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Research Article

Biocompatibility of Dental Implant: Revised

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Abstract

A dental implant is a good example of the integrated framework of science and technology in multiple disciplines, including surface chemistry and physics, biomechanics, from macro-scale to nano-scale manufacturing technologies and surface engineering, among different dental materials and their effective applications. There are important features for dental implant systems, like all other dental materials and products, since the surface of dental implants is directly in contact with vital hard/soft tissue and is subject to both chemical and mechanical bio-environments. Such appliances should include, at the very least, biological compatibility, mechanical compatibility and morphological compatibility with the important tissues surrounding it. Most of the dentists know well biological compatibility but overlook mechanical compatibility, and morphological compatibility. Therefore, this review throws a deliberate sight on these points.

Keywords: Compatibility; Titanium Implants; Biological Compatibility; Mechanical Compatibility; Morphological Compatibility

Introduction

The implantation of equipment for the repair or reconstruction of a body feature imposes exceptional requirements on building materials. The problem of biocompatibility is the most significant among these. Interactions occur between the foreign material and the living tissue, liquid and blood components of the surrounding host. Some of these are adaptive only. Others pose a threat to the survival of the living organism, both in the short and long term [1]. The material must have mechanical and physical characteristics, as well as the structural design that the device should exhibit. Some of these control the device's ability to provide its intended purpose from an engineering perspective. Others, such as tribology (in particular friction and wear), corrosion and mechanical compliance, are significantly linked to the issues of biocompatibility. Applications for human implantation impose more rigorous reliability criteria than any other engineering activity. An implanted device is required to work for the life of the patient in most applications. The lifetime of the product must increase to more than 30 years as the medical profession becomes more emboldened (if follow-up servicing is performed carefully and thoroughly and ex-

cellent patient cooperation is obtained), and very few engineering devices have been designed to function for more than 30 years. In terms of output reliability, it is important to think of thousands of devices for a patient's lifetime and a tolerable expectation of failure of maybe no more than one in one thousand [1,2]. The ability to form a properly stable mechanical unit with the adjoining hard or soft tissues is one of many universal criteria for implants, wherever they are used in the body. A loose implant may operate less effectively or cease to function entirely, or it may cause the tissues to respond abnormally. It may cause the patient discomfort and pain in any case. For implants placed to exhibit biointegration, there are at least three major compatibilities needed to obtain hard tissue and biofucntionality thereafter. These include (1) biological compatibility, (2) mechanical compatibility, and (3) morphological compatibility for host tissue reception [3,4]. The aim of the current mini review was to pay attention of dentists and implantologists to the three pillars of biocompatibility namely: biological, mechanical, and morphological ones.

Biological compatibility (Biocompatibility)

It has been shown that many aspects of the biocompatibility profiles developed for dental implants rely on interrelated biomaterials, tissue, and host factors, which are linked to both surface and bulk properties. Biomaterial surface chemistry can be associated with shorter and longer term *in vivo* host responses, such as purity, surface tension for wetting, topography, and type of tissue incorporation, whether osseous, fibrous, or mixed. In addition, the host environment has been shown to directly affect the biomaterial-to-tissue interface zone unique to the healing and longer-term clinical aspects of load-bearing activity under local biochemical and biomechanical circumstances. The interaction between recipient tissues and implanted material at the interface is confined to the implant surface layer and to a few nanometers in the living tissues. Information of connection (hard or soft tissue) and force transfer resulting in static (stability) or dynamic (instability or motion) conditions have also been shown to substantially alter the clinical longevity of intraoral functional units [5].

Both corrosively and mechanically, the service conditions in the mouth are aggressive. All intraorally located components are continually bathed in saliva, an aerated aqueous solution of approximately 0.1 N chlorides, with varying amounts of mucin, Na, Ca, K, CO2, PO4, and sulphur compounds [6]. The pH value is usually between 5.5 and 7.5, but it may be as low as 2 for plaque deposits. Temperatures can range from ±36.5 °C, and for short periods, a number of food and drink concentrations apply. Loads may be up to 1,000 N (with a normal chewing force of between 150 N and 250 N) [6], often superimposed with impact loads. Trapped food debris can decompose to form sulphur compounds, resulting in discoloration of placed devices [6]. Under such aggressive environments, the biocompatibility of metallic materials is basically equal to corrosion resistance since it is assumed that alloy elements can only penetrate the surrounding organic environment and produce poisonous effects by converting to ions by a chemical or electrochemical phase.

As described above, the success and longevity of the implant placed is strongly controlled by the interface zone between the implant placed and the hard/soft tissue obtained. There are also two main research approaches; one looks at the interface from the material side of the implant, the other from the critical tissue side. Initial healing of the bony compartment after implant placement is characterized by the formation of blood clots at the traumatized wound site and protein adsorption [7]. Then, about two days after implant placement, fibroblasts proliferate into the blood clot, organisation starts, and an extra-cellular matrix is formed. The appearance of osteoblast-like cells and new bone is seen approximately one week after the implant is implanted. Fresh bone reaches the surface of the implant by osseoconduction by bone growth over the surface and bone cell migration over the implant surface [7].

Compared with other alloys, why do titanium and its alloys exhibit such strong biocompatibility?. In general, the answer to this question is that, in aqueous solutions, titanium is passive and the passive film forming on titanium is stable, even in a biological system, including chemical and mechanical environments. In certain instances, such an interpretation is valid. However, when we consider the dynamic interfacial phenomenon between titanium and a biological system, both in biological and biomechanical settings, the existence of the passive film is only part of the solution [8].

For all possible metallic materials, there are many criteria to assess excellent corrosion resistance, including (1) ease of oxidation, (2) strong adhesion of the formed oxide to the substrate, (3) density of the formed oxide and (4) protection of the formed oxide. The Pilling-Bedworth (P-B) ratio is a very simple indicator for determining whether or not the oxide produced is protective [9]. The ox-

ide formed is porous and not protective if the P-B ration is less than 1, since the volume of oxide is smaller than that of the metal. Oxide occupies a large volume when greater than 2 and can flake from the surface, revealing a fresh surface of the substrate that exhibits non-protectiveness. If the P-B ration is between 1 and 2, the oxide volume is close to that of the metal, such that the oxide produced is substrate-adherent, non-porous and protective. The P-B ratio for the formation of TiO2 was estimated at 1.76, which indicates that the TiO2 produced is protective. Titanium is a highly reactive metal which, when exposed to the atmosphere, can react to form an oxide layer within microseconds [10]. While the standard electrode potential was stated for the Ti ↔ Ti3 + electrode reaction in a range from -1.2 to -2.0 volts [11], due to strong chemical affinity to oxygen, a compact oxide film is readily formed, ensuring high metal corrosion resistance. This oxide, which is predominantly TiO2, easily forms because it has one of the highest known reaction heats (ΔH = -915 kJ/mole) (298.16 °-2000 ° K) [12]. Oxygen is also very impenetrable (since Ti's atomic diameter is 0.29 nm, the primary layer of defense is only around 5 to 20 atoms thick) [13]. The developed oxide layer adheres closely to the surface of the titanium substrate. The mean single-bond strength of the TiO2 to Ti substrate was stated to be approximately 300 kcal/mol, whereas for Cr2O3/Cr it was 180 kcal/mol, for Al2O3/Al it was 320 kcal/mol, and for Ta2O5/Ta and Nb2O5/Nb it was 420 kcal/mol [14].

Titanium releases corrosion compounds (primarily titanium oxide or titanium hydro-oxide) into the surrounding tissues and fluids during implantation, even though they are covered by a thermodynamically stable film of oxide [15]. As a function of implantation time an increase in oxide thickness as well as the introduction of elements from the extra-cellular fluid (P, Ca, and S) into the oxide was observed [16]. In addition, *in vitro* releases of titanium corrosion products have been associated with improvements in oxide stoichiometry, structure, and thickness [17]. As factors determining biological performance, oxide properties, such as stoichiometry, defect density, crystal structure and orientation, surface defects, and impurities were suggested [18].

In surgical implant applications, the performance of titanium and its alloys can be examined in relation to their biocompatibility and ability to withstand the corrosive species involved in fluids inside the human body [19]. In an electrochemical reaction, this can be known as an electrolyte. It is well known that titanium materials 'excellent corrosion resistance is due to the formation, as discussed before, of a thick, protective, and strongly-adhered film, which is called a passive film. Such a surface condition refers to passivity or a state of passivation. There is debate about the precise composition and structure of the passive film covering titanium and its alloys. This is the case not only for "natural" air oxide, but also for films formed, as well as those formed anodically, during exposure to different solutions. The 'standard' oxide film on titanium varies in thickness from 2 to 7 nm, depending on factors such as the composition of the metal and the surrounding medium, the maximum temperature obtained during working of the metal and the surface finish. The oxides formed on Ti materials differ according to their general shape; TiOX (1 < x < 2). There are five distinct crystalline oxides depending on the x values, i.e. (1) cubic TiO (ao = 4.24 Å), (2) hexagonal Ti2O3 (ao = 5.37 Å, α = 56°48 '), (3) tetragonal TiO2 (anatase) (ao = 3.78Å, co = 9.50 Å), (4) tetragonal TiO2 (rutile) (ao = 4.58 Å, co = 2.98 Å), and (5) orthorhombic TiO2 (brookite) (ao = 9.17 Å, bo = 5.43 Å, co = 5.13 Å). In addition, (6) non-stoichiometric oxides (when x is not integral) and (7) amorphous oxides are present. Among these oxides, it is generally accepted that only rutile and anatase-type oxides are stable under normal conditions. The choice of rutile formation or anatase formation depends on the acidity of the electrolyte used [20], which is of interest. Various physical properties-interms of surface tension-are demonstrated by the rutile and anatase form oxides. For pure titanium and measured surface contact angles, surface electrochemical potential and roughness, various surface conditions were prepared [21]. The surface covered by the TiO2-type rutile alone was hydrophobic, while the surface covered by the oxide-type rutile and anatase mixture showed hydrophilicity [21].

Using Auger Electron Spectroscopy (AES) to study the shift in titanium surface composition during human bone implantation, the oxide produced on titanium implants has been shown to develop and absorb minerals during implantation [16,22]. Since the adsorbed layer of protein is located on the oxide, growth and uptake occur, meaning that mineral ions move through the adsorbed protein. Using Fourier Transform Infrared Reflection Absorption Spectroscopy (FTIR-RAS), phosphate ions have been shown to be adsorbed to the titanium surface following adsorption of the protein. Using x-ray photoelectron spectroscopy (XPS) [23], oxides from commercially pure titanium and titanium alloy (Ti-6Al-4V) have been shown to convert into complex hydroxyl-containing tita-

nium and calcium phosphate groups binding water by immersion in artificial saliva (pH = 5.2) [24]. Titanium has been shown to be in almost direct contact with bone tissue, differentiated only by an exceptionally thin layer of non-calcified tissue, free of cells. An interfacial hierarchy consisting of a 20-40 nm thick proteoglycan layer within 4 nm of the titanium oxide was exposed by transmission electron microscopy, followed by collagen bundles as near as 100 nm and Ca deposits within 5 nm of the surface [25]. To achieve the steady-state interface described, both the oxide on titanium and the adjacent tissue undergo various reactions. The specific tissue reaction to the materials has been correlated with the physiochemical properties of titanium: these include the biochemistry of released corrosion products, release kinetics and oxide stoichiometry, density of crystal defects, thickness and surface chemistry [26]. All these studies suggest that surface oxides react with mineral ions, water and other constituents of biofluids in titanium materials, and that these reactions, in turn, induce surface remodeling.

In general, as seen in the above, not only does the titanium passivating layer produce good resistance to corrosion, but it also appears to allow physiological fluids, proteins, and hard and soft tissue to come very near and/or deposit directly on it. There are also mostly unknown explanations for this. But it may have something to do with factors like TiO2's high dielectric constant (50 to 170 vs. 4-10 for alumina and dental porcelain), which may result in the bonds of van der Waal on TiO2 considerably stronger than other oxides. The TiO2 oxide film can permit the attachment of a compatible biomolecule layer [27,28].

Mechanical compatibility

Biomechanics engaged in implantology should involve at least the nature of the implant's biting forces, the transition of interfacial tissue biting forces, and the biological reaction of interfacial tissues to conditions of stress transfer. More complex, interrelated issues are interfacial stress transfer and interfacial biology. While several engineering studies have shown that variables such as implant shape, elastic modulus, degree of bonding between implant and bone, etc., can affect stress transfer conditions, the unanswered question is whether there is any biological significance to these variations. The good clinical outcomes obtained with osseointegrated dental implants underscore the fact that these implants can effectively withstand large masticatory loads. Actually, bite forces in patients with these implants have been documented to be comparable to those in patients with natural dentitions. The way in which mechanical stresses are transferred smoothly from the implant to the bone is a crucial feature influencing the success or failure of an implant [29]. Beyond the long-term fatigue ability, it is important that neither implant or bone be stressed. Any relative motion that can produce abrasion of the bone or gradual loosening of the implants must also be avoided. An osseointegrated implant connects the implant directly and relatively stiffly to the bone. This is an advantage because, without any major change in shape or length, it offers a durable design. There is a mismatch between the mechanical properties at the interface of Ti and bone. It is important to note that if the soft layer were between the metal implant and the bone, the shock-absorbing action would be the same from a mechanical perspective. The periodontum that forms a shock-absorbing layer is in this position between the tooth and the jaw bone in the natural tooth [29].

Normal teeth and implants have various characteristics of force transfer to the bone. Compressive strains around natural teeth and implants were caused by static axial loading, while variations of compressive and tensile strains were found during lateral dynamic loading [20,30]. For most regions under all loading conditions, the level of pressure around the natural tooth is slightly lower than for the opposing implant and the occluding implants on the opposite side. It was reported that, under higher loads and especially under lateral dynamic loads, there was a general tendency for increased strains around the implant opposing the natural tooth [31].

Stress-distribution in the bone around implants was measured with and without a stress-absorbing factor by means of finite element (FEM) analysis [32]. Simulations were made with an implant linked to a natural tooth and a freestanding implant. It was noted that the difference in the stress-absorbing portion's elasticity modulus had no effect on the stresses in the freestanding implant's bone. There was little impact on the stresses in the cortical bone when changing the shape of the stress-absorbing feature. A more uniform tension around the implant with a low elasticity modulus of the stress-absorbing factor was the conclusion for the implant connected to a natural tooth and a decrease in peak stress height was shown by the bone surrounding the natural tooth.

The surface area of dental or orthopaedic prostheses should respond to the loading transmission feature. The implant and the

receiving tissues created a distinctive stress-strain field. An interfacial layer should exist between them. During loading with the implant/bone pair, the strain-field continuity should be maintained (if not, it should mean that the implant is not fused to the vital bone), although the stress-field is clearly distinct between the host tissue and the foreign implant material due to different elasticity modulus values (E). That is to say, bone stress B = EB B and implant stress I = EI I. Under the continuous field of strain, εB = εI. However, because of dissimilar material pair condition EB ≠ EI. If the magnitude of the difference in elasticity modulus is high, then the interfacial stress may therefore become so large that a dangerous failure or detachment situation would be faced by implant device. In other words, if interfacial stress is greater than the osteointegrated fused implant retention strength due to stress difference $\Delta\sigma = (\sigma I - \sigma B)$, the positioned impant will fail. Therefore, implant materials or implant surface areas should be mechanically compatible with the mechanical properties (particularly the elasticity modulus) of the receiving tissues to reduce interfacial discrete stress. This is the second compatibility and is referred to as the mechanical compatibility [3,20].

A relationship between yield strength and elasticity modulus of various types of biomaterials and bones that receive useful implant tissue (Figure 1). As can be seen clearly, both log scales have a linear relationship between the strength and rigidity of all biomaterials concerned. From the point of view of strain-continuity, it is ideal to choose any implantable material that has values of strength and rigidity close to those of bone receipt. As both hydroxyapatite (HA) and receiving critical bone have similar chemical compositions, hydroxyapatite coating on titanium implant has been widely adopted, so early adaptation can be strongly expected. At the same time, EHA is positioned between EB and EI values; as a consequence, HA coating will have a second mechanical compatibility function to make the stress a smooth transfer (or to minimize the interfacial stress). This is one of the typical hindsight, as HA-coating is originally performing and still performing due to its chemical composition being similar to bone receiving (Figure 1).

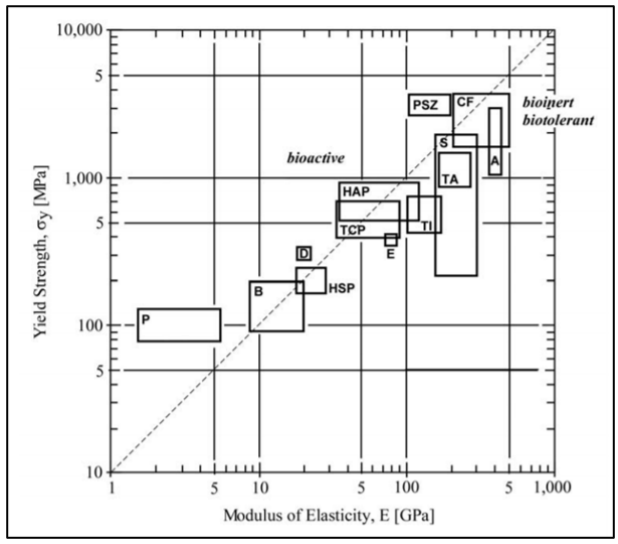

Figure 1: Yield strength and modulus of elasticity relationship of various.

Biomaterials: P: Polymeric Materials, B: Bone, D: Dentin, HSP: High Strength Polymers, E: Enamel, TCP: Tricalcium Phosphate, HAP: Hydroxyapatite, TI: Commercially Pure Titanium, TA: Titanium Alloys, S: 304-Series Stainless Steel, PSZ: Partially Stabilized Zirconia, A: Alumina, CF: Carbon Fiber.

Morphological Compatibility

For four factors, the surface plays a key role in biological interactions [33,34]:

- The biomaterial surface is the only element that is in contact with the bio-environment.
- The surface area of a biomaterial is often distinct in morphology and composition from the bulk as differences arise from molecular rearrangement, surface reaction, and contamination.
- In the case of biomaterials which do not release or leak biologically active or harmful compounds, biological reactions are known to be biological.
- Other surface properties, such as topography, influence the implant/tissue interface's mechanical stability.

The surface morphology of active implants has been found to have upper and lower limitations in mean roughness (1-50 cm) and mean particle size (10-500 cm), irrespective of the form of implant material (either metallic, ceramic or polymeric) [3]. If a particle size is greater than 10 μm, the surface would be more harmful to fibroblastic cells and have an adverse effect on cells, regardless

of any chemical toxic effects, due to their physical presence. The surface zone does not retain adequate structural integrity if the pore is larger than 500 m, since it is too coarse. This is the third compatibility: compatibility with morphology [3,4].

The implant surface preparation methods can significantly affect the resulting surface properties and subsequently the biological responses occurring on the surface [35]. Recent efforts have shown that the success or failure of dental implants can be linked not only to the chemical properties of the surface of the implant, but also to its macromorphological character [36]. From an *in vitro* point of view, surface topography or geometry on a macroscopic basis [36], as well as surface morphology or roughness on a microscopic level [37], can affect the response of cells and tissues at implant interfaces. Undoubtedly, these characteristics influence how cells and tissues respond to different biomaterial forms. Of all the cellular responses, it has been suggested that cellular adhesion is considered to be the most important response needed for the bone/implant interface to develop rigid structural and functional integrity [38]. The entire tissue response to biomaterials is altered by cellular adhesion [39].

The effect of Ti-6Al-4V titanium alloy surface roughness (Ra: 0.320, 0.490 and 0.874 μm) on short-and long-term *in vitro* reaction and protein adsorption of human bone marrow cells was studied [40]. Cell attachment, proliferation of cells, and differentiation (specific activity of alkaline phosphatase) were determined. XPS and radio labeling is used to investigate the protein adsorption of bovine serum albumin and fibronectin from single protein solutions on rough and smooth Ti-6Al-4V surfaces. As the roughness of Ti-6Al-4V increased, cell attachment and proliferation were susceptible to surface roughness and improved; human albumin was ideally adsorbed to a smooth substrate; and higher volumes of total protein (from a culture medium containing 15% serum) and fibronectin (10 times) were bound to the rough substratum than to the smooth one, indicating the importance of rugophilicity [40].

Events leading to the integration of the implant into the bone, and thus to the determination of the device's long-term success, occur mainly at the interface between the tissue and the implant [41]. The architecture of this interface is complex and influenced by several factors, including surface chemistry and foreign material surface topography [42]. Treatment of NiTi at room temperature for 30 seconds by acid-picking in HF-HNO3-H2O (1:1:5 by volume) regulating surface topology and selectively dissolving Ni, resulting in a Ti-enriched surface layer, was a fundamental example of controlling surface topology [43]. The role of surface roughness in the interaction of cells with well-defined topographical titanium model surfaces was investigated by human bone-derived cells (MG63 cells). A kinetic morphological analysis of cell adhesion, spreading, and proliferation was used to study the early phase of interactions.

SEM and double immunofluorescent labeling of vinculin and actin showed that with a higher cell thickness and a delayed appearance of the focal contacts, the cells responded to nanoscale roughness. A peculiar behavior was observed on nanoporous oxide surfaces, where the cells were more extended and displayed longer and more numerous filopods. On electrochemically microstructured surfaces in cavities of 30 or 100 μm in diameter, MG63 cells were able to penetrate, bind and proliferate, while cavities of 10 μm in diameter were not observed. When connecting within the 30 μm diameter cavities, cells took on a 3D form. The results showed that, compared to flat surfaces with the same nanostructure, nano topography on surfaces with 30 μm cavities had little impact on cell morphology, but cell proliferation showed a pronounced synergistic effect of microscale and nanoscale topography [44].

The mechanical properties of the titanium/bone interface, the mechanical interlocking of the interface, and material biocompatibility [45] are influenced by roughness at the macroscopic level (roughness > 10 μm). Surface roughness in the range of 10 nm to 10 mm can also be affected by interfacial biology, as it is the same order as the size of the cells and large biomolecules [10]. At this stage, microroughness involves material defects, such as grain boundaries, measures of dislocation and kinks, and vacancies that are active adsorption sites, thereby affecting the attachment of biomolecules to the implant surface [46]. Microrough surfaces allow slightly better deposition of bone than smooth surfaces, resulting in a higher percentage of bone contact with implants. The mechanical properties of the interface, stress distribution, and bone remodeling [47] can be affected by micro-rough surfaces. Increased contact area and mechanical bone interlocking to a microrough surface can decrease stress levels, resulting in decreased resorption of the bone. Bone resorption occurs shortly after smooth surface implant loading [48], resulting in a coating of fibrous connective tissue, whereas remodelling occurs on rough surfaces [49].

Latest advances in clinical oral implants have focused on topographical improvements in implant surfaces rather than chemical property alterations [35,50]. The presumption that mechanical interlocking between tissue and implant materials depends on surface irregularities at the nanometer to micron level may be based on these attempts. Recent *in vivo* studies have shown considerable improvement in bone tissue reactions by altering the surface oxide properties of Ti implants [51,52]. In animal experiments with oxidized titanium implants, the titanium oxide layer thicker than 600 nm, the porous surface structure and the Ti oxide anatase have been shown to be strongly reinforced in bone tissue reactions, separated with high surface roughness compared to implants that have been turned [51]. This was later confirmed by other researchers who found that the alkali-treated surface of CpTi was predominantly covered with TiO2 anatase and exhibited hydrophilicity, while the acid-treated surface of CpTi was hydrophobic with TiO2 rutile [35,53,54]. In addition to this characteristic crystalline TiO2 structure, it was noted that the heavy osseointegration, bony apposition and cell attachment of Ti implant systems [55] is partly due to the fact that the oxide layer may be the responsible characteristic, with an extremely high dielectric constant of 50-170 depending on the TiO2 concentration [27,28].

Conclusions

A dental implant device uses various disciplines, including surface science and technology, surface alteration and surface physics and chemistry, as a typical and excellent example of an integrated product. Surface characteristics strongly governed the success and longevity of dental implants to accommodate ossteointegration. Factors that successful implants need to have a) not toxic to hard and soft tissues surrounding them (biological compatibility), b) smooth transmission of stress between the implant root and the hard tissue receiving it (mechanical compatibility), and c) accommodate surface rugophilicity and encourage growth of bony cells (morphological compatibility) [56].

Conflict of Interest

No conflict of interest to declare.

Bibliography

1. Brunski JB., *et al*. "Biomaterials and biomechanics of oral and maxillofacial implants: Current status and future developments". *The International Journal of Oral and Maxillofacial Implants* 15 (2000): 15-46.
2. Bannon BP and Mild EE. "In Titanium Alloys in Surgical Implants". Luckey, H.A.; Kubli, F., Ed.; ASTM STP 796, American Society for Testing and Materials: West Conshohocken, PA, USA (1983): 7-15.
3. Oshida Y., *et al*. "Fractal dimension analysis of mandibular bones: Toward a morphological compatibility of implants". *Bio-Medical Materials and Engineering* 4 (1994): 397-407.
4. Oshida Y. "Requirements for successful biofunctional implants". In The 2nd Symposium International of Advanced Bio-Materials; Montreal, Canada (2000): 5-10.
5. Lemons JE. In Contemporary Implant Dentistry. Misch, C.E., Ed.; Mosby, Inc.: St. Louis, MO, USA Chapter 20 (1999): 286-287.
6. Brockhurst PJ. "Dental Materials: New teritories for materials science". (1980): 200-210.
7. Steinmann SG. In Evaluation of Biomaterials. Winter, G.D., Leray, J.L., de Groot, K., Eds.; John Wiley and Sons: New York, NY, USA (1980): 1-34.
8. Greene ND. In Corrosion and Degradation of Implant Materials: Second Symposium. Farker, A.C., Griffin, C.D., Ed.; ASTM STP 859, American Society for Testing and Materials: West Conshohocken, PA, USA (1983): 5-10.
9. Kubaschewski O and Hopkin BE. In Oxidation of Metals and Alloys. Butterworths: London, UK (1962): 38-45.
10. Kasemo B. "Biocompatibility of titanium implants: Surface science aspects". *Journal of Prosthetic Dentistry* 49 (1983): 832-837.
11. Tomashov ND. "Theory of Corrosion and Protection of Metals: The Science of Corrosion". The MacMillan: New York, NY, USA (1966).
12. Ashby MF and Jones DRH. "Engineering Materials. An Introduction to Their Properties and Applications". Pergamon Press: New York, NY, USA (1980): 194-200.
13. Lautenschlager EP and Monaghan P. "Titanium and titanium alloys as dental materials". *International Dental Journal* 43 (1993): 245-253.

14. Coddet C., *et al*. "Measurements of the adhesion of thermal oxide films: Application to the oxidation of titanium". *Journal of Materials Science* 22 (1987): 2969-2974.

15. Ducheyne P., *et al*. "In vivo metal-ion release from porous titanium-silver material". *Journal of Biomedical Materials Research* 18 (1984): 293-308.

16. Sundgren JE., *et al*. "Auger electron spectroscopic studies of the interface between human tissue and implants of titanium and stainless steel". *Journal of Colloid and Interface Science* 110 (1986): 9-20.

17. Ducheyne P., *et al*. In Surface Characterization of Biomaterials. Ratner, B.D., Ed.: Elsevier Science: Amsterdam, Holland (1988): 175-192.

18. Albreksson T and Hansson HA. "An ultrastructural characterization of the interface between bone and sputtered titanium or stainless steel surfaces". *Biomaterials* 7 (1986): 201-205.

19. Solar RJ. In Corrosion and Degradation of Implant Materials. Syrett, B.D., Ed.; ASTM STP 684, American Society for Testing and Materials: West Conshohocken, PA, USA (1979): 259-273.

20. Oshida Y. "Bioscience and Bioengineering of Titanium Materials". Elsevier: Amsterdam, Holland (2007): 217-253.

21. Lim YJ., *et al*. "Surface characterizations of variously treated titanium materials". *The International Journal of Oral and Maxillofacial Implants* 16 (2001): 333-342.

22. McQueen D., *et al*. In Clinical Applications of Biomaterials. Lee, A.J.C., Ed.; Wiley: New York, NY, USA (1982): 179-185.

23. Liedberg B., *et al*. "Fourier transform infrared reflection absorption spectroscopy (FTIR-RAS) of fibrinogen adsorbed on metal and metal oxide surfaces". *Journal of Biochemical and Biophysical Methods* 9 (1984): 233-243.

24. Hanawa T. In The Bone-Biomaterial Interface. Davies, J.E., Ed.; Univ. of Toronto Press: Toronto, ON, Canada (1991): 49-61.

25. Healy KE and Ducheyne P. "Hydration and preferential molecular adsorption on titanium in vitro". *Biomaterials* 13 (1992): 553-561.

26. Healy KE and Ducheyne P. "The mechanisms of passive dissolution of titanium in a model physiological environment". *Journal of Biomedical Materials Research* 26 (1992): 319-338.

27. Brånemark PI. In Tissue-Integrated Protheses. Brånemark, P.I., Ed.; Quintessence Pub.: Chicago, IL, USA, 1985): 63-70.

28. Kasemo B and Lausmaa J. In Tissue-Integrated Protheses. Brånemark, P.I., Ed. Quintessence, Chicago, IL, USA (1985): 108-115.

29. Skalak R. "Biomechanical considerations in osseointegrated prostheses". *Journal of Prosthetic Dentistry* 49 (1983): 843-848.

30. Oshida Y and Tuna EB. In Advanced Biomaterials. Basu, B., Ed.; Wiley: Hoboken, NJ, USA, Chapter 5 (2009): 143-177.

31. Hekimoglu C., *et al*. "Analysis of strain around endosseous implants opposing natural teeth or implants". *Journal of Prosthetic Dentistry* 92 (2004): 441-446.

32. van Rossen IP., *et al*. "Stress-absorbing elements in dental implants". *Journal of Prosthetic Dentistry* 64 (1990): 198-205.

33. Eriksson C., *et al*. "Intercations between human whole blood and modified TiO2-surfaces: Influence of surface topography and oxide thickness on leukocyte adhesion and activation". *Biomaterials* 22 (2001): 1987-1996.

34. Wen X., *et al*. "Microsurface of metallic biomaterials: A literature review". *Journal of Biomedical Materials Research* 6 (1996): 173-189.

35. Keller JC., *et al*. "Characterization of sterilized CP titanium implant surfaces". *The International Journal of Oral and Maxillofacial Implants* 5 (1990): 360-369.

36. Buser D., *et al*. "Interface shear strength of titanium implants with a sandblasted and acid-etched surface: A biomechanically study in the maxilla of miniature pigs". *Journal of Biomedical Materials Research* 45 (1999): 75-83.

37. Murray DW., *et al*. "The influence of the surface energy and roughness of implants on bone resorption". *Journal of Bone and Joint Surgery* 71B (1987): 632-637.

38. Cherhoudi B., *et al*. "Effects of a grooved epoxy substratum on epithelial behavior in vivo and in vitro". *Journal of Biomedical Materials Research* 22 (1988): 459-477.

39. von Recum AF. In Clinical Implant Materials. Heimke, G., Soltesz, U., Lee, A.J.C., EdS.; Elseveier Science Pub.: Amstrdam, The Netherlands (1990): 297-302.

40. Deligianni DD., *et al*. "Effect of surface roughness of the titanium alloy Ti-6Al-4V on human bone marrow cell response and on protein adsorption". *Biomaterials* 22 (2001): 1241-1251.

41. Yang Y., *et al*. "Protein adsorption on titanium surfaces and their effect on osteoblast attachment". *Journal of Biomedical Materials Research Part A* 67 (2003): 344-349.

42. Masuda T., *et al*. "Generalizations regarding the process and phenomenon of osseointegration. Part I. In vivo studies". *The International Journal of Oral and Maxillofacial Implants* 13 (1998): 17-29.

43. Oshida Y., *et al*. "Microanalytical characterization and surface modification of NiTi orthodontic archwires". *Bio-Medical Materials and Engineering* 2 (1991): 51-69.

44. Zinger O., *et al*. "Time-dependent morphology and adhesion of osteoblastic cells on titanium model surfaces featuring scale-resolved topography". *Biomaterials* 25 (2004): 2695-2711.

45. Baro AM., *et al*. "Characterization of surface roughness in titanium dental implants measured with scanning tunneling microscopy at atmospheric pressure". *Biomaterials* 7 (1986): 463-466.

46. Moroni A., *et al*. "Histomorphometry of hydroxyapatite coated and uncoated porous titanium bone implants". *Biomaterials* 15 (1994): 926-930.

47. Keller JC., *et al*. "Quantitative bone remolding resulting from the use of porous dental implants". *Journal of Biomedical Materials Research* 21 (1987): 305-319.

48. Pilliar RM., *et al*. "Dental implant design-effect on bone remodeling". *Journal of Biomedical Materials Research* 25 (1991): 467-483.

49. Gilbert JL and Berkery CA. "Electrochemical reaction to mechanical disruption of titanium oxide films". *Journal of Dental Research* 74 (1995): 92-96.

50. Sul YT. "The significance of the surface properties of oxidized titanium to the bone response: Special emphasis on potential biochemical bonding of oxidized titanium implant". *Biomaterials* 24 (2003): 3893-3907.

51. Sul YT., *et al*. "Resonance frequency and removal torque analysis of implants with turned and anodized surface oxide". *Clinical Oral Implants Research* 13 (2002): 252-259.

52. Sul YT., *et al*. "Oxidized titanium screws coated with calcium ions and their performance in rabbit bone". *The International Journal of Oral and Maxillofacial Implants* 17 (2002): 625-634.

53. Oshida Y. "Surface science and technology – Titanium dental implant systems". 5 (2007): 52-53.

54. Elias CN., *et al*. "Relationship between surface properties (roughness, wettability and morphology) of titanium and dental implant torque". *Journal of the Mechanical Behavior of Biomedical Materials* 1 (2008): 234-242.

55. Lausmaa GJ. "Chemical composition and morphology of titanium surface oxides". *MRS Online Proceedings Library (OPL)* 55 (1986): 351-359.

56. Oshida Y. "Bioscience and Bioengineering of Titanium Materials". Elsevier, Amsterdam, Holland (2007): 406-411.