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Bio-activated titanium surface utilizable for mimetic bone implantation in dentistry—Part III: Surface characteristics and bone–implant contact formation

Jakub Strnad[a], Zdeněk Strnad[a], Jaroslav Šesták[b,*], Karel Urban[c], Ctibor Povýšil[d]

[a]LASAK—Laboratory for Glass and Ceramics, Papírenská 25, CZ—16200 Praha 6, Czech Republic
[b]University of West Bohemia, Faculty of Applied Sciences, Universitni 8, CZ-30614 Pilsen and Institute of Physics, Academy of Sciences of the Czech Republic, Cukrovarnická 10, CZ—162 53 Prague 6, Czech Republic
[c]Orthopedic Clinic, Teaching Hospital, Charles University, Šimkova 870, CZ—500 01 Hradec Králové, Czech Republic
[d]Institute of Pathology, 1st Medical Faculty of Charles University and Institute for Postgraduate Studies, U Nemocnice 4, CZ—128 52 Praha 2, Czech Republic

Abstract

This study was carried out to quantify the effect of an alkali-modified surface on the bone–implant interface formation during healing using an animal model. A total of 24 screw-shaped, self-tapping, (c.p.) titanium dental implants, divided into test group B—implants with alkali-modified surface (Bio surface) and control group M—implants with turned, machined surface, were inserted without pre-tapping in the tibiae of three beagle dogs. The animals were sacrificed after 2, 5 and 12 weeks and the bone–implant contact (BIC%) was evaluated histometrically. The surface characteristics that differed between the implant surfaces, i.e. specific surface area, contact angle, may represent factors that influence the rate of osseointegration and the secondary implant stability. The alkali-treated surface enhances the BIC formation during the first 2–5 weeks of healing compared to the turned, machined surface.

1. Introduction

More than a quarter century ago, two material groups have been found to be able to form a mechanically stable and functional interface with bone. One group consisted of certain soda–lime–silica glasses, with or without addition of phosphorus (*V*) oxide, and the first glass exhibiting the bone-bonding ability (discovered by Hench) [1,2] was named and registered under the name Bioglass. The glasses exhibiting the bone-bonding ability were designated as bioactive by the following definition: "the bioactivity is the characteristics of an implant material which allows it to form a bond with living tissues".

Another material found to exhibit the bone-bonding ability was machined titanium. This characteristic of titanium was first described by Branemark [3] and coworkers and the phenomenon of attachment to bone was named osseointegration with the following definition: "osseointegration represents the formation of a direct contact of a material with bone without intermediate fibrous tissue layer", often when observed by means of a light microscope. The major difference between the two material groups was represented by the materials reactivity and related kinetics of the bone–material interface formation. Very reactive bioactive glasses formed a stable interface with bone within days where as machined titanium required healing periods of several months to reach the same bone–implant contact (BIC). Thanks to high reactivity of bioactive glasses, the course of the glass–body environment interaction could be investigated more easily, and the bone-bonding ability was described and quantified in direct relation to the glass composition [4–7]. Soon other materials like hydroxyapatite, sol/gel prepared glasses or glass ceramics, which were found to

*Corresponding author.
E-mail addresses: strnad@lasak.cz (J. Strnad), sestak@fzu.cz (J. Šesták).

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exhibit similar bone-bonding ability, were included into the "bioactive" group. All these materials had in common a reaction step, which occurred during exposure to body environment and before the formation of the mechanically stable interface with bone. This step was the precipitation of apatite mineral on the surface of the original material as a result of chemical interaction of the materials surface with body environment [1,8].

This apatite formation was accepted as a hallmark of the bioactive materials and it is assumed that this bone mineral formation enables quick formation of the mechanically stable and functional interface of bone and a bioactive material. For initial assessment of potential bioactivity of a material, the apatite formation occurring in vivo was reproduced in vitro in simulated body environment and a good correlation of in vivo and in vitro results was found for the above mentioned, highly bioactive materials [9–11].

The investigation of the osseointegration observed in the titanium group was much more difficult because of the low reactivity of titanium in body environment. Changes detected in the passive oxide layer during the exposure to body environment were not comparable in magnitude to those occurring in bioactive materials [12,13]. With the intention to increase the implant surface available for bone ingrowth and fixation and/or to increase the blood clot retention on the materials surface, machined titanium is most often modified by sand blasting, plasma spraying or acid etching. Resulting roughened surfaces showed higher bone/implant interface strength (removal torque values) and higher BIC after the same healing time compared to machined titanium [1,14–21]. It was suggested that surfaces with the mean roughness parameter *S*a (arithmetic average height deviation) in the interval of 1.0–1.5 μm show stronger bone response than smoother or rougher implant surfaces [22]. These suggestions however do not consider the chemical composition changes introduced to the compared surfaces by the roughening procedures. It was shown that the optimal roughness value varies according to the chemical composition of the tested surfaces [13,23,24]. Some authors also demonstrated the ability of titanium oxide layer to attract preferentially calcium and phosphate ions from simulated body solutions—a characteristic property of bioactive materials [12,25]. Although roughening surface treatments always change both surface chemistry and morphology of the titanium substrate, they are usually regarded as tools for optimization of surface roughness only. The mechanism of bone–titanium attachment of the moderately roughened surfaces is considered to be solely morphology based and dependent on the mechanical interlocking [22,26]. Acceleration of the bone–implant interface and the increase of the BIC in the early phases of healing [27–29], was successfully achieved by plasma spraying of a hydroxyapatite as a bioactive material on the titanium substrate, however, hydroxyapatite plasma sprayed coatings have been the subject of many controversies [30,31] regarding their long-term stability and thickness and low long-term success rates [32,33]. On the other hand, some authors reported mid- and long-term clinical results showing high success rates of hydroxyapatite-coated implants [34–36].

As lately as in the late 1990s, specific surface modifications of machined titanium have been developed with the intention to modify the reactivity of titanium chemically so that it gains the best defined characteristics of well-proven bioactive materials—the ability to induce apatite mineral formation in vitro. Until now, to the knowledge of the authors, only two surface modifications of titanium supporting the precipitation of bone mineral apatite have been developed and clinically introduced. In 1999, alkali treatment [37] was used in combination with sand blasting and acid etching on LASAK implants (Bio surface) [38–41] and in 2000 fluoridated titanium surface (Osseospeed) was introduced by ASTRATECH [42,43].

From the present scientific literature, it seems necessary to evaluate both surface roughness and chemistry in order to be able to draw reliable conclusions regarding the effect of the surface treatment on the bone–implant interface formation. A method of quantitative evaluation of the clinical benefit of a surface treatment has not yet been established. Machined surface with defined surface roughness is often used as a reference when evaluating the effect of a surface treatment. The aim of this study is to evaluate the physicochemical properties and the stability time dependence during healing of potentially bioactive titanium surface and to compare it with the machined surface as a reference. The surface properties of both surfaces were compared to those of other commercially available implant surfaces.

2. Material and methods

Twelve pairs of screw shaped, self-tapping, (c.p.) titanium dental implants, divided into test group B—implants with alkali-treated surface (Bio surface) and control group M—implants with turned, machined surface, were inserted without pre-tapping in the tibiae of three Beagle dogs. The animals were sacrificed after 2, 5 and 12 weeks and the BIC was evaluated histomorphometrically.

Surface roughness of implants was determined using scanning surface topography instrument a Talysurf CLI 1000 with confocal CLA gauge (Taylor Hobson, Leicester, United Kingdom) that provides highly accurate non-contact 3D measurement. Dynamic contact angle measurement was performed using the Wilhelmy plate method, using Tensiometer K15 (Kruss GmbH, Germany). The wetting angle values in water were determined from the dependence of the wetting force on the immersion depth. The mean values of the wetting angle were calculated from four repeated measurements (Table 2). The surface area was calculated by the BET method from the results of the krypton gas absorption study. The surface area is expressed in relation to unit geometric surface area of the implant (Table 2). The determination was performed by absorption of krypton on a ASAP 2010 M instrument (Micromeritics, USA).

A total of three beagle dogs (mean weight 16.2 kg) were used in this study, which was approved by the ethics committee for work with experimental animals at the Teaching Hospital, Charles University, Hradec Králové, Czech Republic. Under total anaesthesia, in a position on its back, following the usual preparation of the operation field and toweling, a surgical cut with a length of 7 cm was made on the anteromedial surface of the tibia. A sharp cut was made in the fascia and then in the periosteum, which was widened to the side with a raspatory. Following uncovering of the surface of the tibia, the positions for drilling the holes for implanting the tested implants were marked. The implant sites were prepared with 1.5 mm, 2.0 mm pilot and 3.0 mm drills at low rpm with simultaneous cooling with a physiological solution. Then a countersink drill was used. The three pairs of implants with alkali etched surface and machined surface were inserted in the tibia side by side. The implants were blinded with screws and, following control of hemostasis, the operation wounds were closed in layers and were finally covered with a sterile bandage. Following completion of the experiment, the dogs were sacrificed after 2, 5 and 12 weeks by an overdose of thiopental and the tibiae were removed, a contact X-ray was made and then they were fixed in 10% formaldehyde prior to histological evaluation.

The tibiae were dissected and blocks of 7 mm thickness containing one implant each were prepared. Non-decalcified (ground) sections were processed according to the method of Donath and Breuner. Thin sections with a thickness of 30–50 μm were stained with toluidine blue and examined using an optical microscope (Olympus BX-60, Tokyo, Japan), equipped with an image system (Quick PHOTO Industrial 2.0, Prague, Czech Republic.). Bone–implant interfaces at the threaded part were histometrically analyzed by evaluating the percentage of BIC. The length of the bone tissue in direct contact with the implant (BC) and the total interface length (IL) were measured. The percentage of BIC is given by the ratio of the direct contact length to the total interface length ($BC/IL \times 100 = BIC\%$) (see Fig. 1). The presented mean values were calculated from three measurements available for both types of implant surfaces (B,M).

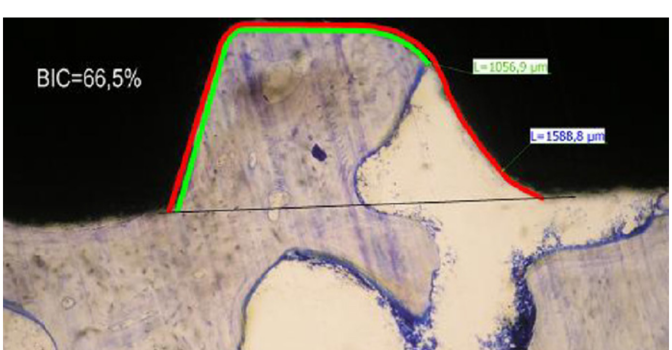

Fig. 1. The histometric analyses. Calculation of the bone–implant contact (BIC,%).

3. Results and discussion

Histological examination of the bone–implant interface was performed for both types of tested implant surfaces 2, 5 and 12 weeks after implantation. Three pairs of implants from each group were evaluated for each time interval. The cervical part of the implants was mostly surrounded by cortical bone, while the thread part is surrounded by trabecular bone. An intimate BIC was frequently observed at the cervical part of the implants with the Bio surface. In contrast, the specimens with turned, machined surfaces showed patchy implant–bone contacts and intermediate soft tissue was indicated in some cases.

The time development of the BICs% at the thread part of the implant was evaluated histometrically. The results of the histometric analysis (mean BIC%(B)$\pm$SD and mean BIC%(M)$\pm$SD) are presented in Fig. 2. Friedman ANOVA revealed statistically significant differences in BIC%(B) (test group) ($p = 0.029$) as well as in BIC%(M) (control group) ($p = 0.032$) throughout the measured intervals during a 12-week follow up. The BIC of the Bio surface increased sharply during the first 2 weeks in contrast to the turned, machined surface, which exhibited a gradual increase starting at a later follow-up time (cf. Fig. 2). Using the Mann–Whitney *U*-test, statistically significant differences between the test and control groups were observed after 2($p = 0.046$), 5($p = 0.049$) and 12 ($p = 0.049$) weeks.

The time dependence of the differences [BIC%IC%(M)] in the first 5 weeks of follow-up was evaluated by the method of linear regressions and the parameters of the straight line (slope and intercept) were determined: $BIC(B)-BIC(M) = 7.93859*t$ (weeks)$+ 10.9210$. The positive slope Δ [BIC%(B) $-$BIC%(M)]/$\Delta t = 7.93859$ BIC%/week$)_{t=0.5}$ of the regression line with correlation coefficient $R = 0.7561$ was found to be statistically significant ($p = 0.013$).

This study presents the results of measurement of changes in the BIC during healing of implants with Bio

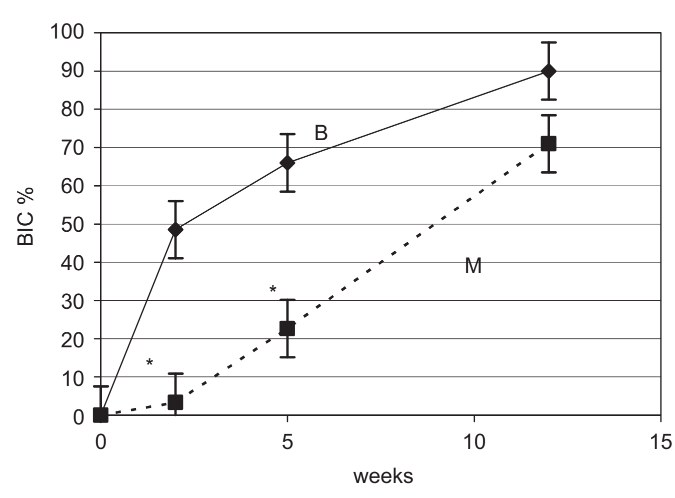

Fig. 2. Mean values of the bone–implant contact (BIC%6$\pm$SD) for the—Bio implants (test group B) and implants with machined surfaces (control group M) 2, 5 and 12 weeks after implantation. (* significant difference ($p<0.05$) at 95% confidence level).

Table 1
Mean roughness parameters of Bio and turned, machined implant surfaces measured at 3 different sites of implant threads

Surface treatments Gaussian filtre size $50 \times 50\,\mu m$	Sites of measurement	S_a (SD) (μm)	S_q (μSD) (μm)	S_{dr} (μSD) (%)	S_{ds} (μSD) (μm^{-2})
Bio surface	Top	1.11(0.13)	1.50(0.19)	15.90(4.5)	0.019(0.002)
	Valley	1.32(0.27)	1.72(0.36)	18.28(7.46)	0.022(0.003)
	Flank	1.15(0.14)	1.55(0.20)	19.99(6.88)	0.031(0.003)
Turned, machined surface	Top	0.57(0.14)	0.73(0.17)	8.35(3.06)	0.025(0.005)
	Valley	0.28(0.03)	0.36(0.03)	2.5(0.04)	0.051(0.009)
	Flank	0.50(0.11)	0.68(0.18)	8.29(4.10)	0.034(0.004)

S_a-arithmetic average height deviation; S_q— root mean square of height deviation; S_{dr}—developed surface ratio, S_{ds}—the number of summits in a unit sampling area.

Table 2
Contact angles and specific surface areas of Bio and turned, machined surfaces

Surface modification	Contact angle $\Gamma \pm$SD(deg.)	Specific surface area $\Gamma \pm$SD (mm^2/mm^2)
Turned,machined surface	79.5±4.6	1.4±0.7
Bio-surface	27.2±6.9	138.0±42.5

surface and a turned, machined surface as a reference. These findings demonstrated that the Bio surface more rapid formation of the BIC in the early stages of healing. It can be speculated that the differences in the rates of osseointegration in the initial stages of healing for the Bio and machined surface could be related to different surface reactivities [44] following from the different surface material properties, e.g. surface area or surface wettability [45]. In general, the surface reactivity, which is a common characteristic of bioactive materials, increases with increasing surface area. Therefore, the three-dimensional macro-, micro- and nano-structured Bio surface, which is more than 100× larger (Table 1) compared to the machined surface, may significantly enhance the surface reactivity with the surrounding ions, amino acids, and proteins, which determine the initial cellular events at the cell–material interface. In addition, easily wettable hydrophilic Bio surface (Table 1) allows the establishment of the contact between the body environment (blood) and the complicated rough and porous structure of the implant, and thus contribute to cell and biomolecule migration and adhesion [46]. Moderately, hydrophilic surfaces (20–40° water contact angle) were also shown to promote the highest levels of cell attachment [47] (Table 2).

The Bio surface, which is rich in hydroxyl groups, in contrast to the machined surface (cf. Fig. 1), rapidly induces adsorption of calcium and phosphate ions on contact with the ions of the blood plasma [48]. The calcium phosphate-rich layer promotes adsorption and concentration of proteins [49] and constitutes a suitable substrate for the first apatite structures of the bone matrix, which are synthesized by the osteogenic cells at the beginning of the formation of the new bone tissue. This mechanism can accelerate the formation of a stable bone–implant interface, formed by fusion of the biological cement line matrix with the reactive calcium phosphate layer on the surface.

4. Conclusion

It was demonstrated that sand-blasted, acid etched and alkali etched titanium surface (Bio) enhances the formation of BIC during the first 2–5 weeks of healing when compared to the machined-turned titanium surface. This phenomenon is likely to be related to the increased roughness and chemical reactivity of the Bio surface. Further investigation is necessary to differentiate the contribution of both surface roughness and surface chemistry.

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