Titanium and its alloys in dental implantology

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Pure titanium and titanium alloys for dental purposes

In contemporary prosthodontics, the use of dental implants is as self-evident as any other established method. Titanium (Ti) and its alloys are still the most widely used materials for dental and orthopaedic applications.[1,2] Titanium has good mechanical stability, low density ($4.5\,g/cm^3$), a high strength-to-weight ratio and favourable biocompatibility.[3] Titanium and its alloys have excellent corrosion resistance owing to the thick, insoluble titanium dioxide (TiO_2) layer that forms on the surface within nanoseconds. This layer can restore itself immediately in the presence of water or air should damage occur.[4]

Four grades of unalloyed, commercially pure (CP) Ti are available for dental applications, designated as Grades 1 to 4. These grades are defined by their oxygen and iron content, as these elements have a substantial effect on the mechanical and physical properties of the metal, even in very small concentrations. As the concentration of oxygen or iron increases, the mechanical strength increases in parallel, while ductility decreases.[5] The Ti-6Al-4V alloy (described later) is also referred to as Grade 5. Grades over 5 are not used in dentistry. A comparison of the mechanical properties of CP Ti and its alloys is given in Table 1.

Grades 1 to 4

As already mentioned, the physical characteristics of CP Ti are predominantly influenced by the oxygen and iron content of the material. The increasing grade number expresses a decreasing amount of these "impurities". Therefore, Grade 1 is the softest and most ductile type of CP Ti, while Grade 4 is significantly stronger and less malleable than the lower grades.[5] Of the unalloyed CP Ti grades, Grade 4 has the highest tensile strength and yield strength. Some disadvantages that Grades 1 to 4 have are relatively low mechanical strength, a high Young's modulus and poor wear resistance. Improving the mechanical

properties without reducing biocompatibility is still a challenge.[6]

Grade 5 (Ti–6Al–4V)

CP Ti is not preferable when high stress tolerance is required. Mechanical properties such as implant strength, creep resistance and formability can be improved by alloying Ti with a wide range of elements (e.g. aluminium, Al; vanadium, V; tantalum, Ta; zirconium, Zr). As shown in Table 1, the mechanical properties of Ti alloys are superior to those of Grades 1 to 4, and therefore it comes as no surprise that Grade 5 is the most widely used Ti alloy for biomedical applications.[3]

In spite of its good mechanical features, corrosion wear and ion release (Al, V) initially raised concerns about its applicability in implant dentistry. De Morais et al. investigated the level of these ions released from orthodontic mini-implants and the potential toxicity of these elements.[7] They concluded that, despite the detectable amounts of Ti, Al and V ions, these values remained below the average nutrition uptake of these ions and did not reach the level of toxicity.[7]

A high Young's modulus is also a problem with Grade 5, but the exact value (115 GPa) does not significantly differ from that of the CP grades. Therefore, this should not raise specific concerns regarding this alloy. Different alloying elements have been used to replace Al and V in the Ti-6Al-4V alloy. One example is the use of niobium (Nb) and Zr in the alloy Ti-13Nb-13Zr. This offers the highest strength-to-weight ratio and a reduced Young's modulus (77 GPa), making Ti-13Nb-13Zr optimal for orthopaedic implants.[8] Ti-13Nb-13Zr's possible dental applicability is still under investigation.[9,10]

Adverse reactions to titanium and titanium alloys

Since Ti is a transition metal, allergy or metal hypersensitivity may be a matter of concern.[11–13] In

Properties	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5 (Ti-6Al-4V)	Ti-13Nb-13Zr
Tensile strength (MPa)	240	345	450	550	860	1,030
Yield strength (0.2 % offset; MPa)	170	275	380	485	795	900
Elongation (%)	24	20	18	15	10	15
Reduction of area (%)	30	30	30	25	25	45

Table 1

Tab. 1: Mechanical properties of titanium and its alloys.[5]

spite of Ti's excellent biocompatibility, allergy to this metal can still be observed in dental implant patients, although its prevalence is very low (0.6 %).[14] Some authors still recommend a metal allergy test for patients with previous hypersensitivity of any kind.[15, 16] While we have no gold standard test for detecting Ti allergy, dermal patch tests or in vitro blood tests such as the lymphocyte transformation test or the memory lymphocyte immunostimulation assay (MELISA®) are frequently used methods, even if the results are often ambiguous.[17] It must be added that Ti exposure from personal care products and biomedical implants is common, and still there is no reliable evidence for actual toxicity or true allergic reactions.

Furthermore, according to a review by Javed et al., Ti per se cannot be identified as a cause of allergic reactions in patients with dental implants.[18] In their opinion, it is the occasional and otherwise negligible impurities (i.e. additional elements besides Ti) that trigger hypersensitivity reactions.[18] Harloff et al. examined common dental implant materials (Grade 1 Ti and Ti alloys, including Grade 5) by spectral analysis.[19] Their results showed that all the investigated materials contained low but detectable amounts of various other elements (nickel, chromium, copper, palladium, manganese) that may induce allergic reactions, especially in people with existing metal sensitivity.

Since it is quite rare for a patient's metal allergy to be diagnosed first upon implant placement, failure due to hypersensitivity can be avoided by careful history taking. However, it can happen that the patient denies knowledge of any metal allergy and an allergic reaction occurs nevertheless. The appearance of a rash, urticaria, oedema, mucosal erythema, swelling, or hyperplastic lesions of the soft tissue after implant placement indicates an allergic reaction.[20] In these cases, a corrosion process is occurring in which ions released from the surface form active complexes with proteins and trigger the characteristic reactions.[21] Such cases, however, are rare, and Ti implants for prosthodontic purposes can be considered safe and reliable for the general population.

Dental implant surface modifications

Bulk properties, such as corrosion resistance and modulus of elasticity, which determine the selection of the appropriate biomaterial for the relevant biomedical application, are important for implant success. However, surface properties also play a significant role. First of all, the geometric configuration of the implant should be designed to achieve an extensive bone–implant contact area for faster osseointegration. This in itself, however, is not sufficient. During osseointegration, the outermost layers of the implant interact with the host tissues and cells. Therefore, developing surfaces that enable a shorter healing time and optimal connection between the biomaterial and the surrounding bone is a major focus of research.

In order to achieve that goal, various surface treatments have been developed, generally classified into two major categories: physicochemical and biochemical. A common feature of these treatments is that they leave the bulk properties unchanged and modify only certain target properties of the surface, such as its roughness or chemical composition.[22–24] Here, we give a brief summary of these methods and their resulting surfaces and discuss the sandblasted, large-grit, acid-etched (SLA) method that combines two physicochemical methods.

Physicochemical methods

Physicochemical methods are usually used to increase the implant's surface roughness. Rougher surfaces yield better bone response and higher bone quality than machined/turned surfaces, as demonstrated by histomorphometric studies.[25–27] Wennerberg and Albrektsson classified surfaces according to their roughness (Sa) as follows: smooth (Sa < 0.5 µm), minimally rough (Sa = 0.5–1 µm), moderately rough (Sa > 1–2 µm) and rough (Sa > 2 µm); and concluded that moderately rough surfaces (such as SLA, detailed later) show the most favourable bone responses.[28] The most widely used physicochemical surface treatments are sandblasting, ion implantation, laser ablation, covering with inorganic calcium phosphates and purely chemical methods, like oxidation and acid etching.[24]
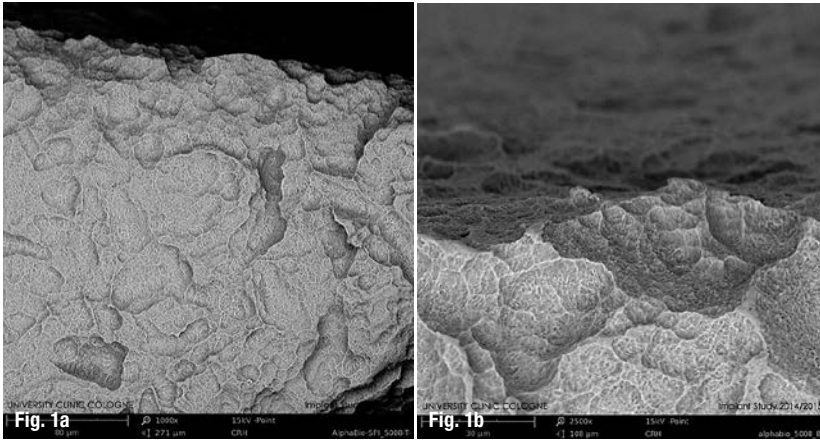
Figs. 1a & b: Scanning electron microscopy images of Alpha-Bio Tec's SLA surface at x 1,000 (a) and x 2,500 (b) magnification.

Biochemical methods

These methods augment the physicochemical processes based on the latest knowledge in biology and biochemistry. The aim is to immobilise various proteins, enzymes and molecules to better control the specific bone–implant interface.[29–31] These molecules can interact with or promote the adsorption of desired proteins to enhance osseointegration. Proteins and/or steroid growth factors have been shown to promote the proliferation of different connective tissue and inflammatory cells.[32,33] Besides promoting the attachment of host cells, the inhibition of bacterial colonisation is desirable and is the focus of intensive research.[34]

In order to prevent the initial attachment of bacteria and biofilm formation, anti-biofouling and bactericidal surfaces have been developed. Anti-biofouling surfaces prevent the initial attachment with specific surface topography or chemistry.[35] In addition, bactericidal surfaces cause the death of the bacterial cell typically on contact.[36] Coatings that release nano-silver, photocatalytic TiO_2 or nitric oxide have been shown to be bactericidal.[37,38]

Sandblasting with large–grit corundum and acid etching

SLA is one of the most widely studied and well-documented Ti implant surface modifiers[39–42] and was originally introduced by Buser et al.[43] As the name suggests, the surface is first sandblasted with large-grit corundum (aluminium oxide) particles, then acid-

etched with hydrochloric acid and sulphuric acid. The result is a moderately rough surface ($Sa \approx 1.5\,\mu m$) characterised by rapid osseointegration and is therefore optimal even for early implant loading.[28] The surface is composed predominantly of TiO_2 with residual Al from the sandblasting process.[44,45] Some studies have reported as high as a 97–100 % success rate with this surface at the five-year follow-up, after early loading at six weeks (Figs. 1a & b).[46,47]

Biocompatibility and clinical applicability of SLA

In vitro studies

Aybar et al. performed an immunohistochemical study of osteoblast-like cells on four different types of Ti discs: SLA1 (Grade 4, Straumann), SLA2 (Grade 5, Alpha-Bio Tec), acid-etched (Grade 5, Alpha-Bio Tec) and machined (Grade 5, Alpha-Bio Tec).[48] Proliferation and DNA synthesis of primary rat calvarial cells were evaluated after one and seven days of incubation. After 24 hours, the highest level of DNA synthesis was observed on SLA1, but after one week, the proliferation of osteoblast-like cells decreased significantly on this surface, while a significant increase of DNA production was observed on the Grade 5 surfaces. In another in vitro study, the adsorption of different human plasma proteins to three different implant surfaces (SLA, machined, acid-etched, Alpha-Bio Tec) was examined. Singh compared polished and SLA surfaces in terms of osteogenetic potential, and found SLA significantly superior (Figs. 2a & b).[55] The quantity and quality of adsorbed plasma proteins (albumin, fibronectin and fibrinogen) was the highest in the SLA group, as demonstrated by enzyme-linked immunosorbent assay and confocal scanning laser microscopy.[49] Implant removal torque testing also resulted in better bone anchorage and higher stiffness values of the SLA surface compared with the machined and acid-etched surfaces.[50]

Clinical studies

Roccuzzo et al. examined 106 implants (53 SLA, 53 control TPS) in 27 patients and found no implant loss after five years' follow-up (100 % success rate).[46] No significant differences were seen in the basic periodontal indices (bleeding on probing, probing pocket depth, bone loss) between the two surfaces,[46] indicating superior biocompatibility. Van Velzen et al. evaluated the ten-year survival of 374 SLA-modified dental implants in 177 patients with special attention to peri-implantitis. The success rate was 99.7 % at the implant level and 99.4 % at the patient level, with 7 % prevalence of symptoms specific to peri-implantitis.[40] In the clinical study of Strietzel et al., the survival of 283 immediately loaded screw-type Alpha-Bio Tec SLA implants was assessed.[47] It was found that,
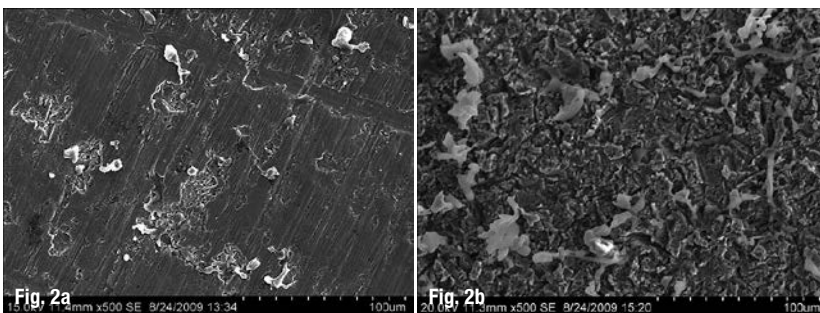
Figs. 2a & b: Scanning electron microscopy images of smooth (a) and SLA (b) surfaces after attachment of human osteosarcoma osteoblast cells.[55]

Authors (year)	Aims of the study	Survival rate (%)	Company	Follow-up
Roccuzzo et al. (2008)	Assessment of the peri-implant condition, early loading	100	Straumann	5 years
Van Velzen et al. (2015)	Long-term survival and incidence of peri-implant disease	99.7	Straumann	10 years
Strietzel et al. (2011)	Comparison of immediately loaded implants (different implant insertion times)	98.2	Alpha-Bio Tec	2.5 years (median)
Artzi et al. (2010)	Success rate of implants loaded immediately after implantation (post-extraction or healed alveoli)	96.9	Alpha-Bio Tec	3 years
Ormianer et al. (2016)	Comparison of long-term bone loss around dental implants with three different thread designs	96.3	Alpha-Bio Tec	107 months (mean)
Kohen et al. (2016)	Comparison of different insertion and loading protocols	95.6	Alpha-Bio Tec, Zimmer Dental, BioHorizons IPH	107 months (mean)

Table 2

Tab. 2: Clinical success rate of SLA-treated dental implants.

regardless of the time of insertion (immediate or delayed), the general survival of these rough-surfaced implants was 98.2 % at follow-up after a median of 2.5 years.

Artzi et al. reported high success rates with immediately loaded, fixed provisional prostheses supported by root form or spiral-shaped Alpha-Bio Tec implants.[51] Of the 676 implants, only 21 (3.1 %) were removed owing to failed osseointegration. The effect of three different implant macrostructure designs on marginal bone loss was compared by Ormianer et al.[52] They investigated 1,361 implants and found the survival rate to be 96.3 %. In their study, one-piece V-thread design implants were associated with the least bone loss and the highest survival rate, probably owing to the absence of micro-gaps between the implant and the abutment. Finally, Kohen et al. reported high implant survival (95.6 %) and minimal bone loss (2.03 mm) in a sample of 1,688 implants, 75 % of which were manufactured by Alpha-Bio Tec.[53] These success rates suggest that the biocompatibility of SLA implants is superior (Tab. 2).

Conclusion

The excellent biocompatibility and physicochemical properties of Ti dental implants position Ti as the gold standard in implant dentistry. While the safety and success of Grade 4 Ti is well documented, Grade 5 offers better physical properties and similarly outstanding biocompatibility and survival. As for the various surface modifications, SLA appears to combine the advantages of the physical and chemical methods successfully, making it a favourable alternative. High levels of osseointegration and favourable long-term survival of SLA dental implants were confirmed by several in vitro and clinical studies. Based on the current literature, we can conclude that Grade 5 Ti with SLA-modified surfaces assures the best dental implantation outcomes. Hypersensitivity or allergic reactions to Ti or other alloy ingredients are extremely rare but still occur, necessitating that the implant dentist be aware of this possibility and pay special attention to the patient's history._
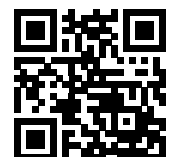
Literature
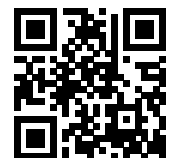
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