone walls and at the base of the defect. In the apical 1/3rd of the defect, newly formed bone appeared to be in





Fig. 7. Ground sections representing submerged sites. (a) The defect adjacent to the sand-blasted, large-grit, acid-etched implant. This defect was filled with newly formed bone. (b) The defect adjacent to the turned implant. In the marginal 2/3rd of this defect, a layer of connective tissue separated the new bone from the implant. In the apical 1/ 3rd of the defect the newly formed bone appeared to be in direct contact with the implant surface (original magnification \times 16).

direct contact with the implant surface. In the marginal 2/3rd of the defect a connective tissue separated the newly formed bone from the implant surface.

Non-submerged sites

Ground sections representing the nonsubmerged implants are presented in Fig. 8. In sites with the SLA implants, the surgically produced defect was healed and filled with new bone (Fig. 8a). In sites with implants designed with a turned surface, defect fill was incomplete (Fig. 8b). Thus, in the major por-



Fig. 8. Ground sections representing nonsubmerged sites. (a) The surgically produced defect around the implant with the sandblasted, large-grit, acid-etched surface was filled with new bone. (b) The defect adjacent an implant with a turned surface exhibited incomplete bone fill. The newly formed bone failed to reach contact with the coronal portion of the titanium surface (original magnification \times 16).

tion of the defect the newly formed bone failed to reach contact with the implant surface.

The paraffin sections illustrated in Fig. 9 represent an experimental site in which an implant with a turned surface had been installed using a non-submerged surgical approach. In the coronal portion of the defect the lateral border of the newly formed bone was not in contact with the implant surface. A layer of connective tissue consistently occupied the region between the implant and the mineralized tissue (Fig. 9a). A dense layer of connective tissue was



Fig. 9. Paraffin sections representing a nonsubmerged site in which an implant with a turned surface had been installed. (a) A hard tissue defect was present after 4 months of healing. In the marginal compartment of the defect a layer of connective tissue occupied the region between the implant and the mineralized tissue (original magnification \times 25). (b) A dense layer of connective tissue, rich in fibers but poor in cells and vessels, was seen to be in direct contact with the implant surface (original magnification \times 100).

seen to be in direct contact with the implant surface (Fig. 9b).

Histometric measurements

The results from histometric measurements performed in the ground sections are presented in Table 1.

The mean distance between M and the most coronal level of BIC (B) in the submerged sites was 0.84 ± 0.37 mm

for SLA implant sites and $3.39 \pm 0.52 \text{ mm}$ for turned implant sites. This difference was statistically significant. The corresponding distances at the non-submerged sites were $0.90 \pm 0.39 \text{ mm}$ and $3.23 \pm 0.68 \text{ mm}$ for the SLA and turned implants, respectively. This difference was statistically significant.

The degree of BIC % in the submerged sites was $64.3 \pm 5.2\%$ for the SLA and $46.8 \pm 10.4\%$ for the turned implants. The BIC % in the non-submerged sites was $64.5 \pm 10.0\%$ for the SLA implants and $38.5 \pm 11.5\%$ for the turned implants. These differences between the SLA and turned implant sites were statistically significant.

The results from histometric measurements performed in the paraffin sections of the non-submerged sites are presented in Table 2. The distance between the margin of the peri-implant mucosa (P) and the apical termination of the barrier epithelium (J) was 1.83 ± 0.17 mm at the SLA and 2.46 ± 0.30 mm at the turned implants. The distance J-B was 1.17 ± 0.32 mm at SLA and 2.15 ± 0.51 mm at turned implants. These differences between the SLA and turned implant sites were statistically significant.

Morphometric measurements

The results from morphometric measurements performed in the ground sections are presented in Table 3.

Submerged sites

The peri-implant tissue present in the "defect area" in the submerged sites at the SLA implants was comprised of $59.6 \pm 6.3\%$ lamellar bone, $18.4 \pm 5.4\%$ woven bone, $19.6 \pm 2.8\%$ bone marrow, and $2.4 \pm 1.9\%$ connective tissue. The corresponding area at the turned implants sites comprised $48.8 \pm 5.5\%$ lamellar bone, $14.8 \pm 3.5\%$ woven bone, $12.3 \pm 3.4\%$ bone marrow, and $24.1 \pm 7.8\%$ connective tissue.

Non-submerged sites

The peri-implant tissue in the "defect area" in the non-submerged sites included $63.4 \pm 1.9\%$ lamellar bone, $16.4 \pm 2.3\%$ woven bone, $16.7 \pm 2.6\%$ bone marrow, and $3.5 \pm 2.0\%$ connective tissue at the SLA implants and $50.1 \pm 3.1\%$ lamellar bone, $15.6 \pm 3.8\%$ woven bone, $10.0 \pm 4.1\%$ bone marrow,

Table 1. The distance between M (Fig. 5) and the most coronal level of bone-to-implant contact (B)

	Su	bmerged si	tes	Non-submerged sites			
	SLA		Turned	SLA		Turned	
M–B (mm) BIC (%)	0.84 (0.37) 64.3 (5.2)	* *	3.39 (0.52) 46.8 (10.4)	0.90 (0.39) 64.5 (10.0)	* *	3.23 (0.68) 38.5 (11.5)	

**p*<0.05

Mean values and standard deviation.

BIC (%), bone-to-implant contact within the original defect area; SLA, implants with a SLA surface; turned, implants with a turned surface; SLA, sand-blasted, large-grit, acid-etched.

Table 2. The distance between the margin of the peri-implant mucosa (P) and the apical termination of the barrier epithelium (J) and between J and the most coronal level of bone to implant contact (B)

	Non-submerged sites					
	SLA		Turned			
P–J (mm) J–B (mm)	1.83 (0.17) 1.17 (0.32)	* *	2.46 (0.30) 2.15 (0.51)			

**p*<0.05.

Mean values and standard deviation.

Assessments performed in the paraffin sections from the non-submerged implant sites. SLA, implants with a SLA surface; Turned, implants with a turned surface; SLA, sand-blasted, largegrit, acid-etched.

and $24.3 \pm 4.8\%$ connective tissue at the turned implants.

The differences between the SLA and turned implant sites regarding proportion of lamellar bone, bone marrow and connective tissue were statistically significant at both submerged and nonsubmerged sites.

Discussion

The present experiment revealed that the surface characteristics of the implants used played an important role for the amount of hard tissue fill and osseointegration that occurred in selfcontained marginal bone defects. On the other hand, no differences could be found with respect to bone formation between sites at which the implants during healing were submerged or nonsubmerged.

Implant surface

The observation that bone healing was superior in bone defects adjacent to implants with a rough as compared with a turned surface topography is consistent with data previously published. Thus, Stentz et al. (1997), in a dog experiment, compared the healing of marginal gaps, 5 mm deep and about 3 mm wide, around implants with turned or HA-coated (hydroxyapatite) surfaces. Some of the defects were filled with demineralized freeze-dried bone allograft and some of the defects were covered with a non-resorbable membrane. After 4 months of healing, there was a minimal amount of new bone formation and osseointegration within the defect region at sites harboring turned implants, while there was a comparatively lager proportion of new bone in direct contact with implants designed with an HA-coated surface.

The present findings are only in part in agreement with data reported from a recent animal experiment by Veis et al. (2004). The authors studied healing around implants, designed with both rough and machined surfaces that were placed in the iliac "wing" portion of dogs. Marginal defects were prepared, the implants installed and the gaps between the implant surface and the bone wall were filled with autogenous bone and covered with a resorbable membrane. After 5 months of healing it was observed that all defects were filled with newly formed bone but that the BIC within the defect region was larger at the rough (46.4%) than at the machined (28.6%) surface portions.

The current observation that bone formation in a marginal defect may not result in optimal osseointegration to an implant with turned surface is in agreement with findings from a study in the dog by Akimoto et al. (1999). Implants were designed with turned surface and placed at sites with marginal defects that were 6 mm in depth and between 0.5 and 1.4 mm wide. Healing was evaluated in histological sections from biopsies obtained 12 weeks after implant installation. The authors reported that while new bone formation and osseointegration had occurred in the apical portion of all defects, a connective tissue consistently separated the implant surface from bone tissue in the marginal compartment. Further, the size of the residual defect depth varied with the width of the surgically created defect. Thus, originally wide marginal defects (1.4 mm) had following healing a longer connective tissue portion facing the implant than small defects (0.5 mm).

Also with respect to bone regeneration and re-osseointegration in defects that developed as a result of periimplantitis, implants with a roughened surface appeared to provide more optimal conditions for healing than smooth surface implants. Wetzel et al. (1999) induced inflammatory lesions around implants with different surface characteristics (Machined, M; Rough, SLA) in beagle dogs. During a 4-month period the inflammatory process resulted in periimplant bone loss that amounted to about 40% of the length of the titanium rod. Treatment included systemic metronidazole, curettage of the craterlike defects and topical application of chlorhexidine on the implant surface. In biopsies obtained after 18 months of healing it was observed that the amount of bone fill in the marginal defect where

Table 3. Results from morphometric measurements of the peri-implant tissues within the original defect area

	Submerged sites			Non-submerged sites		
	SLA		Turned	SLA		Turned
Lamellar bone (%) Woven bone (%) Bone marrow (%) Connective tissue (%)	59.6 (6.3) 18.4 (5.4) 19.6 (2.8) 2.4 (1.9)	* * *	48.8 (5.5) 14.8 (3.5) 12.3 (3.4) 24.1 (7.8)	63.4 (1.9) 16.4 (2.3) 16.7 (2.6) 3.5 (2.0)	* *	50.1 (3.1) 15.6 (3.8) 10.0 (4.1) 24.3 (4.8)

p < 0.05.

Mean values and standard deviation.

SLA, implants with a SLA surface; Turned, implants with a turned surface; SLA, sand-blasted, large-grit, acid-etched.

membrane were used was larger at SLA (83%) than at M implants (61%). Persson et al. (2001) in a similar study induced inflammatory lesions in dogs by placing ligatures in a submarginal position around the neck of implants (with turned or roughened surface characteristics) and by allowing plaque formation. The soft tissue lesions were consistently associated with bone loss of craterlike configuration in the marginal portion of the implant site. Treatment included systemic antibiotics (amoxicillin and metronidazole), surgical curettage of the large bone defects and mechanical cleaning of the implant surface. During healing substantial amounts of new bone formation occurred at all implant sites and in radiographs most marginal defects appeared to be resolved. The histological examination revealed, however, that reosseointegration had been established only at implants designed with a roughened surface.

Davies (1998) suggested that the rough implant surface provides optimal conditions for healing by promoting coagulum stability and the maintenance of contact between the metal surface and the blood clot during the initial phase of healing. Further, it was suggested that a rough implant surface in contrast to a smooth surface may stimulate osteoblast attachment and proliferation. The validity of this hypothesis was recently documented in an experiment in the Labrador dog (Berglundh et al. 2003, Abrahamsson et al. 2004). They used an implant device (chamber) that was prepared with either a turned (T) or roughened (SLA) surface and evaluated bone tissue modeling and remodeling during periods ranging from 2h to 12 weeks. The authors reported that "healing showed similar characteristics with resorptive and appositional events for both SLA and T surfaces " but the rate and degree of osseointegration were superior for the SLA compared with the T chambers".

Submerged *versus* non-submerged installation

In the current study it was observed that defects at implants that during healing were non-submerged exhibited similar amounts of new bone formation and osseointegration as defects that were fully submerged (Table 1). This finding is in agreement with data from previous experiments in the dog by e.g. Fiorellini et al. (1998) and illustrates that during the process of healing the mucosa prevents products from the oral cavity to reach and interfere with modeling events in the defect region.

The histometric measurements disclosed that at all non-submerged implants a mucosal seal had formed that was comprised of a barrier epithelium and a zone of connective tissue attachment. This observation is consistent with data previously published from experiments in the dog (Berglundh et al. 1991, Buser et al. 1992, Abrahamsson et al. 1996, 1999, Berglundh & Lindhe 1996, Weber et al. 1996, Cochran et al. 1997). In the present sample, however, the dimension of the barrier epithelium as well as the connective tissue attachment differed between implants with turned and roughened surface topographies. Thus, the mucosa adjacent to smooth surface implants had a significantly longer barrier epithelium (2.46 mm versus 1.83 mm) and a longer zone of connective tissue (2.15 mm versus 1.17 mm) than the corresponding mucosa at the SLA implants (Table 2). This difference between the 2 implant sites is most likely explained by the difference in the depth of the residual hard tissue defect (3.23 mm versus 0.89 mm; Table 1) and the corresponding height of the peri-implant mucosa.

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