Comparison of Material Properties for Dental Implants: Titanium, Polyetheretherketone, Zirconium and Silicon Nitride

Manuel Aparicio-Razo[1,2], José Luis Jr. Mongalo-Vázquez[3], J. A. Yáñez Ramos[4], Adolfo Navarro-Zárate[3], Víctor Hugo Santos-Enríquez[3], Israel Vivanco-Pérez[3], J. Flores Méndez[1,4,], Genaro Alberto Paredes-Juárez[5]*

This review article presents the biological and technological properties of biomaterials: titanium, polyetheretherketone, zirconium and Si_3N_4, focused on the application of dental implants. The methodology focused on examining different works related to the topics of biocompatibility, biofilm formation and adhesion properties, fibroblast proliferation, bone resorption, peri-implant infection, osseointegration, histology, cytotoxicity, toxicity, carcinogenicity, genotoxicity, hemocompatibility, vascularization, mechanical resistance and approval for use by the FDA. The results of the review show that all four biomaterials have favorable properties that can revolutionize implants, however, more studies are needed to confirm the results in the short and medium term.

Introduction

Oral rehabilitation using osseointegrated dental implants has been a technique used for several decades by professionals around the world with high success rates [**1**]. Dental implants began to be used clinically around 1965 and since then it has been considered one of the treatments of choice for edentulous patients, sometimes exceeding the success rates of fixed prostheses on natural teeth in the case of single absences [**2**]. Dental implants have considerably high success rates according to different human studies depending on the type of dental implant used, reaching ranges of 82.94% [**3**], 90% [**4**] and even 94.7% [**5**].

[1]Facultad de Ciencias de la Electrónica - Benemérita Universidad Autónoma de Puebla, Ciudad Universitaria, Blvd. Valsequillo y Esquina, Av. San Claudio s/n, Col. San Manuel, C.P. 72570, Puebla, Pue, México.
[2]Posgrado en Ciencias de la Ingeniería, Biomédica - Universidad Popular Autónoma Del Estado de Puebla, Calle 21 Sur 1103, Barrio de Santiago, 72410 Puebla, Pue, México.
[3]Departamento de Cirugía Maxilofacial del Hospital Universitario de Puebla. Benemérita Universidad Autónoma de Puebla - Área de la Salud. 25 poniente 1301 Col. Volcanes.
[4]Tecnológico Nacional de México/I.T. Puebla-Departamento de Metal-Mecánica, Av. Tecnológico No. 420, Maravillas, C.P. 72220, Puebla, Pue, México.
[5]Área de Biología - Decanato de Ciencias Biológicas, Universidad Popular Autónoma del Estado de Puebla. 21 sur #1103, Barrio de Santiago C.P. 72410, Puebla, Pue., México.

*Corresponding author:
E-mail: javier.flores@puebla.tecnm.mx, Tel: (+52 1) 222 316 0085

DOI: 10.5185/amlett.2022.011684

Within implantology there are different important circumstances to consider for the materials that will have contact with oral mucosa, bone, blood, among others in the short and long term. One of them is biological effects, which involves different factors such as: biocompatibility [**6**], cytotoxicity [**7**], toxicity [**8**], carcinogenicity [**9**], genotoxicity [**10**], hemocompatibility [**11**] and vascularization [**12**] which are vital to the success of the implant. Another type of cause that is important is related to mechanical resistance, which includes the fracture of the implants and any of their prosthetic components [**13**]. And finally, that related to approval before international organizations such as the Food and Drug Administration (FDA) [**14**].

Currently we have different materials and types of implant body for implantology, among which titanium (Ti) and its alloys stand out, despite the diseases that can be caused by the detachment of particles that cause allergies and peri-implantitis [**15**]. Another material that has gained popularity for several years is zirconium (Zr), which has shown biocompatibility, strength and inert characteristics comparable to that of Ti alloy implants [**16**].

Recent research has evaluated a series of new materials for their application as dental implants, since they have physical and biological characteristics similar to those mentioned above; as is the case with Polyetheretherketone (PEEK) or reinforced and modified PEEK (CFR-PEEK) [**17**] and Silicon Nitride (Si_3N_4) [**18**], which are materials that present even better biological and mechanical properties than traditional implants.

The objective of this article is to review the materials that exist for dental implants "Ti, PEEK, Zr and Si_3N_4" and discuss which one has the best characteristics in the areas of biocompatibility, cytotoxicity, toxicity, carcinogenicity, genotoxicity, hemocompatibility, vascularization, mechanical resistance and approval for use by the FDA.

Methodology

The methodology was focused on carrying out a review of articles related to the topics of biocompatibility, biofilm formation and adhesion properties, fibroblast proliferation, bone resorption, peri-implant infection, osseointegration, histology, cytotoxicity, toxicity, carcinogenicity, genotoxicity, hemocompatibility, vascularity, mechanical resistance and approval for use by the FDA; related in dental implants and materials Ti, PEEK, Zr and Si_3N_4.

The exhaustive review of the articles was carried out in different databases and international scientific portals such as: Wiley Online Library, ScienceDirect and Scopus, Meridian allen press, MDPI, Ingenta Connect, EBSCOhost, Springer Link, Pubmed, Taylor and Francis Online, RSC Publishing, NCBI, Scholar Google, Online bone and joint, Scientific Research Publishing, and ACS Publications.

Developing

Biomaterials are subjected to complex environments and must be capable of not altering the environment or modifying biological processes, in addition to supporting mechanical work and cycles. For that reason, biomaterials are a multidisciplinary science that involves the basic sciences, engineering and the medical area [**19**].

The materials must have a different appearance to function properly so that the material can coexist with the fabrics without undesirable effects. Without a doubt an important aspect is biocompatibility, which focuses on studying biochemical compatibility related to toxicity, irritation, allergies and aspects of carcinogens [**20**]. Another type of relevant aspect is cytotoxicity [**21**], which is a very important aspect when determining whether a material is toxic; as well as genotoxicity, which focuses on studying the genetic mutations of cells in contact with materials [**22**].

Another very important factor for materials that have contact with blood fluids is hemocompatibility, which studies the capacity of red blood cells (thrombogenic property) in a bloodstream that flows over the material [**23**]. On the other hand, it is also important to consider biodegradation, which studies the corrosive effects released in materials by changes in kinetics resulting in the release of ions in tissues by friction and wear [**24**]. In **Fig. 1**, it can be seen which are the most important aspects that should be considered based on our experience to have a good synergy for the biomaterials applied in dental implants.

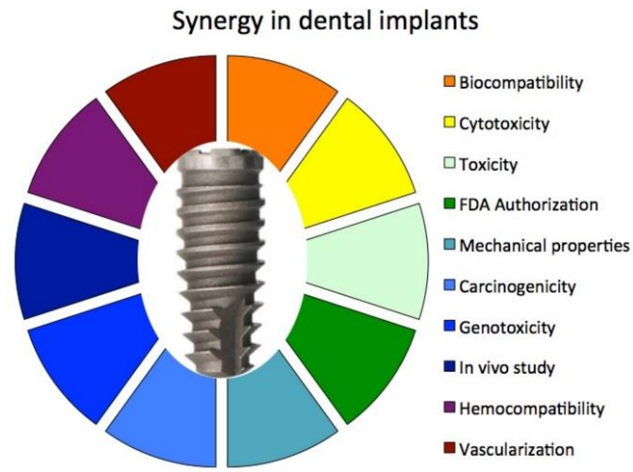

Fig. 1. Synergy and study areas that should be considered in all material for dental implants.

Based on the diagram in **Fig. 1**, the comparison of the different materials Ti, PEEK, Zr and Si_3N_4 related in these areas will be shown below.

Results

Biocompatibility

The term biocompatibility is applied mainly to medical materials in direct, short or prolonged contact with the tissues and internal fluids of the body such as posts for dental implants. Within biocompatibility there are several important aspects to consider; such as biofilm formation, fibroblast proliferation, bone resorption, implant site infections, osseointegration, and histology. These aspects related to the different materials, which are the central theme of the article, will be compared below. The following **Fig. 2** shows the most important aspects of biocompatibility.

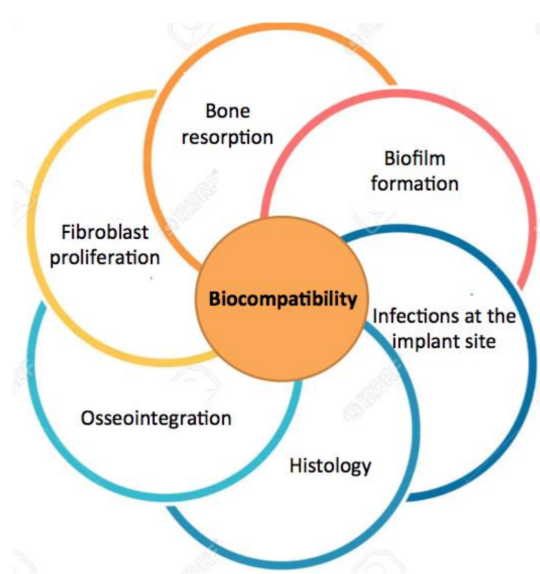

Fig. 2. Most important aspects of biocompatibility.

Biofilm formation

The formation of biofilms or "oral biofilm" is an essential component that is involved in the development of cavities and periodontal diseases. Both pathologies are among the most prevalent in humans with a negative impact on quality of life, being the main cause of tooth loss and contamination of dental implants [**25,26**]. The use of osseointegrated implants as support for fixed or removable prostheses is not free from these problems, so it is believed that oral biofilm plays a fundamental role for implant survival [**27**].

There are a considerable number of publications that have studied biofilm formation on Ti and Zr surfaces [**28-31**]. As a summary we can say that it has been repeatedly found that Zr could have a reduced bacterial adhesion compared to Ti; however, the results of experimental studies are quite controversial so far. However, it can be said that the surfaces of the Zr implants show a statistically significant reduction in the formation of biofilms of human plaque compared to the surfaces of the Ti implants. On the other hand, there are also investigations that report that there are no significant differences between the surfaces of Ti and Zr. Finally, there are also works that have suggested that there is a difference in the microbiota in the formation of oral biofilms associated with Ti and Zr [**32**].

In the case of PEEK, there are few studies that compare the properties of this material with respect to Ti and Zr [**33-36**]. Fundamentally, these publications mention that the surface roughness of unmodified PEEK is significantly lower compared to Ti and Zr, which means that the formation of biofilms is poor, that is, most of the studies do not reveal a significant antimicrobial activity in PEEK. pure. However, other articles have reported that the modification of the surface with nanocomposites seems to improve cell adhesion, influences the structure of the biofilm and reduces the chances of peri-implant inflammation, which makes it an interesting biomaterial in implantology in the near future.

In the case of Si_3N_4, there is currently a limited number of studies applied to the dental area, despite the fact that there are studies of its biological response since 1989 [**37**]. Some interesting characteristics of this material is that it shows resistance to bacteria and to biofilm formation in in vivo studies [**38,39**]. Furthermore, a recent study has shown a direct bactericidal effect against an oral pathogen [**40**]. The antibacterial behavior of Si_3N_4 is probably multifactorial and is related to surface chemistry, surface pH, texture, and electrical charge [**41**]. Optimizing these surface properties for specific implants is a clear advantage of the material.

Finally, a recent study on Si_3N_4, Ti and PEEK surfaces showed that Si_3N_4 has superior resistance to the biofilm of S. epidermis and E. coli compared to other biomaterials [**42**].

Fibroblast proliferation

A fibroblast is the most common type of cell found in connective tissue in dental implants. Fibroblasts secrete collagen proteins that are used to stabilize and maintain a structural framework, as well as play an important role in wound healing.

Currently there are various methods of surface modification in biomaterials to promote a better proliferation of fibroblasts and thus achieve a union between implants and bone. In the different search engines, different studies were found comparing the proliferation of fibroblasts on the surfaces of Ti, Zr and PEEK [**43-46**].

The different studies show that the roughness of the materials is remarkably different according to the results of scanning electron microscopy. In the case of the PEEK surface, it has a better behavior when it is superficially modified, achieving similar roughnesses compared to Ti and Zr, which resulted in cell proliferation and migration equivalent to other materials. On the other hand, studies have found that materials modified with laser and plasma techniques present significantly higher values in adhesion of human gingival fibroblasts than those effected by other techniques, such as soft machining. In general, studies have found that fibroblast cell viability and proliferation is higher on PEEK and Zr surfaces compared to Ti, due to the greater wettability of these materials.

In the case of Si_3N_4, it has been found that the absorption of fibronectin and vitronectin-type proteins are significantly higher compared to Ti and PEEK [**39**]. Furthermore, it has been seen that the surface modification of this material bearing functional primary amine end groups increases fibronectin adsorption and promoted cell proliferation, but there is a delay in differentiation [**47**].

Finally, it has been analyzed that Si_3N_4 has shown the ability to reduce or maintain normal levels of reactive oxygen species (ROS) in macrophages depending on the particle size and dose, which is important since the levels of fibroblasts and ROS are associated in the production of collagen and fibronectin [**48**].

Bone resorption

Bone resorption is the destruction and loss of bone tissue caused by osteoclasts and mononuclear cells. These diseases are a complication of osseointegrated dental implants and cause changes in the bone and soft tissue around the implants. In general terms, this resorption is due to periodontitis or the use of removable prostheses. The small amount of bone resorption around the implant is considered normal for all implants [**49**].

Focusing on biomaterials for dental implants, some have a greater or lesser degree of resorption. In the case of Ti implants, the particles of said material have a negative effect on the peri-implant tissue by activating macrophages that promote the local secretion of inflammatory cytosines, causing bone loss due to a decrease in macrophages [**50,51**]. Other studies have found that there is little bone loss, approximately 0.5 mm during the first postoperative year and 0.06 to 0.08 mm annually thereafter. Poor oral hygiene and teeth clenching significantly influenced bone loss [**52**].

In the case of Zr implants, there are studies that found negative results for bone resorption and no soft tissue recession at 26 months of follow-up [**53**]. Another study in rodents found that the inflammatory response and bone resorption induced by ceramic particles were much smaller than those induced by Ti alloys [**54**]. On the other hand, there are studies that have compared osteoclast reabsorption pits in bone with Ti and Zr surfaces, resulting in surface roughness values of 86 nm in Zr and between 127 and 140 nm in Ti surfaces [**55**].

In the case of the PEEK biomaterial, there are few studies referring to bone resorption, however a study that was carried out of patient-specific subperiosteal implants of Ti and PEEK did not find any radiographic signs of bone resorption, mobility, infection or prosthetic fracture in the patients. implants [**56**]. In addition, studies have evaluated the bone immune response in rabbits in the presence of PEEK and Ti, where it was found that PEEK shows some inhibition of bone resorption compared to Ti at 28 days [**57**].

In the case of Si_3N_4, it was found that it causes a significant inhibition of the phenotypic genetic expressions of osteoclasts, osteoclast formation and bone resorption in vitro [**58**]. On the other hand, another study where the response of Si_3N_4 in bone formation was evaluated, it was found that simultaneous measurements of the bone resorption marker Glu-osteocalcin (that is, an undercarboxylated form of γ-carboxyglutamate) showed significant inhibition of osteoclastogenesis compared to that presented in Ti [**59**]. In addition, this material has been found to promote blood flow, facilitating the release of leukocytes that mediate bone resorption and inflammation [**60**].

Infections at the implant site

Dental implants, like natural teeth, can be affected by infection. The two main types of dental implant infections that cause inflammation in the tissues (bone and gum) surrounding the implant are mucositis and peri-implantitis. Mucositis is an inflammatory reaction that only affects the gingiva surrounding the implant. Its equivalent in teeth is gingivitis. When, in addition to inflammation of the soft tissues, the implant has lost part of the bone that supports it, we speak of peri-implantitis. The equivalent in teeth is periodontitis.

In a study evaluating the presence of human cytomegalovirus-1 (HCMV-1) and Epstein-Barr-1 (EBV-1) in Ti and Zr implants, it was found that 60% of people with Ti abutments had the EBV-1 virus, while 0% in Zr. In the case of HCMV-1, 90% of TI implant participants were found to have HCMV-1 versus 70% in Zr abutments [**61**]. On the other hand, another study found that Zr and Ti implants have a similar adherence to S. mutans bacteria, while Ti has a higher proliferation against P. gingivalis than Zr. In general, Ti showed higher bacterial viability [**62**].

In the case of PEEK, the surface is known to have antibacterial properties, which depends on the topography of the surface and the dimensions of the surface structures [**63**], as well as the surface treatment to which it is subjected [**64**]. In addition, it has excellent antibacterial behavior in vitro, mainly against S. aureus and E. coli [**65**].

In the case of Si_3N_4, it offers an inert surface that is resistant to bacteria and the formation of biofilms [**38,39**]. Furthermore, a recent study has shown a direct bactericidal effect against an oral pathogen [**66**]. The antibacterial behavior of Si_3N_4 is possibly related to surface chemistry, pH, surface texture, and electrical charge [**41**].

Osseointegration

Osseointegration is the process by which a solid bond is produced between a dental implant and the patient's natural bone, or put another way, it's all about scarring. Osseointegration is an essential process for the effectiveness and success of dental implants and is considered the most important stage in the success of implants.

Research results have shown that pure Ti and its alloys show similar osseointegration and mechanical anchoring [**67**]. Ti implants demonstrate a similar ability to integrate soft tissue and bone, but tend to show a faster initial osseointegration process compared to Zr [**68**]. Furthermore, other research found that Zr implants are capable of establishing implant rates in contact with bone close to what is known for the osseointegration behavior of titanium implants with the same surface modification and roughness [**69**]. Finally, another study evaluated that there is no statistical difference between Ti and Zr implants regarding osseointegration [**70**].

In the case of PEEK, some studies show that Ti exhibits a generally more osteogenic behavior than PEEK [**71**]. PEEK implants are considered a viable alternative to Ti implants, but new experimental studies are needed both to investigate chemical modulation and to find combinations that increase the implant bone interface and minimize stress distribution in the peri-implant bone [**72, 73**].

Si_3N_4 has a surface chemistry that accelerates bone repair, allowing osseointegration within the human environment. Elements Si and N stimulate progenitor cell differentiation and osteoblastic activity, ultimately resulting in accelerated bone growth [**74**]. In another study where human osteosarcoma cells were exposed within an osteogenic medium with Si_3N_4 powder, a more balanced combination of collagen and mineral fractions closer to the natural composition of native human bone was observed [**75**].

Histology

Histology is the branch of science that allows to identify and analyze through electron microscopy the relationship between structures and functions of cells in the human body. In the case of superficially modified Ti implants, their histological response has been shown to be good after 5 years [**76**]. Another study in dogs showed that Ti dental implants have similar soft tissue adaptation and adequate bone anchorage (osseointegration). However, more studies are needed to determine long-term clinical feasibility [**77**].

On the other hand, there are studies that have compared the histological response in Ti and Zr implants with modified surfaces. In this study, it was found that there is bone integration for both materials, in addition to not detecting statistically significant differences between both types of implants at any time [**78**]. Other work has verified that surface modified Zr implants show no differences with respect to histological and biomechanical results compared to an established electrochemically modified Ti implant surface [**79**].

In the case of PEEK, it is known that histologically there is an intimate or optimal contact between the bone and this material, in such a way that the histomorphometric evaluation shows high values of the bone area and bone implantation for surfaces modified with hydroxyapatite and PEEK without modifications, which suggesting high bone quality around implants [**80**]. On the other hand, it has been shown that the PEEK biomaterial presents early bone formation with a low degree of mineralization, in fact, in this study no significant differences were found in bone volume densities [**80**].

In the case of Si_3N_4, in vivo biocompatibility has also been demonstrated: implants of this material placed in the intramedullary cavities of rabbit femurs did not initiate any inflammatory reaction, and tissue formation was observed histologically, followed by mature bone formation (after 3 months) around the placed implants [**81**]. Animal studies related to implantation of screws made with Si_3N_4 were associated with satisfactory bone healing, and histological/radiographic evaluations showed a new contact between the bone and the implant on the screw surface. No adverse reactions were observed and the authors concluded that Si_3N_4 was suitable for facial bone surgery as a bio-inert material [**82**]. To conclude, there are also studies that have compared the materials Si_3N_4, Ti and PEEK in calvary rat models, where it was observed that the Si_3N_4 sections present histological characteristics of superior new bone around the implants tested compared to Ti and PEEK [**83**].

Cytotoxicity

The cytotoxicity of dental prostheses frequently consists in evaluating the cytotoxic effect or the capacity they have to integrate into the recipient tissue. Cytotoxicity constitutes one of the effector mechanisms of certain specialized cell populations of the immune system, consisting of the ability to interact with and destroy other cells.

There are studies that have studied the cytotoxicity of Ti and Zr implants, which have reported Ti and Zr concentrations in the bone / tissues near the implants in miniature pig jaws after 12 weeks. Furthermore, the Ti content released by the Ti implants is twice as high as the Zr content released by the Zr implants. In these investigations they concluded that Zr implants showed less cytotoxicity and DNA damage compared to the results reported for Ti in human cells [**84**]. In another in vitro study, they reported that both TI and Zr have similar cytotoxicity [**85**] and that both materials are optimal for general implant application [**86**].

In the case of PEEK, it has been found that in vitro cytotoxicity does not present any evidence of a cytotoxic effect, in addition to showing high in vitro biosafety for its application in implants in general [**87**]. Another study found that this material has no mutagenic or cytotoxic activity, that is, that the material does not release any substance that causes the cells to mutate [**88**].

For Si_3N_4, it has been reported according to in vitro studies based on the ISO 10993 standard, that this material does not show any cytotoxicity behavior, which makes it a suitable material for the development of implantable biomedical microsystems [**89**]. There is also evidence in studies that Si_3N_4 has outstanding characteristics in cytotoxicity studies, confirming that it is extremely inert and biocompatible for medical applications [**90**]. Finally, there are studies that have evaluated different industrial formulations of Si_3N_4 of similar composition and none showed cytotoxicity [**82**].

Toxicity

The toxicity of a material is another very important factor when selecting a biomaterial for implants, because it indicates the harmful effects on a living being, when coming into contact with it.

Although Ti is an inert bioimplant material commonly used in the medical and dental fields, in some cases there are reports of problems caused by Ti. Recent studies regarding the toxicity of Ti have been on the rise and have now expanded. Problems that can arise in Ti-based dental implants include the generation of ions, particles and alloy deposited in the surrounding tissues due to corrosion and wear of the implants, resulting in bone loss due to reactions inflammatory, which can lead to a failure of osseointegration of the dental implant [**91**]. These titanium ions and particles are deposited systemically and can cause toxic reactions in other tissues, such as yellow nail syndrome [**92**]. In addition, implant failure and allergic reactions can occur due to hypersensitivity reactions [**93**].

In the case of Zr, little information is available on the possible adverse effects and the toxic mechanism in human organs associated with this ceramic biomaterial. Studies have reported that nanoparticle exposure leads to persistent oxidative stress and the promotion / inhibition of cell proliferation in various organs. Spleen and brain RNA-Seq results point to significant changes in gene expression. Metabolism was identified as major pathways in the spleen. This study demonstrates that Zr likely has negative impacts on various organs and presents potential disease risks [**94**]. On the other hand, another study found that there are alterations in lipid biosynthesis and metabolism due to the presence of particles of this ceramic. Meanwhile, the results of in vitro studies demonstrated that this material induces oxidative stress, lipid accumulation, cell apoptosis, and activation of the P53-mediated signaling pathway in HepG2 cells. This study shows that Zr has effects on the liver. There is a potential concern about hepatotoxicity of Zr in biomedical applications and occupational exposure through large-scale production [**95**].

The evaluation of CF-PEEK compounds have shown, according to studies, a mild toxicity and no hemolytic reaction. And the histopathological section of the systemic toxicity test showed that CF-PEEK compounds had no obvious acute toxicity to organisms [**96**]. Another study carried out with the incubation of PEEK fibers with seven different genotype variants of the Salmonella bacteria, showed that the toxic reaction in the study material revealed that the number of surviving colonies was within the range or below the solvent control. even in the presence of high concentrations of PEEK. Therefore, in summary, the study found no evidence of cellular damage caused by this material [**88**].

In the case of Si_3N_4, there are studies carried out in animals, where they have evaluated the toxicity in vivo (zebrafish). In summary, this work reports that said material presents null toxicity or developmental anomalies in zebrafish embryos exposed to ionic dissolution products, up to 144 h after fertilization, which makes it a great potential as orthopedic implants, for applications such as spinal fusion cages [**97**]. In another study, the outstanding characteristic has been confirmed in toxicity studies, confirming that it is an extremely inert and biocompatible material, as well as presenting chemical stability against different aqueous media and physiological solutions. In addition, the same study demonstrated its non-toxicity and confirmed that this material can serve as a biomaterial for bone replacement in load-bearing prostheses [**98**].

Carcinogenicity and genotoxicity

In the literature, although the direct carcinogenic and genotoxic role of dental implants has never been established, several theories related to corrosion and release of metal ions from malignant cells through the groove around the implant have been proposed [**99**].

In the case of Ti, it is known that this ion is one of the most inert metal ions and although it has been shown that the particles of this material lead to an increase in the levels of prostaglandin E-2 and interleukin-1, it seems that it has not yet a clear association between Ti particles and cancer has been shown [**100**]. On the other hand, there are also studies that show that the Ti-6A1-4V alloy lacks cytotoxic and genotoxic effects in a test carried out [**101**]. However, we consider it pertinent to show studies related to vanadium and aluminum ions, since they are alloying in the implants used today.

In the case of vanadium, there are no data to indicate that this element is carcinogenic in animals or in man, but since it interferes with mitosis and the distribution of chromosomes, it indicates the possibility that vanadium may be carcinogenic under certain conditions. conditions, so it cannot be ruled out immediately [**102**]. In other studies, in human lymphocytes and leukocytes, the effect of vanadium induced cytotoxic, cytostatic, and chromosomal damage [**103**]. Regarding the carcinogenic potential, studies based on key cells have shown the ability of vanadium to induce genotoxic lesions, cell morphological transformation and antiapoptotic effects in a certain type of cells. Furthermore, contradictory effects of vanadium on immune functions of cells and probable cytotoxic mechanisms in neurons and glial cells have been observed in cell culture studies [**104**].

In the case of aluminum, no conclusive epidemiological evidence has been provided that exposure to aluminum represents a carcinogenic hazard to man. Although, probably due to interference with microtubule polymerization, some aluminum compounds appear capable of producing chromosomal abnormalities [**105**]. New aluminum nanomaterials have also been found to cause size- and dose-dependent genotoxicity based on in vivo studies [**106**].

In the case of Zr, it is known that this material does not cause a mutagenic or transforming effect in cells and can be considered suitable for biomedical applications from the point of view of the effects of its content of radioactive impurities [**107**]. Another in vivo study carried out in insects subjected to Zr nanoparticles, it was reported that this biomaterial is not capable of inducing genotoxic activity, which indicates that the nanoparticulate form of the nanomaterial does not modify the potential genotoxicity of its microparticulate versions [**108**]. However, there are also studies that have found results that support that zirconium oxide nanoparticles induce DNA damage and apoptosis [**109**].

Regarding PEEK, studies have been carried out with fibers of the material with seven different genotype variants of the Salmonella bacteria, finding a null release of substances that cause cell mutation [**88**]. In addition, this material has been reported to be bio-inert and does not show evidence of mutagenicity, teratogenicity, and carcinogenicity [**110**]. As well as in vivo studies have been found that PEEK does not present cytotoxicity, genotoxicity and immunogenesis [**111**].

Finally, for Si_3N_4 there are very few publications that have studied its impact in this area. Among those found is one that reports that Si_3N_4 does not release substances with inflammatory cytotoxic activity, oxidative stress, or genotoxic activity in human peripheral blood mononuclear cells [**112**]. We believe that more studies should be done to expand the long-term carcinogenic and genotoxic effects of this material.

Hemocompatibility

Hemocompatibility is a key property of biomaterials that come into contact with blood. In the case of Ti, there are studies that have proven hemocompatibility that include in vitro clotting time, thrombin time, platelet adhesion and in vivo implantation in the ventral aorta or right atrium in dogs from 17 to 90 days, demonstrating that this biomaterial has excellent hemocompatibility [113]. There are also reports that show that this biomaterial has lower fibrinogen adsorption, cell adhesion, platelet activation and blood clotting, which prevents the generation of thrombosis [**114**]. Furthermore, it has been found that the Ti surface can be potentially useful in tissue engineering constructions for bone and dental applications, as it allows a pre-vascularization binding of scaffolds using early and selective endothelial cells and improved hemocompatibility while at the same time supports proliferation and growth of mesenchymal stem cells [**115**]. In the case of Zr, it is known which thin films of this biomaterial have favorable hemocompatibility and corrosion resistance [**116**]. Furthermore, in vivo evaluation of this material indicates that it has good hemocompatibility in stump bearings of Dex Aide ventricular assist devices [**117**]. Similarly, in vitro studies have found that Zr has good hemocompatilility with values of less than 2% of lysis, which indicates that it is acceptable [**118**].

For PEEK there are studies that have reported a null hemolytic reaction [**119**], as well as other studies have made superficial modifications of this material, improving fibrinogen adsorption, inhibition of adhesion and activation of platelets, achieving better anti-thrombogenicity [**120**]. On the other hand, there are biocompatible and hemocompatible filters for blood filtration that use the biomaterials PEEK and CFR-PEEK, which indicates that this material does not present any risk when used in devices in contact with blood [**121**].

For Si_3N_4 there are few publications related to this topic, however it is known that the superficial modification of medical implants and intervention devices with this biomaterial improves hemocompatibility in addition to acquiring less adhesion and platelet activation [**122**]. In other work, it was found that coatings with Si_3N_4 may be a great candidate for the development of anti-thrombogenic surfaces on materials that come into contact with blood [**123**].

Vascularization

The clinical success of implanted materials depends not only on osseointegration but also on neovascularization in the peri-implant bone. It is well known that the efficient vascularization of dental implants reduces the risks of loss [**124**]. Furthermore, angiogenesis is the physiological process that involves the formation of new blood vessels from the pre-existing vessels formed in the early stage of vasculogenesis. The critical role of angiogenesis in regenerative dental procedures, dealing with the dentin-pulp complex and regeneration of the dental pulp, has recently been highlighted [**125**].

In the case of Ti, there are several studies that have discussed the effect of the alloys of this biomaterial, the characteristics of the surface of dental implants and the treatments on the angiogenesis process. However, in vivo and clinical studies addressing the effect of angiogenesis in treatments using bone grafts and barrier membrane materials are still lacking [**126**]. Furthermore, some studies show that the microenvironment change induced by surface-modified Ti implants promotes adhesion, recruitment and proliferation of derived mesenchymal stem cells and facilitates coupled osteogenesis and angiogenesis in bone healing [**127**]. In other studies where PEEK and Ti biomaterials were compared, it was found that cells stimulated with Ti alloy generate a microenvironment that stimulates the osteogenic-angiogenic. Osteogenic-angiogenic responses to Ti alloy were greater than PEEK and greater in rough Ti alloy than in smooth Ti alloy. The characteristics of the surface regulate the expression of integrins important in collagen recognition. These factors can increase bone formation, improve integration, and improve implant stability in spinal interbody fusions [**128**].

In the case of Zr, studies have found that the 200 μm wide and 100 μm deep microchannels of this material present greater capillarity, thus being promising solutions for promoting the vascularization of implants and consequently better osseointegration [**129**]. In another study carried out with Ti and Zr materials, it was observed that both materials present a similar pattern of bone healing and high vascularization [**130**].

Regarding PEEK, there are studies that have evaluated the biological response of particles of this biomaterial in the spinal cord and nerve roots, finding normal vascularization and adherence of particles to the connective tissue, in addition to not finding necrosis or swelling [**131**]. Also, studies have found the addition of porosity to be a common modification to improve vascularity and methods to create porous PEEKs have been reported [**132**]. Finally, there are mouse models of biomimetic scaffold craniotomy with PEEK, finding excellent osteoinductive and angiogenic properties, which makes it a material for regenerative medical applications [**133**].

For the Si_3N_4 biomaterial, bone-implant contact has been observed in rabbit models through scanning electron microscopy, the development of vascular structures in newly formed bone, which indicates the quality of bone healing [**134**]. Also, in different studies they have found that this biomaterial is a highly porous ceramic, which allows the promotion of angiogenesis and vascularization for bone generation [**135**]. In addition, in rabbit femoral models, the creation of new vessels and bone tissues in

Si_3N_4 was found through micro computational tomography, as well as promoting vascularization, osteogenesis and osseointegration in vivo [**136**].

Mechanical properties

From a biomechanical point of view, the occlusal forces exerted on dental implants by the mandibular muscles present the same type of loads as a natural tooth. For this reason, it is important that the biomaterial of the implants have the mechanical capacity to withstand these forces and moments efficiently without neglecting other important physical characteristics such as weight, hardness, resistance to fatigue, among others.

For Ti-6A1–4V alloy implants it is known that the elastic limit ranges between 270 and 530 Mpa and its maximum compressive strength between 390 and 600 Mpa [**137**], while other studies have evaluated that it presents values of 40 Mpa [**138**]. On the other hand, the fatigue resistance varies according to the surface quality, where the smooth finishes subjected to hydrogen alloy treatments present approximate values of 643-669 MPa, while the fatigue resistance of the same alloy with annealing in β presents the average value of 497 MPa and finally the fatigue resistance of the same alloy but with prebaked and equiaxial is 590 MPa [**139**]. In the case of surface hardness, the Rockwell C hardness is known to be 36 [**140**]. Finally, the flexural strength of this alloy is approximately 48-320 Mpa [**141**].

In the case of Zr, it is known that its properties are similar to those of stainless steel, that is, it has a compressive strength of approximately 2000 MPa [**142**]. In addition, the values of its elastic limit have been reported to be between 250-310 Mpa, while its hardness is approximately 41 Rockwell C and flexural strength is 620 MPa [**143**]. In the case of Zr fatigue, it has been found that it presents values of approximately 1200 Mpa [**144**].

For the PEEK biomaterial in many medical fields, it is known that it presents mechanical properties similar to bone, these iso-elastic characteristics lead to suppose that it could represent a viable alternative to conventional materials in the field of dentistry. The results reported in studies regarding the flexural modulus range between 170.37 ± 19.31 MPa for an unfilled brand and 1009.63 ± 107.33 Mpa for a PEEK reinforced with carbon fiber or CFR-PEEK [**145**]. On the other hand, the elastic limit of this material is 107.62 ± 8.23 MPa for samples of a CFR-PEEK compound [**146**]. In the case of hardness, this material has a value of 85 according to Rockwell M, while it has an approximate value of compressive stress of 138 MPa [**73**]. Finally, in the case of fatigue, it has been reported that the maximum values are between 100-102.5 Mpa [**147**].

In the case of Si_3N_4, it is known that its stress due to bending can vary between the values 552-735 Mpa [**148, 149**]. In the case of compression stress, it has been found to have the value of 720 Mpa, while its hardness 67, Rockwell 45N [**150**] has been evaluated. Regarding the elastic limit, it has been evaluated that it is approximately 160 MPa [**151**]. Finally, the fatigue stress values are known to have the average value of 300 MPa [**152**].

In vivo studies

In vivo studies are undoubtedly one of the most important steps in the application of biomaterials, since it allows us to observe the real behavior within an organism. In the case of Ti, there is a large number of investigations carried out in animals [**153-155**], as well as in humans [**156-158**], making it a relatively safe material. In the case of Zr, the publications are a little more limited, however there are different studies carried out in animals in vivo [**159-161**], and in humans [**162,163**]. For PEEK, in vivo studies in animals are scarce, however interesting results have been found [**164-166**]. On the other hand, in the case of humans, applications have been made mainly focused on surgical procedures such as: spine surgery [**167**], orthopedics [**168**], maxillofacial [**169**] among others [**170**]. Finally, Si_3N_4 there are very few publications in in vivo studies, but despite this there are some works reported in animals [**37,83,171**]. Finally, in the case of human studies, spinal and lumbar prosthetic applications have been made [**172,173**].

FDA authorization

The Food and Drug Administration (FDA) [**174**] is one of the international agencies of the United States government responsible for regulating food (for both humans and animals), drugs (human and veterinary), cosmetics, medical devices (human and animal), biological products and blood derivatives that play a very important role in the acceptance and application of materials for medical uses.

In the case of Ti, it is a widely used material because it began to be used in the 1940s when it was introduced in the field of medicine. It was Bothe, Beaton and Dnvenportl who, through implantation in animals, observed its excellent biocompatibility comparable to that of stainless steel or Vitallium (CoCrMo) [**175**]. Ti is currently an FDA cleared material [**176,177**].

For Zr, it is known that it became more widely known from the fracture of the femoral heads that occurred at the beginning of the year 2000, where it was proposed that this biomaterial could be the solution to these failures. Biomedical-grade zirconia was introduced more than 35 years ago to solve the problem of alumina brittleness and consequent potential implant failure [**178**]. The Zr currently has certifications in Europe (CE) as well as the FDA / Canada [**179,180**] and ANVISA, Brazil [**181,182**] for use in orthodontics and other areas.

In 1998, the Victrex® company commercialized PEEK-OPTIMATM for the first time, a biomaterial for medical use that allows the manufacture of different high-performance implants. Independent testing laboratories have performed biocompatibility tests for the relevant parts of ISO 10993 and for USP Class VI plastics with excellent results. The DMF and MAF files containing the results of these tests have been submitted to the FDA [183]. Currently, the PEEK biomaterial is a biomaterial approved by the FDA for biomedical use, mainly for applications in spinal devices [184]. Today the FDA continues to conduct studies on the application of vertebral disc replacement [185].

Si_3N_4 was first prepared in 1857 and was little more than a chemical curiosity. However, as its benefits became known, the compound began to be used in multiple industries in the late 1940s. Today, it is a key component as it is a biocompatible material that is stronger than bone and bone. PEEK, accepted by the human body, compatible with all imaging technologies, is anti-pathogenic, non-toxic, and well suited for medical device applications [186].

Si_3N_4 is antiviral and antibacterial [187]. Recent studies have shown that AP2 silicon nitride powder kills SARS-CoV-2 faster than other antipathogenic materials [188]. As a biomaterial, it also offers more advantages than titanium or PEEK [189]. This material is currently approved by the FDA for the manufacture of medical devices such as [190]: cervical and thoracic spine devices, joint replacement, and its use for dental implants is even being considered [191].

Discussion

Dental implants based on Ti alloys have proven for years to be the star material, thanks to their various properties. However, new advances in biomaterials have generated the necessary technological conditions to implement and support the physical, chemical, biological and biomechanical conditions necessary in the new generations of dental implants.

As we have seen in the review, there are other materials capable of matching and even exceeding the properties of Ti, however much in vivo research still needs to be done to validate the feasibility of its use in humans, despite the fact that the materials are safe for use. to agencies such as the FDA.

In order to contrast the different materials reviewed in this article, **Table 1** is shown, where the relationship between the studied aspects of each material is found, considering an assessment of 1 to 5 asterisks (*). Where: * = Bad, ** = Regular, *** = Fair, **** = Good and ***** = Excellent.

The weighting shown in **Table 1** was constructed from the studies shown in the review and also based on experience in the area of dental implants and biomedical engineering of materials. We consider that the Peek and Si_3N_4 materials present interesting and promising properties to be considered for the implementation in dental implants. In the case of Zr there are implants in use today and they are being used mainly for having a better aesthetic appearance, resistance, durability, but without a doubt the main advantage is that it is an option for patients allergic to metallic materials. Finally, in the case of Ti, there is a considerable number of studies that reveal, on the one hand, its extraordinary properties for implants, however there are also a number of publications that have found some contraindications that are important to consider.

In the following **Fig. 3**, the implants with the different materials can be seen.

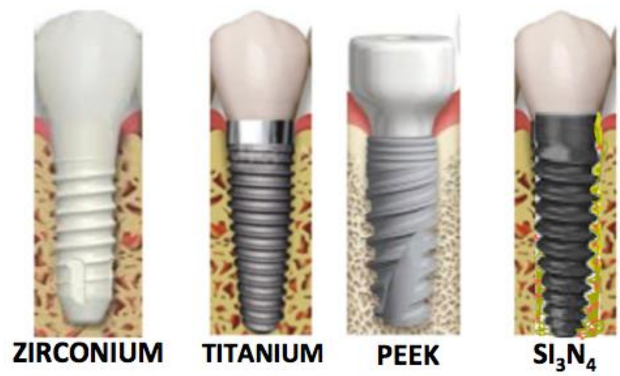

Fig. 3. Dental implants with materials.

Table 1. Comparison of the most important aspects of a biomaterial for implants.

		Ti	Zr	Peek	Si_3N_4
Biocompatibility	Biofilm formation	**	***	****	*****
	Fibroblast proliferation	***	****	****	*****
	Reabsorption	***	****	****	****
	Infection at the implant site	***	****	*****	*****
	Osseointegration	*****	****	***	****
	Histology	***	***	****	*****
	Cytotoxicity	**	***	*****	*****
	Toxicity	**	**	****	*****
	Carcinogenicity / Genotoxicity	****	****	*****	****
	Hemocompatibility	*****	****	*****	****
	Vascularization	*****	****	***	*****
	Mechanical properties	****	*****	***	*****
	In vivo study	*****	****	***	***
	FDA Authorization	Yes	Yes	Yes	Yes

Conclusion & future prospective

Advances in biomaterial engineering is a very promising area of research that will allow the revolutionization of implants in the implantology sector. One of the most optimistic aspects is the creation of devices capable of adapting to increasingly demanding users and offering more efficient implants, which requires having new types of materials.

The biomaterials of Zr, Peek and Si_3N_4 in comparison with the implants of Ti is that today there is more research and evidence. We believe that more studies of these biomaterials are necessary to confirm the promising results in the short and medium term. However, within the framework of the review of this article we can conclude that its predictions of success could approach and even exceed those of Ti.

We believe that in the near future, the development of new implants based on other biomaterials will be able to offer a new generation of properties, with the possibility of being more compatible, light, safe, resistant and at a lower cost for users.

Acknowledgements

The authors acknowledge the support from "Universidad Popular Autónoma Del Estado de Puebla", for providing us the use of the necessary resources regarding technical-scientific information.

Conflicts of interest

All the authors declare that there is no conflict of interest.

Keywords

Implants, titanium, polyetheretherketone, zirconium, Si_3N_4.

References

1. Misch, C.E.; Contemporary Implant Dentistry, 3a Edition. Editorial Mosby, St Louis (Missouri), **2008**, p.621-635.
2. Misch, C. E.: Prótesis Dental Sobre Implantes. Editorial Mosby, Madrid, **2006**, p. 43-53.
3. Simonis, P.; Dufour, T.; Tenebaum, H.; *Clinical Oral Implants Research*, **2010**, *21*, 772.
4. Lang, N.P.; Berglundh, T.; *Journal of Clinical Periodontology*, **2011**, *38*, 178.
5. Jungner, M.; Lundqvist, P.; Lundgren, S.; *Clinical Implant Dentistry and Related Research*, **2014**, *16*, 230-237.
6. Manam, N.S.; Harun, W. S.W.; Shri, D.N.A.; Ghani, S.A.C.; Kurniawan, T.; Ismail, M. H.; Ibrahim, M.H.I.; *Journal of Alloys and Compounds*, **2017**, *701*, 698.
7. Marchi, J.; Ussui, V.; Delfino, C.S.; Bressiani, A.H.; Marques, M. M.; *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, **2010**, *94(2)*, 305.
8. Shahi, S.; Özcan, M.; Maleki Dizaj, S.; Sharifi, S.; Al-Haj Husain, N.; Eftekhari, A.; Ahmadian, E.; *Toxicology Mechanisms and Methods*, **2019**, *29(5)*, 368.
9. Ramos, J.C.; Dos Santos, E.S.; Normando, A.G.C.; Alves, F.A.; Kowalski, L.P.; dos Santos-Silva, A. R.; Lopes, M. A.; *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, **2021**.
10. Ribeiro, D.A.; Yujra, V.Q.; DE MOURA, C. F. G.; Handan, B. A.; Viana, M.D.B.; Yamauchi, L.Y.; Aguiar, O.; *Anticancer Research*, **2017**, *37(8)*, 4017.
11. Yun, Y.H.; Turitto, V.T.; Daigle, K.P.; Kovacs, P.; Davidson, J.A.; Slack, S.M.; *Journal of Biomedical Materials Research: An Official Journal of The Society for Biomaterials and The Japanese Society for Biomaterials*, **1996**, *32(1)*, 77.
12. Benlidayi, M. E.; Gaggl, A.; Bürger, H.; Brandner, C.; Kurkcu, M.; Ünlügenç, H.; *Clinical Oral Implants Research*, **2011**, *22(6)*, 594.
13. Esposito, M.; Hirsch, J.M.; Lekholm, U.; Thomsen, P.; *European Journal of Oral Sciences*, **1998**, *106*, 527.
14. Eckert, S.E.; *The Journal of Prosthetic Dentistry*, **1995**, *74(2)*, 162.
15. Albrektsson, T.; Wennerberg, A.; The impact of oral implants—past and future, 1966-2042. *J Can Dent Assoc.*, **2005**, *71*, 327), (Tarnow DP. Increasing prevalence of peri-implantitis: how will we manage? *J Dent Res.*, **2016**, *95*, 7.
16. Sailer, I.; Philipp, A.; Zembic, A.; Pjetursson, B. E.; Hämmerle, C. H.; Zwahlen, M.; *Clinical Oral Implant Research*, **2009**, *4*, 4.
17. Schwitalla, A.; Müller, W.D.; *Journal of Oral Implantology*, **2013**, *39(6)*, 743.
18. Badran, Z.; Struillou, X.; Hughes, F.J.; Soueidan, A.; Hoornaert, A.; Ide, M.; *Journal of Oral Implantology*, **2017**, *43(3)*, 240.
19. Heimann, R.B.; *Ceramics*, **2021**, *4(2)*, 208.
20. Black, J.; Biological performance of materials: fundamentals of biocompatibility. CRC Press, **2005**.
21. Sismanoglu, S.; Ercal, P.; *Australian Endodontic Journal*, **2021**.
22. Heil, J.; Reifferscheid, G.; Waldmann, P.; Leyhausen, G.; Geurtsen, W.; *Mutation Research/Genetic Toxicology*, **1996**, 368(3-4), 181.
23. Weber, M.; Steinle, H.; Golombek, S.; Hann, L.; Schlensak, C.; Wendel, H.P.; Avci-Adali, M.; *Frontiers in Bioengineering and Biotechnology*, **2018**, *6*, 99.
24. McBane, J. E.; Sharifpoor, S.; Cai, K.; Labow, R.S.; Santerre, J.P.; *Biomaterials*, **2011**, *32(26)*, 6034.
25. Sanz, M.; Beighton, D.; Curtis, M.A.; Cury, J.A.; Dige, I.; Dommisch, H.; Ellwood, R.; Giacaman, R.A.; Herrera, D.; Herzberg, M.C.; Kononen, E.; Marsh, P.D.; Meyle, J.; Mira, A.; Molina, A.; Mombelli, A.; Quirynen, M.; Reynolds, E.C.; Shapira, L.; Zaura, E.; *Journal of Clinical Periodontology*, **2017**, *44 Suppl 18*, S5.
26. Guentsch, A; Antibiotics against periodontal biofilms. Oral Biofilms, **2021**, *29*, p119-132.
27. Lang, N.P.; y Berglundh, T.; *J. Clin. Periodontol*, **2011**, *38 Suppl 11*, 178.
28. Roehling, S.; Astasov-Frauenhoffer, M.; Hauser-Gerspach, I.; Braissant, O.; Woelfler, H.; Waltimo, T.; Gahlert, M.; *Journal of Periodontology*, **2017**, *88(3)*, 298.
29. Do Nascimento, C.; Pita, M.S.; de Souza Santos, E.; Monesi, N.; Pedrazzi, V.; de Albuquerque Junior, R.F.; Ribeiro, R.F.; *Dental Materials*, **2016**, *32(1)*, 93.
30. Kunrath, M.F.; Monteiro, M.S.; Gupta, S.; Hubler, R.: de Oliveira, S.D.; *Archives of Oral Biology*, **2020**, *117*, 104824.
31. De Avila, E.D.; Vergani, C.E.; Junior, F.A.M.; Junior, M.J.; Shi, W.; Lux, R.; *The Journal of Prosthetic Dentistry*, **2017**, *118(4)*, 481.
32. Do Nascimento, C.; Pita, M.S.; de Souza Santos, E.; Monesi, N.; Pedrazzi, V.; de Albuquerque Junior, R.F.; Ribeiro, R.F.; *Dental Materials*, **2016**, *32(1)*, 93.
33. Mishra, S.; Chowdhary, R.; *Clinical Implant Dentistry & Related Research*, **2019**, *21(1)*, 208.
34. Barkarmo, S.; Longhorn, D.; Leer, K.; Johansson, C.B.; Stenport, V.; Franco-Tabares, S.; Sammons, R.; *Clinical and Experimental Dental Research*, **2019**, *5(4)*, 427.
35. Hahnel, S.; Wieser, A.; Lang, R.; Rosentritt, M.; *Clinical Oral Implants Research*, **2015**, *26(11)*, 1297.
36. Brum, R.S.; Labes, L.G.; Volpato, C.Â.M.; Benfatti, C.A.M.; Pimenta, A.D.L.; *Antibiotics*, **2020**, *9(9)*, 609.
37. Gong, Y.; Honda, Y.; Adachi, T.; Marin, E.; Yoshikawa, K.; Pezzotti, G.; Yamamoto, K.; *International Journal of Molecular Sciences*, **2021**, *22(23)*, 13130.
38. Webster, T.J.; Skidmore, G.A.; Lakshminarayanan, R.; "Increased Bone Attachment to Silicon Nitride (Si3N4) Materials Used in Interbody Fusion Cages (IBF) Compared to Polyetheretherketone (PEEK) and Titanium (Ti) Materials - An In vivo Study;" pp. 1–5 in Proc. 2012 Annu. Meet. Orthopeaedic Soc. **2012**.
39. Gorth, D.J.; Puckett, S.; Ercan, B.; Webster, T.J.; Rahaman, M.; Bal, B.S.; *Int. J. Nanomedicine*, **2012**, *7*, 4829.
40. Pezzotti, G.; Bock, R.M.; McEntire, B.J.; Jones, E.; Boffelli, M.; Zhu, W.; Baggio, G.; Boschetto, F.; et al *Langmuir*, **2016**, *32*, 3024.

41. Bock, R.M.; McEntire, B.J.; Bal, B.S.; Rahaman, M.N.; Boffelli, M.; Pezzotti, G.; *Acta Biomater.*, **2015**, *26*, 318.
42. Bock, R.M.; Jones, E.N.; Ray, D.A.; Bal, B.S.; Pezzotti, G.; McEntire, B.J.; *J. Biomed. Mater. Res. Part A*, **2017**, 105(5) 1521.
43. Ramenzoni, L.L.; Attin, T.; Schmidlin, P. R.; *Materials*, **2019**, *12(9)*, 1401.
44. Gheisarifar, M.; An in Vitro Study of Surface Alterations to PEEK and Titanium and Its Effect Upon Human Gingival Fibroblasts, **2019**.
45. da Cruz, M. B.; Marques, J. F.; Peñarrieta-Juanito, G. M.; Costa, M.; Souza, J.; Magini, R. S.; Caramês, J. M. M.; *International Journal of Oral & Maxillofacial Implants*, **2019**, 34(1).
46. Mishra, S.; Chowdhary, R.; *Clinical Implant Dentistry and Related Research*, **2019**, *21(1)*, 208.
47. Heimann, R. B.; *Ceramics*, **2021**, *4*(2), 208.
48. Lal, S.; Hall, R.; Tipper, J.; *In Orthopaedic Proceedings*, **2017**, 99, 98.
49. Roos J.; Sennerby, L.; Lekholm, U.; Jemt, T.; Gröndahl, K.; Albrektsson, T.; *Int. J. Oral Maxillofac Implants*, **1997**, 12, 504.
50. Wang, X.; Li, Y.; Feng, Y.; Cheng, H.; Li, D.; *Journal of Periodontal Research*, **2019**, *54(4)*, 329.
51. Trindade, R.; Albrektsson, T.; Galli, S.; Prgomet, Z.; Tengvall, P.; Wennerberg, A.; *Clinical Implant Dentistry and Related Research*, **2018**, *20(1)*, 82.
52. Lindquist, L.W.; Rockler, B.; Carlsson, G.E.; *The Journal of Prosthetic Dentistry*, **1988**, *59(1)*, 59.
53. Pirker, W.; Kocher, A.; *International Journal of Oral and Maxillofacial Surgery*, **2008**, *37(3)*, 293.
54. Warashina, H.; Sakano, S.; Kitamura, S.; Yamauchi, K. I.; Yamaguchi, J.; Ishiguro, N.; Hasegawa, Y.; *Biomaterials*, **2003**, *24(21)*, 3655.
55. Hefti, T.; Frischherz, M.; Spencer, N. D.; Hall, H.; Schlottig, F.; *Biomaterials*, **2010**, *31(28)*, 7321.
56. Mounir, M.; Atef, M.; Abou-Elfetouh, A.; Hakam, M. M.; *International Journal of Oral and Maxillofacial Surgery*, **2018**, 47(5), 658-664.
57. Trindade, R.; Albrektsson, T.; Galli, S.; Prgomet, Z.; Tengvall, P.; Wennerberg, A.; *Journal of Clinical Medicine*, **2019**, *8(6)*, 814.
58. Mladenović, Ž.; Johansson, A.; Willman, B.; Shahabi, K.; Björn, E.; Ransjö, M.; *Acta Biomaterialia*, **2014**, *10(1)*, 406.
59. Pezzotti, G.; Bock, R. M.; Adachi, T.; Rondinella, A.; Boschetto, F.; Zhu, W.; Mazda, O.; *Applied Materials Today*, **2017**, *9*, 82.
60. Bevilacqua, M.P.; Endothelial-leukocyte adhesion molecules. *Annual Review of Immunology*, **1993**, *11(1)*, 767.
61. Kheur, M.; Harianawala, H. H.; Sethi, T.; Kheur, S.; Acharya, A.; Mattheos, N.; *Journal of Investigative and Clinical Dentistry*, **2016**, *7(4)*, 396.
62. Meza-Siccha, A. S.; Aguilar-Luis, M. A.; Silva-Caso, W.; Mazulis, F.; Barragan-Salazar, C.; del Valle-Mendoza, J.; *International Journal of Dentistry*, **2019**.
63. Mo, S.; Mehrjou, B.; Tang, K.; Wang, H.; Huo, K.; Qasim, A. M.; Chu, P. K.; *Chemical Engineering Journal*, **2020**, *392*, 123736.
64. Liu, C.; Bai, J.; Wang, Y.; Chen, L.; Wang, D.; Ni, S.; Liu, H.; *Dental Materials*, **2020**.
65. Ouyang, L.; Zhao, Y.; Jin, G.; Lu, T.; Li, J.; Qiao, Y.; Liu, X.; *Biomaterials*, **2016**, *83*, 115.
66. Pezzotti, G.; Bock, R.M.; McEntire, B.J.; Jones, E.; Boffelli, M.; Zhu, W.; Baggio, G.; Boschetto, F.; et al., *Langmuir*, **2016**, *32(12)*, 3024.
67. Shah, F. A.; Trobos, M.; Thomsen, P.; *Mater Sci Eng C Mater Biol Appl.*, **2016**, *62*, 960.
68. Roehling, S.; Schlegel, K.A.; Woelfler, H.; Gahlert, M.; *Clin Oral Implants Res.*, **2019**, *30(5)*, 365.
69. Koch, F. P.; Weng, D.; Krämer, S.; Biesterfeld, S.; Jahn-Eimermacher, A.; Wagner, W.; *Clinical Oral Implants Research*, **2010**, *21(3)*, 350.
70. Chacun, D.; Lafon, A.; Courtois, N.; Reveron, H.; Chevalier, J.; Margossian, P.; Grosgogeat, B.; *Dental Materials*, **2021**, *37*(9), 1377.
71. Najeeb, S.; *Journal of Oral Implantology*, **2016**, *42(6)*, 512.
72. Shariq, N.; Zohaib Khurshid BDS; Sana Zohaib BDS; Muhammad Sohail Zafar BDS; *Journal of Oral Implantology*, **2016**, *42*, 512.
73. Skirbutis, G.; Dzingutė, A.; Masiliūnaitė, V.; Šulcaitė, G.; Žilinskas, J.; *Stomatologija*, **2018**, *20(2)*, 54.
74. Pezzotti, G.; Oba, N.; Zhu, W.; Marin, E.; Rondinella, A.; Boschetto, F.; Bal, B.S.; *Acta Biomaterialia*, **2017**, *64*, 411.
75. Marin, E.; Adachi, T.; Boschetto, F.; Zanocco, M.; Rondinella, A.; Zhu, W.; Pezzotti, G.; *Materials & Design*, **2018**, *159*, 79.
76. Mangano, F.; Mangano, C.; Piattelli, A.; Iezzi, G.; *BioMed Research International*, **2017**.
77. Ericsson, I.; Nilner, K.; Klinge, B.; Glantz, P. O.; *Clinical Oral Implants Research*, **1996**, *7(1)*, 20.
78. Gahlert, M.; Röhling, S.; Wieland, M.; Sprecher, C. M.; Kniha, H.; Milz, S.; *Clinical Oral Implants Research*, **2009**, *20(11)*, 1247.
79. Ismail, L.; The Fracture/Fatigue behavior of Zirconia Implants Compared to Titanium Implants (Doctoral dissertation, Nova Southeastern University, **2021**.
80. Johansson, P.; Barkarmo, S.; Hawthan, M.; Peruzzi, N.; Kjellin, P.; Wennerberg, A.; *Journal of Biomedical Materials Research Part A*, **2018**, *106(5)*, 1440.
81. Elschner, C.; Korn, P.; Schulz, M. C.; Jünger, D.; Range, U.; Scheler, U.; Osseointegration of dental PEEK implants: A combined magnetic resonance imaging and histology study, **2014**.
82. Howlett, C. R.; McCartney, E.; Ching, W.; *Clinical Orthopaedics and Related Research*, **1989**, *244*, 293.
83. Kong, X.; Hu, X.; Chai, W.; In-vitro & In-vivo Investigation of the Silicon Nitride Ceramic Hip Implant's Safety and Effectiveness Evaluation, **2021**.
84. Webster, T. J.; Patel, A. A.; Rahaman, M. N.; Bal, B. S.; *Acta Biomaterialia*, **2012**, *8(12)*, 4447.
85. He, X.; Reichl, F. X.; Milz, S.; Michalke, B.; Wu, X.; Sprecher, C. M.; Hickel, R.; *Dental Materials*, **2020**, *36(3)*, 402.
86. Jiawen, S.; Haoyuan, W.; Qifan, H.; Huiqiang, S.; *International Journal of Stomatology*, **2011**, *5*.
87. Marchi, J.: Ussui, V.; Delfino, C. S.; Bressiani, A. H.; Marques, M. M.; *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, **2010**, *94(2)*, 305.
88. Chon, J. W.; Yang, X.; Lee, S. M.; Kim, Y. J.; Jeon, I. S.; Jho, J. Y.; Chung, D. J.; *Polymers*, **2019**, *11(11)*, 1803.
89. Katzer, A.; Marquardt, H.; Westendorf, J.; Wening, J. V.; Von Foerster, G.; *Biomaterials*, **2002**, *23(8)*, 1749.
90. Roy, S.; Fleischman, A. J.; *Sensors Materials*, **2003**, *15*, 335.
91. Mazzocchi, M.; Bellosi, A.; *Journal of Materials Science: Materials in Medicine*, **2008**, *19(8)*, 2881.
92. Kim, K. T.; Eo, M. Y.; Nguyen, T. T. H.; Kim, S. M.; *International Journal of Implant Dentistry*, **2019**, *5(1)*, 10.
93. Baran, R. L.; Vignes, S.;). Yellow nail syndrome. In Advances in Nail Disease and Management, Springer, Cham, **2021**, pp.1-4
94. Wood, M. M.; Warshaw, E. M.; *Dermatitis*, **2015**, *26(1)*, 7.
95. Sun, T.; Liu, G.; Ou, L.; Feng, X.; Chen, A.; Lai, R.; Shao, L.; Journal of Biomedical Nanotechnology, **2019**, *15(4)*, 728.
96. Sun, T.; Liu, X.; Zhan, X.; Ou, L.; Lai, R.; *Process Safety and Environmental Protection*, **2020**, *147*, 134.
97. Li, Y.; Wang, D.; Qin, W.; Jia, H.; Wu, Y.; Ma, J.; Tang, B.; *Journal of Biomaterials Science, Polymer Edition*, **2019**, *30(18)*, 1709.
98. Fu, L.; Xiong, Y.; Carlsson, G.; Palmer, M.; Örn, S.; Zhu, W.; Xia, W.; Applied Materials Today, **2018**, *12*, 260.
99. Mazzocchi, M.; Bellosi, A.; *Journal of Materials Science: Materials in Medicine*, **2008**, *19(8)*, 2881.
100. Bhatavadekar, N. B.; *Journal of Oral Implantology*, **2012**, *38(6)*, 792.
101. Thornhill, T. S.; Ozuna, R. M.; Shortkroff, S.; Keller, K.; Sledge, C. B.; Spector, M.; *Biomaterials*, **1990**, *11*, 69.
102. Velasco-Ortega, E.; Jos, A.; Cameán, A. M.; Pato-Mourelo, J.; Segura-Egea, J. J.; *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, **2010**, *702(1)*, 17.
103. Léonard, A.; Gerber, G. B.; *Mutation Research/ Reviews in Genetic Toxicology*, **1994**, *317(1)*, 81.
104. Xi, W. S.; Li, J. B.; Liu, Y. Y.; Wu, H.; Cao, A.; Wang, H.; *Toxicology*, **2021**, *459*, 152859
105. Zwolak, I.; Toxicology Mechanisms and Methods, **2014**, *24(1)*, 1.
106. Leonard, A.; Leonard, E. D.; Toxicological & Environmental Chemistry, **1989**, *23(1-4)*, 27.

107. Balasubramanyam, A.; Sailaja, N.; Mahboob, M.; Rahman, M. F.; Hussain, S. M.; Grover, P.; *Mutagenesis*, **2009**, *24(3)*, 245.
108. Covacci, V.; Bruzzese, N.; Maccauro, G.; Andreassi, C.; Ricci, G. A.; Piconi, C.; Cittadini, A.; *Biomaterials*, **1999**, *20(4)*, 371.
109. Demir, E.; Turna, F.; Vales, G.; Kaya, B.; Creus, A.; Marcos, R.; *Chemosphere*, **2013**, *93(10)*, 2304.
110. Atalay, H.; Çelik, A.; Ayaz, F.; *Chemico-biological Interactions*, **2018**, 296, 98.
111. Panayotov, I. V.; Orti, V.; Cuisinier, F.; Yachouh, J.; *Journal of Materials Science: Materials in Medicine*, **2016**, *27(7)*, 118.
112. Williams, D. F.; McNamara, A.; Turner, R. M.; *Journal of Materials Science Letters*, **1987**, *6(2)*, 188.
113. Lal, S.; Caseley, E. A.; Hall, R. M.; Tipper, J. L.; *Scientific Reports*, **2018**, *8(1)*, 1.
114. Manivasagam, V. K.; Sabino, R. M.; Kantam, P.; Popat, K.; *Materials Advances*, **2021**.
115. Manivasagam, V. K.; Popat, K. C.; *ACS Omega*, **2020**, *5(14)*, 8108.
116. Liu, Y.; Tan, T. T. Y.; Yuan, S.; Choong, C.; *Journal of Materials Chemistry B*, **2013**, *1(2)*, 157.
117. Liu, Y.; Zhang, D.; Yin, Y.; Liu, X.; Wang, J.; Study on Effect of Annealing Temperature on Zirconia Thin Films Prepared by Sol-gel Method. Hot Working Technology, **2015**, *24*, 48.
118. Saeed, D.; Shalli, S.; Fumoto, H.; Ootaki, Y.; Horai, T.; Anzai, T.; Dessoffy, R.; In vivo evaluation of zirconia ceramic in the DexAide right ventricular assist device journal bearing. Artificial Organs, **2010**, *34(6)*, 512-516.
119. Bargavi, P.; Chitra, S.; Durgalakshmi, D.; Radha, G.; Balakumar, S.; *Materials Today Communications*, **2020**, 101253.
120. Li, Y.; Wang, D.; Qin, W.; Jia, H.; Wu, Y.; Ma, J.; Tang, B.; *Journal of Biomaterials Science, Polymer Edition*, **2019**, *30(18)*, 1709.
121. Tateishi, T.; Kyomoto, M.; Kakinoki, S.; Yamaoka, T.; Ishihara, K.; *Journal of Biomedical Materials Research Part A*, **2014**, *102(5)*, 1342.
122. Mendonca, A.; Ahmadi, M.; Khan, T.; Biocompatible and hemocompatible material and filter. U.S. Patent Application No. 16/312,089, **2019**.
123. Wang, Q. Y.; Yang, P.; Huang, J.; Liang, J.; Sun, H.; Huang, N.; Trans Tech Publications Ltd., *Advanced Materials Research*, **2009**, 79, 727.
124. Shi, Z.; Wang, Y.; Du, C.; Huang, N.; Wang, L.; Ning, C.; *Journal of the Mechanical Behavior of Biomedical Materials*, **2012**, *16*, 9.
125. Pérez, O. P.; Ortega, E. V.; Calzadilla, O. R.; Méndez, A. G.; Olivares, L. G.; Técnicas quirúrgicas complejas en el tratamiento con implantes oseointegrados del maxilar superior. Un seguimiento clínico de dos años. Avances en periodoncia e implantología oral, **2006**, *18(1)*, 10.
126. Saghiri, M. A.; Asatourian, A.; Sorenson, C. M.; Sheibani, N.; Journal of Endodontics, **2015**, *41(6)*, 797.
127. Saghiri, M. A.; Asatourian, A.; Garcia-Godoy, F.; Sheibani, N.; The role of angiogenesis in implant dentistry part I: Review of titanium alloys, surface characteristics and treatments. Medicina oral, patologia oral y cirugia bucal, **2016**, *21(4)*, e514.
128. Chen, W.; Xu, K.; Tao, B.; Dai, L.; Yu, Y.; Mu, C.; Cai, K.; *Acta Biomaterialia*, **2018**, *74*, 489.
129. Olivares-Navarrete, R.; Hyzy, S. L.; Gittens, R. A.; Schneider, J. M.; Haithcock, D. A.; Ullrich, P. F.; Boyan, B. D.; *The Spine Journal*, **2013**, *13(11)*, 1563.
130. Dantas, T. A.; Pinto, P.; Vaz, P. C.; Silva, F. S.; Ceramics International, **2020**.
131. Marques, G.; Padovan, L. E. M.; Matsumoto, M. A.; Júnior, P. D. R.; Sartori, E. M.; Claudino, M.; Bone healing in titanium and zirconia implants surface: a pilot study on the rabbit tibia. RSBO Revista Sul-Brasileira de Odontologia, **2013**, *10(2)*, 110.
132. Rivard, C. H.; Rhalmi, S.; Coillard, C.; *An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials*, **2002**, *62(4)*, 488.
133. Torstrick, F. B.; Evans, N. T.; Stevens, H. Y.; Gall, K.; Guldberg, R. E.; *Clinical Orthopaedics and Related Research®*, **2016**, *474(11)*, 2373.
134. Chubrik, A.; Senatov, F.; Kolesnikov, E.; Orlova, P.; Poponova, M.; Grunina, T.; Karyagina, A.; *Polymer Testing*, **2020**, 106518.
135. e Silva, C. G.; König Jr, B.; Carbonari, M. J.; Yoshimoto, M.; Allegrini Jr, S.; Bressiani, J. C.; *Materials Characterization*, **2008**, *59(9)*, 1339.
136. Sainz, M. A.; Serena, S.; Belmonte, M.; Miranzo, P.; Osendi, M. I.; *Materials Science and Engineering: C*, **2020**, 110734.
137. Dai, Y.; Chu, L.; Luo, Z.; Tang, T.; Wu, H.; Wang, F.; Shang, X.; *ACS Biomaterials Science & Engineering*, **2019**, *5(12)*, 6425.
138. Lifland, M. I.; Kim, D. K.; Okazaki, K.; *Clinical Materials*, **1993**, *14(1)*, 13.
139. Asaoka, K.; Kuwayama, N.; Okuno, O.; Miura, I.; *Journal of biomedical Materials Research*, **1985**, *19(6)*, 699.
140. Kohn, D. H.; Ducheyne, P.; *Journal of Biomedical Materials Research*, **1990**, *24(11)*, 1483.
141. "Titanium Ti-6Al-4V (Grade 5), Annealed". asm.matweb.com. ASM Aerospace Specification Metals, Inc. Retrieved 14 March **2017**.
142. Reig, L.; Tojal, C.; Busquets, D. J.; Amigó, V.; *Materials*, **2013**, *6(10)*, 4868.
143. Tinschert, J.; Natt, G.; Mautsch, W.; Augthun, M.; Spiekermann, H.; *International Journal of Prosthodontics*, **2001**, *14(3)*.
144. Guazzato, M.; Albakry, M.; Swain, M. V.; Ironside, J.; *International Journal of Prosthodontics*, **2002**, *15(4)*.
145. Smirnov, A.; Beltrán, J. I.; Rodriguez-Suarez, T.; Pecharromán, C.; Muñoz, M. C.; Moya, J. S.; Bartolomé, J. F.; *Scientific Reports*, **2017**, *7*, 44922.
146. Schwitalla, A. D.; Spintig, T.; Kallage, I.; Müller, W. D.; *Dental Materials*, **2015**, *31(11)*, 1377.
147. Schwitalla, A. D.; Zimmermann, T.; Spintig, T.; Kallage, I.; Müller, W. D.; *Journal of the Mechanical Behavior of Biomedical Materials*, **2017**, *69*, 163.
148. Berer, M.; Tscharnuter, D.; Pinter, G.; *International Journal of Fatigue*, **2015**, *80*, 397.
149. He, G.P.; Hirschfeld, D.A.; Cesarano III, J.O.S.E.P.H.; Stuecker, J.N.; Robocasting and mechanical testing of aqueous silicon nitride slurries (No. SAND2000-1493C). Sandia National Labs., Albuquerque, NM (US); Sandia National Labs., Livermore, CA (US), **2000**.
150. Zhao, S.; Xiao, W.; Rahaman, M. N.; O'Brien, D.; Seitz-Sampson, J. W.; Sonny Bal, B.; *International Journal of Applied Ceramic Technology*, **2017**, *14(2)*, 117.
151. Amaral, M.; Lopes, M. A.; Silva, R. F.; Santos, J. D.; *Biomaterials*, **2002**, *23(3)*, 857.
152. Kiefer, B.; Shieh, S. R.; Duffy, T. S.; Sekine, T.; *Physical Review B*, **2005**, *72(1)*, 014102.
153. Takahashi, K.; Ando, K.; Murase, H.; Nakayama, S.; Saito, S.; *Journal of the American Ceramic Society*, **2005**, *88(3)*, 645.
154. Qiao, S.; Cao, H.; Zhao, X.; Lo, H.; Zhuang, L.; Gu, Y.; Lai, H.; *International Journal of Nanomedicine*, **2015**, *10*, 653.
155. Pieralli, S.; Kohal, R. J.; Hernandez, E. L.; Doerken, S.; Spies, B. C.; *Dental Materials*, **2018**, *34(2)*, 171.
156. Velasco-Ortega, E.; Alfonso-Rodríguez, C. A.; Monsalve-Guil, L.; España-López, A.; Jiménez-Guerra, A.; Garzón, I.; Gil, F. J.; *Materials Science and Engineering: C*, **2016**, *64*, 1.
157. Salvi, G. E.; Bosshardt, D. D.; Lang, N. P.; Abrahamsson, I.; Berglundh, T.; Lindhe, J.; Donos, N.; Temporal sequence of hard and soft tissue healing around titanium dental implants. Periodontology 2000, **2015**, *68(1)*, 135.
158. He, X.; Reichl, F. X.; Wang, Y.; Michalke, B.; Milz, S.; Yang, Y.; Högg, C.; *Dental Materials*, **2016**, *32(8)*, 1042.
159. Tunchel, S.; Blay, A.; Kolerman, R.; Mijiritsky, E.; Shibli, J. A.; *International Journal of Dentistry*, **2016**.
160. Schierano, G.; Mussano, F.; Faga, M. G.; Menicucci, G.; Manzella, C.; Sabione, C.; Carossa, S.; *BioMed Research International*, **2015**.
161. Gehrke, S. A.; Prados-Frutos, J. C.; Prados-Privado, M.; Calvo-Guirado, J. L.; Aramburú Júnior, J.; Pérez-Díaz, L.; De Aza, P. N.; *Materials*, **2019**, 12(6), 856.
162. Zeller, B.: Stöckli, S.; Zaugg, L. K.; Astasov-Frauenhoffer, M.; Hauser-Gerspach, I.; Waltimo, T.; Zitzmann, N. U.; *Clinical Oral Implants*, **2020**.

163. Sivaraman, K.; Chopra, A.; Narayan, A. I.; Balakrishnan, D.; *Journal of Prosthodontic Research*, **2018**, *62(2)*, 121.
164. Adánez, M. H.; Nishihara, H.; Att, W.; *Journal of Prosthodontic Research*, **2018**, *62(4)*, 397.
165. Kjellin, P.; Vikingsson, L.; Danielsson, K.; Johansson, P.; Wennerberg, A.; *Materialia*, **2020**, 100645.
166. Cai, L.; Pan, Y.; Tang, S.; Li, Q.; Tang, T.; Zheng, K.; Su, J.; *Journal of Materials Chemistry B*, **2017**, *5(42)*, 8337.
167. El Awadly, T. A.; Wu, G.; Ayad, M.; Radi, I. A.; Wismeijer, D.; Abo El Fetouh, H.; Osman, R. B.; Clinical Oral Implants Research, **2020**, *31(3)*, 246.
168. Sahoo P.K.; *Apollo Med.*, **2013**, *10*, 233.
169. Kurtz, S.M.; Devine, J.N.; Biomaterials, **2007**, *28*, 4845.
170. Kim, M.M.; Boahene, K.D.; Byrne, P.J.; *Arch Fac Plast Surg.;* **2009**, *11*, 53.
171. Scolozzi, P.; Martinez, A.; Jaques, B.; *J. Craniofac Surg.*, **2007**, *18*, 224.
172. Pearce, A.; Richards, R.; Milz, S.; Schneider, E.; Pearce, S.; *Eur. Cell Mater.*, **2007**, *13*, 1.
173. Arts, M. P.; Wolfs, J. F.; Corbin, T. P.; *European Spine Journal*, **2017**, *26(9)*, 2372.
174. Youssef, S.L.; Myhre, and B.S. Bal.; *J. Musculoskelet. Disord. Treat.*, **2016**, *2(1)*, 1.
175. FDA.gov (Administración de Medicamentos y Alimentos). Consultado el 13 de enero **2021**.
176. Niinomi, M.; Boehlert, C. J.; Titanium alloys for biomedical applications. In Advances in Metallic Biomaterials, Springer, Berlin, Heidelberg, **2015**, pp. 179-213.
177. Strid, K. G.; Regulatory Aspects in the Use of Titanium-based Materials for Medical Applications. In Titanium in Medicine, Springer, Berlin, Heidelberg, **2001**, pp. 929-947.
178. FDA, U.; Biological Responses to Metal Implants. Food Drug Admistration, **2019**.
179. Lawson, S.; Journal of the European Ceramic Society, **1995**, *15(6)*, 485.
180. Oliva, J.; Oliva, X.; Oliva, J. D.; *International Journal of Oral & Maxillofacial Implants*, **2010**, *25(2)*.
181. Oliva, J.; Oliva, X.; Oliva, J. D.; *International Journal of Oral & Maxillofacial Implants*, **2007**, *22(3)*.
182. Mellinghoff, J.; Erste klinische Ergebnisse zu dentalen Schraubenimplantaten aus Zirkonoxid. Z Zahnärztl Impl, **2006**, *22(4)*, 288-293.
183. Lambrich, M.; Iglhaut, G.; Vergleich der überlebensrate von zirkondioxid-und titanimplantaten. Z Zahnärztl Impl, **2008**, *24(3)*, 182-191.
184. Green, S.; Schlegel, J.; A polyaryletherketone biomaterial for use in medical implant applications. *Polym for the Med Ind Proc, Brussels*, **2001**, 14-15.
185. Graham, J.; Peck, J.; FDA Regulation of PEEK Implants. In PEEK Biomaterials Handbook, William Andrew Publishing, **2019**, pp.431-445.
186. Coric, D.; Guyer, R. D.; Carmody, C. N.; Sasso, R. C.; Musacchio, M. J.; Bae, H. W.; Ohnmeiss, D. D.; *The Spine Journal*, **2020**, *20(9)*, S80.
187. Palmero, P.; De Barra, E.; Cambier, F.; Advances in ceramic biomaterials: materials, devices and challenges. Woodhead Publishing, (Eds.), **2017**.
188. Pezzotti, G.; Ohgitani, E.; Shin-Ya, M.; Adachi, T.; Marin, E.; Boschetto, F.; Mazda, O.; Rapid inactivation of SARS-CoV-2 by silicon nitride, copper, and aluminum nitride. *BioRxiv*, **2020**.
189. Lehman, C. W.; Flur, R.; Kehn-Hall, K.; McEntire, B. J.; Bal, B. S.; Bock, R. M.; Silicon Nitride Inactivates SARS-CoV-2 in vitro. *BioRxiv*, **2020**.
190. Gorth, D. J.; Puckett, S.; Ercan, B.; Webster, T. J.; Rahaman, M.; Bal, B. S.; *International Journal of Nanomedicine*, **2012**, *7*, 4829.
191. Pettersson, M.; Berlind, T.; Schmidt, S.; Jacobson, S.; Hultman, L.; Persson, C.; Engqvist, H.; *Surface and Coatings Technology*, **2013**, *235*, 827-834.
192. Rahaman, M.; Xiao, W.; *International Journal of Applied Ceramic Technology*, **2018**, *15(4)*, 861.

Authors biography

Manuel Aparicio-Razo, is a mechanical engineer graduated from the national system of technological institutes, MSc in electronics and automation, Dr. (c) in biomedical engineering sciences. Full-time research professor at the Faculty of Electronic Sciences of the “Benemérita Universidad Autónoma de Puebla”, Mexico. His research area focuses on the study of new mechanical and electromagnetic properties in materials for biomedical and industrial applications.

Genaro Alberto Paredes-Juárez, is Biologist, with a master's degree in biotechnology from the "Universidad de las Américas, Puebla" (UDLAP) in Puebla, Mexico, and a Ph.D. in Biomedical Engineering from the University of Groningen, in the Netherlands, Postdoctoral fellow in the department of radiology and imaging at Johns Hopkins University, Baltimore, Maryland. He has level 1 of the "National System of Researchers" (SNI) and works as a part-time teacher at the "Universidad Popular Autónoma del estado de Puebla" (UPAEP); research area in immunology and biomaterials with several research papers published in the field.

J. A. Yáñez Ramos, is Mechanical Engineer and Master in Integrated Manufacturing Systems and Quality Strategies. He is Professor-Researcher in the College of Industrial Engineering at the “Instituto Tecnológico de Puebla”, México. His research area focuses in improving and optimizing product designs, manufacturing processes and production systems through software systems.

Israel Vivanco-Pérez, is a Maxillofacial Surgeon graduated from the University Hospital of Puebla of the “Benemérita Universidad Autónoma de Puebla”, certified by the Mexican Council of Oral and Maxillofacial Surgery, collegiate member of the Mexican Association of Oral and Maxillofacial Surgery, currently medic assigned to the service of Maxillofacial Surgery of the University Hospital of Puebla , adjunct professor in the Maxillofacial Surgery specialization course at the University Hospital of Puebla and head of the same service.

José Luis Jr. Mongalo-Vázquez, is a Dental Surgeon from the Autonomous University of Zacatecas. Master in Dental Implantology endorsed by the ICOI. Trainer in dental implantology for dentists around the world in association with various international companies and for his own. Certified as instructor by the IDEFT and director of the dental clinic "ORALIS" in the city of Guadalajara, Jalisco (México). Resident of the specialty in Maxillofacial Surgery at BUAP, in the City of Puebla, México.

Adolfo Navarro-Zárate, is graduated in Stomatology from BUAP. Specialist in Maxillofacial Surgery graduated from the University Hospital of Puebla. Research professor at the BUAP faculty of medicine. Professor of the specialty of Maxillofacial Surgery at the University Hospital of Puebla.

Víctor Hugo Santos-Enríquez, is graduated in Stomatology. Maxillofacial Surgeon graduated from the “Benemérita Universidad Autónoma de Puebla” (BUAP). Professor of the Specialty of Maxillofacial Surgery of the University Hospital of Puebla of the BUAP

J. Flores Méndez, is Doctor in Materials Science. In addition, he has a Master of Science in Mechanical Engineering. Currently, he is a Professor-Researcher at the Faculty of Engineering of the “Benemérita Universidad Autónoma” de Puebla and at the “Instituto Tecnológico de Puebla”, Mexico. He is part of the National System of Researchers of Mexico. His research area focuses on studying the acoustic and electromagnetic response in metamaterials and computational finite element analysis.

Graphical Abstract