J Clin Periodontol 2010; 37: 466–473 doi: 10.1111/j.1600-051X.2010.01533.x

Journal of Clinical Periodontology

Influence of titanium implant surface characteristics on bone regeneration in dehiscence-type defects: an experimental study in dogs

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Schwarz F, Sager M, Kadelka I, Ferrari D, Becker J. Influence of titanium implant surface characteristics on bone regeneration in dehiscence-type defects: an experimental study in dogs. J Clin Periodontol 2010; 37: 466–473. doi: 10.1111/j.1600-051X.2010.01533.x.

Abstract

Objectives: The aim of the present study was to compare bone regeneration in dehiscence-type defects at titanium implants with chemically modified sandblasted/acid-etched (modSLA) or dual acid-etched surfaces with a calcium phosphate nanometre particle modification (DCD/CaP).

Materials and Methods: Buccal dehiscence-type defects were surgically created following implant site preparation in both the upper and the lower jaws of 12 fox hounds. Both types of implants were randomly allocated in a split-mouth design and left to heal in a submerged position for 2 and 8 weeks. Dissected blocks were processed for histomorphometrical analysis [e.g. new bone height (NBH), percentage of bone-to-implant contact (BIC), area of new bone fill (BF), and area of mineralized tissue (MT) within BF].

Results: At 2 and 8 weeks, both groups revealed comparable mean BF (2.3 ± 0.6 to $2.5 \pm 0.6\,mm^2$ *versus* 2.0 ± 0.6 to $1.4 \pm 0.5\,mm^2$) and MT (31.1 ± 14.3–$83.2 \pm 8.2\%$ *versus* 38.9 ± 15.9–$84.4 \pm 6.3\%$) values. However, modSLA implants revealed significantly higher mean NBH (2.4 ± 0.8 to 3.6 ± 0.3 mm *versus* 0.9 ± 0.8 to 1.8 ± 1.4 mm) and BIC (53.3 ± 11.3–$79.5 \pm 6.6\%$ *versus* 19.3 ± 16.4–$47.2 \pm 30.7\%$) values than DCD/CaP implants.

Conclusion: ModSLA implants may have a higher potential to support osseointegration in dehiscence-type defects than DCD/CaP implants.

Key words: bone regeneration; dehiscence-type defect; hydrophilicity; implant surfaces; nanotopography

Accepted for publication 29 November 2009

Predictable bone formation at deficient sites still remains a key issue in implant dentistry. An incomplete bone regeneration in the defect area may compromise the long- or even the short-term success of the implant (Donos et al. 2008, Tonetti & Hämmerle 2008). Recent research activities have indicated that currently available surface modifications of titanium implants may have the potential to support bone formation at deficient sites such as circumferential defects (de Sanctis et al. 2009, Lai et al. 2009, Vignoletti et al. 2009), dehiscence-type defects (Schwarz et al. 2007, 2008a), and even more critical situations such as supraalveolar ridge defects (Wikesjö et al. 2008). The commercially available modifications refer to surface hydrophilicity (Schwarz et al. 2009) and biomimetic coatings such as fluoride phosphate substitution (Berglundh et al. 2007) or discrete crystalline deposition (DCD) of nanometre-scale calcium phosphate (CaP) crystals (Mendes et al. 2007). Another yet experimental approach is the coating of titanium implants using recombinant human bone morphogenetic protein 2 (Becker et al. 2006, Wikesjö

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

The study was in part funded by a grant from Institute Straumann AG, Basel, Switzerland. The study materials were kindly provided by Institut Straumann AG.

et al. 2008). Surface hydrophilicity of chemically modified sand-blasted, large grit, and acid-etched (modSLA) titanium implants is characterized by initial water contact angles of approximately 0° when compared with 139.9° for conventional hydrophobic SLA surfaces (Rupp et al. 2006). The continuous storage in an isotonic NaCl solution at a pH between 4 and 6 was able to retain the high surface energy by reducing the adsorption of potential contaminants from the atmosphere (e.g. hydrocarbons and carbonates) (Zhao et al. 2005). Preliminary experimental studies have indicated that the specific surface properties noted for modSLA titanium implants supported bone formation in dehiscence-type defects without the additional use of a bone graft substitute or a barrier membrane (Schwarz et al. 2007, 2008a). In particular, these surfaces were able to stabilize the blood clot in the defect area (Schwarz et al. 2008a), which was supposed to physiologically induce and amplify the migration, proliferation, and differentiation of endothelial cells (Liu et al. 1990). As angiogenesis precedes new bone formation (Schwarz et al. 2008b), blood clot stabilization was considered as the key feature of this surface technology, thus explaining at least in part the improved bone response to modSLA implants (Schwarz et al. 2009). Fluoride-modified implants possess nanostructured features (50–100 nm) created by TiO_2 blasting, followed by a proprietary hydrofluoric acid treatment (Abron et al. 2001, Cooper et al. 2006), and promoted bone formation and osseointegration in wide marginal defects (Abrahamsson et al. 2008). Similarly, DCD of nanometre-scale CaP particles on a dual acid-etched (DAE) implant surface showed a tendency towards an increase of the new mineralized tissue (MT) fraction during the early stages of wound healing in fresh extraction sockets of dogs. Interestingly, the effects of calcium phosphate nanoparticle-modified dual acid-etched (DCD/CaP) implants were more pronounced at wider socket configurations (Vignoletti et al. 2009). Based on these findings, one might hypothesize that the osteopromotive effects of hydrophilic and nanoscale over conventional titanium implants are particularly pronounced at advanced defect sites. However, since it was recently reported that modSLA implants also feature a specific nanoroughness (Wennerberg & Albrektsson 2010) and the nanotopography of DCD/CaP implants was correlated with hydrophobic characteristics (Gubbi et al. 2007), it remains unclear which surface quality may increase bone response in these specific situations. The observation that conventional SLA titanium surfaces failed to predictably support bone formation and subsequently osseointegration in dehiscence-type defects (Schwarz et al. 2007, 2008a) when compared with marginal defects (Botticelli et al. 2005, Lai et al. 2009) might render this model more suitable for the clarification of this issue. Currently, there are no experimental studies available reporting on bone formation at DCD/CaP titanium implants in a dehiscence-type defect model.

Therefore, the aim of the present study was to histomorphometrically evaluate and compare bone regeneration in standardized dehiscence-type defects at either modSLA or DCD/CaP titanium implants following submerged healing in dogs.

Material and Methods

Animals

A total of 12 fox hounds (mean age 23.3 ± 2.1 months, mean weight 38.4 ± 2.9 kg) were used in the study. All animals exhibited a fully erupted permanent dentition. During the experiment, the dogs were fed once per day with a soft-food diet and water. Animal selection, management, and surgery protocol were approved by the Animal Care and Use Committee of the Heinrich Heine University and the local government of Düsseldorf. The experimental segment of the study started after an adaption period of 4 weeks.

Study design

The experimental part of the study was performed in two surgical phases. In the first phase, extraction of the mandibular and maxillary second, third, fourth premolar as well as the ‘first and second molar (P2-M2) was performed bilaterally in all dogs. After 3 months of healing, standardized buccal dehiscence-type defects were surgically created following implant site preparation in both the upper ($n = 4$ defects per animal) and the lower jaws ($n = 4$ defects per animal). According to a split-mouth design, a total of two modSLA and two DCD/CaP implants each were randomly placed in both the upper and the lower jaws (total $n = 8$ implants per animal).

Randomization was based on a computer-generated list (RandList®, DatInf GmbH, Tübingen, Germany). The animals were sacrificed after 2 and 8 weeks of healing, including 6 animals each.

Surgical procedure

Before each surgical intervention, intramuscular sedation was accomplished with 0.17 mg/kg acepromazine (Vetranquil 1%, Ceva Tiergesundheit, Düsseldorf, Germany). Subsequently, anaesthesia was initiated using 21.5 mg/kg thiopental-sodium (Trapanal 2.5%, Altana GmbH, Konstanz, Germany). During all surgical procedures, inhalation anaesthesia was performed using oxygen and nitrous oxide and isoflurane. To maintain hydration, all animals received a constant-rate infusion of lactated Ringer’s solution while anaesthetized. Intraoperative analgesia was performed by an intravenous injection of 0.4 mg/kg piritramid (Dipidolor®, Janssen-Cilag GmbH, Neuss, Germany) and 4.5 mg/kg carprofene (Rimadyl®, Pfitzer Pharma GmbH, Karlsruhe, Germany). For post-operative treatment, piritramid and carprofene were applied subcutaneously for three days at the same dose as described before.

In the first surgery, mucoperiosteal flaps were reflected bilaterally in both the jaws and P2–M2 were carefully removed after tooth separation. Wound closure was accomplished by means of mattress sutures and the sites were allowed to heal for 3 months. Prophylactic administration of clindamycine (11.0 mg/kg body weight, Cleorobe®, Pharmacia Tiergesundheit, Erlangen, Germany) was performed intra- and post-operatively for 10 days.

In the second surgery, midcrestal incisions were made and full-thickness mucoperiosteal flaps were reflected to expose the respective experimental sites in both the upper and the lower jaws. Surgical implant sites were prepared bilaterally, at a distance of 10 mm apart, using a low-trauma surgical technique under copious irrigation with a sterile 0.9% physiological saline (surgery protocol by Institut Straumann AG, Basel, Switzerland and Biomet 3i, Karlsruhe, Germany).

Following implant site preparation, standardized dehiscence-type defects, approximately 4 mm in height from the crestal bone, 2 mm in depth from the surface of the buccal bone, and 3 mm in width mesiodistally, were created with a straight fissure carbide bur as reported previously by Schwarz et al. (2007, 2008a). The osteotomy procedures were performed under copious irrigation with a sterile 0.9% physiological saline. The defect sizes were standardized using a periodontal probe (PCP12, Hu-Friedy Co., Chicago, IL, USA). Thereafter, screw-type modSLA (Bone Level® SLActive®, ∅ 4.1 mm, length 10 mm, Institut Straumann AG, Basel, Switzerland) and DCD/CaP (Nanotite® Certain Prevail®, ∅ 4/3 mm, length 10 mm, Biomet 3i) titanium implants were inserted with good primary stability (i.e. the lack of clinical implant mobility) in a way so that the implant shoulder (IS) coincided with the bone crest at both mesial and distal aspects. Subsequent to implant placement, the defect areas were gently rinsed with sterile saline to remove any residual bone particles (Fig. 1). Following periosteal-releasing incisions, the mucoperiosteal flaps were advanced, repositioned coronally, and fixed with vertical or horizontal mattress sutures (Resorba®, Nürnberg, Germany) in a way to ensure a submerged healing condition. All surgical procedures were performed by the same experienced operator (F. S.).

Animal sacrifice and retrieval of specimens

After a healing period of 2 and 8 weeks, six animals each were killed by an overdose of sodium pentobarbital 3%, respectively. The oral tissues were fixed by perfusion with 10% buffered formalin administered through the carotid arteries. The jaws were dissected and blocks containing the experimental specimens were obtained. All specimens were fixed in a 10% neutral-buffered formalin solution for 4–7 days.

Histological preparation

The specimens were dehydrated using ascending grades of alcohol and xylene, infiltrated, and embedded in methylmethacrylate (MMA, Technovit 9100 NEU, Heraeus Kulzer, Wehrheim, Germany) for non-decalcified sectioning. During this procedure, any negative influence of polymerization heat was avoided due to a controlled polymerization in a cold atmosphere (−4°C). After 20 h, the specimens were completely polymerized. Each implant site was cut in the bucco-oral direction along with the long axis of the implant using a diamond band saw (Exakt®, Apparatebau, Norderstedt, Germany). Serial sections were prepared from the respective defect areas, resulting in two to four sections of approximately 300 μm in thickness each (Donath 1985). Only implant sections showing an inner thread were chosen for the evaluation of the central defect areas. Subsequently, all specimens were glued with acrylic cement (Technovit 7210 VLC, Heraeus Kulzer) to silanized glass slides (Super Frost, Menzel GmbH, Braunschweig, Germany) and ground to a final thickness of approximately 40 μm. All sections were stained with toluidine blue (TB) to evaluate new bone formation. With this technique, old bone stains light blue, whereas newly formed bone stains dark blue because of its higher protein content (Schenk et al. 1984).

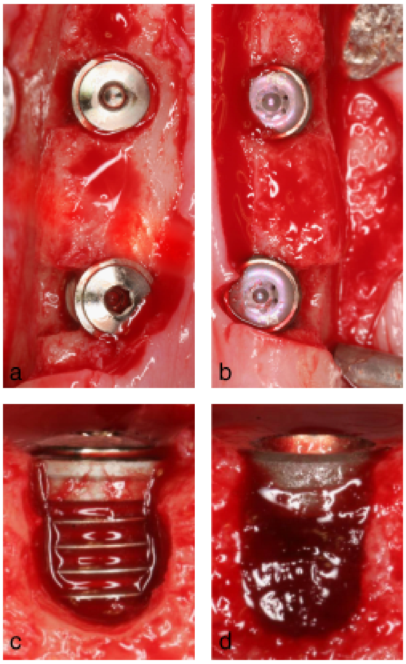

Fig. 1. (a and b) Two standardized dehiscence-type defects (height: 4 mm, width: 3 mm, depth: 2 mm) were surgically created in each quadrant of both the upper and the lower jaws ($n = 8$ defects per animal). Screw-type DCD/CaP (a) and modSLA (b) titanium implants exhibiting a comparable length and diameter were randomly allocated in a split-mouth design and inserted in a way so that implant shoulder coincided with the bone crest at both mesial and distal aspects. To remove any residual bone graft particles, all defect sites were gently rinsed with sterile physiological saline. (c and d) Situation at 5 min. after a gentle irrigation with sterile saline, indicating obvious differences in blood clot stabilization at DCD/CaP (a) and modSLA (b) surfaces. DCD/CaP, calcium phosphate nanoparticle-modified dual acid-etched; modSLA, modified sandblasted, large grit, and acid-etched.

Histomorphometrical analysis

Histomorphometrical analyses as well as microscopic observations were performed by one experienced investigator masked to the specific experimental conditions. For image acquisition, a colour CCD camera (Color View III, Olympus, Hamburg, Germany) was mounted on a binocular light microscope (Olympus BX50, Olympus). Digital images (original magnification ×200) were evaluated using a software program (Cell D®, Soft Imaging System, Münster, Germany).

The following landmarks were identified in the stained sections: IS, the bottom of the bone defect (BD), the most coronal level of bone in contact with the implant at the buccal aspect (CBI). Defect length (DL) was measured from IS to BD (mm), new bone height (NBH) was measured from BD to CBI (mm), per cent linear fill (PLF) was defined as NBH divided by DL, and the amount of new bone-to-implant contact (BIC) in the defect area was measured as a percentage of the distance from BD to IS (Figs 2 and 3). Additionally, the area (mm^2) of new bone fill (BF) was measured from BD to CBI. Within BF, the surface area of MT was automatically assessed (%) by the image analysis software (Fig. 2h). Before the start of the morphometrical analysis, a calibration procedure was initiated for the image analysis software and revealed that repeated measurements of $n = 12$ different sections were similar at $>95\%$ level.

Statistical analysis

The statistical analysis was performed using a commercially available software program (SPSS 17.0, SPSS Inc., Chicago, IL, USA). Mean values and standard deviations among animals were calculated for each variable and group. The data rows were examined using the Kolmogorow–Smirnow test for normal distribution. For the statistical evaluation of the changes within groups over time, the paired *t*-test was used. For the comparisons between groups at each observation period, the unpaired *t*-test was used. The α error was set at 0.05.

Results

The post-operative healing was considered as generally uneventful in all dogs. No complications such as allergic reac-

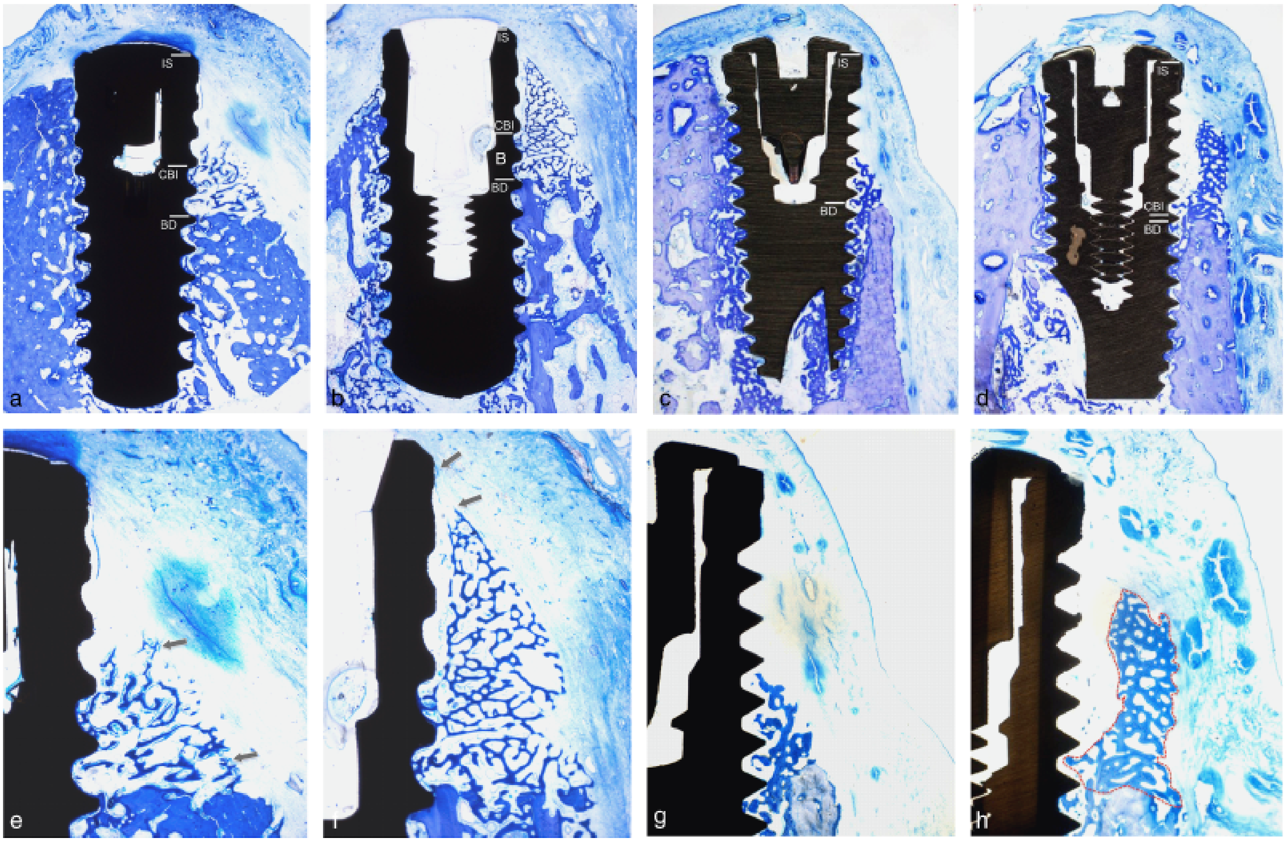

Fig. 2. Representative histological views (Toluidine blue stain) of wound healing at 2 weeks. Both groups showed a woven bone formation of varying extension and mineral density in the former defect area. While modSLA implants commonly established a close contact with the newly formed trabecular bone, DCD/CaP implants frequently revealed the interposition of a non-mineralized tissue. (a) modSLA (lower jaw, original magnification $\times$ 12.5). (b) modSLA (upper jaw, original magnification $\times$ 12.5). (c) DCD/CaP (lower jaw, original magnification $\times$ 12.5). (d) DCD/CaP (lower jaw, original magnification $\times$ 12.5). (e) Higher magnification ($\times$ 40) of the defect area shown in (a). The primary network of woven bone was demarcated by osteoid seams (arrows). (f) Higher magnification ($\times$ 40) of the defect area shown in (b). In the advancing front of mineralization, tiny spots of trabecular bone had started to establish a close contact with the most coronal aspect of the titanium implant surface (arrows). (g and h) Higher magnification ($\times$ 40) of the defect areas shown in (c and d). The interposition of a non-mineralized tissue frequently interfered with the establishment of a close contact of newly formed trabecular bone with the titanium implant surface (h): the red dotted area corresponds to bone fill). DCD/CaP, calcium phosphate nanoparticle-modified dual acid-etched; modSLA, modified sand-blasted, large grit, and acid-etched.

tions, swellings, abscesses, or infections were observed throughout the entire study period. None of the defect sites revealed a premature exposure of the respective titanium implants.

Histological observations/ Histomorphometrical analysis

The mean values of DL, NBH, PLF, BF, MT, and BIC in both modSLA and DCD/CaP groups after 2 and 8 weeks of healing in either the upper or the lower jaws are presented in Tables 1 and 2. Within- and between-group comparisons revealed comparable mean DL values at each observation period ($p > 0.05$; paired- and unpaired t-test, respectively).

At 2 weeks, wound healing in both groups was basically characterized by a woven bone formation in the former defect area. In particular, tiny trabeculae of varying mineral densities that mainly originated from the basal walls of the adjacent alveolar bone had homogeneously started to invade within the defect area in both coronal and central directions (Fig. 2a–d). These areas were demarcated by osteoid seams and osteoblasts indicating an early stage of healing (Fig. 2e). The resulting mean BF values at 2 weeks were comparable in both groups and varied between 2.3 ± 0.6 and $2.4 \pm 0.6\,mm^2$ at modSLA and 2.0 ± 0.6 and $2.1 \pm 0.6\,mm^2$ at DCD/CaP implants ($p > 0.05$; unpaired t-test, respectively) (Tables 1 and 2). However, a distinct difference between groups was observed with respect to the bridging of the implant surface and the defect margin by the newly formed trabecular bone. While BF areas were most commonly separated from DCD/CaP implants by a non-MT, woven bone revealed a close contact to modSLA implants, thus resulting in significantly increased mean NBH, PLF, and BIC values ($p < 0.05$, $p < 0.05$, $p < 0.01$; unpaired t-test, respectively) in both the upper and the lower jaws. Histomorphometrical analysis exhibited varying MT values within both groups (Fig. 2e–h). Even though the mean MT values tended to be higher in the DCD/CaP group, these differences did not reach statistical significance (Tables 1 and 2).

At 8 weeks, wound healing in both groups was mainly characterized by an ongoing bone formation and maturation

Fig. 3. Representative histological views (Toluidine blue stain) of wound healing at 8 weeks. In both the groups, the ongoing bone formation and signs of remodelling were associated with a slight to moderate contour-deforming resorption at the buccal aspect. (a) modSLA (lower jaw, original magnification $\times$ 12.5). (b) modSLA (lower jaw, original magnification $\times$ 12.5). (c) DCD/CaP (lower jaw, original magnification $\times$ 12.5). (d) DCD/CaP (lower jaw, original magnification $\times$ 12.5). (e) Occasionally, the coronal extension of newly formed bone in the defect area even exceeded the lingual aspect of the alveolar ridge undergoing slight crestal bone-level changes (modSLA, lower jaw, original magnification $\times$ 12.5). (f) Higher magnification ($\times$ 40) of the defect area shown in (e). Parallel-fibred bone exhibiting primary and secondary osteons in close contact with the implant surface. Figures 2 and 3. BD, bottom of the bone defect; CBI, the most coronal level of bone in contact with the implant; IS, implant shoulder. DCD/CaP, calcium phosphate nanoparticle-modified dual acid-etched; modSLA, modified sand-blasted, large grit, and acid-etched.

Table 1. Mean values ($\pm$ SD) of DL, NBH, PLF (mm), BF (mm^2), MT, and BIC (%) in the upper jaws after 2 and 8 weeks of submerged healing ($n = 6$ dogs per healing period)

Groups	Weeks	DL	NBH	PLF	BF	MT	BIC	
modSLA	2	4.1 $\pm$ 0.2	2.6 $\pm$ 0.8†	63.3 $\pm$ 19.6†	2.4 $\pm$ 0.6	31.1 $\pm$ 14.3	55.8 $\pm$ 9.7‡	
	8	4.2 $\pm$ 0.1	3.6 $\pm$ 0.3†	86.8 $\pm$ 7.2†	2.3 $\pm$ 0.5†	81.3 $\pm$ 9.4	78.2 $\pm$ 14.5	
		NS	$p<0.05$	NS	NS	$p<0.001$	$p<0.05$	p value*
DCD/CaP	2	4.2 $\pm$ 0.2	0.9 $\pm$ 0.8	21.4 $\pm$ 19.0	2.0 $\pm$ 0.6	38.9 $\pm$ 15.9	20.3 $\pm$ 16.7	
	8	4.2 $\pm$ 0.1	1.8 $\pm$ 1.4	43.0 $\pm$ 34.9	1.6 $\pm$ 0.4	82.7 $\pm$ 8.8	47.2 $\pm$ 30.7	
		NS	NS	NS	$p<0.05$	$p<0.01$	NS	p value*

*Comparisons within groups (paired *t*-test).
Comparisons between groups (unpaired *t*-test): $^{\dagger}P<0.05$, $^{\ddagger}P<0.01$.
DL, defect length; NBH, new bone height; PLF, per cent linear fill; BIC, bone-to-implant contact; MT, mineralized tissue; BF, bone fill; modSLA, modified sand-blasted, large grit, and acid-etched; DCD/CaP, calcium phosphate nanoparticle-modified dual acid-etched; NS, non significant.

of the primary network of spongiosa. In particular, histological observation revealed a continuous filling of the intertrabecular spaces in both the modSLA and the DCD/CaP groups, subsequently resulting in the formation of a mature, parallel-fibred bone (Fig. 3a–d). This was clearly correlated with significantly increased mean MT values in both

Table 2. Mean values (± SD) of DL, NBH, PLF (mm), BF (mm^2), MT, and BIC (%) in the lower jaws after 2 and 8 weeks of submerged healing ($n = 6$ dogs per healing period)

Groups	Weeks	DL	NBH	PLF	BF	MT	BIC	
modSLA	2	4.2 ± 0.1	2.4 ± 0.8†	57.8 ± 19.9†	2.3 ± 0.6	32.3 ± 7.3	53.5 ± 11.3‡	
	8	4.2 ± 0.2	3.4 ± 0.3†	82.5 ± 9.2†	2.5 ± 0.6	83.2 ± 8.2	79.5 ± 6.6†	
		NS	$p<0.05$	$p<0.05$	NS	$p<0.001$	$p<0.001$	p value*
DCD/CaP	2	4.1 ± 0.2	0.8 ± 0.7	17.9 ± 17.6	2.1 ± 0.6	42.1 ± 11.0	19.3 ± 16.4	
	8	4.1 ± 0.1	1.7 ± 1.4	42.1 ± 34.4	1.4 ± 0.5	84.4 ± 6.3	43.3 ± 22.1	
		NS	NS	NS	$p<0.05$	$p<0.001$	NS	p value*

*Comparisons within groups (paired *t*-test).
Comparisons between groups (unpaired *t*-test): †$P<0.05$, ‡$P<0.01$.
DL, defect length; NBH, new bone height; PLF, per cent linear fill; BIC, bone-to-implant contact; MT, mineralized tissue; BF, bone fill; modSLA, modified sand-blasted, large grit, and acid-etched; DCD/CaP, calcium phosphate nanoparticle-modified dual acid-etched; NS, non significant.

groups (upper and lower jaw; $p<0.01$, $p<0.001$; paired *t*-test, respectively). Early signs of remodelling, replacing the primary bone by secondary osteons, were apparent. In both groups, this was associated with a slight to moderate superficial contour resorption at the buccal and lingual aspects (Fig. 3e and f). These changes appeared to be more pronounced in the DCD/CaP groups, thus resulting in a significant decrease in the mean BF values (upper and lower jaw; $p<0.05$; paired *t*-test, respectively). A significant difference in the mean BF values between groups was observed in the upper jaw after 8 weeks of healing ($p<0.05$; unpaired *t*-test) (Tables 1 and 2).

A significant increase in the mean NBH, PLF, and BIC values in either the upper ($p<0.05$, $p>0.05$, $p<0.05$; paired *t*-test, respectively) or the lower jaw ($p<0.05$, $p<0.05$, $p<0.001$; paired *t*-test, respectively) was only observed at modSLA implants. Even though the mean NBH, PLF, and BIC values also tended to increase in the DCD/CaP group at 8 weeks, these differences did not reach statistical significance ($p>0.05$, paired *t*-test, respectively). Accordingly, between-group comparisons revealed significant differences in the mean NBH, PLF (upper and lower jaw; $p<0.05$; unpaired *t*-test, respectively), and BIC (lower jaw; $p<0.05$; unpaired *t*-test) values (Tables 1 and 2).

Discussion

The present study was designed to investigate and compare the potential of modSLA and DCD/CaP titanium implants to support bone formation at dehiscence-type defects in a dog model. Basically, it was observed that both groups exhibited comparable mean BF (i.e. lower jaws) and MT values after 2 and 8 weeks of healing. However, between-group comparisons revealed significantly higher mean NBH, PLF, and BIC values at modSLA implants in both the upper and the lower jaws. In this context, it is important to mention that both types of titanium implants revealed potential differences with respect to the macrodesign (e.g. design and dimensions of threads), and therefore, the influence of these individual design features on the outcome of healing cannot be estimated.

The observation that modSLA titanium implants might have the potential to support bone regeneration in acute dehiscence-type defects without the additional use of any bone augmentation procedure corroborates previous data using the same model (Schwarz et al. 2007, 2008a). In particular, at 2 and 12 weeks of submerged healing, modSLA implants revealed significantly increased mean NBH (1.1 ± 0.2 and 3.3 ± 0.2 mm), PLF (34% and 97%), BF (0.4 ± 0.1 and 2.4 ± 0.3 mm^2), and BIC (27% and 80%) values at the central aspect of the defect area (height: 3 mm; width: 3 mm; depth: 3 mm) (Schwarz et al. 2007). An improved outcome of bone formation was even observed at advanced defect sites considering a shorter healing period of 8 weeks (height: 4 mm; width: 3 mm; depth: 3 mm). In particular, after 2 and 8 weeks of submerged healing, modSLA implants in both the upper and the lower jaws revealed comparable and significant increases in the mean NBH (2 weeks: 3.3 ± 0.5/1.8 ± 0.6 and 8 weeks: 3.7 ± 0.1/3.7 ± 0.1 mm), PLF (2 weeks: 79.4 ± 13.0/41.5 ± 14.4 and 8 weeks: 91.2 ± 1.9/92.4 ± 2.4%), BF (2 weeks: 10.5 ± 0.5/5.2 ± 2.9 and 8 weeks: 6.6 ± 0.9/6.4 ± 0.7 mm^2), and BIC (2 weeks: 67.6 ± 12.0/39.7 ± 12.0 and 8 weeks: 81.4 ± 12.6/82.1 ± 14.8%) values at the central aspect (Schwarz et al. 2008a). The slight discrepancies noted between these data and the present histomorphometrical analysis might primarily be attributed to the use of two implant designs (i.e. Soft Tissue Level® *versus* Bone Level® implants). A potential difference was particularly observed with respect to the mean BF values obtained after 8 weeks of healing. While the mean values varied between 6.4 ± 0.7 and 6.6 ± 0.9 mm^2 at Soft Tissue Level® implants (Schwarz et al. 2008a), the present values obtained with Bone Level® implants appeared to be markedly reduced (2.3 ± 0.5 to 2.5 ± 0.6 mm^2). One might speculate that the individual design of the transmucosal part of this type of one-piece implant was able to maintain space in the defect area for bone regeneration by preventing a collapse of the mucoperiosteal flap. This might be supported by the observation that a non-submerged healing procedure was associated with a marked reduction of the mean BF values after 8 weeks of healing (2.9 ± 1.0 to 4.3 ± 1.5 mm^2) (Schwarz et al. 2008a). Importantly, however, the specific surface characteristics of modSLA implants equally supported the mean NBH values at both types of implant designs. When interpreting the present results, one must realize that these are the first data reporting on bone regeneration at DCD/CaP titanium implants in this type of defect model. Even though the mean NBH, PLF, and BIC values obtained were significantly lower in comparison with modSLA implants, the outcome of healing in the DCD/CaP group might be regarded as improved when compared with previous data reported for conventional SLA surfaces (Schwarz et al. 2007, 2008a). In particular, at 2 and 12 weeks of submerged healing, SLA titanium implants exhibited only minor and non-significant improvements in the mean NBH (0.0 ± 0.0 and 0.4 ± 0.1 mm), PLF (0% and 10%), BF (0.0 ± 0.0 and $0.07 \pm 0.04\,\text{mm}^2$), and BIC (0% and 5%) values at the central aspect of the defect area (height: 3 mm; width: 3 mm; depth: 3 mm) (Schwarz et al. 2007). At advance defect sites (height: 4 mm; width: 3 mm; depth: 3 mm), the mean NBH ($1.4 \pm 1.0/1.2 \pm 0.6$ mm), PLF ($34.5 \pm 24.5/28.9 \pm 15.1$%), BF ($2.6 \pm 0.6/1.9 \pm 0.3\,\text{mm}^2$), and BIC ($34.4 \pm 20.7/26.8 \pm 10.4$%) values at 8 weeks also failed to reach statistical significance in either the upper or the lower jaw (Schwarz et al. 2008a). Considering the potential impact of a difference in implant designs (i.e. Soft Tissue Level® *versus* Certain Prevail® implants), one might assume that the specific surface properties noted for DCD/CaP implants may have a beneficial influence over conventional SLA implants on bone regeneration in this specific defect model. This observation might, at least in part, be supported by recent studies reporting on implant healing in fresh extraction sockets (de Sanctis et al. 2009, Vignoletti et al. 2009). In this specific defect model, the mean BIC values at DCD/CaP implants significantly increased from 13.1 ± 13.0% at 2 weeks to 42.4 ± 21.5% at 8 weeks, but were not significantly different in comparison with a conventional DAE surface. However, a marked difference between groups was observed when the socket location was taken into account. In particular, mean BIC values at wider defect sites were obviously higher in the DCD/CaP group (22.7 ± 9.9% *versus* 11.7 ± 3.1%). In these areas, a beneficial effect of DCD/CaP titanium implants was also found with respect to an increase in either new bone area (between 1 and 2 weeks) or bone formation (between 2 and 4 weeks) (Vignoletti et al. 2009). When comparing bone healing in fresh extraction sockets at 6 weeks, no significant differences in any of the investigated parameters were observed between DCD/CaP and conventional SLA titanium implants. In particular, both groups revealed comparable mean new bone (49.01 ± 19.48% *versus* 49.49 ± 18.53%) and total bone (77.68 ± 12.53% *versus* 74.49 ± 13.74%) areas as well as BIC (58.52 ± 11.83% *versus* 72.11 ± 9.8%) values (de Sanctis et al. 2009). All these data, taken together with the present results, appear to indicate that a beneficial effect of DCD/CaP over conventional SLA surfaces on bone formation is more likely at advanced defect sites during the early stages of wound healing. As a stabilization of the blood clot was not commonly observed for this surface technology (Vignoletti et al. 2009), one might speculate that a release of CaP crystals has potentially enhanced osteogenesis (Knabe et al. 2004). This was supported by a comparable increase in the mean BF values at both DCD/CaP and modSLA titanium implants at 2 weeks of healing. However, further studies are needed in order to investigate their biological mode of action.

Within its limitations, the present study has indicated that modSLA implants may have a higher potential to support osseointegration in dehiscence-type defects than DCD/CaP implants.

Acknowledgements

We kindly appreciate the skills and commitment of Ms. Brigitte Hartig, Mr. Vladimir Golubovic, and Mr. Tim Fienitz (Department of Oral Surgery, Heinrich Heine University, Düsseldorf, Germany) in the preparation of the histological specimens.

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Clinical Relevance

Scientific rationale for the study: Recent experimental studies provide some evidence that currently available surface modifications of titanium implants may have the potential to support bone formation at deficient sites (i.e. circumferential and dehiscence-type defects). The present study intended to compare bone regeneration in a standardized dehiscence-type defect model using titanium implants with either chemically modified sandblasted/acid-etched (modSLA) or DCD/CaP surfaces.

Principal findings: After 2 and 8 weeks of submerged healing in fox hounds, modSLA implants significantly improved NBH, and the percentage of BIC when compared with DCD/CaP implants.

Practical implications: In this type of defect model, modSLA implants may have a higher potential to support osseointegration than DCD/CaP implants.