

Early healing of implants placed into fresh extraction sockets: an experimental study in the beagle dog. II: ridge alterations

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Abstract

Aims: To describe the early phases of healing at the alveolar ridge around dental implants placed into fresh extraction sockets and to study whether (i) the dimension of the socket and (ii) a new implant surface nano-topography may have any influence.

Materials and Methods: Sixteen beagle dogs received 64 test (new surface) and control implants randomly placed at the distal socket of 3P3 and 4P4. The implant shoulder was levelled with the marginal buccal bone crest. Animals were sacrificed at 4 h, 1, 2, 4 and 8 weeks for histological examination.

Results: Bone loss occurred at the buccal crest between the 4-h and 1-week healing intervals, being more pronounced at the third premolar site [vertical bone loss between day 0 and 8 weeks 1.1 (0.5) mm]. The corresponding loss at the fourth premolar site was 0.3 (0.5) mm. Test sites containing implants with discrete crystalline deposition nano-particles' surface exhibited less buccal bone resorption than control sites at 8 weeks.

Conclusion: Dimensions of the socket influenced the process of wound healing of implants placed into fresh extraction sockets, with more bone loss in the narrower sockets; however, the implant surface nano-topography seemed to have a limited effect in the healing of this implant surgical protocol.

Key words: animal model; buccal crest; fresh extraction socket; nano-topography; ridge alterations

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In recent years, immediate implant placement after tooth extraction has become a more common surgical protocol. Different clinical investigations have reported short-term high survival rates (approximately 95%), similar to when implants are placed in healed alveolar ridges (Schropp et al. 2003, Ganeles & Wismeijer 2004, Cornelini et al. 2005, Lang et al. 2007, Schwartz-

Arad et al. 2007). The healing of implants placed using this surgical protocol has also shown a similar histological pattern of osseointegration in both human (Wilson et al. 1998, Paolantonio et al. 2001) and animal experimental studies (Anneroth et al. 1985, Barzilay et al. 1991, 1996a,b, Karabuda et al. 1999). Nevertheless, histometric findings from recent animal studies have revealed that the placement of implants in fresh extraction sockets was associated with marked alterations of the buccal and lingual socket walls, both in terms of height and width. At the buccal bone wall, this vertical reduction averaged 2.6 mm at 3 months when implants were placed

into the distal sockets of P3 and P4 in the beagle dog (Araujo et al. 2005). Further experiments from the same research group showed that the amount of these ridge alterations was dependent on the socket location (molar *versus* premolar) (Araujo et al. 2006b). When both surgical models (extraction socket *versus* healed ridges) were compared experimentally, Botticelli et al demonstrated significant differences in mean vertical bone resorption (2.45 *versus* 0.68 mm at 4 months), concluding that the process of bone modelling and remodelling at an implant placed in a fresh extraction socket differs from the one that occurs following implant installation in an osseous wide

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defect prepared ridge (Botticelli et al. 2006).

One of the possible causes of this different healing behaviour may be that following tooth extraction the socket's dimensions are greater than the diameter of a conventional implant and consequently, a marginal gap usually occurs between the implant surface and the socket wall. Although some authors have reported that a critical bone-implant distance (jumping distance) must exist in order to allow undisturbed osseointegration (Caudill & Meffert 1991, Gotfredsen et al. 1991, Knox et al. 1991, Akimoto et al. 1999), others have argued that this distance might not be that important if implants with rough surfaces are utilized and an undisturbed blood clot is allowed to heal (Botticelli et al. 2003). In fact, experimental evidence from this research group has shown that osseointegration at implants placed in sites with surgically created marginal defects was mostly influenced by the surface characteristics of the implant (Botticelli et al. 2005). Further modifications of the implant surface micro-topography at the nano-scale level have further provided similar evidence of enhanced bone response in both animal experiments (Meirelles et al. 2007, 2008a, b) and human biopsy material (Goene et al. 2007, Orsini et al. 2007).

We, however, lack precise knowledge of the critical factors that may affect the early healing of implants placed in fresh extraction sockets and how implant surface modifications may interact with the vertical and horizontal ridge alterations reported when implants are placed immediately upon tooth extraction. The purpose of this study was, therefore, to investigate these early healing events, focusing on the dimensional changes of

the buccal and lingual walls of fresh extraction sockets following implant installation in a dog model. We studied the influence of the socket dimensions and the surface micro-topography by comparing implants with a calcium-phosphate nano-treated surface (DCD nano-particles, Nanotite[®], Biomet 3i) with a standard dual acid-etched (DAE) surface (Osseotite[®], Biomet 3i).

Materials and Methods

The experimental model used in this study was recently reported (Vignoletti et al. 2009). The sample consisted of 16 female adult beagle dogs with weight between 10 and 20 kg and a mean age of 1.5 years. Throughout the experimental study, the animals were kept on a soft diet and subject to oral hygiene by mechanical cleaning of both teeth and implants using a toothbrush and toothpaste. Animals were divided into five groups according to the following healing intervals: 4 h, 1, 2, 4 and 8 weeks.

Each group included three dogs, except group-5 (8 weeks), which included four. Four cylindrical screw-shaped 3.25 mm diameter implants with lengths varying from 8.5 to 11.5 mm (Miniplant, Osseotite Certain, Biomet 3i, Palm Beach Gardens, FL, USA) were placed in each dog. Control implants had a DAE surface (Osseotite[®], Biomet 3i), while in the test implants their surface was modified by the deposition of discrete crystals of calcium phosphate (CaP), which superimposes a nano-scale surface topography upon an already complex micro-topographic titanium surface produced by acid etching (DCD nano-particles, Nanotite[™], Biomet 3i). This proprietary, so-called discrete crystalline deposition (DCD) is achieved

by immersing the metallic implants in a suspension of CaP crystals, ranging in size between 20 and 100 nm and resulting in approximately 50% of the metallic surface being covered by the crystals, with the remaining surface being metal oxide (Mendes et al. 2008). Test implants were visibly indistinguishable from control implants. All implants had an internal abutment connection into which healing abutments were adapted. Test (DCD nano-particles, Nanotite[™], Biomet 3i) and control (Osseotite[®], Biomet 3i) implants were randomly inserted into the distal sockets of the two rooted mandibular premolars 3P3 and 4P4, thus providing four study sites per dog.

Surgery

This animal experiment was carried out at the Experimental Surgical Centre of the Hospital "Gomez-Ulla" in Madrid, Spain, once the Regional Ethics Committee for Animal Research had approved the study protocol. Sixteen adult female beagle dogs were included. The implant installation procedure was carried out according to the experimental design outlined in Table 1. Buccal and lingual intrasulcular incisions from mesial of the third premolar 3P3 to mesial of the first molar 1M1 were performed on both sides of the mandible. Mucoperiosteal full-thickness flaps were reflected on both the sides to disclose the marginal aspect of the ridge in order to facilitate tooth extraction. The third and fourth mandibular premolars on both sides (3P3 and 4P4) were hemisected and extracted. The distal sockets of each premolar were selected as the study sites while the mesial sockets were allowed to heal without intervention (Fig. 1).

Table 1. Study schedule

Groups	- 1 week	Baseline	1 week	2 weeks	3 weeks	4 weeks	7 weeks	8 weeks
Group-5 (8 weeks)	Prophylaxis	Surgery						Biopsy
Group-2 (1 week)		Prophylaxis	Surgery	Biopsy				
Group-3 (2 weeks)			Prophylaxis	Surgery		Biopsy		
Group-4 (4 weeks)					Prophylaxis	Surgery		Biopsy
Group-1 (4 h)							Prophylaxis	Surgery biopsy

Each group provided four animals (group-5, 8 weeks, included four animals).

Each animal provided four study sites, two tests and two controls.

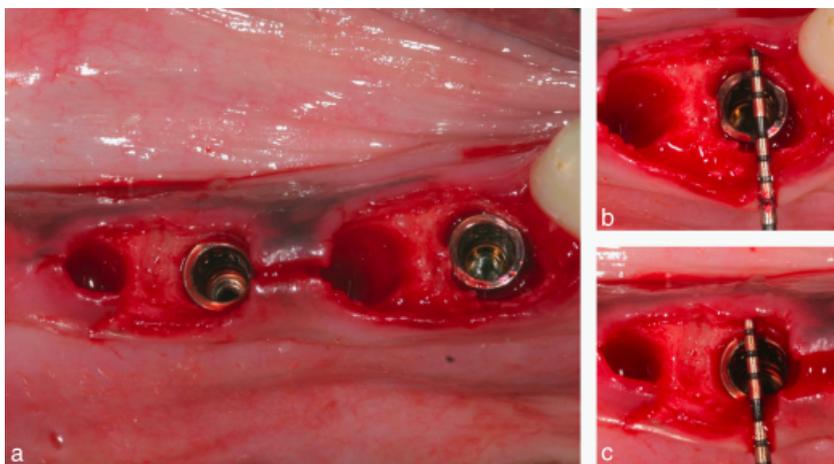


Fig. 1. (a) Implants installation in the distal socket of the third and fourth premolars. Note that the buccal–lingual width of the extraction socket of the fourth premolar (b) is wider than that of the third premolar (c).

Osteotomy preparations were made at the centre of the sockets to the appropriate diameter ensuring that the implant platform was placed at the level of the marginal portion of the buccal plate (Fig. 2). After inserting the implants healing abutments were connected. The flaps were repositioned and sutured with 4-0 vicryl resorbable sutures. The animals were sacrificed with an overdose of sodium-pentothal and perfused with a fixative solution (Karnovsky 1965) through the carotid arteries. Specimens representing five healing periods from 4 h to 8 weeks after implant installation were obtained according to the experimental design depicted in Table 1.

Histological processing

Block biopsies containing the implant and the surrounding periimplant tissues were obtained using a diamond saw. Ground sections were prepared according to the methods described by Donath & Breuner (1982) and in accordance to the protocol reported by Vignoletti et al. (2009).

Histological and histometric evaluation

The histometric evaluation was carried out in a Leitz DM-RBE microscope (Leica, Heidelberg, Germany) equipped with image analysis software (Q-500 MC; Leica).

Four buccal–lingual sections per animal were examined and the following landmarks were identified on the buccal and lingual side of the sections (Fig. 3):

- shoulder of the implant (I);
- marginal bone crest (Bc);

most coronal bone to implant contact (B).

The following distances were calculated on the buccal and lingual aspects and expressed in millimetres:

- I–Bc;
- I–B;
- Bc–B.

Because the bucco-lingual and mesio-distal dimensions of the two sockets were different (Fig. 1), the more distal being wider (Araujo et al. 2005, Blanco et al. 2008), histometric mean measurements of the three outcome variables were compared after stratifying by socket/site location (3P and P3 versus 4P and P4), thus assessing whether a wider gap between the implant surface and the bony walls had any influence on the histological outcome.

Data analysis

The dog was used as the statistical unit of analysis. For each variable a mean value for each animal and healing interval was calculated and used for the data analysis. Histological results were expressed as mean linear distances of buccal and lingual measurements (\pm SD). Comparisons among the different healing periods per group were analysed using the one-way analysis of variance combined with the Bonferroni *post hoc* test. Differences were considered statistically significant when p was <0.05 . This statistical analysis was performed using the software Prism 5.0 (GraphPad, San Diego, CA, USA).



Fig. 2. The shoulder of the implant was leveled with the marginal bone crest on the buccal aspect. Note the different level of the buccal (black arrow) and lingual (yellow arrow) bone crests.

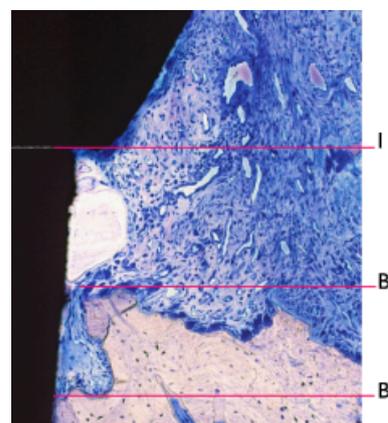


Fig. 3. Landmarks utilized for histometric measurements. I, shoulder of the implant; Bc, marginal bone crest; B, most coronal bone to implant contact. Toluidine-blue staining. Original magnification $\times 16$.

Furthermore, at each healing interval, a mean value of each variable was calculated for test and control implants. Similarly, results were compared after stratifying according to socket site [(3P3) and (4P4)]. Because of the limited number of animals per group, no statistical analysis was performed on such stratified data, and results are presented in a descriptive manner.

Results

Clinically, healing was uneventful for all 64 implants, with no visible signs of inflammation in the peri-implant mucosa. Two healing abutments in one dog in group-4 and four healing abutments in two dogs in group-5 were not present at the day of sacrifice. These implants were covered by a layer of keratinized epithelium and, therefore, the specimens from these implants were excluded from the histometric analysis. One implant

Table 2. Number of animals per group, number of specimens analysed and mean (SD) dimension of the microgap

Healing interval	Group	Number of animals	Number of specimens	Microgap [mean (SD)] (µm)
4 h	1	3	12	151 (199)
1 week	2	3	11	127 (143)
2 weeks	3	3	12	321 (282)
4 weeks	4	3	10	346 (337)
8 weeks	5	4	12	116 (137)

SD, standard deviation.

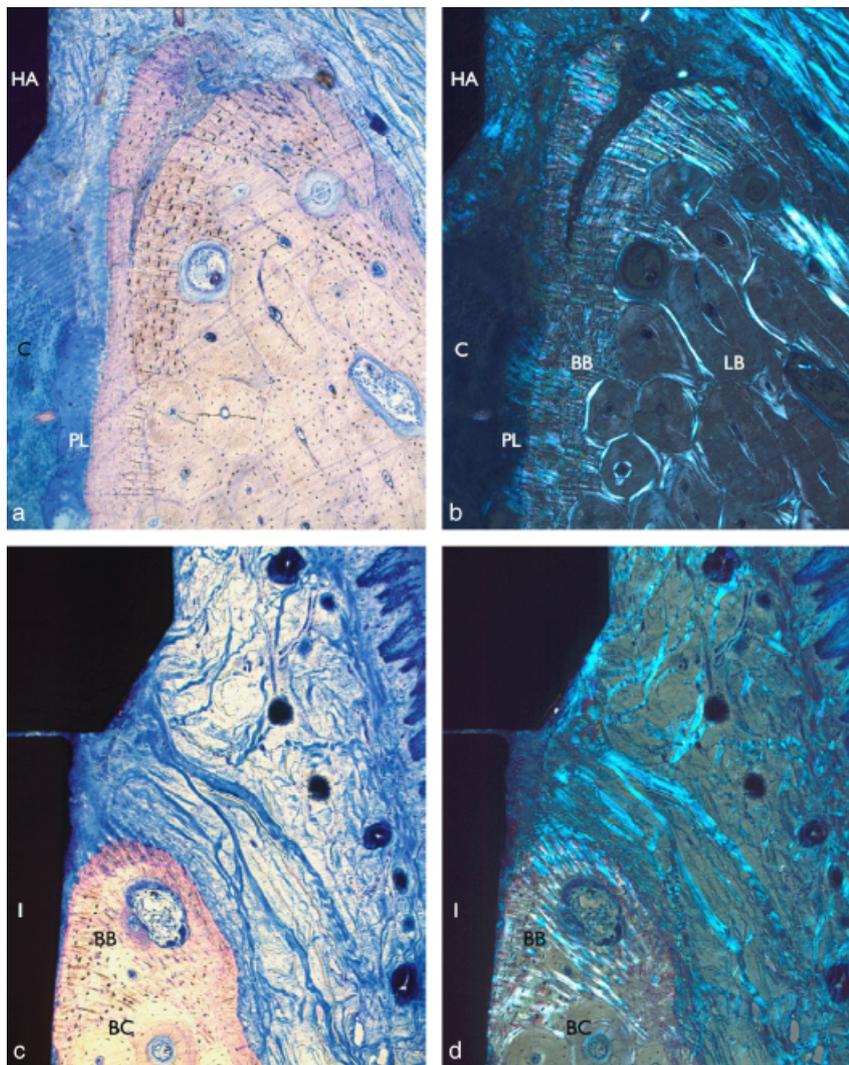


Fig. 4. (a) Ground section representing the coronal portion of the lingual bone crest 4 h after implant installation. A coagulum (C) fills the void between the socket wall and the implant surface (not shown). Toluidine-blue staining. Original magnification $\times 16$. (b) The bone crest is comprised of lamellar bone (LB) and bundle bone (BB). Note the remnants of the periodontal ligament (PL) inserted into the bundle bone in the inner side of the socket wall (HA, healing abutment). Polarized light. (c) Ground section representing the coronal portion of one implant 4 h after installation. The implant (I) is in intimate contact with the buccal bone crest (BC). Note that the marginal bone crest is comprised of bundle bone alone (BB). Toluidine-blue staining. Original magnification $\times 16$. (d) polarized light.

in the third premolar site (3P3) of one dog from group-2 (1 week) suffered a surgical complication during implant placement, and a complete dehiscence

occurred at the buccal aspect of the socket. The specimen from this implant was also excluded from the histometric analysis. The final number of specimens

per group that were histologically evaluated is presented in Table 2.

Histological observations

Since the implant shoulder was placed at the level of the marginal portion of the buccal crest and due to the anatomy of the dog mandible, the position of the implant shoulder at the lingual side was sub-crestal (Fig. 2). This anatomical difference influenced the positioning of the healing abutments that did not always adjust precisely to the implant shoulder (Fig. 8). The mean height (SD) of this microgap calculated at the buccal aspect of each implant is presented in Table 2.

At 4 h the bone crest was comprised by bundle bone alone or by a combination of bundle and lamellar bone (Fig. 4a–d). At this healing period, a coagulum occupied the void between the implant surface and the bone. On the inner side of the socket walls, remnants of the periodontal ligament attached to the bundle bone were observed (Fig. 4b).

In the 1-week specimens, bundle bone was still present at the buccal bone crest, which was located between 0 and 3 mm apical of the implant shoulder (I). In the bone–implant interface no periodontal ligament remnants were observed. The void that was occupied by a coagulum in the 4-h sections was, in this group of specimens, filled by a loose connective tissue rich in inflammatory cells. Numerous osteoclasts in Howship's lacunae lined the bone surface at the top and at the inner part of the crest (Fig. 5a and b).

At 2 weeks, bundle bone was still present in the most coronal part of the ridge (Fig. 6a and b). New bone formation was also observed at the outer part of the bone crest. This latter finding was observed only at the thinner buccal plate (Fig. 7a and b). The newly formed bone was clearly separated from the old lamellar bone by reverse cement lines. Signs of bone remodelling were observed in the old lamellar bone. The apical extension of the connective tissue varied from 1 to approximately 3 mm apical of the implant shoulder (I). Only a small number of inflammatory cells were present at the coronal part of the crest (Fig. 8a and b).

At 4 weeks the buccal crest consisted of lamellar bone, woven bone and occasional remnants of bundle bone. At the bone–implant interface, woven bone for-

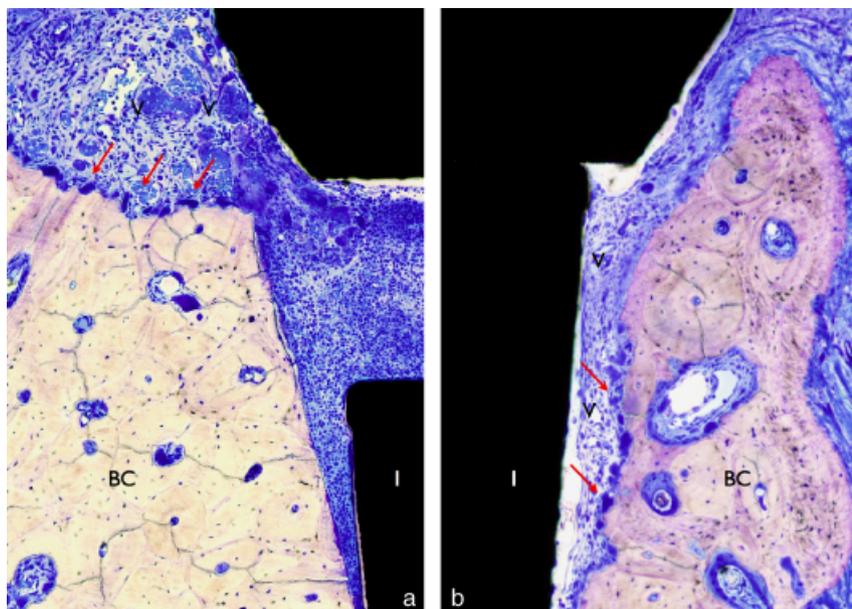


Fig. 5. Ground sections representing implant 1 week after installation. A loose connective tissue rich in inflammatory cells and vessels (V) is interposed between the Implant surface (I) and the bone crest (BC). Note the osteoclasts (arrows) on the marginal portion of the bone crest. (a) Lingual bone crest, (b) buccal bone crest. Toluidine-blue staining. Original magnification $\times 16$.

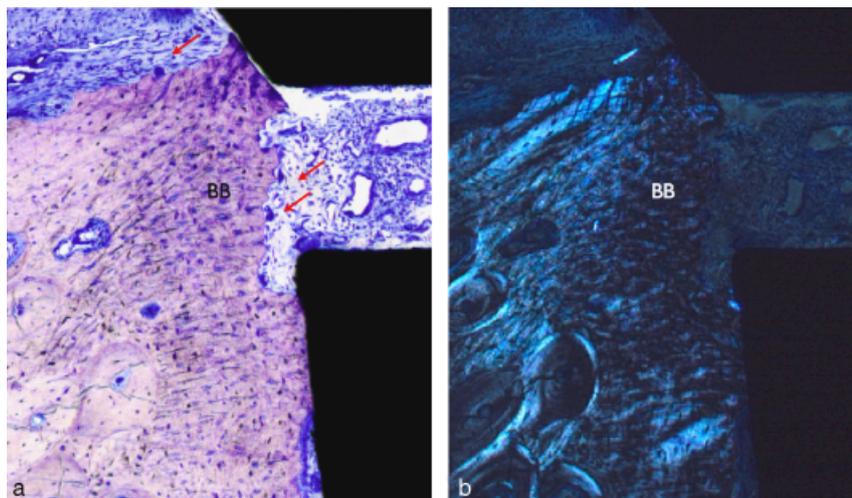


Fig. 6. Ground sections representing one implant 2 weeks after implant installation. (a) Bundle bone (BB) present in the inner part of the socket wall. Osteoclasts (arrows) on the marginal portion of the bone crest. (b) polarized light. Toluidine-blue staining. Original magnification $\times 16$.

mation concomitant with bone remodeling was evident. At the coronal level, the dense fibre-rich collagen tissue extended to a position 1 mm apical of the implant shoulder (I) (Figs 9 and 10).

At 8 weeks, the buccal crest was located either in level with or at various positions apical of the implant shoulder (I) (Fig. 11a and b). Bundle bone was not identified. Similar to the 4-week specimens, a densely packed collagen tissue in

close contact with the implant surface was located in a zone limited to approximately 1 mm apical of the implant shoulder.

Histometric analysis

The results from the histometric measurements (mm) of I–Bc, I–B and Bc–B, assessed at the buccal and lingual aspects of the analysed sections, are depicted in Tables 3–5, respectively.

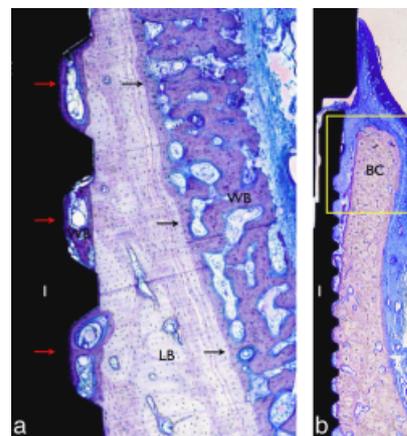


Fig. 7. (a) Ground sections representing implant 2 weeks after installation. Newly formed bone (dark stained areas, WB) is clearly separated from the lamellar bone (LB) and identified in contact (red arrows) with the implant surface (I) and at the outer part of the thin buccal crest (black arrows). Toluidine-blue staining. Original magnification $\times 10$. (b) Ground section representing implant 2 weeks after installation. Newly formed bone (dark stained areas, WB) is observed at the inner part of the buccal bone crest (BC). (I, Implant surface) Inset: Fig. 8. Toluidine-blue staining. Original magnification $\times 5$.

I–Bc

There was a marked difference in the healing pattern between buccal and lingual alveolar walls. While there was an overall mean vertical difference of the buccal socket wall averaging 0.6 mm between day 0 and 8 weeks, such a difference was not observed at the lingual wall. The vertical buccal bone loss occurred mainly from baseline to 1 week (0.7 mm). From 1 week till the end of the study, the buccal bone crest remained at the same level (0.6 mm apical of the implant shoulder). The differences between baseline (4 h) and 1, 2, 4 and 8 weeks were statistically significant (Table 3).

When implants were stratified according to their different surface topographies, sites that contained implants with DCD nano-particles' surface exhibited less buccal bone resorption than the control sites at 8 weeks. Similarly, when implants were stratified according to their socket location, differences between the third (3P3) and the fourth (4P4) premolar site were observed. At the distal socket of the third premolar an overall vertical mean difference of 1.1 (0.5) mm was observed between day 0 and 8 weeks. The corresponding value for the fourth premolar site was 0.3 (0.5) mm. In both types of

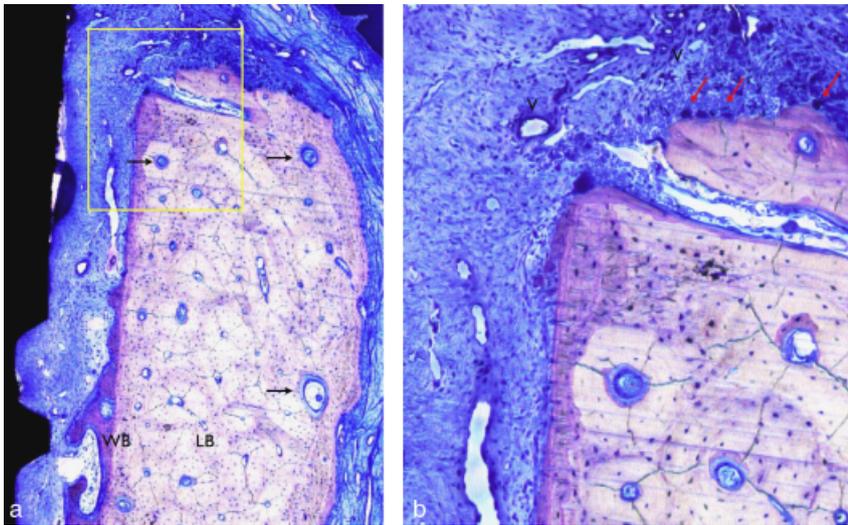


Fig. 8. (a) Bone remodelling was observed in the old lamellar bone (black arrows). Trabecules of woven bone (WB) are continuous with the lamellar bone (LB). Toluidine-blue staining. Original magnification $\times 16$ (b). Detail of (a). Only a small number of inflammatory cells were present in the connective tissue, mainly in the proximity of vessels (V). Note the osteoclasts (red arrows) on the marginal portion of the bone crest. Toluidine-blue staining. Original magnification $\times 20$.

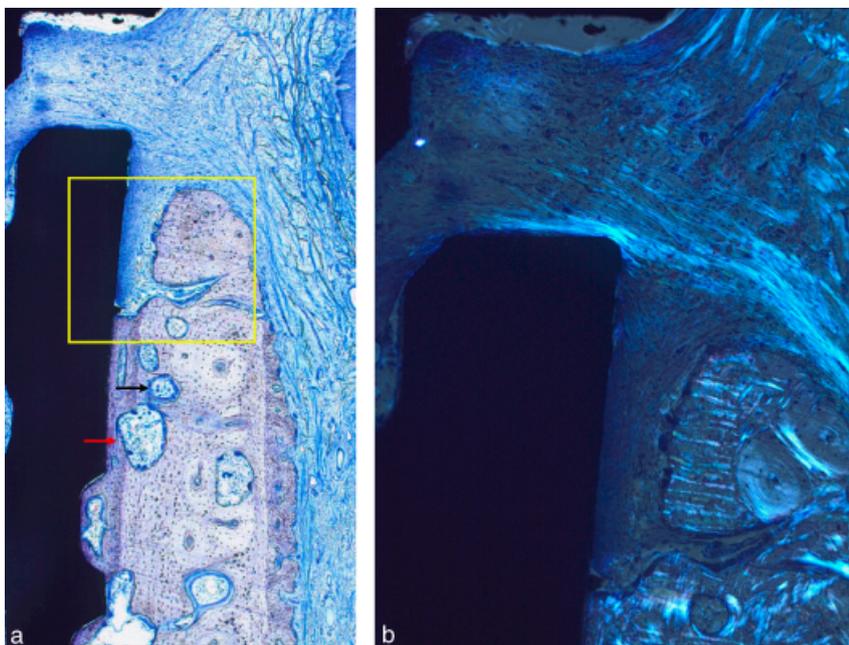


Fig. 9. (a) Ground sections representing implant 4 weeks after installation. Signs of bone remodelling are observed in the old lamellar bone (black arrows) and in the newly formed bone (red arrows). Inset: Fig. 12. Toluidine-blue staining. Original magnification $\times 16$. (b) Higher magnification of (a). Note the dense fiber rich collagen tissue. Polarized light.

sockets, the total amount of vertical bone resorption occurred between baseline and 1 week (Table 3).

I-B

At baseline, the distance between the implant shoulder and the bone to

implant contact was 2.47 (0.70) and 3.65(1.50)mm at the buccal and lingual walls, respectively. From 4 h to 1 week, there were almost no changes, while between 1 and 2 weeks, 50% of the changes occurred, mostly at the lingual wall, where these changes were statistically significant ($p < 0.05$). At the end of

the study, I-B measured almost the same at both sides (1.3 mm) (Table 4).

Table 4 depicts the results from the I-B measurements when implants were stratified according to their surface topography. Data from histometric analysis demonstrated that the I-B distance was independent of the surface treatment. Conversely, when implants were stratified according to their socket location, the first bone to implant contact at the fourth premolar site was located more apically than at the third premolar site. At the distal socket of the third premolar (3P3), a marked vertical bone resorption was observed, with the I-B distance declining from 1.3 (0.7)mm at day 0 to 3.2 (2.7)mm at 1 week. The I-B distance then reverted to baseline values at 8 weeks [1.2 (0.5)mm]. Conversely, at the distal socket of the fourth premolar (4P4), the distance I-B consistently diminished, from 3.6 mm (1) at 4 h to 2 (1.3) mm at 1 week and then to 1.4 (0.5) mm at 8 weeks (Table 4).

BC-B

The distance between the bone crest and the most coronal bone to implant contact represented the infrabony component measured at the buccal and lingual aspects of the implant. At baseline, this distance was higher at the buccal side. Although this distance diminished at each time interval, still at 8 weeks, the infrabony component measured 0.8 (0.7) mm at the buccal and 1.8 (0.9) mm at the lingual aspect, respectively (Table 5).

When comparing implants according to their surface topography, the infrabony component was very similar between sites that contained test and control implants at baseline (Table 5). The Bc-B distance reduced to 2.05 (1.09) and 0.83 (0.90) mm at 1 week for test and control implants, respectively. The infrabony component was gradually reduced to 1.10 (0.94) and 0.39 (0.32) mm for sites that contained implants with DCD nano-particles and DAE surfaces, respectively. When comparing implants according to their socket location, large differences between the third and the fourth premolar sites were observed. At baseline, the infrabony component was 1.2 (0.8) and 3.9 (1.1)mm, at the third and fourth premolars, respectively. From 4 h until the end of the study, the BC-B distance was reduced mainly at the fourth premolar site. After 8 weeks of healing, the distance between the bone crest and the

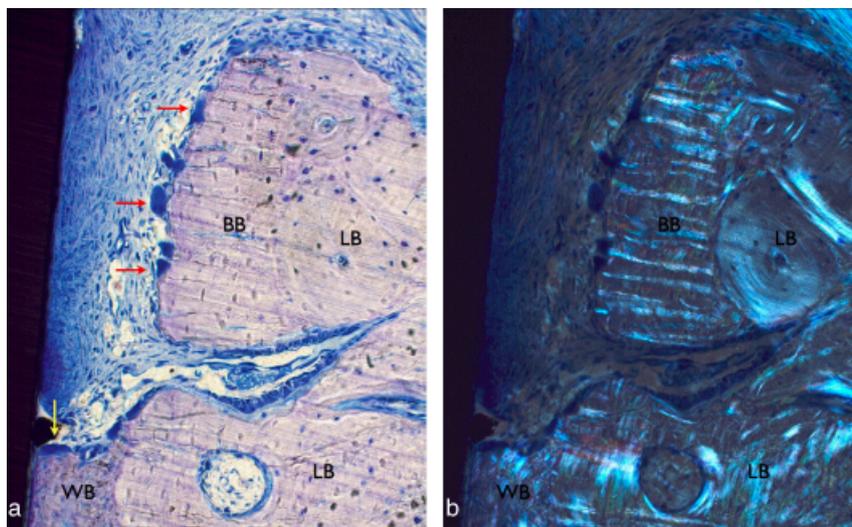


Fig. 10. (a) Detail of Fig. 9. Coronal portion of the buccal bone crest comprised of bundle bone (BB), woven bone (WB) and lamellar bone (LB). Dense collagen tissue rich in elongated fibroblasts is interposed between the implant surface (I) and the bone. Osteoclasts (red arrows) are present on the surface of the bundle bone (BB) and the newly formed bone (yellow arrows). Toluidine-blue staining. Original magnification $\times 20$. (b) Note the different fibers orientation of the 3 types of bone. Polarized light.

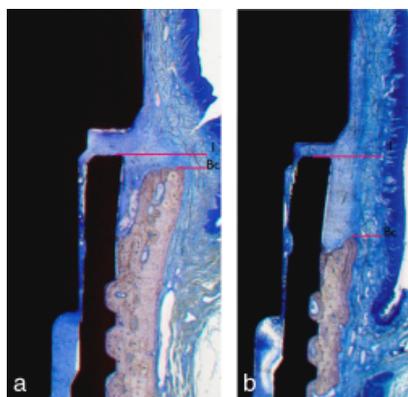


Fig. 11. Ground sections representing implant 8 weeks after installation. The buccal plate (BC) was observed either in level (a) or at various positions (b) apical of the implant shoulder (I). Toluidine-blue staining. Original magnification $\times 5$.

most coronal bone to implant contact was approximately 0 and 1 mm at the third and fourth premolars, respectively (Table 5).

Discussion

This investigation evaluated the early dimensional changes (from 4 h to 2 months) of the buccal and lingual crests after placing implants into fresh extraction sockets. Furthermore, we aimed to assess whether the socket dimension as well as a new surface micro-topography

(DCD nano-particles) influenced the crest healing dynamics.

In the present animal experiment the overall mean resorption of the vestibular plate amounted to 0.6 (0.7) mm at 8 weeks after implant placement. This vertical resorption was not observed at the lingual wall. These findings are consistent with data published by Araujo et al. (2005). They observed bone resorption of approximately 2–2.5 mm at the buccal crest 3 months after implant placement. In this study, implants 4.1 mm in width were placed into the distal sockets of 3P3 and 4P4. The higher buccal vertical bone resorption reported by Araujo et al. (2005), compared with this investigation, may in part be explained by the different implant diameters used and by the longer healing period evaluated in the study by Araujo. Another study from the same research group (Araujo et al. 2006a) investigated the ridge alterations at 1 and 3 months after immediate implant placement in dogs. It was observed that most of the buccal crest resorption occurred between 1 and 3 months. These findings are not in agreement with the results of this study, in which most of the resorption occurred between day 0 and 1 week. A possible explanation for this difference may be the smaller implant diameter used in the current study. In a recent study in the beagle dog, (Blanco et al. 2008) compared flapped *versus* flapless surgery on placing 3.3 mm wide

implants into fresh extraction sockets of 3P3 and of 4P4. They reported that at 3 months of healing 1.33 and 0.8 mm of buccal bone resorption occurred at the 3P3 and 4P4 sites, respectively. The amount of buccal bone resorption in the flapless group reported by Blanco et al. (2008) is thus consistent with the results presented in this study.

The possible influence of the socket dimension on the ridge alterations was one of the main aims of this experimental study. While a small vertical bone loss (0.3 mm) occurred between baseline and 8 weeks at the buccal plate at the fourth premolar sites, the corresponding change at the third premolar site was about 1 mm. Furthermore, at the 3P3 sites no vertical defects were present at the marginal bone–implant interface due to the pronounced resorption of the buccal plate, while at the fourth premolar sites the vertical infrabony component of the defect amounted to approximately 1–1.5 mm (Fig. 11a and b). This possible influence of a wider gap between the implant surface and the bone bed was also investigated by Araujo, when placing implants immediately following tooth extraction (Araujo et al. 2006b). They observed less bone height reduction when implants were placed into molar than into premolar sockets. It was concluded that the wider the combined defect–bone wall dimensions, the more coronal the contact between bone and implant surface. It is unclear, however, whether it is the thicker bone wall or the wider gap between the implant surface and the bone wall that is relevant in the prevention of the buccal crest resorption. The larger fraction of bundle bone that occupies the buccal bone of the socket wall, compared with the lingual side (Araujo et al. 2005) and the observed lack of bone resorption at the lingual aspect of the crest in the present experiment, suggests that the crest thickness may play an important role in this respect. Another important difference to consider when evaluating the healing at the third and fourth premolar in the present study is the presence of the first molar 1M1 distal to the fourth premolar site. The tooth and its attachment apparatus may have in part prevented the buccal plate resorption.

Because of the anatomical differences between the buccal and the lingual bone marginal crest, the healing abutments could not fit precisely to the shoulder of the implant in some sites (Table 2). A microgap at the implant–abutment

Table 3. Results of the histometric measurements (mean and SD)

I-Bc	Buccal (test+control)	Statistics	Lingual (test+control)	Statistics	DAE*	DCD nano-particles*	Third premolar site* (test+control)	Fourth premolar site* (test+control)
4 h	-0.07 (0.07)		-0.73 (0.24)		-0.03 (0.01)	-0.11 (0.25)	0.08 (0.19)	-0.22 (0.10)
1 week	0.73 (0.80)		-0.60 (0.16)		1.82 (2.96)	0.58 (1.25)	1.33 (1.90)	0.10 (0.28)
2 weeks	0.77 (0.35)		-0.71 (0.31)		0.65 (0.49)	0.82 (0.89)	1.11 (0.68)	0.28 (0.28)
4 weeks	0.70 (0.24)		-0.25 (0.46)		0.62 (0.20)	0.67 (0.57)	0.97 (0.32)	0.33 (0.11)
8 weeks	0.73 (0.28)		-0.63 (0.18)		0.94 (0.66)	0.24 (0.46)	1.13 (0.55)	0.30 (0.53)

$P < 0.05$
 $P < 0.01$
 $P < 0.001$

*Buccal measurements. See Fig. 4 for landmarks.

DAE, dual acid-etched surface; DCD, discrete crystalline deposition; SD, standard deviation; I, shoulder of the implant. Bc, marginal bone crest.

Table 4. Results of the histometric measurements (mean and SD)

I-B	Buccal (test+control)	Statistics	Lingual (test+control)	Statistics	DAE*	DCD nano-particles*	Third premolar site* (test+control)	Fourth premolar site* (test+control)
4 h	2.47 (0.70)		3.65 (1.50)		2.21 (1.63)	2.73 (1.49)	1.29 (0.69)	3.64 (1.09)
1 week	2.38 (1.29)		2.94 (1.57)		2.66 (2.88)	2.63 (1.33)	3.20 (2.77)	2.09 (1.29)
2 weeks	1.87 (0.80)		1.48 (2.19)		1.57 (0.90)	2.04 (1.27)	1.60 (1.04)	2.00 (1.15)
4 weeks	1.38 (0.47)		0.44 (0.78)		1.10 (0.29)	1.44 (0.63)	1.30 (0.68)	1.25 (0.28)
8 weeks	1.36 (0.28)		1.21 (0.29)		1.34 (0.43)	1.34 (0.57)	1.24 (0.52)	1.41 (0.46)

$P < 0.05$
 $P < 0.01$
 $P < 0.001$

*Buccal measurements. See Fig. 4 for landmarks.

I, shoulder of the implant; B, most coronal bone to implant contact; DAE, dual acid-etched surface; DCD, discrete crystalline deposition; SD, standard deviation.

Table 5. Results of the histometric measurements (mean and SD)

Bc-B	Buccal (test+control)	Statistics	Lingual (test+control)	Statistics	DAE*	DCD nano-particles*	Third premolar site* (test+control)	Fourth premolar site* (test+control)
4 h	2.54 (0.67)		4.39 (1.75)		2.24 (1.77)	2.84 (1.68)	1.21 (0.76)	3.87 (1.17)
1 week	1.65 (0.95)		3.55 (1.70)		0.83 (0.90)	2.05 (1.09)	0.89 (0.60)	1.99 (1.34)
2 weeks	1.09 (0.46)		2.20 (2.28)		0.91 (1.18)	1.21 (1.14)	0.49 (0.54)	1.72 (1.31)
4 weeks	0.67 (0.24)		0.70 (0.32)		0.47 (0.46)	0.76 (0.38)	0.32 (0.37)	0.92 (0.23)
8 weeks	0.63 (0.27)		1.84 (0.19)		0.39 (0.32)	1.10 (0.94)	0.10 (0.11)	1.10 (0.66)

$P < 0.05$
 $P < 0.01$
 $P < 0.001$

*Buccal measurements. See Fig. 4 for landmarks.

Bc, marginal bone crest; B, most coronal bone to implant contact; DAE, dual acid-etched surface; DCD, discrete crystalline deposition; SD, standard deviation.

interface has been considered a potential factor influencing bone resorption in two-piece implants (Ericsson et al. 1996). The influence of the size and

position of this microgap on crestal bone changes has been experimentally studied by Hermann et al (2001). These authors placed experimental implants

(1- or 2-piece implants) with three different type of microgaps (<10, 50 or 100 μm) in the edentulous mandible of five dogs and reported crestal bone

changes independent of the size of the microgap, with more crestal bone loss observed in the two-piece implants. In this investigation we could not see any relationship between the presence of this microgap and crestal bone loss around these implants. Nevertheless, the misfit of the healing abutments shown in this study in some of the specimens should be taken into consideration when evaluating the histological outcomes.

The influence of implant surface topography on the dimensional changes of the crest could not be evaluated due to the limited number of animals in each healing group. Mean values indicated that less resorption of the buccal plate occurred at the test than at the control implants after 8 weeks of healing.

In conclusion, results from the present investigation showed a moderate resorption of the buccal bone crest of about 0.6 (0.7) mm at 2 months after implant placement. Most of the resorption occurred at the third premolar site during the first week of healing. In sites with thick bone walls and with a gap between the implant surface and the bone wall, the risk of bone resorption was lower. These findings confirm results from clinical studies that showed that this surgical protocol of placing implants into fresh extraction sockets does not provide a predictable outcome (Evans & Chen 2008). More experimental and clinical studies are needed to further understand the risk factors involved in the outcomes after implant placement in fresh extraction sockets.

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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.

Anneroth, G., Hedstrom, K. G., Kjellman, O., Kondell, P. A. & Nordenram, A. (1985) Endosseous titanium implants in extraction sockets. An experimental study in monkeys.

International Journal of Oral Surgery **14**, 50–54.

Araujo, M. G., Sukekava, F., Wennstrom, J. L. & Lindhe, J. (2005) Ridge alterations following implant placement in fresh extraction sockets: an experimental study in the dog. *Journal of Clinical Periodontology* **32**, 645–652.

Araujo, M. G., Sukekava, F., Wennstrom, J. L. & Lindhe, J. (2006a) Tissue modeling following implant placement in fresh extraction sockets. *Clinical Oral Implants Research* **17**, 615–624.

Araujo, M. G., Wennstrom, J. L. & Lindhe, J. (2006b) Modeling of the buccal and lingual bone walls of fresh extraction sites following implant installation. *Clinical Oral Implants Research* **17**, 606–614.

Barzilay, I., Graser, G. N., Iranpour, B. & Natiella, J. R. (1991) Immediate implantation of a pure titanium implant into an extraction socket: report of a pilot procedure. *International Journal of Oral and Maxillofacial Implants* **6**, 277–284.

Barzilay, I., Graser, G. N., Iranpour, B., Natiella, J. R. & Proskin, H. M. (1996a) Immediate implantation of pure titanium implants into extraction sockets of *Macaca fascicularis*. Part II: histologic observations. *International Journal of Oral and Maxillofacial Implants* **11**, 489–497.

Barzilay, I., Graser, G. N., Iranpour, B. & Proskin, H. M. (1996b) Immediate implantation of pure titanium implants into extraction sockets of *Macaca fascicularis*. Part I: clinical and radiographic assessment. *International Journal of Oral and Maxillofacial Implants* **11**, 299–310.

Blanco, J., Nunez, V., Aracil, L., Munoz, F. & Ramos, I. (2008) Ridge alterations following immediate implant placement in the dog: flap versus flapless surgery. *Journal of Clinical Periodontology* **35**, 640–648.

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

Botticelli, D., Berglundh, T., Persson, L. G. & Lindhe, J. (2005) Bone regeneration at implants with turned or rough surfaces in self-contained defects. An experimental study in the dog. *Journal of Clinical Periodontology* **32**, 448–455.

Botticelli, D., Persson, L. G., Lindhe, J. & Berglundh, T. (2006) Bone tissue formation adjacent to implants placed in fresh extraction sockets: an experimental study in dogs. *Clinical Oral Implants Research* **17**, 351–358.

Caudill, R. F. & Meffert, R. M. (1991) Histologic analysis of the osseointegration of endosseous implants in simulated extraction sockets with and without e-PTFE barriers. 1. Preliminary findings. *International Journal of Periodontics and Restorative Dentistry* **11**, 207–215.

Cornelini, R., Cangini, F., Covani, U. & Wilson, T. G. Jr. (2005) Immediate restoration of implants placed into fresh extraction sockets for single-tooth replacement: a prospective clinical study. *International Journal of Periodontics and Restorative Dentistry* **25**, 439–447.

Donath, K. & Breuner, G. (1982) A method for the study of undecalcified bones and teeth with attached soft tissues. The Sage–Schliff (sawing and grinding) technique. *Journal of Oral Pathology* **11**, 318–326.

Ericsson, I., Nilner, K., Klinge, B. & Glantz, P. (1996) Radiographical and histological characteristics of submerged and nonsubmerged titanium implants. An experimental study in the Labrador dog. *Clinical Oral Implants Research* **7**, 20–26.

Evans, C. D. & Chen, S. T. (2008) Esthetic outcomes of immediate implant placements. *Clinical Oral Implants Research* **19**, 73–80.

Ganeles, J. & Wismeijer, D. (2004) Early and immediately restored and loaded dental implants for single-tooth and partial-arch applications. *International Journal of Oral and Maxillofacial Implants* **19** (Suppl.), 92–102.

Goene, R. J., Testori, T. & Trisi, P. (2007) Influence of a nanometer-scale surface enhancement on de novo bone formation on titanium implants: a histomorphometric study in human maxillae. *International Journal of Periodontics and Restorative Dentistry* **27**, 211–219.

Gottfredsen, K., Warrer, K., Hjorting, H. & Karring, T. (1991) Effect of membranes and porous hydroxyapatite on healing in bone defects around titanium dental implants. An experimental study in monkeys. *Clinical Oral Implants Research* **2**, 172–178.

Hermann, J., Buser, D., Schenk, R. & Cochran, D. (2000) Crestal bone changes around titanium implants. A histometric evaluation of unloaded non-submerged and submerged implants in the canine mandible. *Journal of Periodontology* **71**, 1412–1424.

Karabuda, C., Sandalli, P., Yalcin, S., Steffik, D. E. & Parr, G. R. (1999) Histologic and histomorphometric comparison of immediately placed hydroxyapatite-coated and titanium plasma-sprayed implants: a pilot study in dogs. *International Journal of Oral and Maxillofacial Implants* **14**, 510–515.

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**, 364–375.

Lang, N. P., Tonetti, M. S., Suvan, J. E., Pierre Bernard, J., Botticelli, D., Fourmousis, I., Hallund, M., Jung, R., Laurell, L., Salvi, G. E., Shafer, D. & Weber, H. P. (2007) Immediate implant placement with transmucosal healing in areas of aesthetic priority. A multicentre randomized-controlled clinical trial I. Surgical outcomes. *Clinical Oral Implants Research* **18**, 188–196.

Meirelles, L., Albrektsson, T., Kjellin, P., Arvidsson, A., Franke-Stenport, V., Andersson, M., Currie, F. & Wennerberg, A. (2008a) Bone reaction to nano hydroxyapatite modified titanium implants placed in a gap-heal-

- ing model. *Journal of Biomedical Material Research Part A* **87**, 624–631.
- Meirelles, L., Arvidsson, A., Albrektsson, T. & Wennerberg, A. (2007) Increased bone formation to unstable nano rough titanium implants. *Clinical Oral Implants Research* **18**, 326–332.
- Meirelles, L., Arvidsson, A., Andersson, M., Kjellin, P., Albrektsson, T. & Wennerberg, A. (2008b) Nano hydroxyapatite structures influence early bone formation. *Journal of Biomedical Material Research Part A* **87**, 299–307.
- Mendes, V. C., Moineddin, R. & Davies, J. E. (2008) Discrete calcium phosphate nanocrystalline deposition enhances osteoconduction on titanium-based implant surfaces. *Journal of Biomedical Material Research Part A*. June 18 (Epub ahead of print).
- Orsini, G., Piattelli, M., Scarano, A., Petrone, G., Kenealy, J., Piattelli, A. & Caputi, S. (2007) Randomized, controlled histologic and histomorphometric evaluation of implants with nanometer-scale calcium phosphate added to the dual acid-etched surface in the human posterior maxilla. *Journal of Periodontology* **78**, 209–218.
- Paolantonio, M., Dolci, M., Scarano, A., d'Archivio, D., di Placido, G., Tumini, V. & Piattelli, A. (2001) Immediate implantation in fresh extraction sockets. A controlled clinical and histological study in man. *Journal of Periodontology* **72**, 1560–1571.
- Schropp, L., Kostopoulos, L. & Wenzel, A. (2003) Bone healing following immediate versus delayed placement of titanium implants into extraction sockets: a prospective clinical study. *International Journal of Oral and Maxillofacial Implants* **18**, 189–199.
- Schwartz-Arad, D., Laviv, A. & Levin, L. (2007) Survival of immediately provisionalized dental implants placed immediately into fresh extraction sockets. *Journal of Periodontology* **78**, 219–223.
- Vignoletti, F., Johansson, C., Albrektsson, T., de Sanctis, M., San Roman, F. & Sanz, M. (2009) Early healing of implants placed into fresh extraction sockets: an experimental study in the beagle dog. De novo bone formation. *Journal of Clinical Periodontology* **36**, 265–277.
- Wilson, T. G. Jr., Schenk, R., Buser, D. & Cochran, D. (1998) Implants placed in immediate extraction sites: a report of histologic and histometric analyses of human biopsies. *International Journal of Oral and Maxillofacial Implants* **13**, 333–341.

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Clinical Relevance

Scientific rationale for the study: Immediate implant installation into fresh extraction sockets is a surgical protocol aimed at preserving the tissue alterations that usually take place at the alveolar ridge after tooth extraction. Evidence from experimental studies, however, has failed to show that immediate implants influence the physiological process of bone modelling and remodelling after tooth loss. Yet, there is limited information on (i) the early phases of healing of the alveolar ridge, (ii) the influence of the socket dimensions

on bone modelling and remodelling and (iii) whether implants with an improved surface nano-topography may influence this process. Thus, the aim of this investigation is to describe in detail the early healing phases of implants placed immediately upon tooth extraction.

Principal findings: The healing of the alveolar ridge after implant placement occurred with a concomitant vertical bone resorption. This bone loss was variable and occurred mainly at the buccal crest between the 4-h and the 1-week time intervals. The dimensions of the socket

influenced this process, with a more pronounced bone loss at the narrower third premolar site. The improved surface nano-topography seemed to have a limited effect on the healing process.

Practical implications: When implants adapt more intimately to thin socket walls, a marked buccal vertical bone loss should be expected. Ridge alterations that occurred after immediate implant placement were very variable in this animal model. This heterogeneity in the outcomes should alert the clinician when using this surgical protocol.

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