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Impact of guided bone regeneration and defect dimension on wound healing at chemically modified hydrophilic titanium implant surfaces: an experimental study in dogs

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Abstract

Objectives: The aim of the present study was to evaluate the impact of guided bone regeneration and defect dimension on wound healing at chemically modified titanium implant surfaces (modSLA).

Materials and Methods: ModSLA implants were placed at chronic-type lateral ridge defects of different heights (H1–H4: 2, 4, 6 and 8 mm) and randomly allocated to either (a) GBR (polyethylene glycol membrane + biphasic calcium phosphate) or (b) untreated control. At 2 and 8 weeks ($n = 6$ dogs each), dissected blocks were processed for histomorphometrical analysis [e.g., percentage linear fill (PLF), regenerated area (RA)].

Results: At 8 weeks, both groups revealed comparable mean PLF (%) [Control: H1 (26.1 $\pm$ 5.8)–H4 (60.4 $\pm$ 11.8); GBR: H1 (8.3 $\pm$ 5.3)–H4 (50.7 $\pm$ 23.1)] and RA (mm^2) [Control: H1 (2.5 $\pm$ 0.4)–H4 (7.4 $\pm$ 4.1); GBR: H1 (1.8 $\pm$ 1.0)–H4 (10.8 $\pm$ 5.9)] values. A significant difference was observed for the mean PLF values at H1 defects.

Conclusion: It was concluded that (i) modSLA titanium implants supported bone regeneration and osseointegration at H1–H4 defects and (ii) the present GBR procedure did not seem to improve the outcome of vertical bone regeneration, but tended to increase the mean RA values.

Key words: animal study; chronic-type defect; guided bone regeneration; hydrophilicity; implant surfaces

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Conflict of interest and source of funding statement

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Previous experimental animal studies have indicated that chemically modified sandblasted, large-grid and acid-etched titanium implant surfaces (modSLA) supported bone regeneration in standardized buccal dehiscence-type defects without the additional use of guided bone regeneration (GBR) and/or bone augmentation procedures (Schwarz et al. 2007b, 2008b). After 2 weeks of either submerged or non-submerged healing in Beagle dogs, newly formed woven bone started to invade the dehiscence area, resulting in a nearly complete defect closure at 8 and 12 weeks. A specific immunohistochemical key feature was the initial stabilization of a fibrin clot at modSLA implants featuring a pronounced proliferation of vascular structures that mainly originated from the adjacent periosteum (Schwarz et al. 2008b). Because angiogenesis plays a key role in bone formation (Mair et al. 2007), it was suggested that blood clot stabilization in the defect area may be considered as the key feature of this new surface technology (Schwarz et al. 2007a, c, 2009a). In particular, the physico-chemical properties of hydroxylated/hydrated modSLA implants are mainly characterized by an increased surface free energy and hydrophilicity with initial water contact angles of about 0° compared with 139.9° for conventional SLA surfaces (Rupp et al. 2006). In addition, the specific production process (i.e. rinsing the titanium surface after the etching procedure under protective N_2 gas conditions) and 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, such as hydrocarbons and carbonates (Zhao et al. 2005). Even though the surgical creation of standardized buccal dehiscence-type defects in dogs is a commonly used model to evaluate bone regeneration at titanium implants (Stentz et al. 1997, Cho et al. 1998, Oh et al. 2003), acute-type defects have a certain tendency of spontaneous healing. Accordingly, from a clinical point of view, the defect model used in previous studies on modSLA implants may not reflect the biological situation encountered in chronic-type defects (Schwarz et al. 2007b, 2008b). Moreover, it remains unknown to what extent the outcome of healing is potentially influenced by the defect dimension (i.e. height) and whether an additional GBR procedure might have a beneficial effect on healing at respective sites. Preliminary histological data indicate that a GBR procedure in acute-type dehiscence defects using several types of barrier membranes was mainly associated with an initial bone formation along the surface of modSLA implants in the coronal direction (Schwarz et al. 2008a). Recently, an in situ gelling hydrogel composed of two polyethylene glycol (PEG) components was introduced and suggested to serve as a new material for barrier membranes. In particular, hydrogel formation is based on a cross-linking reaction of two PEG compounds and proceeds fast and selectively at physiological temperature and pH (Elbert et al. 2001). Experimental data provide clear evidence that PEG hydrogels are highly biocompatible, cell-occlusive and biodegradable (Jung et al. 2006, Wechsler et al. 2008, Herten et al. 2009, Thoma et al. 2009). Moreover, animal and clinical studies have indicated that a PEG hydrogel membrane may be as effective as a native collagen membrane to predictably support bone regeneration in dehiscence-type defects in conventional SLA titanium implants (Jung et al. 2009a, b). In order to facilitate its application over the defect area, the PEG hydrogel membrane is basically intended to be used in combination with either bone grafts or bone graft substitutes (Jung et al. 2009a, b). So far, this new GBR procedure has not been evaluated in modSLA titanium implants.

Consequently, the aim of the present study was to histomorphometrically evaluate bone regeneration in modSLA titanium implants in experimentally induced chronic-type alveolar ridge defects of different dimensions (i.e. height) with or without a GBR procedure using a PEG hydrogel membrane in combination with a synthetic bone graft substitute.

Material and Methods

Animals

In the present study, a total of 12 fox hounds (age 20–26 months, weight 33–43 kg) were included. 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 study was performed in three surgical phases.

In the first phase, extraction of the mandibular and maxillary (i.e. traumatic injury protection of the defect sites) second, third and fourth premolar as well as the first and second molar (P2-M2) was performed bilaterally in each dog.

After 3 months of healing, a total of four standardized box-shaped defects (mesio-distal width: 6 mm; depth: 6 mm) exhibiting different heights (H1: 2 mm; H2: 4 mm; H3: 6 mm; and H4: 8 mm) were prepared bilaterally at the buccal aspect of the alveolar ridge in both lower quadrants ($n = 8$ defects per animal) and left to heal in a submerged position.

At 4 weeks, modSLA titanium implants (24 per defect subgroup, corresponding to a total of 96 implants) were inserted into the respective chronic-type defects, and randomly allocated in a split-mouth design to either (a) a GBR procedure or (b) untreated sites.

Randomization of the GBR and untreated control sites was performed according to a computer-generated list (RandList®, DatInf GmbH, Tübingen, Germany). The animals were killed after a submerged healing period of 2 and 8 weeks, including $n = 6$ 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 postoperative treatment, piritramid and carprofene were applied subcutaneously for 3 days at the same dose as described before.

Surgical phase 1 (tooth extraction)

In the first surgery, mucoperiosteal flaps were reflected bilaterally in both 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 postoperatively for 10 days.

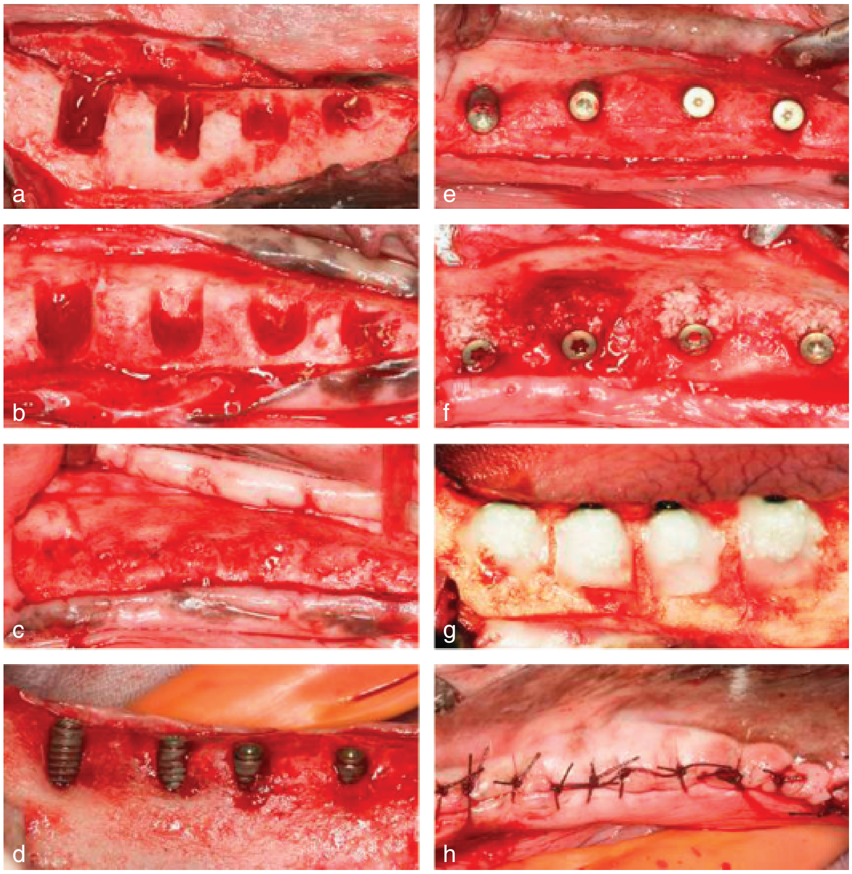


Fig. 1. (a) At 3 months after tooth extraction, a total of $n=8$ standardized box-shaped defects (width: 6 mm; depth: 6 mm) were bilaterally created at a distance of 5 mm in the lower jaws of 12 dogs. In each hemimandible, the defects revealed the following variations in height: H1: 2 mm; H2: 4 mm; H3: 6 mm; H4: 8 mm (mesial to distal). (b) Occlusal view indicating that the lingual bone plate was left intact. (c) Chronic-type defect situation after a submerged healing period of 4 weeks. The residual granulation tissue was carefully removed from each defect site. (d) Situation following placement of screw-type modSLA titanium implants at the central aspect of each defect site. The implant shoulder coincided with the crestal bone level at both mesial and distal aspects. (e and f) Occlusal view indicating that the titanium implants did not exceed the bony envelope. According to a split-mouth design, the defects were either left untreated (e) or homogeneously augmented with a biphasic calcium phosphate (f). (g) Following grafting, respective sites were covered by a polyethylene glycol hydrogel membrane. (h) All sites were left to heal in a submerged position.

Surgical phase 2 (defect creation and chronification)

After 3 months of healing, midcrestal incisions were made and mucoperiosteal flaps were reflected to expose the alveolar bone in the lower jaws. Four standardized box-type defects of different heights were subsequently prepared bilaterally in the buccal bone at a distance of 5 mm with a straight fissure carbide bur. In particular, all defects revealed a mesio-distal width of 6 mm and a depth of 6 mm, as measured from the surface of the buccal bone. The height of the defects, as measured from the crestal bone, varied to the following extent: 2 mm (H1), 4 mm (H2), 6 mm (H3) and 8 mm (H4) (from mesial to distal) (Figs 1a and b). The defect sizes were standardized using a periodontal probe (PCP12, Hu-Friedy Co., Chicago, IL, USA). The design of the chronic-type lateral ridge defects was modified on the basis of the surgical procedure reported in previous studies using the same model (von Arx et al. 2001a, b, Araújo et al. 2002, Schwarz et al. 2007a). All osteotomy procedures were performed under copious irrigation with sterile 0.9% physiological saline. After primary wound closure by means of mattress sutures (Resorba®, Nürnberg, Germany), the sites were allowed to heal for 4 weeks.

Surgical phase 3 (implant placement and GBR)

In the third surgery, midcrestal incisions were made and mucoperiosteal flaps were reflected to expose the experimental sites for implant placement. All granulation tissue was carefully removed from the residual defect areas (Fig. 1c). Implant sites were prepared bilaterally, at the central aspect of each defect site, using a low-trauma surgical technique under copious irrigation with sterile 0.9% physiological saline (surgery protocol by Institut Straumann AG, Basel, Switzerland). Thereafter, screw-type modSLA (Bone Level® SLActive®, ∅4.1 mm, length 10 mm, Institut Straumann AG) titanium implants were inserted with good primary stability (i.e. lack of clinical implant mobility) in a way so that the implant shoulder at best coincided with the bone crest at both mesial and distal aspects (Fig. 1d). Particular care was taken to ensure that the titanium implant did not exceed the bony envelope (i.e. its dehisced surface did not exceed the vestibular aspect of the adjacent alveolar bone) (Fig. 1e). Following implant placement, the defect areas were gently rinsed with sterile saline to remove any residual bone particles. No perforations of the lingual bone plate were performed to enhance bleeding at the respective defect sites.

Subsequently, all defect sites randomly selected for the GBR procedure were homogeneously filled with a biphasic calcium phosphate (60% HA+40% β-TCP, Straumann Bone Ceramic®, pore diameters: 100–500 μm, Institute Straumann AG) (BC). Before grafting, 0.5 g BC was moistened with 0.5 ml of sterile saline and implanted after a rehydration time of 5 min. In particular, the resulting putty was applied in a way as to homogeneously fill each defect site (Fig. 1f). Following grafting, the PEG hydrogel membrane (Institute Straumann AG) was applied in a viscous form as to cover 2–3 mm of the surrounding alveolar bone and to ensure stability of the graft material. After approximately 60 s, the PEG membrane had set to its gelated status (Jung et al. 2009b) (Fig. 1g). The corresponding contralateral control defects were left untreated (i.e. without application of BC and PEG).

Following periosteal-releasing incisions, the mucoperiosteal flaps were advanced, repositioned coronally and fixed with vertical or horizontal mattress sutures (Resorba®) in a way to ensure a submerged healing condition (Fig. 1h).

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 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 central defect area, resulting in two to four sections of approximately 300 μm thickness each (Donath 1985). 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).

Histomorphometrical analysis

Histomorphometrical analyses as well as microscopic observations were performed by one experienced investigator masked to the specific experimental conditions (T. F.). 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 $\times$ 200) were evaluated using a software program (Cell D®, Soft Imaging System, Münster, Germany).

The following landmarks were identified in the stained sections: the implant shoulder (IS), the bottom of the bone defect (BD) and 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 was measured as percentage of the distance from BD to IS, serving as 100% (Fig. 2). Additionally, the regenerated area (RA) (mm^2) was measured from BD to CBI. Within RA, the surface area of mineralized (MT) and non-mineralized tissue (NMT) as well as BC was automatically assessed (mm^2) using the image analysis software. 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.

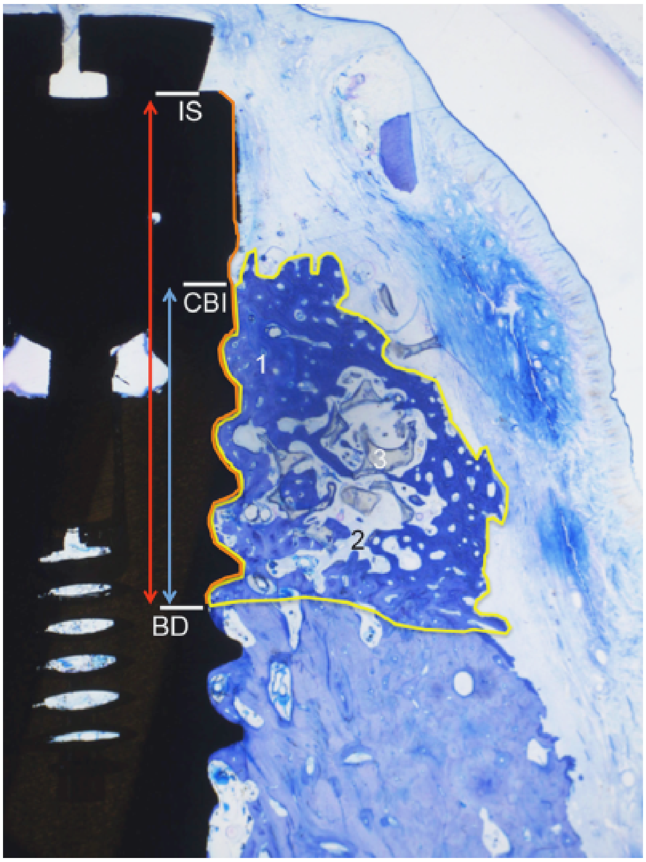


Fig. 2. The following landmarks were identified in the stained sections: IS, implant shoulder; BD, the bottom of the bone defect; CBI, the most coronal level of bone in contact with the implant at the buccal aspect; RA, regenerated area (yellow) was measured from BD to CBI. Within RA, the surface area of mineralized- (1) and non-mineralized tissue (2) as well as BC (3) were automatically assessed (mm^2) by the image analysis software. DL, defect length was measured from IS to BD (red line); NBH, new bone height was measured from BD to CBI (blue line); BIC, bone to implant contact was measured as a percentage of the distance from BD to IS, serving as 100% (orange line). Higher magnification ($\times$ 40) of the defect area shown in Fig. 5c.

Statistical analysis

The statistical analysis was performed using a commercially available software program (PASW Statistics 18.0, 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 a normal distribution. For comparisons between groups in each observation period, the unpaired *t*-test was used. The α error was set at 0.05.

Results

The postoperative healing was considered as generally uneventful in all dogs. No complications such as allergic reactions, swellings, abscesses or infections were observed throughout the whole study period. None of the defect sites revealed a premature exposure of the respective titanium implants.

The mean values of DL, NBH, PLF, RA, MT, NMT, BC and BIC in both GBR and control groups at H1, H2, H3 and H4 defects after 2 and 8 weeks of healing are presented in Tables 1–4. Basically, TB stain did not reveal any histological signs of the individual structure of the PEG hydrogel membrane in different groups at each specific time point. Thus, its specific pattern of biodegradation could not be evaluated.

H1 defects (2 mm)

Between-group comparisons revealed comparable mean DL values at both observation periods ($p > 0.05$; unpaired *t*-test, respectively) (Table 1).

At 2 weeks, the initial pattern of wound healing was comparable in both groups, because tiny trabeculae of woven bone had started to invade the defect area in the coronal direction (Figs 3a and b). Histologically, these areas of mineralization appeared to originate from open marrow spaces at BD and were clearly demarcated by osteoid seams and osteoblasts, indicating an early stage of healing. GBR-treated sites commonly exhibited a slight dislocation of BC granules in the caudal direction (Fig. 3a). Histomorphometrical analysis indicated comparable mean NBH, PLF, RA, MT, NMT and BIC values in both groups ($p > 0.05$; unpaired *t*-test, respectively) (Table 1).

At 8 weeks, the histological pattern of wound healing was mainly characterized by an ongoing bone formation and maturation of the trabecular network in the former defect area. This newly formed parallel-fibred bone appeared to be in close contact with the modSLA titanium implant surfaces (Figs 3c and d). An osseous integration of BC could not be observed in any of the GBR specimens (Fig. 3c). At these sites, residual granules of the bone graft substitute were commonly dispersed and located in a caudal position along the jawline.

Histomorphometrical analysis revealed a significantly higher increase in the mean NBH, PLF and RA values in the control sites ($p < 0.05$; unpaired *t*-test, respectively) (Table 1).

H2 defects (4 mm)

Between-group comparisons revealed comparable mean DL values during both observation periods ($p > 0.05$; unpaired *t*-test, respectively) (Table 2).

At 2 weeks, histological observation commonly indicated a stabilization of BC granules in the defect area at GBR-treated sites, thus resulting in pronounced BC values. While the control specimens were frequently characterized by an undisturbed woven bone formation within the defect area, mineralization was obviously hindered by the well-stabilized BC scaffold in the GBR group. In particular, trabecular bone formation mainly followed along the surface of modSLA titanium implants rather than BC particles (Figs 4a–d). Even though the increase in the mean NBH, PLF and BIC values tended to be higher in the control group, these differences did not reach statistical significance. Similarly, both groups revealed comparable mean RA, MT and NMT values ($p > 0.05$; unpaired *t*-test, respectively) (Table 2).

At 8 weeks, both GBR and control groups exhibited continuous bone formation and filling of the intertrabecular spaces. However, this was commonly accompanied by a slight to moderate superficial contour resorption at the buccal aspect of the newly formed alveolar bone (Figs 4e and f). Histomorphometrical analysis revealed comparable mean NBH, PLF, RA, MT and NMT values in both groups. Even though the mean BIC values tended to be higher in the control group, this difference did not reach statistical significance ($p > 0.05$; unpaired *t*-test, respectively). Similar to H1 defects, RA at GBR-treated sites was composed of minute amounts of BC (Table 2).

H3 defects (6 mm)

Between-group comparisons revealed comparable mean DL values during both observation periods ($p > 0.05$; unpaired *t*-test, respectively) (Table 3).

At 2 weeks, the histological characteristics of wound healing were comparable with the results observed in H2 defects (Figs 5a and b). In particular, trabecular bone formation mainly followed along the surface of modSLA titanium implants in the coronal direction and obviously appeared to be initially impeded by residual BC particles. These were frequently condensed at BD, thus resulting in decreased BC values in the coronal compartment of the defect area (Fig. 5a). Even though increases in the mean NBH, PLF and BIC tended to be higher in the control sites, these differences did not reach statistical significance. The corresponding RA, MT and NMT values were comparable in both groups ($p > 0.05$; unpaired *t*-test, respectively) (Table 3).

At 8 weeks, both GBR and control sites were characterized by a newly

Table 1. Mean values (± SD) of DL, NBH, PLF (in mm), RA, MT, NMT, BC (in mm^2) and BIC (in %) at *H1 (2 mm) defects* ($n = 6$ dogs per healing period)

Weeks	Groups	DL	NBH	PLF	RA	MT	NMT	BC	BIC	
2	GBR	2.5 ± 0.4	2.1 ± 0.7	16.1 ± 8.7	1.8 ± 0.3	0.3 ± 0.2	1.0 ± 0.4	0.5 ± 0.3	16.6 ± 13.7	
	Control	2.4 ± 0.4	2.1 ± 0.5	12.5 ± 7.5	1.1 ± 0.5	0.4 ± 0.1	0.7 ± 0.4	–	7.6 ± 10.7	
		NS	NS	NS	NS	NS	NS	–	NS	*p* value*
8	GBR	2.4 ± 0.4	2.2 ± 0.5	8.3 ± 5.3	1.8 ± 1.0	1.1 ± 0.4	0.7 ± 0.5	0.0 ± 0.0	9.9 ± 12.6	
	Control	2.3 ± 0.5	1.7 ± 0.6	26.1 ± 5.8	2.5 ± 0.4	1.6 ± 0.5	0.9 ± 0.4	–	21.9 ± 15.7	
		NS	$p < 0.05$	$p < 0.05$	$p < 0.05$	NS	NS	–	NS	*p* value*

*Comparisons between groups (unpaired *t*-test): $p < 0.05$.

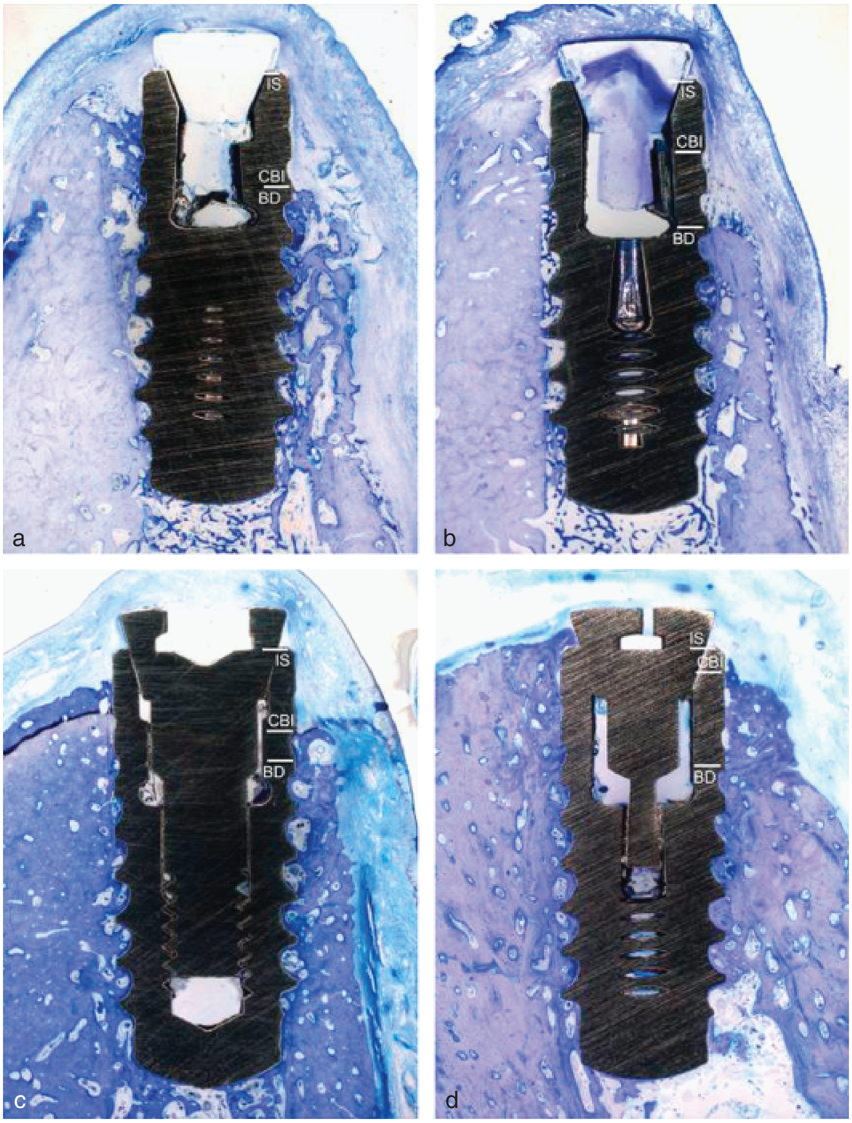


Fig. 3. Representative histological views (Toluidine blue stain) of wound healing at *H1 (2 mm) defects* (original magnification × 12.5). At 2 weeks, both groups exhibited a comparable initial woven bone formation that originated from BD. A dislocation of BC particles was frequently observed at GBR-treated sites. (a) GBR (2 weeks). (b) Control (2 weeks). At 8 weeks, both groups revealed varying amounts of parallel-fibred bone in the former defect area, which appeared to be in close contact with the surface of modSLA titanium implants. (c) GBR (8 weeks). (d) Control (8 weeks). BD, bottom of the bone defect; CBI, the most coronal level of bone in contact with the implant; IS, implant shoulder.

formed mineralized tissue that had homogeneously invaded within the former defect area in close contact with the surface of modSLA titanium implants (Figs 5c and d). The resulting increases in the mean NBH, PLF and BIC values tended to be higher in the control group, but failed to reach statistical significance ($p > 0.05$; unpaired t-test, respectively) (Table 3). Histological analysis revealed that residual BC particles were homogeneously integrated into this second formed network of spongiosa. However, these areas were demarcated by an increased amount of NMT (Fig. 5c). Accordingly, the mean RA values tended to be higher in the GBR-treated sites, but also failed to reach statistical significance (Table 3). At these sites, histological signs for a contour deforming bone remodelling appeared to be less pronounced when compared with the control defects (Figs 5c and d).

H4 defects (8 mm)

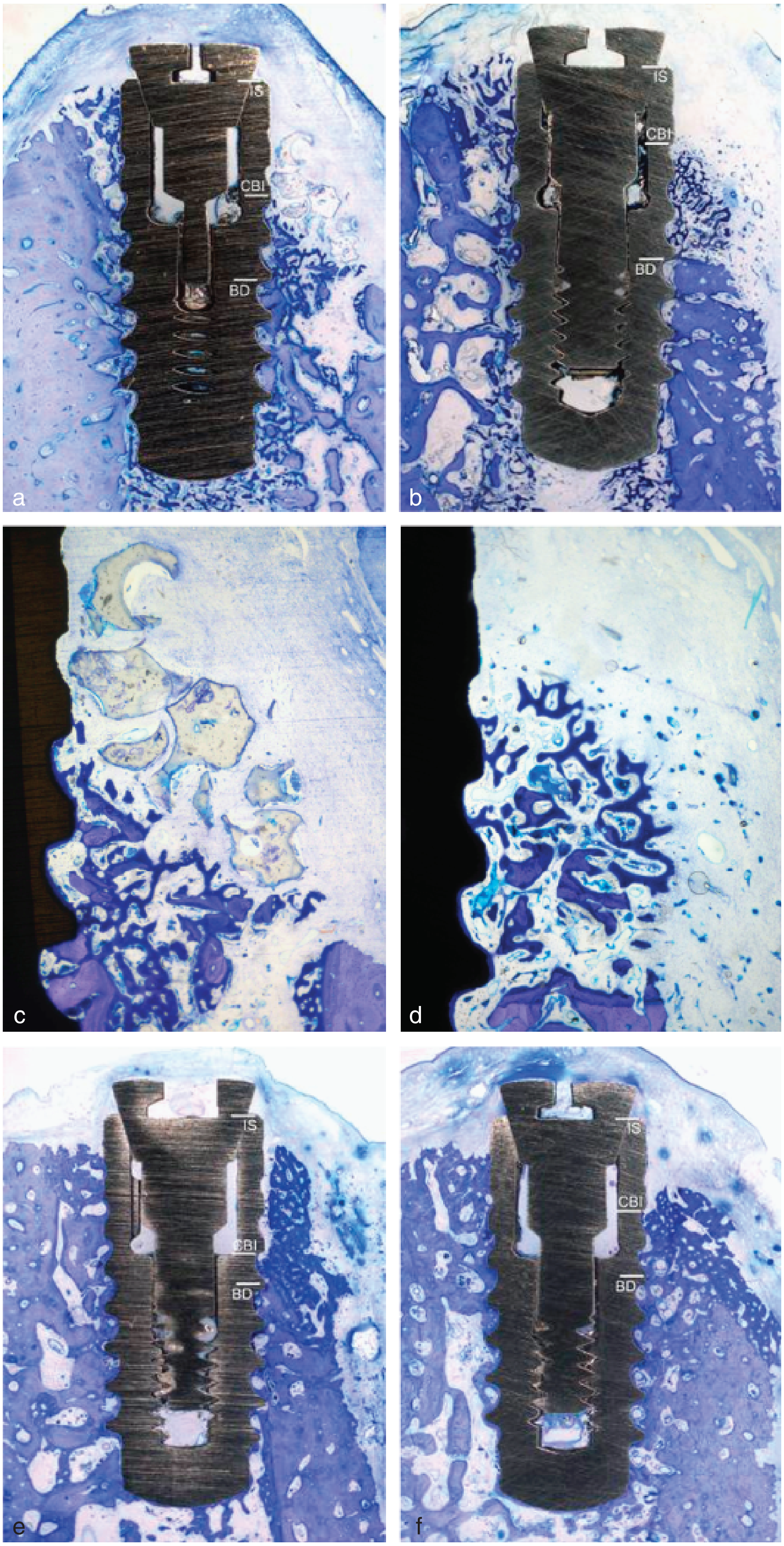
Between-group comparisons revealed comparable mean DL values during both observation periods ($p > 0.05$; unpaired t-test, respectively) (Table 4).

At 2 weeks, the difference in initial woven bone formation at either GBR or control sites was even more pronounced when compared with H2 or H3 defects. In particular, the control sites were characterized by an undisturbed trabecular bone formation within the former defect area, along and in close contact to the modSLA titanium implant surface. Because most of the GBR specimens revealed good and homogeneous stabilization of BC particles in the defect area, woven bone formation was mainly limited to the titanium implant surface facing the basal wound compartment (Figs 6a and b). The resulting increases in the mean NBH, PLF, MT and BIC appeared to be higher in the control sites, but still failed to reach statistical

Table 2. Mean values (± SD) of DL, NBH, PLF (in mm), RA, MT, NMT, BC (in mm^2) and BIC (in %) at *H2 (4 mm) defects* ($n = 6$ dogs per healing period)

Weeks	Groups	DL	NBH	PLF	RA	MT	NMT	BC	BIC	
2	GBR	3.7 ± 0.7	3.1 ± 0.7	12.7 ± 17.3	4.2 ± 1.9	0.7 ± 0.6	2.1 ± 1.5	1.4 ± 0.7	12.5 ± 19.1	
	Control	3.9 ± 0.4	3.0 ± 1.0	24.7 ± 22.4	3.2 ± 1.4	0.6 ± 0.9	2.6 ± 0.4	–	24.3 ± 21.5	
		NS	NS	NS	NS	NS	NS	–	NS	p value*
8	GBR	4.1 ± 0.4	2.3 ± 0.5	43.3 ± 11.0	4.0 ± 1.7	1.7 ± 1.2	1.9 ± 0.7	0.4 ± 0.2	32.7 ± 16.6	
	Control	4.0 ± 0.5	2.5 ± 1.1	39.0 ± 23.1	2.8 ± 1.4	1.6 ± 0.5	1.2 ± 0.9	–	38.9 ± 7.2	
		NS	NS	NS	NS	NS	NS	–	NS	p value*

*Comparisons between groups (unpaired t-test): NS.



significance when compared with the respective GBR defects ($p > 0.05$; unpaired *t*-test, respectively) (Table 4).

At 8 weeks, the ongoing bone formation and maturation appeared to follow primarily along the surface of modSLA titanium implants. Residual BC particles were inhomogeneously incorporated into RA and frequently surrounded by NMT (Fig. 6c). In contrast, the amount and mineral density of newly formed bone tended to be higher in the control group (Fig. 6d). However, between-group comparisons of the mean NBH, PLF, RA, MT, NMT and BIC values were not statistically significant (Table 4).

Discussion

The present study was designed to histomorphometrically evaluate the impact of defect configuration on bone regeneration at modSLA titanium implants and to assess whether a GBR procedure may improve the outcome of healing additionally at respective sites. Basically, it was observed that H1, H2, H3 and H4 defects in both GBR and control groups revealed comparable increases in the mean NBH, PLF, RA and BIC values after 2 and 8 weeks of healing. A statistically significant difference between groups was only observed for H1 defects at 8 weeks, showing significantly higher mean NBH, PLF and RA values at control sites. Even though increases in the mean histomorphometrical parameters (i.e. NBH, PLF, MT, BIC) also tended to be higher in the control group at H2, H3 and H4 defects,

Fig. 4. Representative histological views (Toluidine blue stain) of wound healing at *H2 (4 mm) defects*. At 2 weeks, stabilization of BC particles in the defect area appeared to impede vertical bone formation, which mainly followed along the surface of modSLA titanium implants. (a) GBR (2 weeks) (original magnification × 12.5). (b) Control (2 weeks) (original magnification × 12.5). (c) Higher magnification view (× 100) of the defect area shown in (a). (d) Higher magnification view (× 100) of a serial section derived from the defect area shown in (b). At 8 weeks, both groups featured a slight contour resorption at the buccal aspect of the regenerated area. (e) GBR (8 weeks) (original magnification × 12.5). (f) Control (8 weeks) (original magnification × 12.5). BD, bottom of the bone defect; CBI, the most coronal level of bone in contact with the implant; IS, implant shoulder.

Table 3. Mean values (± SD) of DL, NBH, PLF (in mm), RA, MT, NMT, BC (in mm^2) and BIC (in %) at *H3 (6 mm) defects* ($n = 6$ dogs per healing period)

Weeks	Groups	DL	NBH	PLF	RA	MT	NMT	BC	BIC	
2	GBR	5.7 ± 0.4	4.9 ± 0.4	11.7 ± 11.2	5.1 ± 3.3	0.4 ± 0.4	3.1 ± 3.1	1.6 ± 0.7	7.5 ± 6.2	
	Control	5.6 ± 0.4	4.4 ± 1.5	20.5 ± 28.6	4.8 ± 1.9	0.9 ± 1.0	3.9 ± 0.9	–	21.7 ± 33.0	
		NS	NS	NS	NS	NS	NS	–	NS	*p* value*
8	GBR	5.6 ± 0.5	3.3 ± 1.5	40.7 ± 25.3	7.4 ± 2.9	2.4 ± 1.7	3.9 ± 2.0	1.1 ± 0.8	37.0 ± 21.6	
	Control	5.5 ± 0.4	2.5 ± 0.7	53.8 ± 9.6	5.6 ± 2.2	2.6 ± 0.9	3.0 ± 0.9	–	44.4 ± 7.1	
		NS	NS	NS	NS	NS	NS	–	NS	*p* value*

*Comparisons between groups (unpaired *t*-test): NS.

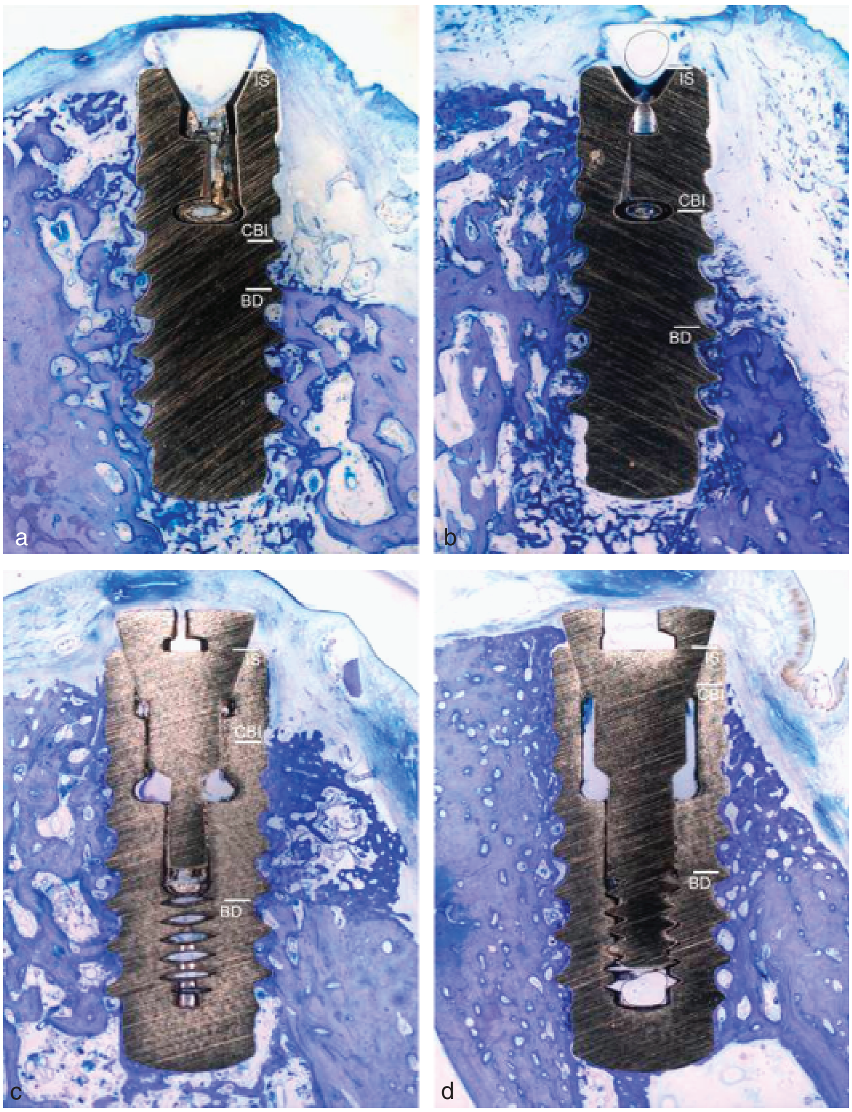


Fig. 5. Representative histological views (Toluidine blue stain) of wound healing at *H3 (6 mm) defects* (original magnification × 12.5). At 2 weeks, the control sites commonly revealed an undisturbed woven bone formation within the former defect area when compared with the GBR-treated sites. (a) GBR (2 weeks). (b) Control (2 weeks). At 8 weeks, BC particles were homogeneously integrated into the regenerated area, but also appeared to be surrounded by an increased amount of NMT. The mean CBI tended to be higher in the control group. (c) GBR (8 weeks). (d) Control (8 weeks). BD, bottom of the bone defect; CBI, the most coronal level of bone in contact with the implant; IS, implant shoulder.

these differences did not reach statistical significance. In contrast, the GBR groups generally revealed higher RA values when compared with the respective control groups. However, these differences also failed to reach statistical significance. When interpreting these data, one must keep in mind the potential clinical relevance of an experimentally induced chronic-type defect model, because it features no tendency towards spontaneous regeneration and therefore possesses similarities to the biological environment of a true compromised jawbone configuration. Accordingly, in recent years, this chronic-type lateral ridge defect model has been increasingly used for the assessment of a variety of biomaterials and surgical techniques (von Arx et al. 2001a, b, Araújo et al. 2002, Schwarz et al. 2007a, 2009a, Jung et al. 2009b). However, a potential disadvantage is related to difficulties in the standardization of the defect sizes subsequent to the chronification period. This might be particularly true for the horizontal dimension of the adjacent alveolar bone (i.e. BD), which has been reported to be an important determinant of bone regeneration (Polimeni et al. 2004). Because the present study aimed at investigating the impact of small differences in defect heights (i.e. H1–H4) on the outcome of wound healing, the chronification period was reduced to a period of 4 weeks, thus preserving the vertical dimensions at the best. In this context, however, it must be emphasized that bone remodelling subsequent to the surgical phase 2 may not have been completed at implant placement, and therefore, possibly influenced bone regeneration at both GBR and untreated control sites.

For the time being, these are the first experimental data reporting on different

Table 4. Mean values (± SD) of DL, NBH, PLF (in mm), RA, MT, NMT, BC (in mm^2) and BIC (in %) at *H4 (8 mm) defects* ($n = 6$ dogs per healing period)

Weeks	Groups	DL	NBH	PLF	RA	MT	NMT	BC	BIC	
2	GBR	7.7 ± 0.5	5.4 ± 1.4	26.2 ± 29.2	6.8 ± 3.6	0.3 ± 0.2	3.7 ± 3.1	2.8 ± 0.4	14.3 ± 9.7	
	Control	7.5 ± 0.3	4.9 ± 1.5	34.6 ± 22.4	3.6 ± 2.6	1.1 ± 0.6	2.5 ± 2.1	–	23.4 ± 16.4	
		NS	NS	NS	NS	NS	NS	–	NS	*p* value*
8	GBR	7.5 ± 0.3	3.7 ± 1.4	50.7 ± 23.1	10.8 ± 5.9	4.2 ± 3.7	5.2 ± 3.1	1.4 ± 0.4	35.7 ± 21.6	
	Control	7.7 ± 0.6	3.1 ± 1.2	60.4 ± 11.8	7.4 ± 4.1	4.7 ± 3.3	2.7 ± 1.7	–	43.4 ± 15.5	
		NS	NS	NS	NS	NS	NS	–	NS	*p* value*

*Comparisons between groups (unpaired *t*-test): NS.

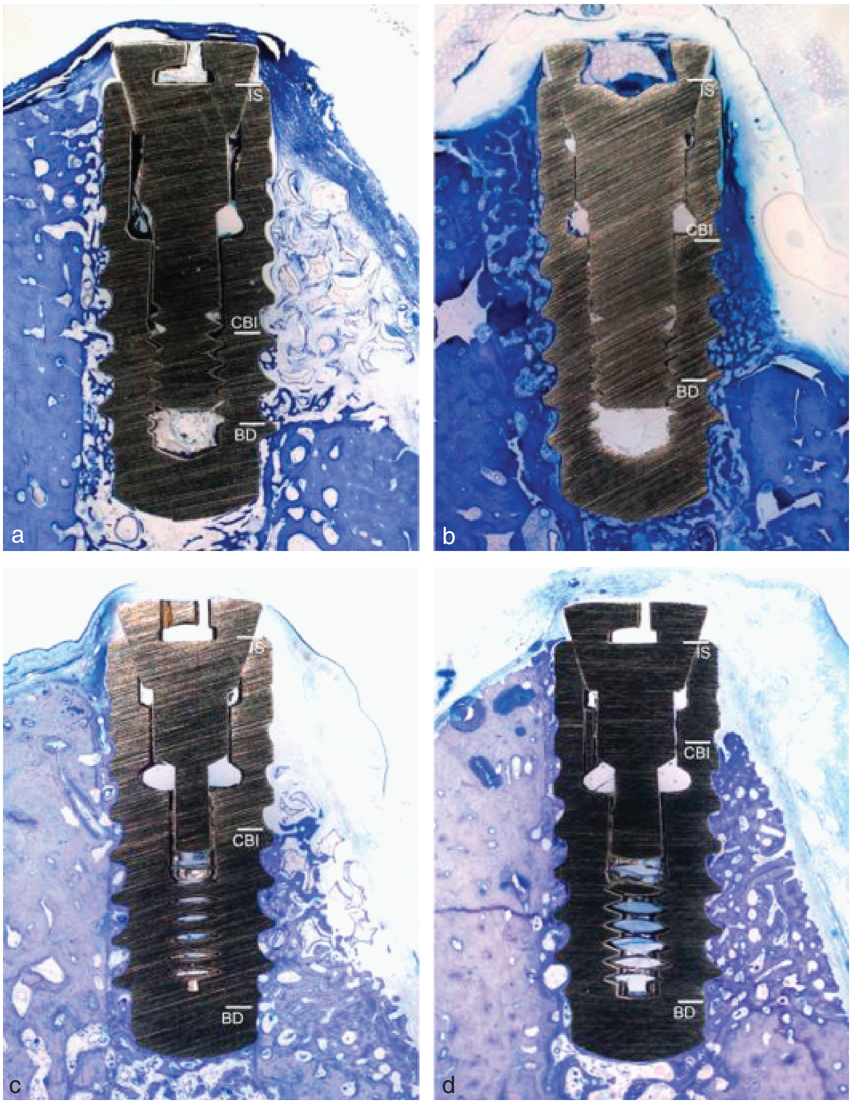


Fig. 6. Representative histological views (Toluidine blue stain) of wound healing at *H4 (8 mm) defects* (original magnification × 12.5). At 2 weeks, modSLA titanium implants appeared to be more attractive for an initial vertical woven bone formation than the stabilized BC particles. (a) GBR (2 weeks). (b) Control (2 weeks). At 8 weeks, residual BC particles were inhomogeneously integrated into the newly formed bone area. The mean CBI tended to be higher in the control group. (c) GBR (8 weeks). (d) Control (8 weeks). BD, bottom of the bone defect; CBI, the most coronal level of bone in contact with the implant; IS, implant shoulder.

defect heights (i.e. H1–H4) at modSLA titanium implants. Furthermore, the implementation of titanium implants without the addition of a GBR procedure has, so far, not been considered. However, in a recent experimental animal study performed in Beagle dogs, Jung et al. (2009b) assessed several types of GBR procedures for the treatment of chronic-type dehiscence defects (height: 6 mm) in conventional SLA titanium implants. This also included the application of the same PEG hydrogel membrane in combination with BC as a scaffold. While the mean PLF values decreased slightly from 45 ± 21% at 2 months to 35 ± 19% at 6 months, the corresponding mean BIC values increased from 82 ± 13% at 2 months to 91 ± 11% at 6 months (Jung et al. 2009b). These data seemed to be within the range of the present histomorphometrical results noted for GBR-treated H3 defects. In particular, the mean PLF values increased from 11.7 ± 11.2% at 2 weeks to 40.7 ± 25.3% at 8 weeks, thus resulting in an increase of the mean BIC values from 7.5 ± 6.2% at 2 weeks to 37.0 ± 21.6% at 8 weeks. Interestingly, Jung et al. (2009b) observed that the amount of BC within the former defect area varied considerably, because two out of five defects did not reveal any residual particles of this specific bone graft substitute after 6 months. This observation is, to a certain extent, in agreement with the present histological data, also pointing to a decrease of the mean BC values within RA over time. While these changes might in part be explained by an initial resorption of BC at 8 weeks (Jensen et al. 2007), the specific pattern of biodegradation noted for the PEG hydrogel membrane may also have contributed to a reduction of the mean BC values (Herten et al. 2009). In particular, first signs of a hydrolytic dissolution of the PEG matrix were observed at 2 weeks following subcutaneous implantation in rats. While the ongoing dissolution resulted in the formation of larger interstices in the membrane body at 4 weeks, a complete disruption of the PEG matrix into numerous fragments was commonly observed after 8 weeks of healing (Herten et al. 2009). This observation was also supported by Jung et al. (2009b), because histological evaluation merely revealed the presence of fragments of the PEG membrane at 2 months. Accordingly, one might speculate that the hydrolytic disruption of the PEG matrix caused a slight dispersion of the bone graft substitute after 8 weeks of healing, thus resulting in a reduced amount of BC within RA. In this context, however, it must be emphasized that the mean PLF and BIC values as noted for GBR-treated H3 defects at 8 weeks were on a level equivalent or even superior to those values obtained at defect sites treated with a native collagen membrane + BC after either 2 or 6 months of healing (Jung et al. 2009b).

When interpreting the present results, it was noted that residual BC particles were homogeneously integrated into a second formed network of spongiosa, which is basically in agreement with previous experimental data (Jensen et al. 2007, Schwarz et al. 2007d, Jung et al. 2009b). However, the specific histological pattern of wound healing in GBR-treated sites has indicated that initial woven bone formation mainly followed along the surface of modSLA titanium implants rather than the residual BC particles. This observation corroborates, to a certain extent, the histological data from a previous animal study investigating several types of GBR procedures at modSLA titanium implants in acute-type dehiscence defects in dogs (Schwarz et al. 2008a). In particular, all defects were augmented with a collagen-coated bovine-derived xenograft (BDX) and were subsequently either covered by a barrier membrane (i.e. native and cross-linked collagen, expanded polytetrafluorethylene, titanium mesh) or left uncovered. In all groups investigated, histological analysis revealed that initial trabecular bone formation also originated from open bone marrow spaces at BD, and had started to invade within the dehiscence areas mainly along and in contact with the modSLA implant surface (Schwarz et al. 2008a). These findings, taken together with the results from the present study, seem to indicate that modSLA titanium implants featured at least a higher osteoconductivity than either BC or BDX particles. In these studies, however, conventional SLA implants were not included, and therefore any conclusions on the potential influence of the specific surface characteristics noted for modSLA titanium implants on the outcome of wound healing at either GBR or untreated control sites need to be drawn with caution. As mentioned above, recent experimental studies performed in beagle dogs have pointed to a high potential of modSLA titanium implants to support bone formation in acute-type dehiscence defects without the additional use of a bone graft/substitute or GBR procedure (Schwarz et al. 2007b, 2008b, 2010). In particular, after 2 and 12 weeks of submerged healing, modSLA titanium implants revealed significantly increased mean PLF (34% and 97%), RA (0.4 ± 0.1 and $2.4 \pm 0.3\,mm^2$) 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. 2007b). These values appeared to be even improved at slightly advanced defect sites (height: 4 mm; width: 3 mm; depth: 3 mm) after 2 and 8 weeks of submerged healing in both the upper and the lower jaws [PLF (2 weeks: $79.4 \pm 13.0/41.5 \pm 14.4$ and 8 weeks: $91.2 \pm 1.9/92.4 \pm 2.4\%$), RA (2 weeks: $10.5 \pm 0.5/5.2 \pm 2.9$ and 8 weeks: $6.6 \pm 0.9/6.4 \pm 0.7\,mm^2$) and BIC (2 weeks: $67.6 \pm 12.0/39.7 \pm 12.0$ and 8 weeks: $81.4 \pm 12.6/82.1 \pm 14.8\%$) values] (Schwarz et al. 2008b). Basically, slight discrepancies noted between these data and the present histomorphometrical analysis might primarily be attributed to differences in the defect characteristics (i.e. acute-type *versus* chronic-type) but also to the use of two implant designs (i.e. Soft Tissue Level® *versus* Bone Level® implants). However, most recent data on submerged modSLA Bone Level® implants in the same acute-type defect setting (height: 4 mm, width: 3 mm, depth: 2 mm) revealed comparable outcomes of bone regeneration in both the upper and the lower jaws [PLF (2 weeks: $63.3 \pm 19.6/57.8 \pm 19.9$ and 8 weeks: $86.8 \pm 7.2/82.5 \pm 9.2\%$), RA (2 weeks: $2.4 \pm 0.6/2.3 \pm 0.6$ and 8 weeks: $2.3 \pm 0.5/2.5 \pm 0.6\,mm^2$) and BIC (2 weeks: $55.8 \pm 9.7/53.5 \pm 11.3$ and 8 weeks: $78.2 \pm 14.5/79.5 \pm 6.6\%$) values] (Schwarz et al. 2010). As wound healing at conventional SLA titanium implants was commonly characterized by the ingrowth of a dense connective tissue within the defect area (Schwarz et al. 2007b, 2008b), this type of surface technology was not considered to serve as an additional control group in a more challenging chronic-type defect model. All these data seem to indicate that the regenerative potential of a defect site may increase with its initial size. In particular, the present results have pointed out that the mean PLF values at 8 weeks consistently tended to increase with the defect height. This appeared to be particularly true for the control sites [H4 $(60.4 \pm 11.8) >$ H3 $(53.8 \pm 9.6) >$ H2 $(39.0 \pm 23.1) >$ H1 (26.1 ± 5.8)], and, to a certain extent, also for the GBR sites [H4 $(50.7 \pm 23.1) >$ H3 $(40.7 \pm 25.3) =$ H2 $(43.3 \pm 11.0) >$ H1 (8.3 ± 5.3)]. In this context, however, it must be emphasized that all GBR-treated defects tended to reveal higher mean RA values after 8 weeks of healing. Based on these findings, one might assume that the GBR procedure supported bone volume gain in the defect area, rather than the primary osseointegration of modSLA titanium implants. Considering blood clot stabilization as a biological key property of modSLA titanium implant surfaces (Schwarz et al. 2009b), it has to be questioned to what extent this feature might have been impaired by this specific GBR procedure using BC as a scaffold. Further studies using earlier observation periods are necessary in order to clarify these issues.

Within its limitation, the present study has indicated that (i) modSLA titanium implants might have the potential to support bone regeneration and osseointegration at H1–H4 defects and (ii) the present GBR procedure did not seem to improve the outcome of vertical bone regeneration, but generally tended to increase the mean RA values.

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References

Araújo, M. G., Sonohara, M., Hayacibara, R., Cardaropoli, G. & Lindhe, J. (2002) Lateral ridge augmentation by the use of grafts comprised of autologous bone or a biomaterial. An experiment in the dog. *Journal of Clinical Periodontology* **29**, 1122–1131.

Cho, K. S., Choi, S. H., Han, K. H., Chai, J. K., Wikesjö, U. M. & Kim, C. K. (1998) Alveolar bone formation at dental implant dehiscence defects following guided bone regeneration and xenogeneic freeze-dried demineralized bone matrix. *Clinical Oral Implants Research* **9**, 419–428.

Donath, K. (1985) The diagnostic value of the new method for the study of undecalcified bones and teeth with attached soft tissue (Säge-Schliff (sawing and grinding) technique). *Pathology Research and Practice* **179**, 631–633.

Elbert, D. L., Pratt, A. B., Lutolf, M. P., Halstenberg, S. & Hubbell, J. A. (2001) Protein delivery from materials formed by self-selective conjugate addition reactions. *Journal of Control Release* **76**, 11–25.

Herten, M., Jung, R. E., Ferrari, D., Rothamel, D., Golubovic, V., Molenberg, A., Hämmerle, C. H., Becker, J. & Schwarz, F. (2009) Biodegradation of different synthetic hydrogels made of polyethylene glycol hydrogel/RGD-peptide modifications: an immunohistochemical study in rats. *Clinical Oral Implants Research* **20**, 116–125.

Jensen, S. S., Yeo, A., Dard, M., Hunziker, E., Schenk, R. & Buser, D. (2007) Evaluation of a novel biphasic calcium phosphate in standardized bone defects: a histologic and histomorphometric study in the mandibles of minipigs. *Clinical Oral Implants Research* **18**, 752–760.

Jung, R. E., Halg, G. A., Thoma, D. S. & Hämmerle, C. H. (2009a) A randomized, controlled clinical trial to evaluate a new membrane for guided bone regeneration around dental implants. *Clinical Oral Implants Research* **20**, 162–168.

Jung, R. E., Lecloux, G., Rompen, E., Ramel, C. F., Buser, D. & Hämmerle, C. H. (2009b) A feasibility study evaluating an in situ formed synthetic biodegradable membrane for guided bone regeneration in dogs. *Clinical Oral Implants Research* **20**, 151–161.

Jung, R. E., Zwahlen, R., Weber, F. E., Molenberg, A., van Lenthe, G. H. & Hämmerle, C. H. (2006) Evaluation of an in situ formed synthetic hydrogel as a biodegradable membrane for guided bone regeneration. *Clinical Oral Implants Research* **17**, 426–433.

Mair, B., Fuerst, G., Kubitzky, P., Tangl, S., Bergmeister, H., Losert, U., Watzek, G. & Gruber, R. (2007) The anti-angiogenic substance TNP-470 impairs peri-implant bone formation: a pilot study in the rabbit metaphysis model. *Clinical Oral Implants Research* **18**, 370–375.

Oh, T. J., Meraw, S. J., Lee, E. J., Giannobile, W. V. & Wang, H. L. (2003) Comparative analysis of collagen membranes for the treatment of implant dehiscence defects. *Clinical Oral Implants Research* **14**, 80–90.

Polimeni, G., Koo, K. T., Qahash, M., Xiropaidis, A. V., Albandar, J. M. & Wikesjo, U. M. (2004) Prognostic factors for alveolar regeneration: bone formation at teeth and titanium implants. *Journal of Clinical Periodontology* **31**, 927–932.

Rupp, F., Scheideler, L., Olshanska, N., de Wild, M., Wieland, M. & Geis-Gerstorfer, J. (2006) Enhancing surface free energy and hydrophilicity through chemical modification of microstructured titanium implant surfaces. *Journal of Biomedical Materials Research A* **76**, 323–334.

Schenk, R. K., Olah, A. J. & Herrmann, W. (1984) Preparation of calcified tissues for light microscopy. In: Dickson, G. R. (ed). *Methods of Calcified Tissue Preparation*, pp. 1–56. Amsterdam, Elsevier.

Schwarz, F., Ferrari, D., Herten, M., Mihatovic, I., Wieland, M., Sager, M. & Becker, J. (2007a) Effects of surface hydrophilicity and microtopography on early stages of soft and hard tissue integration at non-submerged titanium implants: an immunohistochemical study in dogs. *Journal of Periodontology* **78**, 2171–2184.

Schwarz, F., Herten, M., Sager, M., Wieland, M., Dard, M. & Becker, J. (2007b) Bone regeneration in dehiscence-type defects at chemically modified (SLActive) and conventional SLA titanium implants: a pilot study in dogs. *Journal of Clinical Periodontology* **34**, 78–86.

Schwarz, F., Herten, M., Sager, M., Wieland, M., Dard, M. & Becker, J. (2007c) Histological and immunohistochemical analysis of initial and early osseous integration at chemically modified and conventional SLA((R)) titanium implants: preliminary results of a pilot study in dogs. *Clinical Oral Implants Research* **18**, 481–488.

Schwarz, F., Rothamel, D., Herten, M., Wustefeld, M., Sager, M., Ferrari, D. & Becker, J. (2008a) Immunohistochemical characterization of guided bone regeneration at a dehiscence-type defect using different barrier membranes: an experimental study in dogs. *Clinical Oral Implants Research* **19**, 402–415.

Schwarz, F., Sager, M., Ferrari, D., Herten, M., Wieland, M. & Becker, J. (2008b) Bone regeneration in dehiscence-type defects at non-submerged and submerged chemically modified (SLActive(R)) and conventional SLA titanium implants: an immunohistochemical study in dogs. *Journal of Clinical Periodontology* **35**, 64–75.

Schwarz, F., Sager, M., Ferrari, D., Mihatovic, I. & Becker, J. (2009a) Influence of recombinant human platelet-derived growth factor on lateral ridge augmentation using biphasic calcium phosphate and guided bone regeneration: a histomorphometric study in dogs. *Journal of Periodontology* **80**, 1315–1323.

Schwarz, F., Sager, M., Kadelka, I., Ferrari, D. & Becker, J. (2010) Influence of titanium implant surface characteristics on bone regeneration in dehiscence-type defects: a experimental study in dogs. *Journal of Clinical Periodontology* **37**, 466–473.

Schwarz, F., Sculean, A., Wieland, M., Horn, N., Nuesry, E., Bube, C. & Becker, J. (2007d) Effects of Hydrophilicity and Microtopography of Titanium Implant Surfaces on Initial Supragingival Plaque Biofilm Formation. A Pilot Study. *Mund Kiefer Gesichtschirurgie* **11**, 333–338 (in German).

Schwarz, F., Wieland, M., Schwartz, Z., Zhao, G., Rupp, F., Geis-Gerstorfer, J., Schedle, A., Broggini, N., Bornstein, M. M., Buser, D., Ferguson, S. J., Becker, J., Boyan, B. D. & Cochran, D. L. (2009b) Potential of chemically modified hydrophilic surface characteristics to support tissue integration of titanium dental implants. *Journal of Biomedical Materials Research B Appl Biomater* **88**, 544–557.

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.

Thoma, D. S., Halg, G. A., Dard, M. M., Seibl, R., Hämmerle, C. H. & Jung, R. E. (2009) Evaluation of a new biodegradable membrane to prevent gingival ingrowth into mandibular bone defects in minipigs. *Clinical Oral Implants Research* **20**, 7–16.

von Arx, T., Cochran, D. L., Hermann, J. S., Schenk, R. K. & Buser, D. (2001a) Lateral ridge augmentation using different bone fillers and barrier membrane application. A histologic and histomorphometric pilot study in the canine mandible. *Clinical Oral Implants Research* **12**, 260–269.

von Arx, T., Cochran, D. L., Hermann, J. S., Schenk, R. K., Higginbottom, F. L. & Buser, D. (2001b) Lateral ridge augmentation and implant placement: an experimental study evaluating implant osseointegration in different augmentation materials in the canine mandible. *International Journal of Oral and Maxillofacial Implants* **16**, 343–354.

Wechsler, S., Fehr, D., Molenberg, A., Raeber, G., Schense, J. C. & Weber, F. E. (2008) A novel, tissue occlusive poly(ethylene glycol) hydrogel material. *Journal of Biomedical Materials Research A* **85**, 285–292.

Zhao, G., Schwartz, Z., Wieland, M., Rupp, F., Geis-Gerstorfer, J., Cochran, D. L. & Boyan, B. D. (2005) High surface energy enhances cell response to titanium substrate microstructure. *Journal of Biomedical Materials Research A* **74**, 49–58.

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Clinical Relevance

Scientific rationale for the study: Previous animal studies provide some evidence that hydrophilic modSLA titanium implants may support bone regeneration at an acute-type lateral ridge (i.e. dehiscence) defects. So far, however, it remains unknown to what extent these findings can be transferred to an experimentally induced chronic-type defect situation of varying dimensions (i.e. heights of H1: 2 mm; H2: 4 mm; H3: 6 mm; H4: 8 mm) and whether an additional GBR procedure might have a beneficial effect on healing at respective sites.
Principal findings: After 2 and 8 weeks of submerged healing, both GBR and control groups basically revealed a comparable linear defect fill (PLF), bone-to-implant contact and new bone formation at H1–H4 defect configurations. The mean PLF values consistently tended to increase with the defect height, which appeared to be particularly true for the control sites. However, the total regenerated area generally tended to be increased at all GBR-treated sites.
Practical implications: The specific surface properties noted for modSLA titanium implants may promote vertical bone regeneration at H1–H4 defects even without the addition of a GBR procedure.