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Effects of titanium surface topography on bone integration: a systematic review

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Conflicts of interest:
The authors' laboratory is, or has been, involved in research projects with several oral implant companies during the last five years.

Key words: bone integration, surface roughness, surface topography, titanium implants

Abstract

Aim: To analyse possible effects of titanium surface topography on bone integration.

Materials and methods: Our analyses were centred on a PubMed search that identified 1184 publications of assumed relevance; of those, 1064 had to be disregarded because they did not accurately present *in vivo* data on bone response to surface topography. The remaining 120 papers were read and analysed, after removal of an additional 20 papers that mainly dealt with CaP-coated and Zr implants; 100 papers remained and formed the basis for this paper. The bone response to differently configurated surfaces was mainly evaluated by histomorphometry (bone-to-implant contact), removal torque and pushout/pullout tests.

Results and discussion: A huge number of the experimental investigations have demonstrated that the bone response was influenced by the implant surface topography; smooth ($S_a < 0.5\,\mu m$) and minimally rough (S_a 0.5–1 μm) surfaces showed less strong bone responses than rougher surfaces. Moderately rough ($S_a > 1$–$2\,\mu m$) surfaces showed stronger bone responses than rough ($S_a > 2\,\mu m$) in some studies. One limitation was that it was difficult to compare many studies because of the varying quality of surface evaluations; a surface termed 'rough' in one study was not uncommonly referred to as 'smooth' in another; many investigators falsely assumed that surface preparation per se identified the roughness of the implant; and many other studies used only qualitative techniques such as SEM. Furthermore, filtering techniques differed or only height parameters (S_a, R_a) were reported.

Conclusions:

- Surface topography influences bone response at the micrometre level.
- Some indications exist that surface topography influences bone response at the nanometre level.
- The majority of published papers present an inadequate surface characterization.
- Measurement and evaluation techniques need to be standardized.
- Not only height descriptive parameters but also spatial and hybrid ones should be used.

Date:
Accepted 20 May 2009

To cite this article:
Wennerberg A, Albrektsson T. Effects of titanium surface topography on bone integration: a systematic review.
Clin. Oral Impl. Res. **20** (Suppl. 4), 2009; 172–184.
doi: 10.1111/j.1600-0501.2009.01775.x

Already by the beginning of the 1980s, surface structure was identified as one of the six factors particularly important for implant incorporation into bone (Albrektsson et al. 1981), a statement that has been confirmed in later published research. Faster and stronger bone formation may confer better stability during the healing process, thus allowing more rapid loading of the implant.

In a review covering both *in vitro* and *in vivo* studies related to implant surfaces, Cooper (2000) concluded that an increase in the surface roughness of cp titanium implants improved bone integration with respect to the amount of bone formed at the interface, increased osteoconduction and osteogenesis. The report summarized results from studies where mainly 'machined' surfaces were used as controls. A systematic review of surface roughness and bone healing was published by Shalabi et al. (2006). A total number of 14 articles were analysed and the conclusion was that there existed a positive correlation between surface roughness and bone-to-implant contact and pushout strength. The authors also concluded the studies to be too heterogeneous to be compared; however, they did not include a critical analysis of different techniques for surface analyses, and thus what was regarded as 'smooth' in one study could very well be termed 'rough' in another.

Le Guéhennec et al. (2007) concluded in their review over surface treatments that surface roughness did enhance osseointegration although the exact role of chemistry and topography in the early events of bone integration is still poorly understood. Not only bone formation may be stimulated by an increase of surface roughness; bone resorption may also be prevented. Cosyn et al. (2007) found microtextured collars to prevent bone resorption when compared with turned collars. Unfortunately, no analyses of the different surface topographies were reported in this review of five published clinical studies.

For many years, the Brånemark implant was the gold standard for implant surfaces. This implant was machined with a turning process with specific topographical properties such as anisotropy and a rather small average height deviation. When described in scientific publications this surface is only mentioned as being 'machined'. However, a machined surface can actually be turned, electro discharged, end milled, ground, sandblasted, fly cut, bored, slap milled or polished, to mention just a few techniques (Stout et al. 1990). Such surfaces have very different topographies and different machining methods can be detected due to differences in the topographical appearance. In oral implant research, machined surfaces have been used synonymously with a Brånemark turned implant without reflecting on the particular turning process applied for this implant. Thus, very different surfaces have been used as 'machined' controls when investigating new and rougher surfaces.

An increasing number of surface modifications are introduced and despite a majority of studies comparing 'machined' surfaces with new rough surfaces, it is not clear whether, in general, one surface modification is better than another. To further add to the confusion, not only is surface topography changed with many techniques but also surface chemistry and altered topography commonly results in a change in the chemistry and vice versa. Albrektsson & Wennerberg (2004) suggested smooth surfaces to have an S_a value of $<0.5\,\mu m$; minimally rough surfaces were identified with an S_a of 0.5–1 μm, moderately rough surfaces with S_a 1–2, and rough surfaces with an S_a of $>2\,\mu m$. This review will summarize our present knowledge of surface configurations of implant surfaces.

Material and methods

This literature review is based on articles published in International peer-reviewed journals before 1 July 2008. A database (PubMed) was used with the following key words: surface roughness, implant, bone integration, surface roughness and implant bone healing, clinical studies, experimental studies, surface topography, surface roughness and bone used in different combinations. This search resulted in 1189 papers of potential interest. A supplementary search for new publications was performed 31 October 2008. Duplicates were then sorted out, and because the topic was surface topography of importance for bone integration, all papers with an *in vitro* design and material characterization were excluded. Studies on orthopaedic hip prostheses were also excluded since the majority of such studies referred to Co–Cr and stainless steel, materials that are not relevant for dental applications. Furthermore, orthopaedic implant placement in reamed femoral bone as well as their loading conditions are quite different from oral implants, which was a further criterion for exclusion. This left 165 publications; abstracts for these studies were read and an additional assortment was made according to the above exclusion criteria. This left 120 publications and after exclusion of an additional 20 papers that mainly dealt with CaP-coated and Zr implants, 100 papers remained and formed the basis for this paper.

In the present review, the bone response was evaluated with histomorphometry (bone-to-implant contact), removal torque analyses and pushout/pullout tests in the experimental analyses. A few clinical studies were included in which parameters such as marginal bone loss and implant survival were evaluated and compared with different surface roughness.

Results and discussion

A general observation is that more studies are now presenting roughness measurements than was the case by the beginning of the 1990s (Wennerberg 1996). However, there are still several poorly described surface analyses and there is no consensus on 'smooth' and 'rough' surfaces. If the surface topography is measured, only a few studies characterize the surface topography more than in the height direction. The height-descriptive two-dimensional parameters (profiles) R_a, R_q, R_z and R_t are by no comparison the most commonly used parameters; sometimes, their three-dimensional counterparts S_a, S_q, S_z and S_t appear. This is slightly surprising because modern implant surfaces are often modified with different techniques such as blasting and etching, where the etching will leave high-frequency components in addition to the longer wavelengths produced by the blasting technique. Height-descriptive parameters, in combination with spatial, hybrid or functional parameters, preferably in three-dimensions, would provide a much better characterization for all modern implant surfaces.

Even if some different height parameters were found in the reviewed papers, the discussion almost always centred on the R_a or the S_a value. Therefore, it is possible to compare the different studies based on this parameter alone.

Because some confusion still remains about the different parameters, a short description will follow:

R_a (S_a for 3D) is the arithmetic mean deviation of a profile (R_a) or a surface (S_a).

This is a robust and stable height-descriptive parameter.

R_q (S_q for 3D) is the root mean square deviation of the profile (R_q) or surface (S_q). R_q gives almost the same information as R_a but is slightly more sensitive to high peaks and low valleys.

R_z (S_z for 3D is the 10-point height i.e. the average of the five lowest valleys and the five highest peaks within the profile (R_z) or the surface (S_z).

R_t (S_t for 3D) is the maximum peak to valley of the profile (R_t) or the surface (S_t), an extreme parameter that easily varies over different areas.

Many different techniques exist to both smoothen and roughen implant surfaces. For bone integration, smoother surfaces like electro- or mechanically polished ones will be too smooth for proper clinical integration but may still be used in research if certain surface properties have to be investigated. However, the huge majority of investigated implant surfaces are turned and rougher than the turned surfaces. Some techniques for surface alteration have been proven to be unsuitable such as spark erosion. This method produces a rather rough surface but without particular promise for bone integration, possibly due to impurities incorporated into the surface (Wennerberg et al. 1997b).

Commonly used techniques to alter surface topography

Some techniques add material on the bulk metal; thus, a surface with bumps (convex profile) will be created in contrast to techniques where particles will be removed from the surface, creating pits or pores on the surface (concave profile).

Examples of subtractive processes

Electropolishing
Mechanical polishing
Blasting
Etching
Oxidation

Examples of additive processes

Hydroxylapatite (HA) and other Calcium phosphate coatings.
Titanium plasma-sprayed (TPS) surfaces.
Ion deposition.

Surface topography

The surface topography is dependent on surface orientation and roughness. Different machining procedures will produce different orientations (Stout et al. 1990). Furthermore, different machining processes like the ones listed above will influence orientation as well as roughness.

Surface orientation

A surface with a clear orientation as for example a turned or a milled surface is called an anisotropic surface and a surface with no orientation at all is an isotropic surface. Blasted and etched surfaces may be isotropic.

Gotfredsen et al. (1992) compared machined (turned) and blasted surfaces. The R_a value for machined implants was 1 and 1.1 μm for the blasted implants i.e. a similar height deviation. Significantly higher removal torque was found for the blasted implants but there was no difference in bone-to-implant contact.

Huré et al. (1996) compared two types of surfaces, described by SEM. From these images, it is clear that one surface was isotropic and the other was anisotropic. After 6 months, in sheep tibia, no differences were found in histomorphometry . Whether or not the surface roughness differed among the two modifications is unclear. However, in a study by Göransson & Wennerberg (2005), blasted and turned implants with similar roughness were compared in a rabbit model. The S_a was 0.70 μm for the turned implants and 0.78 μm for the blasted ones. No difference was found in the amount of bone in contact with the implant surface . This study confirmed the work by Hallgren Höstner et al. (2001a, 2001b, 2003), who found blasted surfaces with no dominating pattern to display significantly stronger bone integration than surfaces with a clear orientation. *Whether the surface is isotropic or anisotropic seems to be of no importance for implant incorporation into bone.*

Surface roughness – micrometre surface configurations

Turned/machined

Turned or polished or milled surfaces are often called machined in oral implantology and have been commonly used as controls to other surfaces, most often rougher surfaces. However, some exceptions exist. Lucchini et al. (1996) compared two machined implants from two different companies in a sheep model. The topography was measured with a stylus instrument, and it is unclear whether the actual integrated areas of the implants or only suitable areas for the stylus technique were evaluated. The parameter S_{pa} was presented. S_{pa} is the unfiltered version of R_a. One implant surface had a value of 0.4 μm and the other 0.26. No difference in bone-to-implant contact was registered after 12 weeks.

Grizon et al. (2002) compared 'smooth' and 'rough' surfaces in a sheep model. The 'smooth' surface had an R_a value of 0.16 μm and the 'rough' surface had an R_a value of 0.21 μm as measured using an optical profilometer. No difference in bone formation between the two surfaces was found after 3, 6, 8 and 12 months. These surfaces were, in fact, all smooth ones and a small S_a increase from 0.16 to 0.21 μm is unlikely to be statistically significant. *There was no difference in bone formation when smooth surfaces were compared.*

Substractive machining processes

Blasted surfaces

Some studies of blasted surfaces have found indications of an optimal surface roughness. Wennerberg et al. (1995, 1996a, 1996b, 1996c, 1997a, 1997b, 1998) compared blasted surfaces with different roughnesses and compared them with turned surfaces. The investigated surfaces had S_a values ranging from 0.6 to 2.1 μm. The blasted surfaces demonstrated a stronger bone response than the turned implants in rabbit bone up to a healing period of 1 year. The strongest bone response in terms of peak removal torque and bone-to-implant contact was found for a blasted surface with an S_a value of 1.5 μm, an average wavelength of 11 μm and surface enlargement of 50%. The amount of Ti ions released was similar for the different surfaces as investigated in a study published by Wennerberg et al. (2004); thus, the study did not support the hypothesis that one reason for rough surfaces to be less well integrated may be an increased ion release.

In a series of studies, Rønold & Ellingsen (2002) and Rønold et al. (2003a, 2003b) used coin-shaped blasted and blasted + etched implants prepared with different roughnesses and evaluated with respect to the tensile strength. The S_a ranged from 0.6 to 11 μm. Up to an S_a value of 3.9 μm, a positive correlation was found between tensile strength and increasing roughness. A further increase in roughness demonstrated a decrease in tensile strength. Although the absolute value for an optimal height deviation seemingly differs, when compared with the studies by Wennerberg and colleagues, these results support the notion of a window of an optimal bone response. In fact, due to differently applied measurement techniques, the quoted S_a values may even be comparable to one another in the Rønold & Ellingsen and Wennerberg colleagues studies, respectively.

Other studies demonstrate a positive correlation between increasing roughness and bone integration for blasted when compared with machined/turned implants. Piatelli et al. (1998) investigated R_a up to 2.1 μm, Han et al. (1998) S_a up to 1.6 μm and Ivanoff et al. (2001) S_a up to 1.2 μm. It is possible that the limit for optimal roughness was not included in these studies.

Duyck et al. (2007) compared turned (R_a 0.45 μm) vs. rough blasted implants (R_a 2.75 μm). They found implant loading not to affect bone formation for the different surfaces but observed a bone-stimulating effect for the rough surface in the vicinity of the implants.

Blasted implants made either from a cobalt–chromium, a (Co–Cr) or a titanium alloy Ti6Al4V were compared in a study by Jinno et al. (1998). Co–Cr implants had an R_a of 3 μm and the Ti6Al4V implants had an R_a of 4 μm. Rods were implanted in rabbit and evaluated after 3, 6 and 12 weeks. Less bone-to-implant contact and lower interfacial strength were demonstrated for the Co–Cr implants compared with titanium alloy ones. The result may be dependent on the chemistry and/or the topography but in relation to topography a positive correlation was found between surface roughness and bone integration.

Either chemistry or topography may likewise explain the results obtained by Ellingsen et al. (2004), who investigated TiO_2-blasted implants with and without HF etching. The blasted + HF acid-etched surface had an S_a of 0.91 μm whereas the blasted implant had an S_a of 1.12 μm. The blasted + etched surface demonstrated significantly higher removal torque after 3 months and significantly more bone-to-implant contact after 1 and 3 months in rabbit bone. Even if the differences in height deviation may have been minor, the less rough surface demonstrated the firmest osseointegration, possibly due to the chemical influence of the HF acid etching.

The blasting material leaves chemical remnants on the surface; thus, some blasting materials may be preferable to others. Two different studies where different blasting materials were compared but with similar R_a/S_a values have been found in the literature. Müeller et al. (2003) compared implants blasted with aluminium oxide and bioceramic particles. R_a was estimated to be around 0.5 μm for both modifications. No significant difference was found in the bone response. Nor were any differences found in a study by Wennerberg et al. (1996a) when they compared TiO_2 and Al_2O_3 blasting particles resulting in S_a values of about 1 μm.

Clinical studies comparing different surface topographies. In a 5-year prospective study, Wennström et al. (2004) compared Astra Tech implants with either a turned or a TiO_2particle-blasted surface in periodontitis-susceptible patients. They found minor bone loss for both surface modifications and no difference between the surfaces.

Karlsson et al. (1998) compared Astra Tech TioBlast with machined Astra Tech implants and found no difference in the survival rate or marginal bone loss after 2 years of loading.

No topographical characterization was presented.

Mazor & Cohen (2003) characterized the surface topography of an MTX implant (grit-blasted surface with hydroxyapatite paticles), Osseotite (double acid etched) and SLA (sandblasted and etched). Seventeen different topographic parameters were used, 15 height descriptive and two hybrid ones. The R_a was 0.76 μm for the MTZ implants, 0.80 μm for Osseotite and 2.10 μm for the SLA surface. The MTX implants were then evaluated for 48 months when used for single crown restoration. A 100% clinical success rate was reported, with a marginal bone loss of < 1 mm. No comparison was made between the other two implant brands.

TiO_2-blasted implants were followed up to 3 years (average follow-up of 2.3 years) in a study published by Warren et al. (2002). This retrospective study included 102 implants positioned in 48 patients. A marginal bone resorption of < 1 mm was reported, which was less than expected. The implant surface roughness was claimed to be one reason for the findings although no topographical characterization was published.

Blasted implants demonstrate better bone integration than turned/machined implants. The clearly different R_a/S_a values reported in the studies may be a result of different measurement equipments and evaluation techniques. In contrast to animal studies, clinical studies often fail to find any major advantages or disadvantages with blasted implants when compared with turned implants.

Etched surfaces

Titanium is a corrosion-resistant metal even though some acids can be used for etching i.e. removing a small amount of material to create pits on the surface. Acids like HCl, H_2SO_4 and HF are examples of often-used chemical agents for the etching of titanium. The surface area may increase but not necessarily the average height deviation. Another effect of the etching procedure is to transform anisotropy to isotropy.

The etching technique has been investigated in some studies, such as Att et al. (2007), who compared one- and two-step etching procedures. R_a was 0.9 for the one-step etched surface and 0.6 μm for the 2-step procedure. No difference in the pushin test was found. Cho & Park (2003) compared three etched groups treated with increasing concentrations of HF acid, again without finding any differences between the groups. However, implants etched with 24% HF achieved significantly higher removal torque than the turned controls.

Butz et al. (2006) found surrounding bone around etched surfaces to be significantly harder than bone around turned implants in a rat study, where no topographical evaluation was performed.

Etched surfaces have been compared with machined surfaces in other animal studies (Klokkevold et al. 1997; Pebé et al. 1997) as well as in human bone (Lazzara et al. 1999). The acid-etched surface required higher torque than machined and blasted ones in all three investigations but because SEM was the only method for the description of topography, it is unknown whether the surface roughness actually differed between the machined and the etched surfaces. Surface measurements were performed in other studies, Ogawa et al. (2000) using an AFM and Abrahamsson et al. (2001) using an interferometer. The machined implants in the study by Ogawa and colleagues had an R_a of 0.063 μm and the etched ones 0.159 μm. The acid-etched surface in that study showed a significantly greater pushin value than the machined cylinders after 0, 2, 4 and 8 weeks of healing. In the Abrahamsson (2001) study, the S_a was 0.53 μm for the standard and 0.94 μm for the Osseotite implant. After 9 months in a dog model the etched implants had a statistically higher amount of bone in contact with the implant surface than the standard implants while the bone density was similar for the two types of surfaces.

Etched surfaces have been compared with other machined surface modifications and found to display stronger bone responses independent of the etched surfaces being rather smooth. London et al. (2002) inserted double-etched, Ha-coated, TPS and machined implants into rabbit bone. The surface roughness was measured with an interferometer and three height-descriptive parameters were presented in a diagram; despite being somewhat difficult to interpret, the R_a was approximately 0.5 μm for the machined, 0.7 μm for etched implants, 9 μm for the HA-coated implants and 10 μm for the TPS surfaces. The authors found more bone-to-implant contact for the double-etched implants but no difference among the others. R_a as rough as 9–10 μm may be too rough for proper osseointegration. If so, this may be one explanation for the contrasting results presented in a study by Klokkevold et al. (2001). Machined, dual-etched and TPS surfaces were used in a rabbit model. The three different surfaces had R_a values of 185 nm, 494 nm and 7.01 μm. The removal torque was evaluated at 1, 2 and 3 months. The etched and TPS surfaces had higher removal torque compared with the machined surfaces at all three times, and the TPS demonstrated higher removal torque than the etched surface after 2 and 3 months of healing. Even though the TPS surface may have been slightly too rough for an optimal bone response, the comparison was made with a very smooth machined, presumably polished surface, and the R_a value of the etched surface was very low as well. Yet another study was published comparing machined, acid-etched, blasted and TPS surfaces (Cordioli et al. (2000). The R_a values were 0.29, 0.62, 1.26 and 9.10 μm, respectively. After 5 weeks in rabbit bone the etched surfaces demonstrated higher removal torque and bone-to-implant contact than the other three surface modifications.

D'Lima et al. (1998) found similar values in pushout tests of acid-etched implants; R_a was reported to be 18 μm, grit-blasted implants had an R_a of 6 μm and fibre mesh-coated implants had an R_a of 400 μm. Nevertheless, there was more bone in contact with the acid-etched surface. The study is indicative of an optimal roughness window although topographical characterization was poor and the R_a values were very difficult to interpret.

Clinical studies comparing different surface topographies. Shibli et al. (2007a, 2007b) investigated failed implants retrieved from smokers. They found no material-related causes for implant failure, but several periodontal pathogens were detected independent of the surface topography. Turned Nobel Biocare, Göteborg Sweden implants were compared with double-etched Osseotite (3i Implant Innovations, West Palm Beach, FL, USA) in a retrospective clinical study by Al-Nawas et al. (2007). No surface characterization was performed. After 49 months, no significant difference in the survival rate was found. However, for patients treated with osteoplastic procedures, significantly more turned implants were lost than double-etched ones.

Khang et al. (2001) compared machined implants with double-etched implants. Ninety-seven patients and 432 implants were included in an RCT study. After 36 months of healing, the cumulative success rate was 95% for the dual-etched implants and 86.7% for the machined implants, a statistically significant difference claimed to be related to surface characteristics. No topographical evaluation was performed and the precise characteristics of the machined surface were not mentioned; it may have been polished.

Etched surfaces demonstrate better osseointegration than machined/turned implants in animals. The etching procedure leads to a small increase or even a decrease of average height deviation. Etched surfaces have been found to achieve a stronger osseointegration than rougher surfaces in animal experiments but contrasting conclusions can also be found in the literature. No major clinical differences are reported when comparing etched surfaces and turned implants.

Blasted and etched surfaces

A combination of blasting and etching has been a commonly used surface modification technique during the last one and a half decade. The reason for the combination of methods is that the blasting procedure hypothetically achieves a roughness optimal for mechanical fixation whereas the additional etching smoothens out some sharp peaks and may add a high-frequency component on the implant surface with potential importance for protein adhesion, considered to be important for the early bone-healing process. The first *in vivo* study was published by Buser et al. (1991). They compared electropolished, blasted and etched and HA-coated implants with R_a values ranging from 0.6 to 50 μm. The blasted + etched surface demonstrated the highest amount of bone-to-implant contact although this surface was not the roughest.

In a later study, Buser et al. (1998, 1999) compared machined, dual-etched and TPS implants with sandblasted + etched surfaces in a pig model. The R_a for the machined, etched and TPS surfaces was 0.15, 1.3 and 3.1 μm, respectively, and the R_a was 2 μm for the blasted + etched surface. The removal torque was significantly higher for the blasted + etched implants. The results can be interpreted in that optimal roughness also exists for blasted + etched surfaces or that the additional micropits added to the surface may be more important than a further increase of the height deviation. Similar findings with blasting + etching implants were published by Abron et al. (2001) when they histomorphometrically evaluated machined, blasted, and blasted + acid-etched implants after 3 weeks in rat bone. The surface roughness was measured with AFM. The R_a was 0.14 for the machined surfaces, 0.58 for the blasted and 0.77 μm for the blasted + etched ones. The actual measurements were performed on discs treated similarly as the implants, which may be one explanation for the rather low R_a values. The rat model was also used by Marinho et al. (2003) when they compared machined (R_a 0.85 μm) and blasted + etched surfaces, and similar to Abron et al. (2001), they found the strongest bone response after 5, 15, 30 and 60 days to blasted + etched implants, this time with an R_a value of 2.1 μm.

Hsu et al. (2007) compared 'machined' vs. sandblasted plus laser irradiated and dual-etched surfaces in a rabbit model using removal torque after 12 weeks of healing. The roughness of the two surfaces was measured with a stylus profilometer. R_a was 0.2 μm for the machined surface and 2.3 μm for the blasted + laser + etched surface. Furthermore, AFM in the tapping mode and a diameter of 15 nm were used for nanometre roughness characterization. R_a in the nanometre scale was 11 nm for the machined surface and 40 nm for the other surface modification. A significantly higher removal torque was found for the roughest surface, hypothesized by the authors to be due to a higher degree of osteoconductivity. Vandamme et al. (2008) investigated two different surfaces: one turned with an R_a of 0.70 μm, the other blasted + etched, R_a 2.75 μm, under unloaded and loaded conditions in a rabbit model. They concluded that increased roughness increased bone formation under unloaded conditions, while no difference was found between the two surfaces when loaded. However, they hypothesized that a well-controlled load would stimulate bone healing and pointed out the possible influence of surface roughness to further stimulate bone formation around implants.

There were no differences in bone-forming capacity after 3 months between minimally rough, moderately rough (oxidized and blasted + etched) and rough (TPS) surfaces in a loaded dog model (Al-Nawas et al. 2008).

Szmukler-Moncler et al. (2004) compared blasted + etched with machined + etched implants i.e. investigating the influence of the blasting procedure for blasted + etched implants. After 10 weeks in a pig model significantly higher removal torque was required for the SLA implants. Surface roughness was measured with laser profilometry; the machined + etched had an R_a value of 0.90 μm and the blasted + etched surface had an R_a value of 1.53 μm, i.e. a roughness that has been found to be optimal for blasted implants.

Blasted and etched surfaces were investigated by Deyneka-Dupriez et al. (2007) in relation to interfacial shear strength. Two different etching procedures were used: sandblasting + HF/HNO_3 and sandblasting + HCl/H_2SO_4. Scanning Probe Microscopy (SPM) was used to measure the different surfaces. The authors aimed to find topographical parameters correlating with shear strength. R_a, R_q, R_t and delta q i.e. only height-descriptive parameters were used. The HCl/H_2SO_4 resulted in an R_a value of approximately 2 μm and the HF/HNO_3 etched technique in an R_a of about 4 μm. After 1 year of implantation the smoother implant demonstrated the highest removal torque, a 'smooth' surface in the range of optimal roughness as described in other studies. The authors suggested that the parameters used were not sufficient to characterize the investigated surfaces but firstly the use of SPM with a maximum vertical measuring range of 6 μm may be inappropriate for the surfaces used (an R_a of 4 μm will require a vertical range of about 40 μm) and secondly if etched surfaces are to be separated the most important differences are the density of summits and the high-frequency components included in the surfaces not evaluated by the authors.

The bone resorption under unloaded and loaded conditions was found to be significantly less for blasted and etched compared with TPS implants (Cochran et al. 1996). To mimic compromised implant sites, Novaes et al. (2004) compared TPS and SLA in a dog model where the implant sites had been prepared with periodontitis before extraction. Implants were inserted into extraction alveolus and bone-to-implant contact was calculated after 12 weeks, without any differences between the two surfaces. Immediate insertion into periodontally compromised sites was successful for both SLA and TPS extraction site implants.

No difference was found between the etched or blasted + etched Ti rods with respect to cell migration and osteogenesis by Kawahara et al. (2006a, 2006b) in an electron microscopic evaluation on cell migration of two different surface topographies. R_a was 0.4 μm for the etched surface and 2 μm for the blasted + etched surface.

Blasted + etched microimplants have been evaluated in human bone (Grassi et al. 2006). After 2 months in human bone (unloaded) the sandblasted + etched surface demonstrated significantly higher amount of bone-to-implant contact than the machined surface. The machined had an R_a value of 0.3 μm and the blasted + etched surface had an R_a value of 0.7 μm as measured in an optical profilometer.

The etching procedure may create a titanium hydride on the surface in addition to titanium oxide. The influence of titanium hydride is mainly unknown. However, Perrin et al. (2002) investigated sandblasted and acid-etched surfaces with and without titanium hydride in a pig model. Both surfaces showed a large amount of bone in contact with the implant surface: 82% bone-to-implant contact without hydride and 75% with hydride. The conclusion was that the surface topography and not the chemical composition was responsible for the good results although the surface topography was not measured.

To further improve blasted + etched surfaces, a deliberate change from hydrophobic to hydrophilic surfaces has been suggested. Buser et al. (2004) used sandblasted and acid-etched implants and compared with implants that, in addition, had been submerged in NaCl under nitrogen protection before acid etching. The additional treatment created a very clean hydrophilic surface. The S_a value was 1.16 μm for the blasted + etched and 1.16 μm for the additionally treated hydrophilic surface. More bone-to-implant contact was found after 2 and 4 weeks in minipigs on the hydrophilic surface. After 8 weeks, no difference could be observed.

Clinical studies comparing different surface topographies. No such studies have been found.

Blasted + etched are often compared with machined surfaces and, with no exception, are found to be stronger integrated in bone. Comparing blasted + etched with other surfaces the outcome is less certain;

however, TPS surfaces often demonstrate less strong bone response than the blasted + etched surfaces. The reported surface topography varies, probably depending on different measuring equipments and evaluation techniques but the blasting and etching procedure may differ as well. However, in the vast majority of studies blasted + etched implants are moderately rough.

Oxidized surfaces

All titanium implants have a native oxide layer but oxidized implants have been prepared with a thicker oxide layer, commonly achieved with heat treatment or with the implant placed as an anode in a galvanic cell with a suitable electrolyte. After passing current through the galvanic cell, the surface oxide will grow from the native state of some 5 nm thickness to 1 mm or even more. A positive correlation between increasing height deviation and implant incorporation was found by Choi et al. (2006) when they investigated oxidized implants prepared at different voltages. SEM and optical interferometry were used to characterize the topography. R_a was the only parameter presented; implants oxidized with 500 V had an R_a of 5.2 μm, 550 V prepared implants had an R_a of 3.8 μm, the 300 V implants had an R_a of 0.8 μm and 300 V implants had an R_a of 1.7 μm. They found a voltage of 500–550 to increase the removal torque and bone-to-implant contact as compared with 300 and 400 V.

Sul et al. (2002) compared different oxidized surfaces with S_a from 0.96 to 1.03 μm with machined surfaces as controls and with an S_a value of 0.83 μm. The oxide thickness was from 200 to 1000 μm. After 6 weeks in rabbit bone, the oxidized implants demonstrated a stronger bone response than the machined implants and the oxide thickness of 600–1000 μm was found to result in the strongest bone response.

Sul et al. (2001, 2002, 2005a, 2005b, 2006a, 2006b) and Sul (2003) investigated, in a series of studies, the influence of surface chemistry and topography in relation to oxidation processes applying the micro-arc technique and using different acids as electrolytes. Electrolytes containing P, S, Ca and Mg changed the chemical composition and the topography. The surface topography was measured with confocal laser scanning profilometry and interferometry. Turned implants were used as controls. The chemically modified implants demonstrated higher removal torque and more bone-to-implant contact than the controls; especially, the Ca- and Mg-reinforced surfaces showed significantly stronger osseointegration. The S_a/R_a value was in a range from 0.7 to 1 μm for the test implants and 0.5 for the turned controls.

Li et al. (2004) confirmed the results by Sul and colleagues comparing machined and oxidized implants in a rabbit study. After 4 weeks the oxidized implants with an estimated R_a of 2.5 demonstrated significantly higher removal torque than machined implants' R_a of 0.3 μm. These values were extracted from a diagram that also showed R_z values that were lower than R_a for the oxidized implants, but not really possible according to the mathematical definition for the two parameters. A positive correlation between increasing minimal roughness and osseointegration was demonstrated by Park et al. (2007). They compared turned implants with three different groups of oxidized implants. The roughness was measured with an interferometer and the parameter R_a was presented. Turned implants had an R_a of 0.54 μm, group 1 oxidized implants had an R_a of 0.68 μm, group 2 oxidized had an R_a of 0.80 μm and group 3 oxidized implants had an R_a of 0.88 μm. After 6 weeks in rabbit bone, group 3 oxidized implants demonstrated significantly more bone-to-implant contact and higher removal torque than the other groups of implants.

Oxidized implants, as well as other surface modifications, have been inserted into human bone to mimic the clinical situation, using microimplants. Ivanoff et al. (2003) and Shibli et al. (2007) investigated oxidized and turned implants. The S_a value in the study by Ivanoff was 0.78 μm for the turned and 1.17 μm for the oxidized implants. The corresponding values were 0.32 and 0.87 μm, respectively, in the study by Shibli and colleagues. Both studies concluded that oxidized implants demonstrated more bone-to-implant contact than turned surfaces.

Blasted implants have been used as controls and compared with oxidized surfaces in animal experiments by Kim et al. (2003), who investigated blasted implants (two sizes of blasting particles) with and without thermal oxidation. The S_a for the blasted implants was 1.25 μm and that for blasted + oxidized implants was 0.94 μm. Blasted + thermal oxidated implants were significantly stronger than bone-anchored after 4 weeks compared with blasted implants; however, after 12 weeks no difference was found.

In some studies, particulate ions have been added to the electrolyte to improve the bioactivity. Sul et al. (2006b) compared Mg-oxidized implants with dual-etched implants (Osseotite, 3i, Implant Innovation) and another oxidized implant (TiUnite, NobelBiocare, Göteborg, Sweden). The surface topography was evaluated with an interferometer. The S_a was 0.69 for the Mg oxidized, 0.72 μm for the Osseotite and 1.35 μm for the TiUnite implants. After 3 and 6 weeks in rabbit bone, the Mg-oxidized implants showed significantly higher removal torque and bone-to-implant contact than Osseotite, but no statistically significant difference when compared with TiUnite. Sul et al. (2009) also compared the Mg-reinforced oxidized surface with blasted and turned surfaces. The roughness was measured with an interferometer and height, spatial and hybrid parameters were presented. The smoothest surface was the turned surface evidenced by all three parameters but there was no difference in terms of the density of peaks or surface enlargements between the Mg-oxidized and the blasted surface. The Mg-oxidized surface had a significantly lower average height (S_a) compared with the blasted surface. The Mg-reinforced surface demonstrated higher removal torque than the turned implants after 3 and 6 weeks while the blasted implants demonstrated a stronger bone response after 6 weeks compared with the controls but not at 3 weeks. Not every study confirms an improved performance for oxidized implants. Giavaresi et al. (2002) prepared cp Ti rods with two different modifications and inserted them into sheep cortical bone. One surface was sandblasted and acid etched, and the other was Ca–P anodized + hydrothermally treated; three height-descriptive parameters were used. The R_a for the blasted + etched surface was 0.80 μm and R_a for the Ca–P anodized + heat-treated implants was 1.17 μm. After 8 and 12 weeks, no difference in pushout force or amount of bone in the interface could be observed. No positive effect of increasing roughness from 0.8 to 1.1 or changing the chemistry was noted. In further studies, Giavaresi et al. (2003a, 2003b) inserted machined, acid-etched, Ha-sprayed and CaP-anodized implants into sheep. The topography was measured with an optical profilometer and two height-descriptive parameters were used: R_a and S_k. The R_a was approximately 0.2, 0.5, 1.1 and 2.2 μm for machined, etched, HA-coated and CaP-anodized implants, respectively (slightly difficult to determine from the diagram). After 8 weeks no differences in bone-to-implant contact were observed, and after 12 weeks the acid-etched surface had the lowest bone contact among those investigated. In most studies etched surfaces are more strongly bone anchored than machined surfaces; however, the machined surfaces (polished?) and the etched surfaces were smooth and an increase from 0.2 to 0.5 μm in the height deviation may not contribute towards better osseointegration.

Clinical studies comparing different surface topographies. Rocci et al. (2003) compared turned Brånemark implants with TiUnite from the same manufacturer (Nobel Biocare, Göteborg, Sweden), an interesting comparison because this is one of few studies comparing different surfaces where the implant design was the same. In an immediate loading protocol, the authors found a significantly higher success rate for the oxidized TiUnite implants compared with the turned ones. In a recently published study by Friberg & Jemt (2008), the TiUnite surface showed a significantly higher survival rate when compared with turned Brånemark implants 1 year after a one-stage surgery.

In general, oxidized implants demonstrate stronger bone anchorage than machined implants, in animal as well as in human experiments. There seems to be an advantage with the use of oxidized implants if the implants are to be loaded during healing. For oxidized surfaces there is often no correlation between height deviation and bone integration. However, often, the anodized implants are minimally rough and the comparison is often made with other minimally rough surfaces. The oxidation may change topographical properties other than the height deviation and the evaluation of other parameters is seldom carried out.

Additive processes

TPS

Titanium particles applied on implant surfaces with a plasma spraying technique (TPS) yield a bumpy surface configuration. The results from studies investigating the possible benefits of TPS surfaces have reached different conclusions. In three studies in a goat model by Vercaigne et al. (1998a, 1998b, 1998c), no correlation between surface roughness and implant incorporation could be found. Their three TPS-coated cylindrical implants had R_a values ranging from 16 to 40 μm. Al_2O_3-blasted implants with an R_a of 4.7 μm were used as controls. After 3 months, in goat bone, no significant differences in bone-to-implant contact or pullout strength were found for the four different surfaces. The surface roughness was measured with a stylus profilometer, but no information about profile length or other measuring conditions was included. Therefore, it is difficult to determine whether the TPS surfaces were so much rougher than in other studies investigating the same surface modification. It is of course possible that the investigated surfaces may have been too rough and no further benefit from increasing roughness can be gained.

Other studies have found TPS surfaces to be better integrated in bone compared with smoother implants. Gotfredsen et al. (2000) compared turned, TiO_2-blasted implants of three different roughnesses and TPS surfaces. The R_a was 0.37 μm for the turned, 1.05, 1.16 and 1.45 for the TiO_2 blasted and finally 3.54 μm for the TPS surfaces. Implants were inserted into rabbit tibia for 6, 9 and 12 weeks. TPS and blasted implants demonstrated significantly higher removal torque than the turned implant.

Suzuki et al. (1997) investigated plasma-sprayed titanium implants and so-called machined implants. The roughness R_a was claimed to be 0.7 and 4 μm, respectively, but without mentioning which method was used for the evaluation and without other important information regarding roughness characterization. More bone was found in contact with the TPS implant surface than with machined implant surfaces. The authors postulated the finding to be related to a smaller degree of remodelling around the rough compared with the smoother surface.

Lee et al. (2004) compared smooth surfaces with plasma-sprayed surfaces with and without alkali heat treatment. No topographical evaluation was published. After 4 weeks, in dog bone, the TPS and TPS + alkali heat treatment demonstrated higher pullout strength than the smooth implants. With the study design, it is impossible to determine the topographical influence on osseointegration but most probably the two TPS surfaces were rougher than the so-called smooth surface.

Clinical studies comparing different surface topographies. In clinical reports TPS surfaces have often been found to cause more marginal bone resorption than other minimally to moderately rough surfaces (Roynesdal et al. 1998, 1999; Åstrand et al. 2000; Becker et al. 2000).

An increase in height deviation from 0.7 to 4.7 μm results in a stronger bone response for TPS surfaces but no effect if the roughness is further increased to approximately 10 μm. Clinical researches show some disadvantages with respect to marginal bone resorption around TPS surfaces when compared with turned implants.

Nanometre surface configurations

In vivo electropolished surfaces

Larsson et al. (1996, 1997) investigated electropolished and machined surfaces with and without a thicker oxide layer achieved with anodic oxidation. Machined implants had an R_q value of 30.3 nm and an oxide thickness of 3–5 nm, machined + oxidized implants had an R_q value of 40.8 nm and an oxide thickness of 180–200 nm, electropolished implants had an R_q value of 2.9 nm and an oxide thickness of 2–3 nm and electropolished and oxidized implants an R_q of 2.7 nm and an oxide thickness of 180–200 nm. The topography was measured with AFM with a measuring area of 1 × 1 μm. After 6 weeks the electropolished implants had less bone in contact compared with the other three modifications; however, after 1 year there were no differences.

Pearce et al. (2008) investigated the removal torque of five different surface topographies in a sheep model. The topography was measured with an optical instrument and R_a values were given for polished stainless steel, electropolished titanium, microrough titanium, electropolished titanium alloy (Ti6Al7Nb) and microrough titanium alloy. The R_a varied from 0.09 to 1.04 μm. The alloy was rougher compared with the titanium surfaces irrespective of whether electropolished or microrough surfaces were investigated and the removal torque was higher for the alloys. In this particular study, the aim was to find a surface that allowed for removal of cortical screws and the conclusion was that a better polishing technique would be needed. There was a positive correlation between removal torque and surface roughness.

Mendes et al. (2007) investigated the influence of calcium phosphate nanocrystals on the bone-bonding capability. Double etched Ti and titanium alloy (Ti6Al4V) implants with and without a coating were inserted into rats. The alloy implants demonstrated higher tensile forces than the cp Ti, and the calcium phosphate-coated samples demonstrated higher tensile forces than the non-coated implants. SEM was the only method to investigate the different surface topographies. Although the chemistry and topography may have contributed to the result, chemical investigations gave no proof of chemical bonding. The authors concluded that the nanometre structures had a positive effect on the bone-forming process. A similar conclusion drawn by Meirelles et al. (2008a, 2008b, 2008c) when they, in a series of studies, modified electropolished cylinders and blasted screw-shaped implants with nanometre particles of CaP. The cylindrical implants were also coated with nanometre TiO_2 to differentiate the influence of nanometre structures from the chemical influence. A rabbit model was used in the three above-cited papers and an enhanced bone formation was demonstrated for implants modified with nanometre particles independent of whether those were CaP or TiO_2.

Li et al. (2008) compared oxidized implants with and without nanometre CaP particles in a minipeg model. SEM was the only method used to characterize the surface topography. After 8 weeks an enhanced osseointegration was found for the CaP-coated implants, although no statistical analyses were performed. Goené et al. (2007) inserted microimplants into human maxilla and compared dual-etched surfaces with and without nanometre deposits of Calcium Phosphate. SEM was the only method used to characterize the implant surface. After 4 and 8 weeks, significantly more bone was in contact with the CaP-treated surface.

Clinical studies comparing different surface topographies. No such studies have been found.

So far, few studies exist that have investigated the importance of nanometre structures on implant integration in bone but the few that exist indicate nanometre structures to have an impact on the early bone healing. However, the optimal size and distribution of nanometre particles or pores applied on implant surfaces is still unknown.

Concluding remarks

A huge number of experimental investigations have clearly demonstrated that the bone response is influenced by the implant surface topography. There is a general consensus that roughening the implant surface above the level seen with most turned, milled or polished surfaces (i.e., surfaces quoted as 'machined' in oral implant research) leads to a stronger bone response. However, it is very difficult to compare different studies, particularly because the techniques used for surface topographical characterization vary considerably; hence, a surface that is termed rough in one study may be termed smooth in another. Unfortunately, many studies even omit all attempts to topographical characterization, in the false belief that the surface preparation *per se* will determine the roughness of the implant. In reality, even a machined surface may vary considerably in roughness as is the case for blasted, acid etched or anodized surfaces. Yet other studies use only qualitative techniques such as SEM for surface description without recognizing that such techniques are very imprecise and the present results that may be interpreted quite differently. The few investigators who use appropriate techniques for surface topographical description such as interferometry may use different filtering techniques; hence, different results may be reported of the same surface (Wennerberg 1996; Wieland et al. 2001). Height parameters alone are by far the most quoted parameters, but a proper description of a surface minimally needs to include one height as well as at least one spatial or hybrid parameter, such as Sds% and Sdr (Wennerberg & Albrektsson 2000).

To add to the complexity of surface understanding, interpretations of a tissue response that has altered after changing the surface topography need not necessarily reflect the performed change of the surface alone; when the surface topography is changed, the surface chemistry or physics may change simultaneously, if accidentally. Furthermore, when the surface microtopography is changed, the nanotopography of the same surface also usually changes, even if this was not planned by the investigator. In other words, it is tempting to claim that the bone response to a new, surface-related alteration is what affects its bone response or even its clinical performance; however, reality is more complicated than this. Take, for example, the novel surface characteristics of some of our major oral implant systems; it would seem attractive to accept that OsseoSpeed from Astra Tech presents stronger bone responses than its predecessor TioBlast due to fluoride ions, that Nanotite from 3i presents stronger bone response than its predecessor Osseotite due to a particular nanotopography or that SLActive from Straumann presents a stronger bone response than its predecessor SLA due to hydrophilia of the former implant. In reality, all these new implants differ from their respective predecessors in several instead of one single parameter each; Osseospeed has not only surface-attached fluoride ions, its microroughness as well as its nanoroughness differ from Tioblast; Nanotite not only has a particular nanosurface, its chemistry (HA) as well as its microroughness differ from Osseotite; and SLActive not only has a hydrophilic surface, its microroughness as well as its nanoroughness differ from SLA (Wennerberg & Albrektsson 2009).

One parameter closely related to, if not influenced by, surface microroughness is the surface nanoroughness. However, whereas there are several scientific investigations of surface microroughness, we have incomplete knowledge of the potential influence of the surface nanoroughness.

Admittedly, there are many *in vitro* studies allegedly supporting the importance of nanoroughness for the bone response, but *in vitro* studies lack *in vivo* characteristics such as the delicate balance between osteoblasts and osteoclasts; furthermore, vascular, hormonal and loading influences are lacking in the *in vitro* environment, making it too artificial to allow for any reliable conclusions with respect to generalization of results to the *in vivo* situation. The few *in vivo* studies that support the notion that nanoroughness is of substantial importance for implant incorporation suffer from either artificial study designs or poor control of the influence of other non-topographical surface parameters. Therefore, at the present level of knowledge, whether or not nanoroughness is important for the tissue response to an oral implant remains unknown; it is possible that the discrete changes reported in *in vivo* in fact will be so dominated by surface microroughness in the clinical reality that the nanoindentations play no significant role.

The mechanisms behind an optimal bone response to an S_a level of between 1 and 2 μm and an Sds of 50% (moderate roughness according to Albrektsson & Wennerberg 2004; Wennerberg & Albrektsson 2009) remain largely unknown. Naturally, one hypothesis behind the poor osseointegration of polished, very smooth surfaces may be purely mechanical, friction is too small to allow for proper retention, but may further relate to cells flattening out on such surfaces, which prevents their nutrition. The moderate roughness is optimal due to the perfect fit to connective tissue/bone cells (but if we concentrate on the size of cellular processes, then nanosurfaces would benefit). Very rough surfaces may leave such a distance between peaks that cells perceive them as smooth surfaces. Naturally, the retention of the rough surface may be poor due to purely mechanical reasons too; they will only reach a peak contact with the bone. Skalak & Zhao (2000) even believed that machined implants would show the same strong bone response as moderately rough implants if the former were placed in undersized defects, a possible interpretation if the difference in tissue response between surface microtopographies is entirely due to mechanical reasons. Other possible mechanisms between the different tissue responses to different surface topographies have been presented based on *in vitro* studies with a due uncertainty in interpretation of course. However, what does seem to be certain is that it is possible to present a review such as this one, but any attempt to present meta-analyses of what is known about surface topography based on the published evidence would need to disqualify papers with improper surface characterization, i.e. the great majority of published papers on this topic.

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