Pongnarisorn NJ, Gemmell E, Tan AES, et al. Inflammation associated with implants with different surface types. Clin Oral Impl Res 2007; 18:114-25. (35 refs)

Purpose: The purpose of this study was to determine the nature of the inflammatory infiltrate associated with different transmucosal implant surfaces in dogs. In addition, putative periodontal pathogens were identified and quantified using real-time polymerase chain reaction (PCR).

Materials and Methods: Eight healthy greyhound dogs were used in this study. Lower premolar teeth were removed and allowed to heal for 1 month. Then, three experimental and one control single-stage implants were randomly placed on each side of the jaw in eight dogs, for a total of 64 implants. All implants had the same fixture surface, TiUnite, while the transmucosal portion of the test implants consisted of an acid-etched surface (type A), a machined surface with a circumferential groove (type C), and a surface prepared by mild anodic oxidation (type D). The control was a standard machined surface (type B). In order to determine the response to the different surfaces, plaque control was carried out twice weekly following placement of the implants for the entire experimental period. Clinical and radiographic evaluations were performed monthly. At 6 months, gingival biopsies and plaque samples were obtained. Sections were cut from three sites of each biopsy (mesial, buccal, and distal). The area of inflammatory infiltrate and the nature of the infiltrating cell types were determined using immunohistology. Real-time polymerase chain reaction was used to identify putative periodontal pathogens, *Actinobacillus actinomycetemcomitans*, *Tannerella forsythia*, *Fusobacterium nucleatum*, and *Porphyromonas gingivalis*.

Findings: All peri-implant tissues showed no clinical signs of inflammation, although minimal supragingival plaque was present on each implant. Inflammatory infiltrates were associated with all implant surfaces and were commonly found subepithelially and perivascularly. Statistical analysis showed that the type C surface (machined with a groove) had significantly larger inflammatory infiltrates than the control surface (machined). No statistically significant differences were found with respect to the size of the inflammatory infiltrates or in terms of the nature of infiltrating cells. However, despite the plaque control regime, plaque was present on all implant surfaces at the time of biopsy 6 months after placement. T cells were the predominant infiltrating cell type in all lesions, associated with the different surfaces. In all lesions, the CD4:CD8 ratio was approximately 2:1. *Aa* was not detected in any of the 64 samples. All other implant samples had similar numbers of *Tannerella forsythia*, *Fusobacterium nucleatum*, and *Porphyromonas gingivalis*, with variations from 10^2 to 10^9 cells/mg protein of plaque.

Conclusions: These results suggest that 1) the development of inflammation in the peri-implant soft tissues is independent of the type of surface of the implant; 2) The presence of a circumferential groove forms an area for subgingival plaque accumulation leading to increased inflammation; and 3) Implant surface type doest not seem to be significant in the development of the peri-implant microbiota or on the nature of the infiltrate, with T cells being the predominant cell type in all lesions.

Liu Y, Huse RO, de Grool K, Buser D, Hunziker EB. Delivery mode and efficacy of BMP-2 in association with implants. Angle Orthod 2006;76:721-7. (21 refs)

Purpose: To investigate the osteoinductive efficacies of biomimetic calcium-phosphate coatings bearing either adsorbed, incorporated, or incorporated and adsorbed BMP-2 at ectopic (subcutaneous) ossification sties in rats.

Materials and Methods: Titanium-alloy discs were coated biomimetically with a layer of calcium phosphate. BMP-2 was adsorbed onto or incorporated into coatings. The amount of BMP-2 passively adsorbed onto or incorporated into the coating was quantified by ELISA. A total of 330 implants were inserted subcutaneously into 165 young adult male Wistar rats among the 16 experimental and control groups. They were retrieved 1, 2, 3, and 5 wks after surgery and were processed for histologic and histomorphometric evaluation. Six saw-cuts were prepared from each embedded implant, polished, and surface-stained. The mean volume of bone tissue per unit area of implant and the mean volume of coating per unit area of implant were determined from 2D light micrographs.

Results: Calcium-phosphate coatings had a thickness of 22μm. With the 3 different bathing concentrations of BMP-2 namely, 0.1μg, 1μg, and 10μg per mL, the amounts of the drug incorporated into the coating were estimated by ELISA to be 0.56 μg, 0.61μg and 1.70μg per implant, respectively. The immersion of coated discs in PBS containing BMP-2 at 10μg per mL resulted in the passive adsorption of 1μg of the drug per implant. The immersion of naked discs in a similar medium for the same time resulted in no passive adsorption of BMP-2. One week after implantation, ectopic bone formation was observed only in associated with coating bearing the highest initial loading dose of adsorbed BMP-2. At the lower and intermediate doses of incorporated BMP-2 no ectopic bone formation was observed during the five-week monitoring period. At the highest dose, osseous tissue first appeared after the 2nd week. Between the 2nd and 5th weeks, the volume of bone deposited increased significantly. When adsorbed onto a calcium-phosphate coating, it was osteoinductive, but not highly efficacious. When BMP-2 was incorporated into calcium-phosphate coating, it was a potent bone-inducer, whose efficacy was compromised, not potentiated, by the additional deposition of an adsorbed pool.

Conclusions: Simple manipulation in the mode of drug delivery by biomimetic calcium-phosphate coating can effect vast improvements in the osteoinductive efficacy of the system. With an expensive drug such as BMP-2, improvements of this kind are all-important in the development of marketable, functionalized prostheses, which are solely needed to enhance and expedite osseointegration at compromised implantation sites.

Pier-Francesco A, Adams RJ, Waters MGJ, et al. Titanium surface modification and its effect on the adherence of *Porphyromonas gingivalis*: an *in vitro* study. Clin Oral Impl Res 2006; 17: 633-637. (21 refs.)

Purpose: To chemically and physically modify pure titanium surfaces in order to assess the effects of such modifications on the adhesion of the peri-implant pathogenic bacterium, *Porphyromonas gingivalis.*

Materials and Methods: Twenty samples of commercially pure titanium were obtained for this experiment. In order to assess the effects of modifications on surface roughness (physical modifications), sixteen samples were divided into four groups-- each group was subjected to a specific polishing technique: the first group, designated as "very smooth," was hand polished with rotary brushes for a mirror finishing process; the second group, designated as "smooth," was polished only with an Eco mini dry rotating machine; the third group, designated as "rough," was sandblasted with glass beads; and the fourth group, designated as "very rough," was sandblasted with aluminum oxide beads. Six additional commercially pure titanium samples were used to analyze the effects of modifications on titanium surface hydrophobicity (chemical modifications). These six samples were equally divided into three groups: the first group did not have its titanium surface hydrophobicity modified, so it was designated as the control group, while the second and third groups were chemically modified to different extents with an Emscope sputter coater, an argon plasma discharge, and a specific silane to produce surfaces of different hydrophobicities. Subsequently, all titanium samples were placed in a broth containing laboratory cultured *P. gingivalis* and incubated by rotation on a mixer at 37 degrees Celsius for one hour. Following the one-hour incubation period, titanium samples were taken from the broth and washed with phosphate buffered solution (PBS.) The titanium samples were then stained with 0.1% w/v acridine orange for 60 seconds so that any adherent bacteria still attached to the surface could be viewed under fluorescent microscopy. The number and the total percentage area covered by adherent bacteria were assessed.

Findings: An analysis of the relationship between physically modified surfaces and *P. gingivalis* adhesion indicated a statistically significant difference between the "very smooth" (Ra = 34nm) samples and the three other sample groups. There was, however, no difference in bacterial adherence between these three other sample groups. For instance, no statistically significant differences in percentage coverage of *P. gingivalis* were noted between the "smooth" (Ra = 155nm) and the "very rough" surfaces (Ra = 449nm.) Thus, a lowered a surfaced roughness ranging from 34 to 155 should result in a reduced adhesion of *P. gingivalis*. In assessing the relationship between chemical modification of the titanium surface and bacterial adhesion, no difference was noted between samples of different hydrophobicities. This is evident by the fact that the controls (from this group of six titanium samples) and the silane-treated samples were very similar in terms of bacterial adherence. This would suggest that chemical factors are not as influential in bacteria retention as physical factors.

Conclusions: Surface roughness is more influential in plaque accumulation and retention around an implant than surface-free energy.

Schwarz F, Herten M, Sager M, et al. Bone regeneration in dehiscence-type defects at chemically modified (SLActive®) and conventional SLA titanium implants: a pilot study in dogs. J Clin Periodontol 2007;34:78-86. (36 refs)

Purpose: To evaluate histomorphometrically in a beagle dog model bone regeneration in acute-type buccal dehiscence-type defects at submerged chemically modified SLA (modSLA) and SLA titanium implants.

Materials and Methods: The sample size consisted of 4 beagle dogs. The study was performed in 2 surgical phases. In the 1st phase, extractions were performed bilaterally in all dogs. After 4 months of healing, the 2nd surgical phase was characterized by standardized buccal dehiscence defects being created following implant site preparation in both the maxilla and mandible. These volumes of the defects were standardized by the use of a periodontal probe. The defects were created with straight fissure carbide bur and the dimensions were as follows: 3 mm in height from the crestal bone, 3 mm in depth from the surface of the buccal bone, and 3 mm in width mesiodistally. Three modSLA and 3 SLA implants were then randomly inserted into the edentulous areas according to a split-mouth design. The implants were 3.3 mm x 8 mm in length. In total, 24 implants were placed and each animal received 4 implants bilaterally in the mandible (2 modSLA and 2 SLA) and 2 implants bilaterally in the maxilla (1 modSLA and 1 SLA). The implants were inserted so that the implant shoulder was located 2 mm coronally to the bone crest at both the buccal and oral aspects. Radiographs were obtained before and after the extractions of the teeth and the placement of the implants. The animals were then sacrificed after 2 weeks and 12 weeks of submerged healing. The jaws of each dog were dissected and blocks containing the experimental specimens were prepared for histologic evaluation. Histomorphometrical analyses as well as light microscopic observations were performed. The following landmarks were identified within the stained sections: 1) New bone height (NBH); 2) the most coronal level of bone in contact with the implant at both buccal and oral sites (CBI-b/o); 3) Defect length (DL) was measured from the BTB to the bottom of the defect (BD); 4) Percent linear fill (PLF) was defined as the NBH divided by DL; 5) The amount of new bone to implant contact (BIC) was measured as a percentage of the distance from the BD to BTB (BIC-D); 6) Area of new bone fill (BF); 7) The difference in buccal and oral dimension of the coronal level of bone in contact with the implant (D-CBI). The data collected were analyzed via statistical analyses.

Findings: No surgical complications were noted during the procedures or throughout the study period. There were also no signs of any wound dehiscence or exposure of the transmucosal part of the implant body in both groups. At 2 weeks, there were no statistically significant differences in the mean defect length values between modSLA and SLA implants at both the central and lateral aspects of the defects.

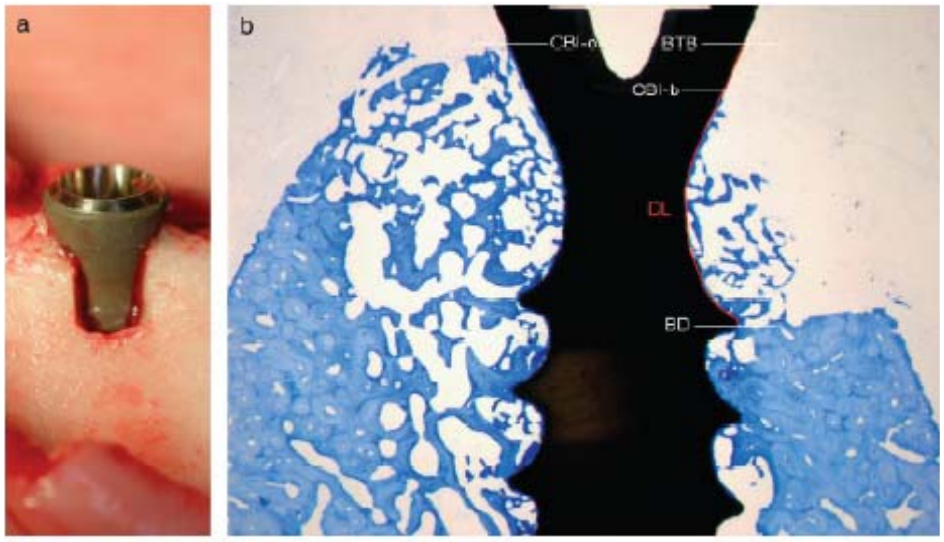
SLA Implants: Histological evaluation of the SLA implants at 2 and 12 weeks revealed that wound healing in all dehiscence defects was characterized by the formation of a poorly vascularized, dense connective tissue. Minute amounts of bone formation were observed at the most apical part of the defect. Both histomorphometrical and statistical analyses did not demonstrate any significant increases of mean NBH, BIC-D, BF, or PLF values in the respective defect areas. In some dogs, an apically directed down-growth of the connective tissue was present on the buccal aspects of the SLA implants underneath the dehiscence-type defects. Histomorphometrical analysis revealed a remodeling process that resulted in both a vertical and horizontal loss of alveolar bone at the buccal aspect of some of the dogs at 12 weeks. After 12 weeks, there was an increase in the mean D-CBI at both the central and lateral aspects.

ModSLA Implants: Histological evaluation revealed a complete defect fill at 12 weeks following implant placement. At 2 weeks, newly formed trabeculae of woven bone originating at both the lateral walls and the bottom of the defect were starting to invade the dehiscence areas. The mean values of NBH, PLF, BIC-D and BF appeared to be the highest at the lateral aspects of the respective defects. No de novo bone formation was demonstrated originating from the implant surface. After 12 weeks, wound healing was characterized by the ongoing formation of new bone within the defects areas. Histological evaluation demonstrated that the modSLA implants were surrounded by a firmly attached

mature, parallel-fibred woven bone. Early signs of remodeling i.e. the replacing of primary bone by secondary osteons were also apparent. According to both statistical and histomorphometric analysis, there were significant increases in BF (2.3 ± 0.4 mm^2), BIC-D (82%), PLF (98%), and NBH (3.2 ± 0.3 mm) values in the respective central and lateral defect areas. Both at the central and lateral mean D-CBI values decreased significantly at the 12 week period demonstrating that the newly formed buccal aspects of the alveolar bone reached the level of the respective oral aspects. ModSLA implants revealed significantly higher bone to implant contact in the non-defect areas (BIC-ND) when compared to the BIC-ND values of SLA implants at the 2 week period.

At the non-defect areas at 2 weeks, the SLA implants were surrounded by newly formed trabeculae of woven bone covering most parts of the endosseous surfaces. In contrast, the modSLA implants appeared to be surrounded by a firmly attached mature, parallel-fibred woven bone. After 12 weeks, new bone formation was seen in the non-defect areas of both groups. The SLA surfaces exhibited a firmly attached mature, parallel-fibred woven bone.

Conclusions: It was observed in this study that modSLA implants exhibited a complete defect fill at 12 weeks following implant placement, while wound healing in the defect areas of the SLA implants was characterized by the formation of a dense connective tissue at both the 2 and 12 week time period, without any increases in mean NBH, BF, PLF, and BIC-D values. ModSLA titanium surfaces may promote bone regeneration in acute-type buccal dehiscence defects when placed in a submerged position.



Buser D, et al. Enhanced bone apposition to a chemically modified SLA titanium surface. J. Dent. Res. 83 2004:(7)529–33.

Purpose: To examine the bone apposition to a modified sand blasted /acid-etched (modSLA)in the maxilla of miniature pigs as compared with the standard SLA surface.

Materials and Methods: Two surgical interventions were performed on 6 adult miniature pigs, first the anterior teeth in the maxilla were removed and were allowed to heal for 6 months. In the second surgery the implants were inserted and good primary stability attained. The implants used were of identical cylindrical shape with a core diameter of 2.7mm and 3 rings with an outer diameter of 4.2mm. The control implants had the standard SLA surface(sandblasted with large grits of 0.25 to 0.5mm and acid etched with HCL/ H2SO4).the test implants were produced with the same sandblasting and acid-etched procedure but were rinsed under N2 protection and continuously stored in an isotonic Nacl solution. The miniature pigs were sacrificed at 2, 4, 8 weeks for histological examinations.

Findings: Significant difference in wettability of surface type was noted. Dynamic contact angle measurements indicated that SLA was hydrophobic (DCA= 138.3± 4.2) and mod SLA was hydrophilic (DCA=0). The mod SLA had increased oxygen and titanium concentration (O=55.0± 2.0 at % Ti= 18.4± 1.6 at %). The mod SLA surface demonstrated reduced carbon concentration (C =18.4 ± 2.7 at%) than the standard SLA (C= 37.3± 3.4 at %). Test implants demonstrated significantly greater mean percentage of bone implant contact as compared with controls at 2 weeks (49.30 vs 29.42%) and 4 weeks (81.91 vs 66.57) of healing. At 8 weeks similar results were observed.

Conclusion: From the results of the study we can conclude that Mod SLA surface promoted enhanced bone apposition during early stages of bone regeneration.

Masaki C, Schneider GB, Zaharias R, et al. Effects of implant surface microtopography on osteoblast gene expression. Clin. Oral Impl. Res. 2005;16:650-56.

Purpose: To evaluate how topographical effects on titanium surface alter the expression of bone-related genes and transcription factors.

Matherials and Methods: Human palatal mesenchymal cell were cultured on titanium disks of various surface characteristics. The following titanium surface characteristics were used in this study: titanium dioxide grit blasted (Astra TiO2 Blast), titanium grit blasted and electrochemically etched in dilute hydrofluoric acid (Astra Osseospeed), large grit Al2O3 and H2SO4/HCl hot liquid etched (Straumann SLA-I), and modified SLA-2 created by blasting, etching and rinsing under N2 protection. Tissue culture plastic was used as a control. The 4 titanium disks were UV sterilized. Scanning electron microscopy (SEM) was utilized to study the cell morphology on the treated surfaces after 72 hours. High density cultures were plated in triplicate on each of the 5 surfaces. After 1 hour of attachment, samples were flooded and at 24 hours the media was removed with the percentage of unattached cells being calculated from the retrieved media. Changes in osteoblast gene expression for alkaline phosphatase (ALP), core-binding factor α1 (Cbfa I), Osterix, Type I collagen, Osteocalcin, and bone sialoprotein II (BSPII) were analyzed using PCR.
Cbfa I→ essential transcription factor protein which mediates osteoblast differentiation and skeletal formation during embryonic development
Osterix→ plays a key role for the ongoing differentiation within the osteogenic pathway
BSPII→ major component of bone matrix, mediates attachment of cells to collagen
ALP→ hydrolytic enzyme which removes phosphate group from proteins, nucleotides, and alkaloids
Osteocalcin→manufactured by osteoblasts and often used as a biochemical marker for bone formation

Findings: Cells on the SLA-1 and SLA-2 disks were mostly flattened with multiple cytoplasmic extensions while cells cultured on TiO2 and Osseospeed disks were more flattened with fewer cytoplasmic extensions. SLA-2 cultures demonstrated a significant increase in ALP gene expression when compared to the other surfaces. Cbfa I expression was significantly increased on the Osseospeed and TiO2 surfaces when compared to the SLA surfaces. Osterix expression was significantly decreased on the SLA surfaces as compared to the Osseospeed surface. Type I collagen was significantly increased on the SLA-2 surface when compared to the control and to SLA-1. No significant difference was noted among titanium disks in regards to osteocalcin and BSPII gene expression.

Conclusions: Implant surface properties may contribute to the regulation of osteoblast differentiation and mineralization by influencing the level of gene expression of bone-associated regulatory transcription factors.

Ellingsen JE, Johansson CB, Wennerberg A, Holmen A. Improved retention and bone-to-implant contact with fluoride-modified titanium implants. Int J Oral Maxillofac Implants 2004;19: 659-66.

Purpose: To compare TiO_2-blasted titanium implants with and without fluoride-modified surfaces with respect to bone-to-implant (BIC) contact, bone area in threads, and removal torque resistance in rabbit tibia 1 and 3 months after placement.

Materials and Methods: 3 test and 3 control implants were subjected to surface analysis with optical profilometry. 80 implants (3.5 mmD x 8 mmL) were used for this animal study. 20 male New Zealand white rabbits were included. 2 test implants (fluoride-modified TiO_2-blasted titanium) were placed in the tuberosity of one tibia and 2 control implants (only TiO_2-blasted titanium) were placed in the other. One implant in each leg was used for removal torque tests and the other implant was used for BIC contact and bone evaluations.

Results:

(1) Surface characterization

- Fluoride-modified implant had a slightly smoother surface (Sa = 0.91±0.14 μm) compared to the control implant (Sa = 1.12 ±0.24 μm). *Sa: average height deviation

(2) Removal torque

- 1-month healing period: No difference
- 3-month healing period: Fluoride-modified (85±16 Ncm) > Control (51±12 Ncm)

(3) Shear strength

- 3-month healing period: Fluoride-modified (23±9 N/mm2) > Control (15±5 N/mm2)

(4) Percentage of BIC contact (All treads)

- 1-month healing period: Fluoride-modified (35±14 %) > Control (26±8 %)
- 3-month healing period: Fluoride-modified (39±11 %) > Control (31±6 %)

(5) Percentage of BIC contact (3 best)

- 1-month healing period: Fluoride-modified (55±15 %) ≈ Control (47±10 %)
- 3-month healing period: Fluoride-modified (70±11 %) > Control (53±10 %)

(6) Percentage of bone area (All treads)

- 1-month healing period: Fluoride-modified (29±4 %) ≈ Control (29±5 %)
- 3-month healing period: Fluoride-modified (31±8 %) ≈ Control (39±15 %)

(7) Percentage of bone area (3 best)

- 1-month healing period: Fluoride-modified (55±9 %) < Control (56±11 %)
- 3-month healing period: Fluoride-modified (54±13 %) < Control (68±13 %)

(8) Qualitative observation

- 1-month healing period: No difference
- 3-month healing period: The fluoride-modified implants seemed to be covered by a thin collar of bone outside of which there were marrow spaces. The control implants showed mature bone which filled a larger amount of the threads.

Conclusions: The fluoride-modified titanium implants showed higher biomechanical anchorage in bone compared to unmodified titanium implants.

Shalabi MM, Gortemaker A, Van't Hof M.A, et al. Implant surface roughness and bone healing: a systematic review. J Dent Res 2006; 85(6):496-500.

Purpose: To perform a systematic analysis of the data regarding implant surface roughness, to determine its relationship, if any, with bone healing and biomechanical tests.

Materials and Methods: A Medline search was performed for dental articles written in English between 1953 and 2003. The key word used was "dental implant". Two independent readers carried out a selection of the references. Inclusion criteria included: 1) animal studies in vivo, 2) studies dealing with implant surface roughness and bone healing, 3) implant surface roughness and bone healing, 4) healing period of 3 months, 5) surface roughness parameters measured (Ra or Sa), 6) bone to implant contact measured, and 7) the use of biomechanical tests. Exclusion criteria included descriptive studies, and studies not meeting the inclusion criteria. Statistical analysis was performed via slopes of regression lines and 95% confidence intervals were used to express the relationship with the roughness. If only two values for roughness were available, the student's t test was applied, and the slope could easily be calculated.

Findings: The Medline search resulted in a list of 5966 hits. Only 14 papers fulfilled the inclusion criteria and escaped the exclusion criteria. Ra/Sa was the only was the only common measurement for surface roughness. 15 out of the 16 comparisons showed a positive relation between surface roughness and bone to implant contact (BIC).
In regards to biomechanical testing, 9 papers used a removal torque test to investigate the relation between biomechanical properties and surface roughness and expressed the results in NCM. Five papers described push-out tests and expressed the strengths in MPa. In all the push-out investigations the push-out strength increased with the increase in surface roughness. On the other hand the relationship between the torque test and the surface roughness was less clear with nearly 50% of the studies showing conflicting results.

Conclusions: The wide variation in slope values indicated substantial heterogeneity among the studies. Due to the lack of homogeneity, it is not permissible for the data to be combined for interference. Consequently, the data from the separate studies cannot be combined, and overall slopes be presented.