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Biocompatibility of Dental Implants: Literature Review

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Abstract

Over the past few decades, the installation of dental implants replacing lost teeth has become a common clinical practice in the field of dentistry. The osseointegration of these implants has been marked as a complex procedure where the surfaces of the implant objects play a crucial role. In this literature review, we aim to review aspects of dental implants biocompatibility. Dental implants can be chemically classified into three groups including metals, ceramics, and polymers, while biologically they can be classified into being bio-tolerant, bioinert, and bioactive. Any of these materials are subjected to both In vitro and In vivo testing before being validated for human consumption. In vitro approach can be used for the assessment of cytotoxicity, cell function, cell growth, and mutagenesis. In vivo approach is generally done to validate the biocompatibility and safety of the dental implants in a biological environment that may be similar to human biology. In general, they can be used to assess whether the implants can introduce any kind of harm to the underlying tissues in patients where these devices are installed.

Keywords: *Implant; Dentistry; Biocompatibility; In Vitro; In Vivo; Implantology*

Introduction

Over the past few decades, the installation of dental implants replacing lost teeth has become a common clinical practice in the field of dentistry. The osseointegration of these implants has been marked as a complex procedure where the surfaces of the implant objects play a crucial role [1]. Besides, irregularities that have arithmetic roughness parameters [Ra or Sa] have been associated with the favorable use of rough surfaces for the process of osseointegration. These irregularities are usually found to be 1 - 2 µm nearly with an existed surface area ratio (Sdr) that is rising 50% [2,3]. To get better outcomes regarding the process of biochemical anchoring in the target bone tissue, grit blasting together with acid etching (H2SO4/HNO3), and alumina particles (Al2O3). This process has been found to render the

surfaces of most dental implants rough. Alumina particles have also been found to contaminate the implant surfaces which can decrease the osteointegration and biocompatibility of the used implants [4-11].

Among the variously reported dental implants, not all of them are biocompatible. Implants derived from calcium phosphate biomaterials are similar to the bone tissue and derivatives, and therefore, these materials have been deemed compatible. In particular, biphasic calcium phosphate (BCP), or hydroxyapatite (HA) beta-tricalcium phosphate (TCP) has been reportedly compatible with favorable outcomes that are attributable to being able to interact with the underlying bony materials following implantation [12, 13]. These biomaterials have been used to fill the bones as synthetic porous materials for many years. Additionally, they have shown the tendency to dissolve in acids which can be used to eliminate the entrapped foreign bodies in the applied titanium surfaces that were used in the process of tissue grafting. This novel approach of using calcium phosphates has shown great potential in increasing the profiles of mean height on the roughness of the used implants [14].

Not many studies have investigated the biocompatibility of such approaches in the recent literature. Branemark *et al*. [15] have conducted several observations and based on these, they come to a definition of osseointegration as being a stable and direct anchorage installation of a previously determined implant by forming a bony tissue with no potential fibrosis formation at the site of the implant installment. Determinants of osseointegration of the dental implants are various including the shape, and materials, and the proper use of surface modifications [16]. These implants should also achieve certain characteristics regarding the function, physiology, and satisfaction, by which they can be deemed successful and biocompatible [17]. In this literature review, we aim to review aspects of dental implants biocompatibility.

Methods

A systematic search was conducted to identify relevant studies in the following databases: PubMed, Medline, Web of Science, Embase, Google Scholar, and Scopus. As appropriate, the search was conducted using the medical subject headings (MeSH) or a combination of all possible related terms. Moreover, reference lists were manually searched to identify additional relevant studies meeting inclusion criteria. Papers discussing the aspects of dental implants biocompatibility were screened for relevant information. No restrictions were applied.

Types of dental implant materials

Dental implants can be chemically classified into three groups including metals, ceramics, and polymers, while biologically they can be classified into being intolerant, bioinert, and bioactive [18,19]. All of the identified metals are either tolerant [gold, cobalt-chromium alloys, stainless steel, zirconium, niobium, tantalum] or bioinert (commercially pure titanium, titanium alloy (Ti-6Al-4V), but none of them are bioactive. On the other hand, ceramics are bioinert and bioactive and are not tolerant while polymers are tolerant only [20,21]. On a clinical aspect, two major implants materials are widely used clinically. These include the Ti-6Al-4V and the commercially pure titanium [22]. Previous reviews found in the literature have summarized the types and classification of these materials in more specific details [23,24].

Biocompatibility meaning and measures

The general definition of biocompatibility is the ability of the introduced or installed object to biologically interact with the cells of the body without causing any pathological concerns. Therefore, it is generally accepted that some materials can not be biologically compatible with certain body applications. Consequently, considering the introduced object biologically compatible or not depends mainly on the physical function of this object in the body and playing the role it was meant for. For instance, osseointegration is considered as the appropriate biocompatibility function of dental implants. The measurement of dental implants biocompatibility is a complex process. However, novel methods are always generated with better approaches due to the increasing advancements in this field as technologies

that assess the interaction between implants and oral tissues enhance over time. A variety of measurements are being used in this field to ensure the biocompatibility of the objects for implantation. These include *in vitro*, *in vivo*, and usage tests [24].

In vitro evaluation approaches

This method requires the introduction of the implant materials of their components into an *in vitro,* and isolated biologically-like system including an enzyme, cell, and other environments that can be obtained from other living organisms and modified according to the intended test. The process can be done directly or indirectly and materials applied in the direct approaches can be used physically, as a whole, or by using a sample [or extract] from this material and applying it. This approach can be used for the assessment of cytotoxicity, cell function, cell growth, and mutagenesis [25,26]. Moreover, many advantages have been reportedly associated with modality. These include the fact that they are relatively quicker, can be standardized, and are cost-effective when compared to animal approaches. Moreover, they are efficacious in large-scale screening; unlike other modalities. However, there one major disadvantage which may hold-back the use of these modalities as *in vitro* assays have been observed to non-relevant to the final *in vivo* application of the test outcome. Other disadvantages as the shortages of anti-inflammatory and tissue-protective mechanisms in these media and cannot be used alone to judge the biocompatibility of the used materials [27].

Standardization and cells used for *in vitro assays*

This process has been marked as a primary concern process that requires attention. The cells used for *in vitro* approaches are either primary single cells or cell lines that are continuously growing cells. The primary cells can be obtained directly from animals and are then cultured to grow for some time and are always consistent with the characteristics of the *in vivo* approaches. These cells have also been observed to be more efficacious than cell line modalities in measuring cytotoxicity outcomes. However, these modalities usually lose their *in vivo* properties once cultures or early after, and their functions can also be altered by viral or bacterial infections based on their unified sources and the limitation of their genetic variability [27]. On the other hand, cell lines may overcome these advantages as they periodically divide although the main disadvantage for these modalities would be losing the *in vivo* characteristics. Based on these features, these cells have been effectively used in standardization methods for assessment of the genetic and metabolic stability. Among the various cell lines that were reported for this purpose, human fetal osteoblast cell line 1.19 (hFOB 1.19) has been reported to play a homogenous and rapidly proliferating medium that can be used for assessment of normal osteoblastic differentiation and physiology in addition to other hormonal and growth factors and other aspects that can alter the normal osteoblastic activity and differentiation [28]. In the same context, immortalized human gingival fibroblasts (hTERT) has also been reported to assess the biocompatibility of the applied dental materials in addition to their cytotoxic effect [29]. Both primary, single, and cell lines should be used simultaneously for *in vitro* assessment modalities.

Cell adhesion, viability, and proliferation

After completing the process of implantation, another challenge regarding cell adhesion, protein adsorption, and bacterial adhesions rises and should be considered [30]. The focal adhesions and desmosomes are the responsible structures for adhesions to occur between the host cells and the implanted substances. Besides, various treatment modalities have been proposed to enhance the adhesion processes by improving the biological characteristics of these structures. On the surface of the host cells, cell-matrix adhesions play a crucial role in this process and the underlying interactions [31]. They have been identified to play major roles in cell migration, rolling, differentiation, homeostasis, and tissue remodeling. Integrins, among other cell-matrix adhesion proteins, have been well-studied and reported to play major roles in the process of adhesion [32]. The evaluation of these adhesions can be done through immunohistochemistry techniques that can successfully detect whether the antigen is expressed and biocompatible in the body or not which may detect any abnormalities that lead to implant rejections and other complications in the long run. Assessment of biocompatibility can be also done through cell-

based assays. These assays can be used to determine whether the *in vitro* implanted cells are vital for implantation and present with no serious side effects as cytotoxicity and subsequent cell death. They have been proven as successful measurements for signal transduction and receptor binding, organ functions, genetic expression, and monitoring of cellular components [24]. A substantial essay to this one also includes the identification of healthy cells that were viable by the end of the implantation process. The MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide] is one of the commonest essays that has been widely used in *in vitro* experiments. This essay is based on the biological conversion of MTT into formazan crystals, and through which the mitochondrial activity can be determined. Consequently, this method has been used to study the effect of many materials on the mitochondrial activity, and the subsequent events as cytotoxicity, and therefore, it was considered an efficient way for assessing the biocompatibility of implants within *in vitro* experiments [7, 12, 24].

In vivo evaluation approaches

This approach is generally done to validate the biocompatibility and safety of dental implants in a biological environment that may be similar to human biology. In general, they can be used to assess whether the implants can introduce any kind of harm to the underlying tissues in patients where these devices are installed. The process can be done by the inoculation of a matrix from the intended implant in an animal. Certain measures should be considered for the validity of such testing as making sure that the used sample is the same as the used dental implants. Besides, the used samples should have relative size and surface textures. The obtained sample can be inoculated within a muscle or a cortical bone.

Osseointegration of dental implants

The definition of these characteristics can be summarized in the presence of a direct connection between the dental implant (which must be endosseous, load-carrying on a microscopic level), and the underlying bone tissue [24]. Besides, Albrektsson *et al*. [33] proposed another definition assessing the function and tolerability of dental implants. The authors defined osseointegration by being an asymptomatic process that is based on a time-dependant pattern of healing with the achievement and maintenance of alloplastic materials rigid fixation in the underlying bone tissues on a functional level. Healing of bone directly, or following a primary lesion, or as osseointegration can be done by an automatic activation by the presence of any lesion in the underlying bony tissue. This happens as growth factors and non-collagenous proteins, which take part in the healing process, are released from the underlying lesion in the bony matrix when it is exposed to the surrounding extracellular matrix. Following this process, osseointegration is then activated following this biologically-based pathway that can be divided into three stages: [1] being incorporated through the formation of woven bone, [2] adaptation and deposition of parallel and lamellar-fibred bony dispositions, [3] remodeling of bones by adaptation of the bone structures [34]. This process also requires several factors including the primary stability of the pre-existing bony materials, and the facilitation of the regenerator materials to be deposited in the lesion that is caused by the implant materials. Integrated dental implants, therefore, achieve biocompatibility, stability, and load-bearing.

Bone-implant contact (BIC)

This modality has been widely used in the assessment of dental implants on a histomorphometric analysis and is defined as the proportion of the mineralized surface areas of the bones that come in contact with the surfaces of the dental implants. This approach can be used to describe this area as it was not stated in the osseointegration definition. By histomorphometric assays, it can be used for measuring the extent of osseointegration and the fraction of the healed dental implants by measuring the BIC percentages. In situ sections of a dental implant, grounds are deemed relatively thick ones comprising around 20-40 µm which makes it difficult to obtain many sections using a bone-implant block. Moreover, the appearance of the shadow effect at the periphery of the used sections indicates the fact that bone-implant blocks have been thoroughly cut [35]. Previous *in vivo* animal studies showed that better anchorage in the bone tissue was obtained by dental implants with relatively roughened surfaces together with obtaining better BIC percentages when compared to other

dental implants with smoother surfaces [36, 37]. These results were also reported by human studies which showed similar results [38-41]. Installment of titanium dental implants with relatively rough surfaces successfully in the clinical practice has been marked as the cornerstone for inaugurating additional novel topographies to enhance peri-implant osseointegration.

Conclusion

In conclusion, dental implants have been gaining increasing popularity among clinicians over the past years and can be used as the first line of treatment. Many types of dental implants have been identified with different biological characteristics and favorable outcomes. For a dental implant to succeed, the right and suitable material should be determined at first. Evaluation of the implant materials can also be done through a variety of methods before being validated for human consumption. Moreover, previous *in vivo* animal studies showed that better anchorage in the bone tissue was obtained by dental implants with relatively roughened surfaces together with obtaining better BIC percentages when compared to other dental implants with smoother surfaces.

Bibliography

1. Le Guéhennec L., *et al.* "Surface treatments of titanium dental implants for rapid osseointegration". *Dental Materials* 23.7 (2007): 844-854.

2. Wennerberg A and Albrektsson T. "On implant surfaces: a review of current knowledge and opinions". *International Journal of Oral and Maxillofacial Implants* 25.1 (2010): 63-74.

3. Wennerberg A and Albrektsson T. "Suggested guidelines for the topographic evaluation of implant surfaces". *International Journal of Oral and Maxillofacial Implants* 15.3 (2000): 331-344.

4. Balshe AA., *et al.* "A Retrospective Study of the Survival of Smoothand Rough-Surface Dental Implants". *International Journal of Oral and Maxillofacial Implants* 24.6 (2009): 1113-1118.

5. Doundoulakis JH. "Surface analysis of titanium after sterilization: role in implant-tissue interface and bioadhesion". *Journal of Prosthetic Dentistry* 58.4 (1987): 471-478.

6. Kim Y-H., *et al.* "A histomorphometric analysis of the effects of various surface treatment methods on osseointegration". *International Journal of Oral and Maxillofacial Implants* 18.3 (2003): 349-356.

7. Mathieu LM., *et al.* "Architecture and properties of anisotropic polymer composite scaffolds for bone tissue engineering". *Biomaterials* 27.6 (2006): 905-916.

8. Müeller WD., *et al.* "Evaluation of the interface between bone and titanium surfaces being blasted by aluminium oxide or bioceramic particles". *Clinical Oral Implants Research* 14.3 (2003): 349-356.

9. Piattelli A., *et al.* "Histologic and histomorphometric analysis of the bone response to machined and sandblasted titanium implants: an experimental study in rabbits". *International Journal of Oral and Maxillofacial Implants* 13.6 (1998): 805-810.

10. Engel E., *et al.* "Streptococcus sanguinis adhesion on titanium rough surfaces: effect of shot-blasting particle". *Journal of Materials Science: Materials in Medicine* 22.8 (2011): 1913-1922.

11. Yurttutan ME and Keskin A. "Evaluation of the effects of different sand particles that used in dental implant roughened for osseointegration". *BMC Oral Health* 180.1 (2018): 47.

12. Lin A., *et al.* "The role of titanium implant surface modification with hydroxyapatite nanoparticles in progressive early bone-implant fixation *In vivo"*. *International Journal of Oral and Maxillofacial Implants* 24.5 (2009): 808-816.

13. Poulos NM., *et al.* "Evaluation of a Novel Calcium Phosphate-Coated Titanium Porous Oxide Implant Surface: A Study in Rabbits". *International Journal of Oral and Maxillofacial Implants* 26.4 (2011): 731-738.

14. Citeau A., *et al.* "*In vitro* biological effects of titanium rough surface obtained by calcium phosphate grid blasting". *Biomaterials* 26.2 (2005): 157-165.

15. Brånemark PI., *et al.* "Intra-osseous anchorage of dental prostheses. I. Experimental studies". *Scandinavian Journal of Plastic and Reconstructive Surgery* 3.2 (1969): 81-100.

16. Wang W., *et al.* "Recent Applications of Nanomaterials in Prosthodontics". *Journal of Nanomaterials* (2015): 408643.

17. Esposito M., *et al.* "Biological factors contributing to failures of osseointegrated oral implants, (I). Success criteria and epidemiology". *European Journal of Oral Sciences* 106.1 (1998): 527-551.

18. Osborn JF and Newesely H. "The material science of calcium phosphate ceramics". *Biomaterials* 1.2 (1980): 108-111.

19. Legeros R and Craig R. "Strategies to affect bone remodeling: Osteointegration". *Journal of Bone and Mineral Research: The Official Journal of the American Society For Bone and Mineral Research* 8.2 (2009): S583-S596.

20. Sykaras N., *et al.* "Implant materials, designs, and surface topographies: their effect on osseointegration. A literature review". *The International Journal of Oral and Maxillofacial Implants* 15.5 (2000): 675-690.

21. Ellingsen J., *et al.* "Advances in dental implant materials and tissue regeneration". *Periodontology 2000* 41 (2006): 136-156.

22. Ananth H., *et al.* "A Review on Biomaterials in Dental Implantology". *International Journal of Biomedical Science: IJBS* 11.3 (2015): 113-120.

23. Saini M., *et al.* "Implant biomaterials: A comprehensive review". *World Journal of Clinical Cases* 3 (2015): 52-57.

24. Moztarzadeh A. "Biocompatibility of Implantable Materials Focused on Titanium Dental Implants (2017).

25. Saini M., *et al.* "Implant biomaterials: A comprehensive review". *World Journal of Clinical Cases* 3.1 (2015): 52-57.

26. Alghamdi HS. "Methods to Improve Osseointegration of Dental Implants in Low Quality (Type-IV) Bone: An Overview". *Journal of Functional Biomaterials* 9.1 (2018): 7.

27. Schmalz G and Garhammer P. "Biological interactions of dental cast alloys with oral tissues". *Dental Materials* 18.5 (2002): 396-406.

28. Harris SA., *et al.* "Development and characterization of a conditionally immortalized human fetal osteoblastic cell line". *Journal of Bone and Mineral Research* 10.2 (1995): 178-186.

29. Kwon Y-D., *et al.* "Cellular viability and genetic expression of human gingival fibroblasts to zirconia with enamel matrix derivative (Emdogain®)". The journal of advanced prosthodontics 6 (2014): 406-414.

30. Gristina AG., *et al.* "Biomaterial-Centered Infections: Microbial Adhesion versus Tissue Integration". In: Wadström T, Eliasson I, Holder I, Ljungh Å, editors. Pathogenesis of Wound and Biomaterial-Associated Infections. London: Springer London (1990): 193-216.

31. Sitbon Y. "Epithelial cells attachment on five different dental implant abutment surface candidates (2009).

32. Li Z., *et al.* "Molecular mechanisms of mechanotransduction in integrin-mediated cell-matrix adhesion". *Experimental Cell Research* 349.1 (2016): 85-94.

33. Albrektsson T., *et al.* "The long-term efficacy of currently used dental implants: A review and proposed criteria of success". *The International Journal of Oral and Maxillofacial Implants* 1 (1986): 11-25.

34. Parithimarkalaignan S and Padmanabhan TV. "Osseointegration: an update". *The Journal of the Indian Prosthodontic Society* 13.1 (2013): 2-6.

35. Rahbek O., *et al.* "Sealing effect of hydroxyapatite coating on peri-implant migration of particles: An Experimental Study In Dogs". *The Journal of Bone and Joint Surgery British* 83 (2001): 441-447.

36. Cordioli G., *et al.* "Removal torque and histomorphometric investigation of 4 different titanium surfaces: an experimental study in the rabbit tibia". *The International Journal of Oral and Maxillofacial Implants* 15.5 (2000): 668-674.

37. Piattelli M., *et al.* "Bone Response to Machined and Resorbable Blast Material Titanium Implants: An Experimental Study in Rabbits". *The Journal of Oral Implantology* 28 (2002): 2-8.

38. Khang W., *et al.* "A Multi-Center Study Comparing Dual Acid-Etched and Machined-Surfaced Implants in Various Bone Qualities". *Journal of Periodontology* 72 (2001): 1384-1390.

39. Davarpanah M., *et al.* "A Prospective Multicenter Evaluation of 1,583 3i Implants: 1- To 5-year Data". *The International Journal of Oral and Maxillofacial Implants* 17 (2001): 820-828.

40. Trisi P., *et al.* "Bone-implant contact and bone quality: evaluation of expected and actual bone contact on machined and osseotite implant surfaces". *The International Journal of Periodontics and Restorative Dentistry* 22.6 (2002): 535-545.

41. Trisi P., *et al.* "Bone-Implant Contact on Machined and Dual Acid-Etched Surfaces After 2 Months of Healing in the Human Maxilla". *Journal of Periodontology* 74 (2003): 945-956.

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