J Clin Periodontol 2004; 31: 309–317 doi: 10.1111/j.1600-051X.2004.00502.x
Printed in Denmark. All rights reserved

Journal of Clinical Periodontology

Resolution of bone defects of varying dimension and configuration in the marginal portion of the peri-implant bone

An experimental study in the dog

Daniele Botticelli, Tord Berglundh and Jan Lindhe

Department of Periodontology, Institute of Odontology, Sahlgrenska Academy, Göteborg University, Göteborg, Sweden

Botticelli D, Berglundh T, Lindhe J: Resolution of bone defects of varying dimension and configuration in the marginal portion of the peri-implant bone. An experimental study in the dog. J Clin Periodontol 2004; 31: 309–317. doi: 10.1111/j.1600-051X. 2004.00502.x © Blackwell Munksgaard, 2004.

Abstract

Background: It was demonstrated that a marginal defect of about 1 mm between the bone wall and the metal surface after implant installation can heal with a high degree of bone fill and osseointegration.

Objective: The aim of the present animal experiment was to study bone healing at implant sites with hard tissue defects of varying dimensions and configuration.

Material and Methods: Four Labrador dogs were used. All mandibular premolars and first molars were extracted. After 3 months of healing, five experimental sites, two control (C1, C2) and three test (T1, T2, T3) sites, were identified. In all five sites, custom-made implants with a sand-blasted, large-grit, acid-etched (SLA) surface and with an outer dimension of 3.3 × 10 mm, were used. In site C1, traditional implant installation was performed. In site C2, the marginal 5 mm of the canal, prepared for the implant, was widened to 5.3 mm using a step-drill. Thus, following the installation of the implant, a circumferential gap occurred between the bone tissue and the metal rod that was 5 mm deep and between 1 and 1.25 mm wide. In test site T1, the canal was widened to establish a marginal gap of 2–2.25 mm. In test sites T2 and T3, the marginal 5 mm of the canal was first widened to 5.3 mm (T2) or 7.3 mm (T3). The buccal bone wall opposite the defect was subsequently removed. Following the placement of a cover screw in sites C2, T1, T2, and T3, a resorbable membrane was placed over the defect. All implants were submerged. After 4 months of healing, block biopsies of each implant site were dissected and processed for ground sectioning.

Results: The observations disclosed that four-wall defects of different dimensions (1–2.25 mm wide) that occurred in the marginal portion of the recipient sites following implant installation were resolved during healing. Further, at sites where the buccal bone wall during defect preparation was intentionally removed, healing resulted in defect resolution at the mesial, distal, and lingual aspects. At the buccal aspects, healing was incomplete but the dimension of the defect was reduced by the limited amounts of new bone formation extending from the lateral and apical borders of the defect.

Conclusion: Wide marginal defects may during healing be filled with bone. In such defects a high degree of osseointegration may occur to implants designed with an SLA surface.

Key words: bone; defect; dental implant; healing; histometry; membrane; morphometry; osseointegration; SLA surface

Accepted for publication 13 June 2003

Findings from clinical studies and case report series indicated that the installation of implants in fresh extraction sites may allow for proper healing and long-term implant survival (for review see Schwartz-Arad & Chaushu 1997, Mayfield 1999). Further, results reported in animal experiments revealed that a marginal gap that occurred between the hard tissue and the implant immediately following its installation, during healing may be resolved with new bone formation and proper osseointegration (Todescan et al. 1987, Becker et al. 1991, Warrer et al. 1991, Gotfredsen et al. 1993, 1994, Kohal et al. 1998, Alliot et al. 1999).

On the other hand, it was also reported in similar studies that marginal defects ranging from 0.35 to about 2 mm wide often failed to properly resolve following healing periods varying between 6 and 12 weeks (e.g. Carlsson et al 1988, Caudill & Meffert 1991, Knox et al. 1991, Clemens et al. 1997, Akimoto et al. 1999).

In a recent experiment, Botticelli et al. (2003a) described a model in the dog for the study of bone reaction to implant installation and bone regeneration in marginal defects lateral to titanium rods. The authors observed that self-contained, that is, four-wall, marginal defects after a 4-month period of submerged healing were more or less fully resolved and that the newly formed bone was in direct contact with the sand-blasted, large-grit, acid-etched (SLA) surface of the implant. The defects studied by Botticelli et al. (2003a) were about 5 mm deep and 1.25 mm wide, that is, larger than the size that would allow for proper hard tissue bridging, that is, the ''jumping distance'' (Schenk & Willenegger 1977, Harris et al. 1983, Schenk 1994). In a subsequent experiment, Botticelli et al. (2003b) showed that such hard tissue bridging is a time-dependent phenomenon. Thus, using the dog model it was demonstrated that healing periods of 1 and 2 months were not long enough to allow hard tissue to form on the SLA surface of the implant in the defect region. In other words, the resolution of defects adjacent to implants seems to be dependent both on defect size and time of healing.

The aim of the present investigation was to study if larger marginal defects, self-contained or buccally open, lateral to implants may heal with proper bone fill and osseointegration.

Material and Methods

The study protocol was approved by the Regional Ethics Committee for Animal Research. Four 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). Further, 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.

In each dog the mandibular premolars and first molars were extracted. After 3 months of healing a surgical procedure including defect preparation and implant installation was performed in the

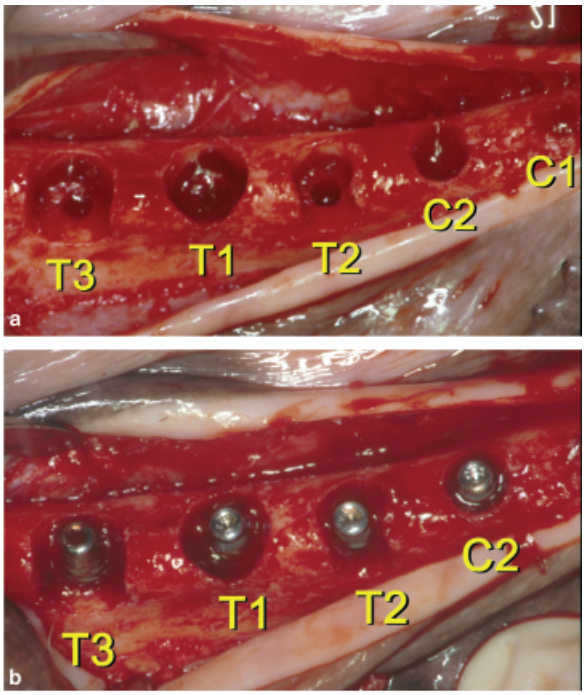

Fig. 1. Clinical photographs illustrating the five recipient sites after defect preparation (a) and the marginal defects around implants after installation (b). C1 and C2 = control sites. T1, T2 and T3 = test sites. C1 = no defect; C2 = small defect; T1 = wide defect; T2 = small and buccally open defect; T3 = wide and buccally open defect.

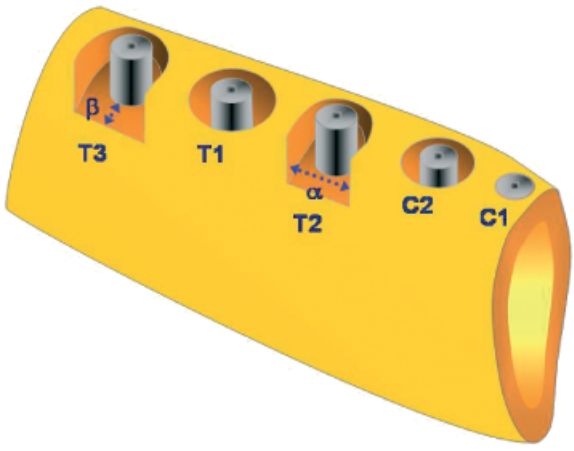

Fig. 2. Schematic drawing illustrating the five recipient sites. Two control sites (C1 and C2) and three test sites (T1, T2 and T3). C2 and T1 represent contained defects while T2 and T3 represent open defects, at which the buccal plate was removed before implant installation. α indicates the mesio-distal width of the buccally open defects. β indicates the distance between the implant surface and the buccal bone margin.

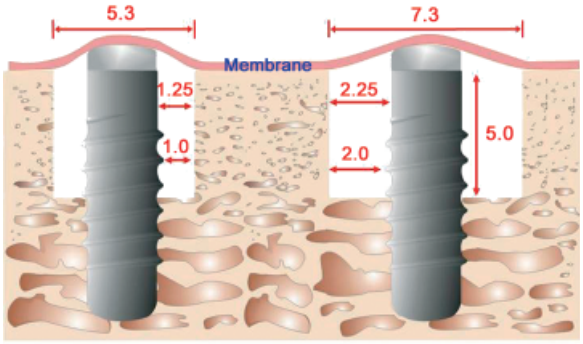

Fig. 3. Schematic drawing illustrating the dimensions of the defects in sites C2 and T2 (left) and in sites T1 and T3 (right). The white areas around the marginal portion of the implants indicates the defect. A membrane was placed to protect the defect sites.

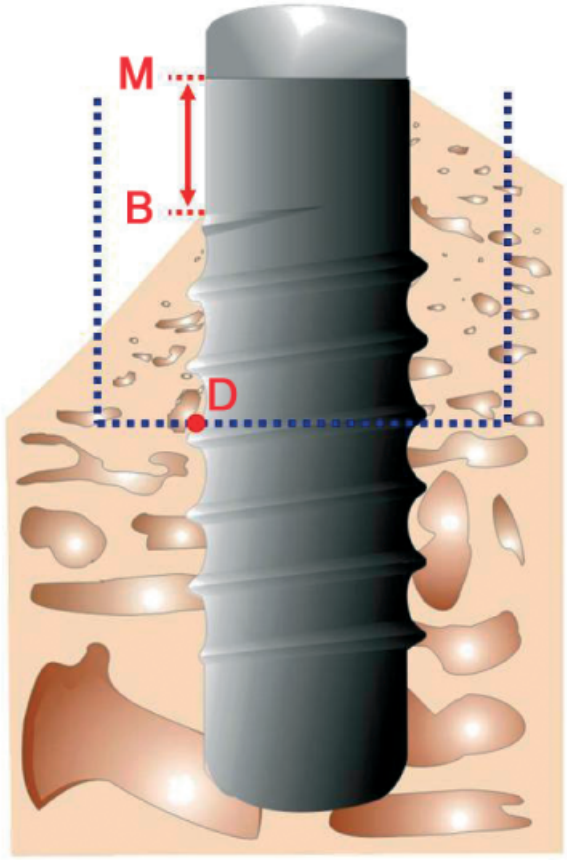

Fig. 4. Schematic drawing illustrating in the buccal–lingual plane the landmarks used for the histological assessments. The dotted frame indicates the dimensions of the original defect. M = implant margin; B = most coronal level of contact between bone and implant; D = base of the original bone defect.

right side of the mandible. Following crestal incision and elevation of buccal–lingual full-thickness flaps, five recipient sites were identified, two control (C1, C2) and three test (T1, T2, T3) sites (Fig. 1a).

In all five sites, custom-made implants with an SLA surface (Straumann AG; Waldenburg, Switzerland), and with an outer dimension of 3.3 × 10 mm, were used (Fig. 1b).

Control sites (C1 and C2)

In site C1, traditional implant installation was performed and in accordance with recommendations for the ITI® system (Straumann AG, Waldenburg, Switzerland).

In site C2, the marginal 5 mm of the canal prepared for the implant was widened to 5.3 mm using a step-drill procedure previously described by Botticelli et al. (2003a). Thus, following the installation of the implant, a circumferential gap occurred between the bone tissue and the metal rod that was 5 mm deep and between 1 and 1.25 mm wide (Figs 1b, 2, and 3).

Test sites (T1, T2, and T3)

In test site T1, the surgical procedure described for site C2 was repeated with the exception that the canal was widened to 7.3 mm using a step-drill device. The circumferential gap, hereby established between the bone and the subsequently installed implant, was 2–2.25 mm in width and 5 mm in height (Figs 1b, 2, and 3).

In test sites T2 and T3, the marginal 5 mm of the canal was first widened to 5.3 mm (T2) or 7.3 mm (T3). The buccal bone wall opposite of the defect was thereafter removed with the use of fissure burs and chisels. The implants were installed (Fig. 1b). The mesio-distal width of the buccally open defect was about 5.3 mm (T2) and 7.3 mm (T3) and the base from the implant rod and the bone margin was on the average of about 2.9 mm (T2) and 3.4 mm (T3) (Fig. 2).

Primary stability of the implant at sites C2, T1–T3 was obtained through the bone-to-implant contact (BIC) zone in the apical 5 mm.

Following the placement of a healing cup in sites C2, T1, T2, and T3, a resorbable membrane (Bio-Gide®, Geistlich AG, Wolhusen, Switzerland) was placed over the defect and surrounding 3–4 mm of bone tissue. The soft tissue flaps were replaced and secured with sutures. After 2 weeks the sutures were removed.

Four months after the implant installation the animals were sacrificed with an overdose of pentothal sodium (Abbot Laboratories, Chicago, IL, USA) and were perfused with a fixative (Karnovsky 1965) through the carotid arteries. The mandibles were removed; block biopsies of the implant sites were dissected using a diamond saw (Exakt®, Apparatebau, Norderstedt, Germany) and placed in the fixative.

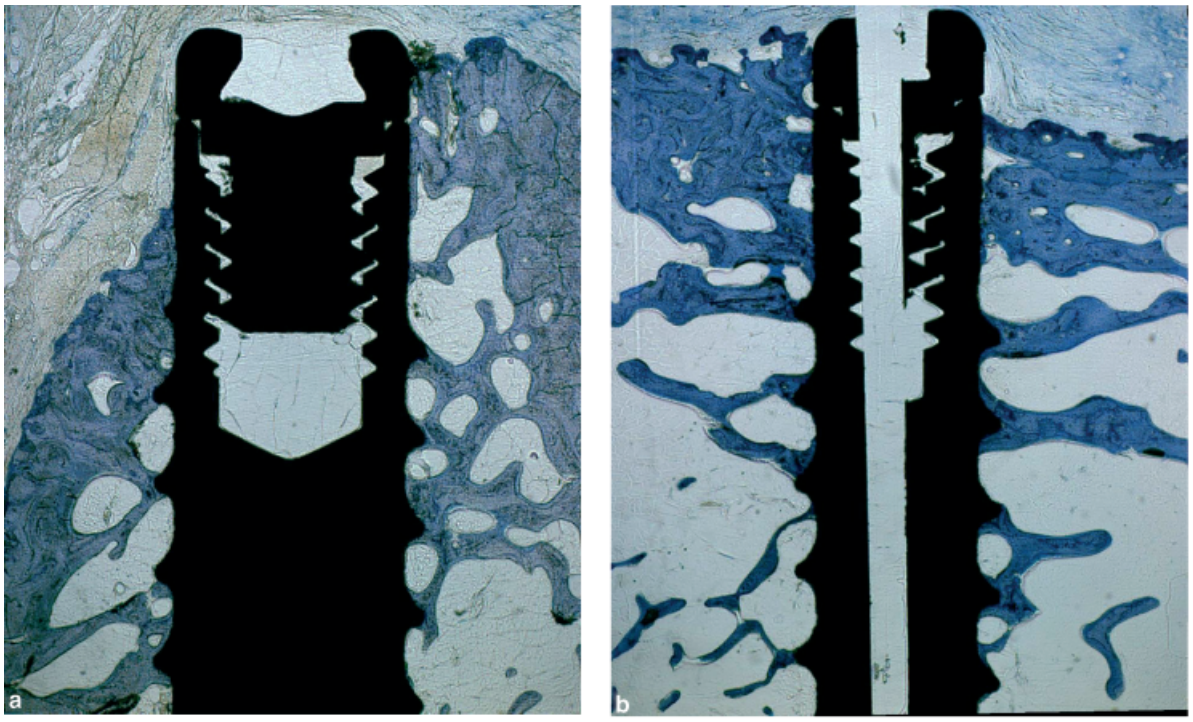

Fig. 5. Ground sections representing one control site C1 after 4 months of healing in (a) buccal–lingual and (b) mesial–distal planes (magnification ×16).

Table 1. Results from histometric measurements made in the defect region

		M–B (mm)		BIC (%)	
all aspects	C1	0.56	(0.19)	69.9	(10.9)
	C2	0.54	(0.38)	68.1	(9.7)
	T1	0.75	(0.50)	66.5	(10.7)
	T2	0.86	(0.21)	65.6	(6.7)
	T3	0.89	(0.36)	65.9	(4.1)
buccal aspect	C1 B	0.99	(0.53)	68.1	(13.4)
	C2 B	0.96	(0.71)	74.3	(14.3)
	T1 B	1.82	(0.33)	76.4	(16.9)
	T2 B	2.20	(0.35)	68.6	(13.1)
	T3 B	2.26	(0.45)	76.7	(6.4)
lingual aspect	C1 L	0.53	(0.18)	65.0	(10.7)
	C2 L	0.36	(0.11)	58.4	(10.4)
	T1 L	0.45	(0.62)	58.7	(12.4)
	T2 L	0.50	(0.59)	59.9	(10.8)
	T3 L	0.50	(0.16)	61.2	(13.6)
mesial aspect	C1 M	0.26	(0.21)	77.8	(13.1)
	C2 M	0.54	(0.54)	71.5	(16.3)
	T1 M	0.36	(0.51)	65.1	(10.2)
	T2 M	0.35	(0.49)	66.0	(11.7)
	T3 M	0.48	(0.37)	62.8	(8.3)
distal aspect	C1 D	0.45	(0.12)	68.7	(12.8)
	C2 D	0.32	(0.17)	68.3	(10.8)
	T1 D	0.39	(0.55)	65.6	(7.0)
	T2 D	0.38	(0.12)	69.8	(6.3)
	T3 D	0.34	(0.47)	63.0	(7.4)

Mean values and standard deviations (SD) are reported for each implant (C1, C2, T1, T2, T3) and for each single site: buccal = B, lingual = L, mesial = M and distal = D.

The tissue blocks were prepared for ground sectioning according to Donath & Breuner (1982) and Donath (1988). The specimens were dehydrated in ethanol, embedded in methylmethacrylate (Technovit® 7200 VLC, Kulzer, Friedrichsdorf, Germany), and cut in a buccal–lingual plane using a diamond saw (Exakt®, Apparatebau, Norderstedt, Germany). From each implant site, two central sections were harvested and reduced to a final thickness of about 20 μm by microgrinding and polishing using a cutting–grinding device (Exakt®, Apparatebau, Norderstedt, Germany). The remaining mesial and distal portions were cut in a perpendicular (mesial–distal) direction and two central sections were prepared from each unit. The sections were stained in toluidine blue (Donath 1993).

Histological examination

The examinations were made in a Leitz DM-RBE® microscope (Leica, Wetzlar, Germany) and the following assessments were made at the mesial, distal, buccal and lingual aspect of each site (Fig. 4): the distance between the implant margin (M) and the most coronal level of contact between bone and implant (B); the *degree* of bone-to-implant contact (BIC%) in the zone between B and the bottom of the defect (D); and the *composition* of the newly formed bone tissue in the ''defect'' region between B and D. Thus, a lattice comprising 100 light points (Schroeder

& Münzel-Pedrazzoli 1973) was superimposed over the tissue in the defect region (magnification ×200) and the percentage area occupied by lamellar bone, woven bone, and bone marrow was determined. Mean values and standard deviations were calculated for each variable, implant and animal.

Results

Control sites (C1 and C2)

Ground sections from a C1 site (traditional implant installation; no defect) are illustrated in Fig. 5a (buccal–lingual) and Fig. 5b (mesial and distal).

The overall mean distance between the implant margin (M; Fig. 4) and the most coronal level of BIC (B) (M–B; Table 1) at site C1 was 0.56 ± 0.19 mm. When the M–B distance for the various aspects was considered, it was observed that M–B was longer at the buccal (0.99 ± 0.53 mm) than at the lingual (0.53 ± 0.18 mm) and the interproximal aspects (mesial = 0.26 ± 0.21 mm; distal = 0.45 ± 0.12 mm). The degree of bone-to-implant contact (BIC%; Table 1) in the marginal portion of the alveolar ridge, corresponding to the ''defect area'' in sites C2, T1–T3, was 66.9 ± 10.9%. The peri-implant bone within the ''defect area'' was comprised of 70.1 ± 9.0% lamellar bone, 5.3 ± 0.9% woven bone and 24.6 ± 8.5% bone marrow (Table 2).

In site C2 (small, self-contained defect) the 1–1.25 mm wide defect was, after 4 months of healing, filled with newly formed bone (Fig. 6a, b). The overall mean distance between M and B was 0.54 ± 0.38 mm (Table 1). Also at this site the M–B distance was longer at the buccal (0.96 ± 0.71 mm) than at the lingual (0.36 ± 0.11 mm) and the interproximal aspects (mesial = 0.54 ± 0.54 mm; distal = 0.32 ± 0.17 mm). The overall BIC in the defect area was 68.1 ± 9.7% (Table 1).

The newly formed bone within the defect region was composed of 51.8 ± 8.3% lamellar bone, 21.3 ± 4.9% woven bone, and 26.9 ± 7.9% bone marrow (Table 2).

Table 2. Results from the morphometric measurements of the newly formed bone tissue within the defect area

	Lamellar bone		Woven bone		Bone marrow	
C1	70.1	(9.0)	5.3	(0.9)	24.6	(8.5)
C2	51.8	(8.3)	21.3	(4.9)	26.9	(7.9)
T1	55.2	(6.9)	25.9	(10.5)	18.8	(5.7)
T2	58.0	(6.4)	21.7	(11.1)	20.3	(6.7)
T3	59.8	(5.8)	22.7	(7.0)	17.6	(4.0)

Mean values (%) and standard deviations (SD).

Test sites (T1–T3)

Also in site T1 the originally 2–2.25 mm wide defect was, after the healing interval, occupied with newly formed bone (Fig. 7a, b). The overall mean distance between M and B was 0.75 ± 0.50 mm (Table 1). The distance M–B was considerably longer at the buccal (1.82 ± 0.33 mm) than at the lingual (0.45 ± 0.62 mm) and at the interproximal aspects (mesial = 0.36 ± 0.51 mm; distal = 0.39 ± 0.55 mm).

The overall amount of BIC in the defect region was 66.5 ± 10.7% (Table 1). The newly formed bone within this

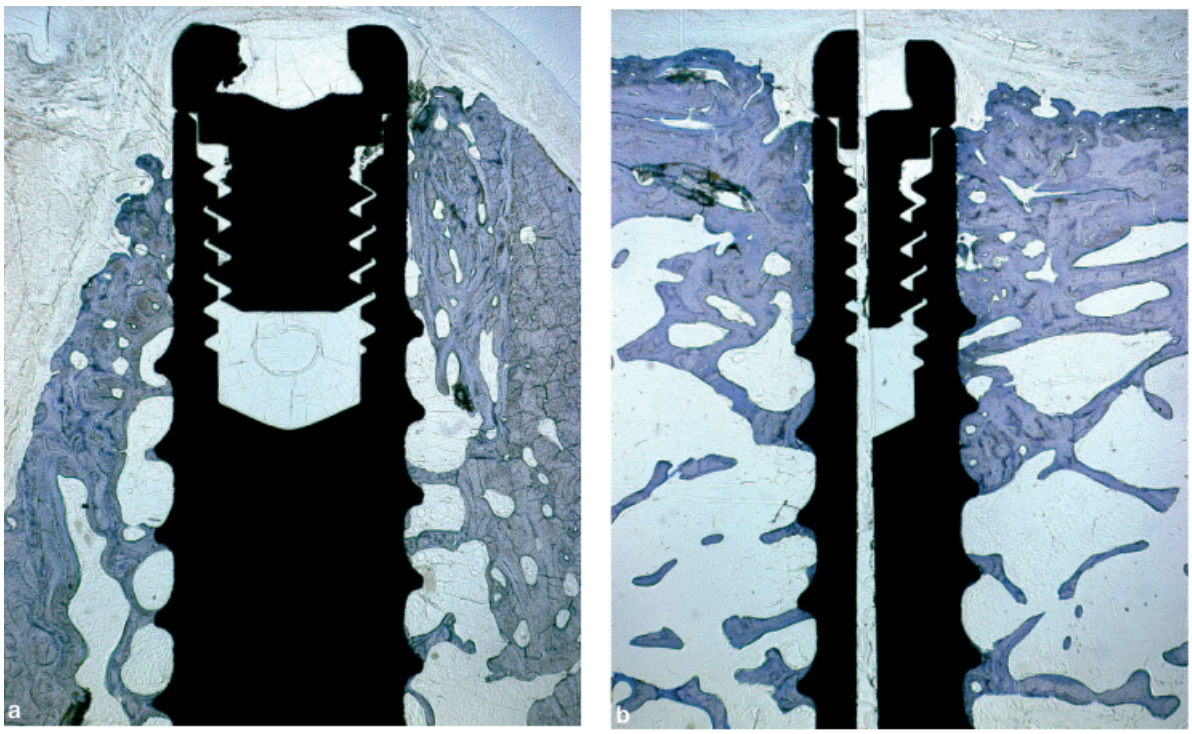

Fig. 6. Ground sections of one control site C2 after 4 months of healing in (a) buccal–lingual and (b) mesial–distal planes (magnification ×16). The amount of new bone formation was, in the 1–1.25 mm wide and 5 mm deep defect, more pronounced at the mesial, distal and lingual aspect than at the buccal portion of the implant.

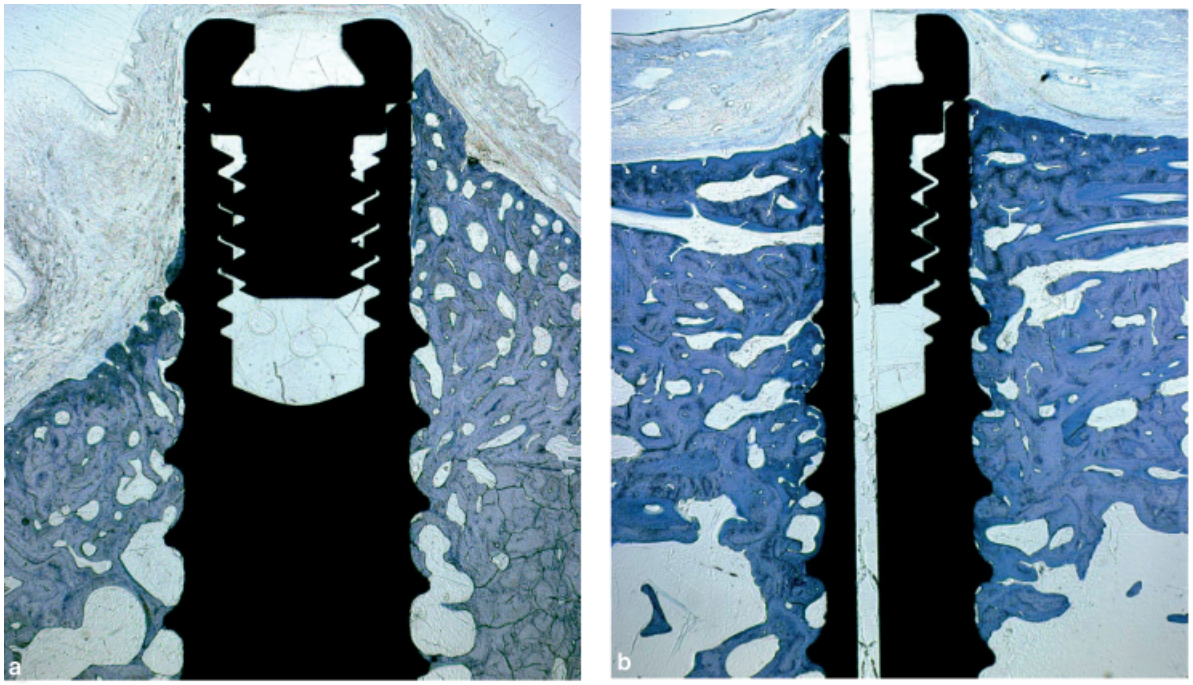

Fig. 7. Ground sections of one test site T1 after 4 months of healing in (a) buccal–lingual and (b) mesial–distal planes (magnification ×16). The wide defect was filled with new bone in the mesial, distal and lingual aspects of the implant, but to a less extent at the buccal aspect.

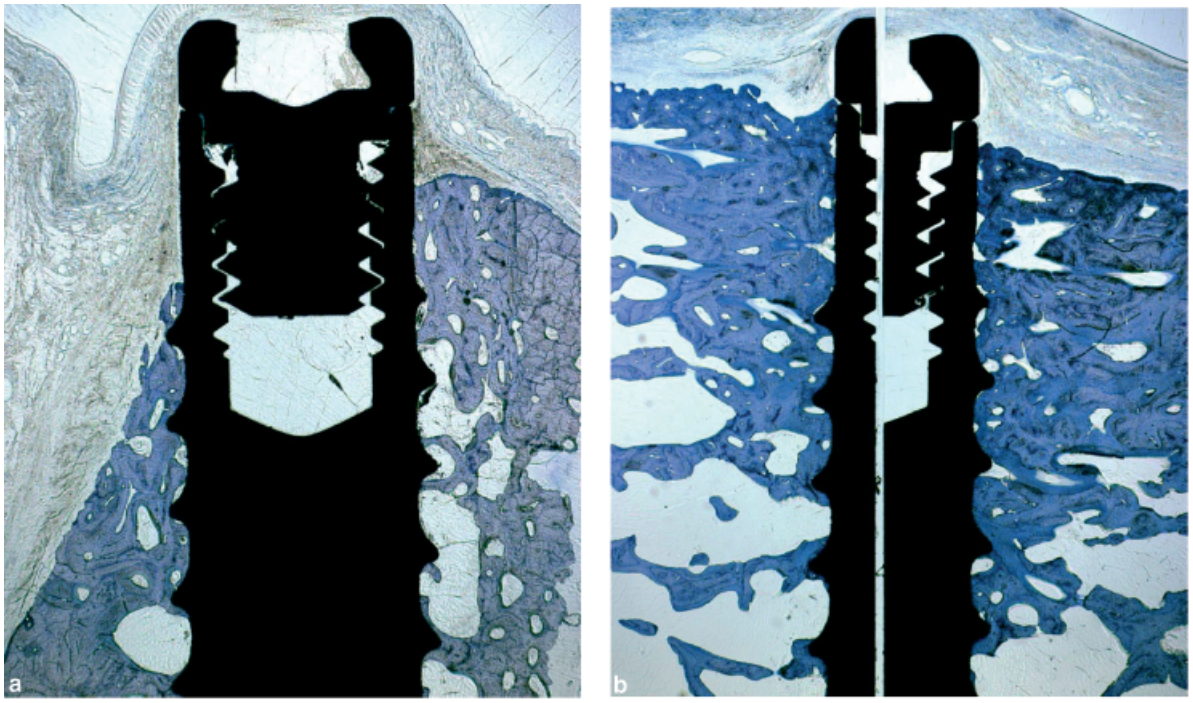

Fig. 8. Ground sections of one test site T2 after 4 months of healing in (a) buccal–lingual and (b) mesial–distal planes (magnification ×16). The buccal plate of the small defect was removed at the time of implant installation. After 4 months of healing the defect was filled with newly formed bone at the mesial, distal and lingual but to a less extent at the buccal aspects.

region was composed of lamellar bone (55.2 ± 6.9%), woven bone (25.9 ± 10.5%), and bone marrow (18.8 ± 5.7%) (Table 2).

In sites T2 (Fig. 8a, b) and T3 (Fig. 9a, b) the overall mean distance between M and B was 0.86 ± 0.21 mm and 0.89 ± 0.36 mm, respectively. The average M–B distance representing the lingual and interproximal (mesial and distal) aspects varied within a small range between 0.34 and 0.50 mm (Table 1).

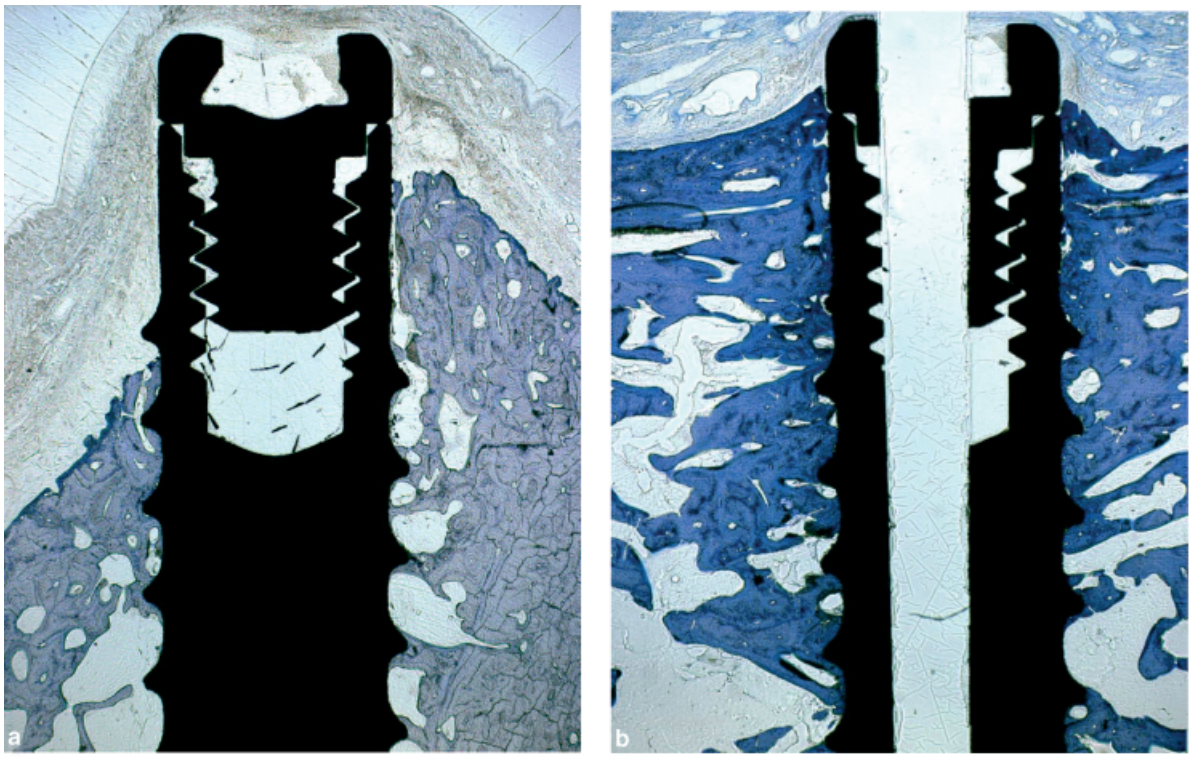

Fig. 9. Ground sections of one test site T3 after 4 months of healing in (a) buccal–lingual and (b) mesial–distal planes (magnification ×16). The buccal plate of the wide defect was removed at the time implant installation. Also in this case the defect became completely filled with newly formed bone at all but the buccal aspects.

The corresponding distance representing the buccal aspect was considerably longer and varied between 2.2 ± 0.35% (T2) and 2.26 ± 0.45% (T3).

The overall BIC in the defect region was 65.6 ± 6.7% (T2) and 65.9 ± 4.1% (T3). The hard tissue found in the defect of sites T2 and T3 varied on the average between 58 ± 6.4% (T2) and 59.8 ± 5.8% (T3) (lamellar bone), 21.7 ± 11.1% (T2) and 22.7 ± 7% (T3) (woven bone), and 20.3 ± 6.7% (T2) and 17.6 ± 4% (T3) (bone marrow) (Table 2).

Discussion

The observations made in the current experiment disclosed that four-wall, self-contained defects of different dimensions (1–2.25 mm wide) that occurred in the marginal portion of the recipient sites following implant installation were resolved during healing. This was accomplished through some resorption of marginal bone tissue and substantial amounts of new bone formation originating from the lateral and ''apical'' walls of the mechanically produced defect. Further, at sites where the buccal bone wall during defect preparation was intentionally removed, healing resulted in defect resolution at the mesial, distal, and lingual aspects. At the buccal aspects, healing was incomplete and the defect was not entirely resolved and reduced in dimension by newly formed bone that extended from the lateral and apical borders of the defect.

The finding that self-contained marginal defects during healing were resolved is in agreement with data previously reported from this laboratory (Botticelli et al. 2003a). In the study referred to, marginal defects, 1–1.25 mm wide, became filled with newly formed bone during a 4-month interval of healing. The present results, however, documented that also defects of larger dimensions could be resolved without the use of filler materials.

There are reasons to suggest that the surface characteristics of the implant used in the experiment may have influenced the amount of new bone that formed in the marginal defects. In this context the current findings should be compared with those reported by, for example, Carlsson et al. (1988) and Akimoto et al. (1999) who in their experiments used implants with a turned surface topography. Carlsson et al. (1988) installed implants in the tibia of rabbits. Bone formation that occurred in defects (⩽0.85 mm wide) that were surgically produced in the cortical bone lateral to the implant, were examined following a 6–12-week period of healing. The authors concluded that a gap that was 0.35 mm wide exhibited only small amounts of new bone formation and that defects with larger dimensions were not resolved with new bone. Akimoto et al. (1999), in a dog model, studied the healing after 12 weeks of self-contained peri-implant defects that were 6 mm deep and 0, 0.5, 1, or 1.4 mm wide. The authors reported that at the end of the 12-week interval, the amount of new bone that was found to be in contact with the implant seemed to be dependent on the original width of the defect. Thus, it appears that when implants with a turned surface are used, the larger the marginal gap is, less amount of de novo peri-implant bone will form.

Knox et al. (1991) used both HA coated and grid-blasted implants in a dog model to study the healing of marginal defects of different dimensions. They concluded that HA-coated implants appear to be superior to those with grid blasted titanium. This was especially true in sites where marginal bone gaps greater than 0.5 mm exist.

The assumption that the quality of the implant surface is of decisive importance for bone formation in marginal defects is further supported by data presented by, for example, Stentz et al. (1997) and Persson et al. (2001). Stentz et al. (1997), in a dog model, compared the healing of marginal gaps, about 3 mm wide, adjacent to implants with turned or HA-coated surfaces. Barrier membranes were used to protect the defects at some but not all sites. The authors reported that, after 4 months of gap healing at sites with turned implants, there was a minimal amount of new bone formation and osseointegration. Further, newly formed bone was only seen within the apical portion of the defect. At corresponding sites with HA-coated implants there was a larger proportion of new bone in contact with the implant surface. Persson et al. (2001) compared the healing of marginal bone defects that occurred following experimental peri-implantitis at sites in dogs with implants designed with either turned or SLA surface topographies. They reported that, while only small amounts of re-osseointegration occurred to implants with a turned surface, defects lateral to implants with an SLA surface were almost entirely resolved.

Based on the findings made in the current experiment and in the studies referred to, it can be argued that it may not be the size of the marginal gap per se but rather the formation of a coagulum in the defect, its retention and replacement with a provisional matrix that determine whether defect resolution will occur. This hypothesis is supported by findings presented by Scipioni et al. (1997). They used the so-called ''edentulous ridge expansion technique'' (Scipioni et al. 1994) in a dog experiment and demonstrated that defects larger than 5 mm could be entirely resolved. Further, it was recently demonstrated that defects (sockets) of comparatively large dimensions that occurred following extraction of premolars in dogs within a 1-month period were filled with newly formed bone (Cardaropoli et al. 2003).

In the present study it was observed that the buccally open defect at sites T2 and T3 healed with less new bone formation than that which was observed at the lingual, mesial, and distal aspects of the same site. There are reasons to suggest that this compromised bone fill to some extent may be related to an inadequate space making effect offered by the barrier membrane used. Thus, the collagen barrier may during the early phase of healing has collapsed into the buccal defect and hence reduced the space available for new tissue formation at this particular aspect of the defect. This assumption seems to be corroborated by data presented by, for example, Lekholm et al. (1993). They used a dog model and placed implants (turned surface) into fresh extraction sockets after the buccal bone had been removed. Dehiscence type defects about 5 mm high, 3 mm wide, and 3 mm deep were hereby established. The defect sites were protected with a rigid expanded polytetrafluoroethylene (ePTFE) membrane, with proper space maintaining properties, and were fully submerged. After 16 weeks of healing, it was observed that the buccal dehiscence defect at such membrane-protected sites was almost entirely resolved. Similar results were obtained by Becker et al. (1995) in a corresponding dog model after 12 weeks of healing, in sites protected with a ePTFE membrane.

In the present study it was also observed that less new bone formation occurred at the buccal aspect of the T1 sites than at the lingual, mesial, and distal aspects (Table 2). The height of the newly formed bone at the buccal aspect in site T1 was shorter than at corresponding buccal surfaces of the control sites (C1 and C2), but longer in relation to other test sites (T2 and T3). This finding may be explained by the fact that the preparation of the large defects at T1 sites exceeded the buccal–lingual dimension of the alveolar ridge and thus, compromised the buccal ''wall'' of the defect. For this reason the buccal crest was, after defect preparation, at a more ''apical'' level than at the mesial, distal and lingual aspects, partly simulating the situation that occurred at the defect where the buccal plate was mechanically removed.

Acknowledgments

This study was supported by grants from the ITI Foundation.

References

Akimoto, K., Becker, W., Persson, R., Baker, D. A., Rohrer, M. D. & O'Neal, R. B. (1999) Evaluation of titanium implants placed into simulated extraction sockets: a study in dogs. *International Journal of Oral and Maxillofacial Implants* **14**, 351–360.

Alliot, B., Piotrowski, B., Marin, P., Zahedi, S. & Brunel, G. (1999) Regeneration procedures in immediate transmucosal implants: an animal study. *International Journal of Oral and Maxillofacial Implants* **14**, 841–848.

Becker, W., Becker, B. E., Handelsman, M., Ochsenbein, C. & Albrektsson, T. (1991) Guided tissue regeneration for implants placed into extraction sockets: a study in dogs. *Journal of Periodontology* **62**, 703–709.

Becker, W., Schenk, R., Higuchi, K., Lekholm, U. & Becker, B. E. (1995) Variations in bone regeneration adjacent to implants augmented with barrier membranes alone or with demineralized freezed-dried bone or autologous grafts: a study in dogs. *International Journal of Oral and Maxillofacial Implants* **10**, 143–154.

Botticelli, D., Berglundh, T., Buser, D. & Lindhe, J. (2003a) The jumping distance revisited. An experimental study in the dog. *Clinical Oral Implant Research* **14**, 35–42.

Botticelli, D., Berglundh, T., Buser, D. & Lindhe, J. (2003b) Appositional bone formation in marginal defects at implants. An experimental study in the dog. *Clinical Oral Implant Research* **14**, 1–9.

Carlsson, L., Röstlund, T., Albrektsson, B. & Albrektsson, T. (1988) Implant fixation improved by close fit. Cylindrical implant–bone interface studied in rabbits. *Acta Orthopedica Scandinavica* **59**, 272–275.

Caudill, R. F. & Meffert, R. M. (1991) Histological analysis of the osseointegration of endosseous implants in simulated extraction sockets with and without e-PTFE barriers. Part I. Preliminary findings. *International Journal of Periodontics and Restorative Dentistry* **11**, 207–215.

Cardaropoli, G., Araújo, M. & Lindhe, J. (2003) Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs. *Journal of Clinical Periodontology* **30**, 809–818.

Clemens, J. A., Klein, C. P., Sakkers, R. J., Dhert, W. J., de Groot, K. & Rozing, P. M. (1997) Healing of gaps around calcium phosphate-coated implants in trabecular bone of the goat. *Journal of Biomedical Material Research* **36**, 55–64.

Donath, K. (1988) Die Trenn-Dünnschliff-Technik zur Herstellung histologischer Präparaten von nicht schneidbaren Geweben und Materialen. *Der Präparator* **34**, 197–206.

Donath, K. (1993) *Preparation of Histologic Sections (by Cutting–Grinding Technique for Hard Tissue and Other Material not Suitable to be Sectioned by Routine Methods) – Equipment and Methodical Performance*. Norderstedt: EXACT – Kulzer Publication.

Donath, K. & Breuner, G.-A. (1982) A method for the study of undecalcified bones and teeth

with attached soft tissues. The Säge-Schliff (sawing and grinding) technique. *Journal of Oral Pathology* **11**, 318–326.

Gotfredsen, K., Nimb, L., Buser, D. & Hjorting-Hansen, E. (1993) Evaluation of guided bone generation around implants placed into fresh extraction sockets: an experimental study in dogs. *Journal of Oral and Maxillofacial Surgery* **51**, 879–884.

Gotfredsen, K., Nimb, L. & Hjorting-Hansen, E. (1994) Immediate implant placement using a biodegradable barrier, polyhydroxybutyrate-hydroxyvalerate reinforced with polyglactin 910. An experimental study in dogs. *Clinical Oral Implants Research* **5**, 83–91.

Harris, W. J., White, R. E., McCarthy, J. C., Walker, P. S. & Weinberg, E. H. (1983) Bony ingrowth fixation of the acetabular component in canine hip joint arthroplasty. *Clinic Orthopedic* **176**, 7–11.

Karnovsky, M. J. (1965) A formaldehyde–glutaraldehyde fixative of high osmolarity for use in electron microscopy. *Journal of Cell Biology* **27**, 137A–138A.

Knox, R., Caudill, R. & Meffert, R. (1991) Histologic evaluation of dental endosseous implants placed in surgically created extraction defects. *International Journal of Periodontics and Restorative Dentistry* **11**, 365–375.

Kohal, R. J., Mellas, P., Hurzeler, M. B., Trejo, P. M., Morrison, E. & Caffesse, R. G. (1998) The effects of guided bone regeneration and grafting on implants placed into immediate extraction sockets. An experimental study in dogs. *Journal of Periodontology* **69**, 927–937.

Lekholm, U., Becker, W., Dahlin, C., Becker, B., Donath, K. & Morrison, E. (1993) The role of early versus late removal of GTAM membranes on bone formation at oral implants placed into immediate extraction sockets. An experimental study in dogs. *Clinical Oral Implants Research* **4**, 121–129.

Mayfield, L. J. A. (1999) Immediate, delayed and late submerged and transmucosal implants. In: *Proceedings of the Third European Workshop on Periodontology*, eds. Lang, N. P., Karring, T. & Lindhe, J., pp. 520–534. Berlin: Quintessence Verlags-GmbH.

Persson, L., Berglundh, T., Sennerby, L. & Lindhe, J. (2001) Re-osseointegration after treatment of peri-implantitis at different implant surface. An experimental study in the dog. *Clinical Oral Implant Research* **12**, 595–603.

Schenk, R. K. (1994) Bone regeneration: biologic basis. In: *Guided Bone Regeneration in Implant Dentistry*, eds. Buser, D., Dahlin, C. & Schenk, R. K., pp. 49–100. Berlin: Quintessence Book.

Schenk, R. & Willenegger, H. (1977) Zur Histologie der primären Knochenheilung. Modifikationen une Grenzen der spaltheilung in Abhängigkeit von der Defktgrösse. *Unfallheilkunde* **80**, 155.

Schroeder, H. E. & Münzel-Pedrazzoli, S. (1973) Correlated morphometric and biochemical analysis of gingival tissue. *Journal of Microscopy* **99**, 301–329.

Schwartz-Arad, D. & Chaushu, G. (1997) Placement of implants into fresh extraction sites: 4 to 7 years retrospective evaluation of 95 immediate implants. *Journal of Periodontology* **68**, 1110–1116.

Scipioni, A., Bruschi, G. B. & Calesini, G. (1994) The edentulous ridge expansion technique: a five-year study. *International Journal of Periodontal and Restorative Dentistry* **14**, 451–459.

Scipioni, A., Bruschi, G. B., Giargia, M., Berglundh, T. & Lindhe, J. (1997) Healing at implants with and without primary bone contact. An experimental study in dogs. *Clinical Oral Implants Research* **8**, 39–47.

Stentz, W. C., Mealey, B. L., Gunsolley, J. C. & Waldrop, T. C. (1997) Effects of guided bone regeneration around commercially pure titanium and Hydroxyapatite-coated dental implants. II. Histologic analysis. *Journal of Periodontology* **68**, 933–949.

Todescan, R., Pilliar, R. M. & Melcher, A. H. (1987) A small animal model for investigating endosseous dental implants: effect of graft materials on healing of endosseous, porous-surfaced implants placed in a fresh extraction socket. *International Journal of Oral and Maxillofacial Implants* **2**, 217–223.

Warrer, L., Gotfredsen, K., Hjorting-Hansen, E. & Karring, T. (1991) Guided tissue regeneration ensures osseointegration of dental implants placed into extraction sockets. An experimental study in monkeys. *Clinical Oral Implants Research* **2**, 166–171.

Address:
Daniele Botticelli
Department of Periodontology
Institute of Odontology
Sahlgrenska Academy
Göteborg University
P.O. Box 450
SE-40530 Göteborg
Sweden
Fax: +46 31 7733791
E-mail: daniele.botticelli@odontologi.gu.se