Study on the Zirconia Surface Modification and Osseointegration

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Abstract: Zirconia was proposed as an alternative material to titanium implant. Considering the condition of osseointegration and the stability of the implant, surface modifications of zirconia were attracting more and more attention. This study provides an overview of recent surface treatment technologies that have shown potential in augmenting the biological and osseointegration aspects of zirconia dental implants. These methods include non-thermal plasma treatment, laser texturing, TiO_2 and hydroxyapatite coatings, carbon and nitrogen implantation, and the use of bioactive molecules. we concluded that the surface modification of zirconia can enhance the osseointegration effect by inducing surface roughness, increasing the surface energy and potential, and introducing functional units to the surface. Moreover, dimensional changes in nanoscale-structure are not invariably dominant in osseointegration of all surface modification methods.

1. Introduction

Titanium is known for its excellent biocompatibility and stability, and is commonly used as dental implant material. However, previous studies have reported allergic reaction, peri-implant inflammation and hypersensitivity to titanium, which can be aggravated by the released titanium particles from bio-tribocorrosion[1,2]. In addition, while used as the implant, blue-greyish shimmering of titanium may lead to a negative aesthetic impact, causing an obvious color difference with the thin gingival tissues of adjacent teeth[3]. The high aesthetic expectations of patients nowadays and certain concerns about titanium allergies have caused the rising demand for alternative materials. Although the alumina implant was proposed as a substitute, the heterogeneity of this first generation of ceramic implant resulted in its temporary disappearance from commercial scene[4].

Zirconia was subsequently introduced as a surrogate ceramic material with improved performance. Nowadays, zirconia ceramic has been regarded as a promising replacement to titanium for dental implants because of their tooth-like white-opaque appearance, excellent biocompatibility, as well as appropriate characteristics such as high fracture toughness, high flexural strength and high anticorrosion property. Furthermore, studies have shown that zirconia may exhibit antibacterial properties, as well as the ability to regulate vesicular transport, cell cycle modulation and immunity [5–7].

Nevertheless, the biological inertia of zirconia surfaces is not favorable to the construction of chemical linkages with native bone[8]. zirconia showed less effective osseointegration and immediate loading compared with titanium in the absence of surface modification[9,10]. Moreover, the bioinert of zirconia leads to higher bone loss, which raises the risk of implant surgery failure and compromises the long-term outcome of zirconia implant[11].

Therefore, there is increasing interests in surface modifications to promote early healing and strengthen the bone-formation and bone-implant integration effect on zirconia implants. Previous publications have gone to great lengths to adapt the topographical and bioactive aspects of zirconia surfaces to facilitate appropriate cellular behavior during the healing process. For modifying zirconia surfaces, certain physicochemical methods were employed including sand blasting, UV light irradiating, laser texturing, and so on. Coatings with various ingredients such as dopamine, magnesium, hydroxyapatite and calcium phosphate onto the zirconia also demonstrated favorable biological and osseointegration outcomes.

In this study, we aim to perform a literature review on surface modifications that enhance the osseointegration and bioactivity of zirconia dental implants in latest years.

2. Nonthermal atmospheric pressure Plasma

Nonthermal atmospheric pressure plasma (NTP), otherwise referred to as cold atmospheric plasma (CAP), was reported to present analogous potency to the antibacterial effect of 0.2% chlorhexidine digluconat, which further facilitates its application on periodontal and peri-implant treatment. Not only can it inhibit the inflammatory response, but also enhance bone formation around the implant. Adjunctive NTP treatment of zirconia implant surfaces has shown promising results in poor bone conditions. Besides, NTP treatment using oxygen plasma was found to improve the attachment, proliferation and vitality of soft tissue cells on polished zirconia, while argon plasma treatment demonstrated minimal effects on the soft tissue cytocompatibility. NTP

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treatment on zirconia surface for 60s increased the attachment of osteoblasts, and exhibited in sterilization and inhibition effects of Porphyromonas gingivalis. Prolonged treatment times, however, exhibited a contrary result of the increase in P.gingivalis adhesion. Further studies are recommended to investigate the effects of NTP treatment to other types of common oral bacteria on zirconia.

NTP treatment has been shown to enhance the initial attachment of osteoblasts and bone-implant integration through increased hydrophilicity, as demonstrated in a study by Duske et al. (2012) where the treatment significantly improved the wettability and cell spreading on dental implant metals. It shares similar mechanisms as ultraviolet (UV) light irradiation in enhancing the bioactivity of implant surfaces. Both the UV-light and NTP treatment improve the hydrophilic property of the zirconia surfaces by inducing in composition of the surface oxide layer. These physicochemical alternations are mainly related with the direct photolysis of hydrocarbons induced by UV light or the formation of reactive oxygen species by NTP. The hydrophilic effect induced by NTP treatment is positively correlated with the initial wettability and surface roughness. Although Non tropical atmospheric pressure plasma (NTP) processing has shown positive effects, there are also some challenges. For example, Duske et al. (2012) found that prolonged NTP treatment may lead to increased bacterial adhesion, which may limit its long-term effectiveness in clinical applications. Future research needs to further explore the optimal balance between NTP processing time and effectiveness.

A comparative study between the influences of NTP and UV light on zirconia implants revealed that both treatments markedly reduced organic content and enhanced oxidizing of the surface. There was an increase in wettability and improvement in cellular environment for osteoblasts, meanwhile the surface topography and roughness were not altered. Oxygen plasma showed a slight advantage in cell growth when comparing NTP with UV light treatment. Furthermore, NTP treatment exhibited better performance in enhancing cell proliferation and attachment of zirconia than UV light. Another in vitro study revealed that Helium plasma had the better effect on human gingival fibroblasts adhesion, proliferation compared to UV light, especially on collagen synthesis.

However, according to an in vivo study, there were no statistically significant differences in bone-to-implant contact (BIC) and bone area fraction occupancy (BAFO) values between the non-treated group, UV light treated group, and NTP treated group. It was mentioned that the chosen animal model of this study might be a limitation, as high turnover rate of the juvenile pig may contribute to the unsignificant differences on BIC and BAFO among the tested groups. Another limitation was that the calvarial bone model cannot provide an ideal long-term osseointegration environment due to the absence of masticatory forces load.

In regard to different types of plasma gases, oxygen plasma favors fibroblasts and osteoblasts on cell attachment and proliferation compared to argon plasma. A study revealed that N_2 plus Ar plasma treatment showed the best performance in optimizing the bioactivity and bonding ability of 3Y-TZP among the tested groups including N_2, Ar, He/O_2, and N_2/Ar. In the N_2/Ar group, microstrain and the alternation in crystallite size induced by the displacements of oxygen atom were detected.

It's worth noticing that non-thermal oxygen plasma treatment offers a chairside method for modifying hydrophobic implants to enhance the wettability. The future consideration of plasma-sensitive properties in biomaterial design allows for the customization of implant surface features towards tissue-adapted biomaterials.

3. Laser texturing

Compared to other surface modification methods, laser texturing offers distinct advantages and is garnering increasing attention in current research. Initially, the treatment process is entirely contactless, thus preventing any contamination on the surface of the implant. Secondly, laser treatments can be utilized for any materials, regardless of their hardness or mechanical strength. Thirdly, laser treatments are capable to control the wettability of the implant by producing distinct hierarchical surface structures and increasing surface energy.

A hierarchical structure morphology encompassing meso-, micro-, and nano-scale roughness on zirconia (Y-TZP) surface created by solid-state laser has been reported. The surface was textured by uniformly carved meso-scale grooves, micro-scale valleys, and nano-scale nodules. The design was built on the supposition that meso-scale roughness enhances the intermeshing between the bone and implant surface, as well as the micro-scale and nano-scale roughness stimulate and strengthen bone formation, therefore reinforce the implant anchorage. After the treatment, the average roughness was remarkably higher than those of machined zirconia in multiples. The laser-roughened zirconia surface exhibited greater hydrophobic and a higher carbon content compared to machined zirconia. Interestingly, this laser-roughen zirconia and polished zirconia exhibited similar rates of osteoblastic proliferation in vitro, but the degree of osteoblastic differentiation was notably promoted on laser-roughen zirconia. Higher push-in values and bone–implant integration on the laser-roughen zirconia were also observed in vivo.

Subsequently, the research team created a hybrid zirconia surface by laser in a crisscrossing manne. The laser carved out grooves in a vertical and horizontal pattern, leaving unengraved areas resembling spikes, thereby controlling the height of the meso-scale spikes. Average roughness surged from 0.10 μm (polished smooth surface) to a remarkable value of 18.14 μm (80 μm-high spikes), coinciding with the increase of surface area in multiples. Among all the tested samples, the laser-modified surface with 40 μm-high spikes exhibited remarkable osteoblastic differentiation capacity as well as in vivo bone-implant integration. The push-in values of zirconia implants featuring this surface topography were about 40 N after 2 weeks, and increased to 72 N after an additional 2 weeks of healing. In comparison, common acid-etched titanium implants were reported push-in values at 15 N and 28 N after the same healing periods in the same animal model.

Further study demonstrated that the biological significance of the nano-trabecula changing in size was comparatively modest to that generated by the hybrid rough topography or different sizes of meso-spike. Another interesting result is that both tested modified surface were hydro-repellent, while the small nano-trabecula size group showed slightly greater hydrophobicity than the other groups. This study also revealed how osteoblasts attach and spread on hierarchically textured implant surfaces at the meso-scale for the first time.

This crisscross laser-treated hybrid surface may have provided another strategy for enhancing bone-implant integration, which is to promote osteoblastic differentiation, and minimize the decline in available osteoblasts for implant-related bone regeneration. The balance between attachment/proliferation rate and osteoblastic differentiation is critical to optimize bond-implant integration. Although laser texturing can accurately control surface roughness, this technology may require high equipment investment and professional operating skills, which to some extent limits its feasibility in wider clinical applications.

However, the wettability of a surface is affected not only by the surface morphology but also by the surface free energy. Further study utilizing technology like non-thermal plasma or ultraviolet light could potentially optimize the biological performance by increasing the surface free energy, enhancing the hydrophilic effect and removing residual carbon without alternating the hierarchy surface structure.

4. TiO_2 coating

TiO_2 was identified to promote cell attachment, spreading, proliferation and differentiation, which further affected by its structural characteristics including morphology, nanostructured features and crystal phase. Hydroxyl groups on TiO_2 surface triggered proteins attachment and promoted mineralization in vitro, consequently inducing a highly bioactive response. Most importantly, the TiO_2 coating prevent the zirconia matrix from low-temperature degradation effect and prolong the service lifespan of the zirconia implant. However, there are certain challenges ensuring appropriate bonding strength with the zirconia substrate using sol-gel method, or maintaining the mechanical qualities of composite materials produced by mixing commercial titania and Y-TZP powders together.

A novel TiO_2 coating technique was devised involving the immersion of zirconia in a composite of TiO_2 and $ZrOCl_2$ suspension followed by water bath treatment prior to zirconia sintering. Tang et al. (2021) found that a TiO2 coating prepared with zirconium oxychloride and titania on zirconia surfaces significantly enhanced surface roughness and wettability, while maintaining the mechanical integrity of the zirconia. The treated surface forms a TiO_2, $TiZrO_4$ and ZrO_2 gradient layer of reduced hardness, further to mitigate the shortcomings of high elastic modulus of zirconia implants. In vitro investigations showed that this TiO_2 coating exhibited favorable biocompatibility and promoted the spreading, proliferation, differentiation and mineralization of osteoblast-like cells. After UV light treatment, hydroxyl group content and wettability were remarkably heightened while the surface topography remained unaltered. The contact angle of the UV light treated TiO_2-modified zirconia (9.33°) was significantly higher than that of TiO_2-modified zirconia without UV light treatment (43.95°). The coating exhibited sufficient bonding strength to withstand loading. In vitro studies demonstrated that UV-light-treated TiO_2-coated zirconia promote cell spreading, proliferation and differentiation. Moreover, in vivo evaluation confirmed that UV light treatment on TiO_2-coated zirconia implants maximally facilitated osseointegration.

A study explored another manner to produce a tightly bonded TiO_2 coating on zirconia surface and synchronously establish a micro-/nano-scale hierarchical structure. The TiO_2 nanocoating was deposited on a previously acid etched zirconia surface with microscale morphology by atomic layer deposition (ALD) technology. Further annealing transformed the amorphous TiO_2 to anatase, generating nanoscale topography. The anatase TiO_2 coated surface exhibited greater hydrophilicity than acid etched surface and amorphous TiO_2 coated surface, as well as better osteoblast attachment, proliferation, osteogenic differentiation and mineralization properties. Despite the nanocoating and annealing processes did not affect the micro-roughness of the zirconia surface, the nanomorphology of the TiO_2 coating varied with different annealing conditions. Regular wavy nanostructure was generated after annealing at 800°C for 5 minutes, which showed the best performance both in vivo and in vitro. This anatase TiO_2 coating with wavy nanostructure promoted the early integration between zirconia implants and bone in vivo. The study pointed out that these positive effects may be caused by the nanostructure through the canonical Wnt/β-catenin pathway. Although TiO2 coatings can enhance the biological activity of the zirconia surface, ensuring long-term stability and wear resistance between the coating and the zirconia substrate remains a technical challenge, which may affect the long-term performance and success rate of implants.

5. Hydroxyapatite coating

Hydroxyapatite (HA) serves as the primary inorganic component of teeth and bone. It has been widely applied as orthopedical and dental implant coating for its pivotal role in bone mineralization and demonstrated capacity to expedite rapid osseointegration. Nano-structured HA constructed by micro-arc oxidation could facilitate the conductivity and inductivity of bones, along with angiogenesis on the titanium surface. Regarding the application of HA coating onto zirconia surfaces, it is important to ensure the coating bond strength and control the production of byproducts.

A study investigated the use of sol-gel technique to establish a HA layer on zirconia surface. The HA sol composition was prepared and subsequently applied to zirconia using the dip-coating technique before sintering. The crystal phase and structure of the sol–gel-obtained HA coating were accommodated by regulating the sintering temperature. At a sintering temperature of 800 °C, the HA surface demonstrated a nano-porous structure without any byproducts. Results from the peel-off test yielded an adhesive strength of 40 MPa. This sol-gel-obtained HA coated zirconia exhibited similar performance to titanium in vitro and in vivo.

Another study explored depositing a fluorinated hydroxyapatite (FHA) film on zirconia (NANOZR) surface using pulsed laser deposition. After treatment, the surface roughness escalated from 2 nm toward 43 nm, whereas the contact angle was reduced to 48°. Tensile test revealed a bonding strength of 17 MPa. This FHA coating exhibited better biological performance in vitro, with a notably heightened amount of newly generated peri-implant bone on FHA-coated implants in contrast to bare NANOZR implants. Furthermore, the addition of fluoride stimulated osteoblasts and osteoprogenitor cells to proliferate and differentiate, as well as the calcium phosphate to mineralize and crystallize during bone formation.

6. Carbon and nitrogen plasma

A nitrogen plasma modified surface was demonstrated to establish a preferable microenvironment to modulate the osteoblasts differentiation. A study introduced nitrogen functional groups on the zirconia surface to generate osteo-inductive microenvironment via applying plasma immersion ion implantation (PIII) technology. Nevertheless, direct exposure to nitrogen proves ineffective in generating functional groups on zirconia due to the absence of a carbon chain skeleton. To overcome this limitation, carbon was implanted onto the zirconia surface using PIII technique so as to construct an in situ carbonized layer, and then implanted nitrogen to form a new chemical structure. Following the treatment, the nitrogen-containing functional groups with high potential were introduced, and the surface hardness increased significantly, meanwhile the surface morphology characteristics and the stability of zirconia remained unaffected. Nanoindentation test revealed no peeling under a load of 100 mN. In vitro study indicated the nitrogen functionalities facilitated a desirable extracellular environment to promote the attachment, proliferation and osteogenic differentiation of osteoblasts. The high surface potential of this modified zirconia also demonstrated remarkable antibacterial effects against common oral bacteria. Drug resistance was barely induced even after six generations of bacterial cultivation.

7. Bioactive molecule

In recent years, researchers have shown a keen interest in methods that immobilize bioactive molecules for surface modification to promote the healing process of titanium implants. The following bioactive molecules are used for titanium surface modification:(1) bone morphogenetic proteins (BMPs), (2) non-BMP growth factors, (3) extracellular matrix (ECM), and (4) peptides components. During the initial intercommunicating process of the implant surface, proteins and ligands are responsively ingested at the surface. This is followed by a subsequent inflammatory release, culminating in bone formation around the surface. Over multiple cycles of remodeling, the surface attains the utmost level of organization and biomechanical competence.

Aung et al. (2023) reported that the immobilization of fibronectin on zirconia surfaces using allylamine significantly enhanced the viability, proliferation, and differentiation of osteoblasts, as well as upregulated the expression of mRNA associated with bone formation in osteoblast-like cells. The incorporation of allylamine formed amine functionalities, further promoted the binding of bioactive proteins on the surface. Zirconia samples were treated by allylamine synthesis in a glow discharge plasma machine, followed by immersion in cross-linking agent solution to trigger an allylamine-fibronectin chain reaction, and then submerged in fibronectin solution. Notably, surface irregularity and water affinity were greatly improved after the treatment. The allylamine and fibronectin concentrations were positively correlated to the contact angle as well as surface roughness. In addition, organic functional groups were detected on the surface after the treatment.

A systematic review and meta-analysis indicated/revealed that the BMPs subgroup exhibited the highest efficacy in terms of coating when compared to peptides and ECM in vivo. The introduction of BMP-2 onto textured zirconia surfaces, aided by genipin for immobilization, demonstrated notable effectiveness in promoting attachment and mineralization of human mesenchymal stem cells (hMSCs). Genipin, a naturally extracted cross-linker for proteins, offers superiority to glutaraldehyde for its cellular toxicity, biological compatibility, mechanical qualities, and antidegradation from enzyme. Moreover, importantly, the grafting process for the complete fibronectin modification merely entails immersing the sample in distinct solutions. All of these attributes collectively render this surface modification technique operationally and economically advantageous. Although immobilization of bioactive molecules can enhance the surface bioactivity of implants, the stability and long-term effects of the immobilization process still need further research to ensure the bioactivity and function of these molecules after implantation.

8. Conclusion

In this study, we conducted an exhaustive examination of assorted zirconia surface modification techniques that have been developed in recent years. The augmentation of zirconia surfaces through modifications has demonstrated remarkable potential to enhance osseointegration. This enhancement is achieved by inducing surface roughness, elevating surface energy and reactivity, and introducing functional units onto the surface. In addition, preferable osseointegration outcomes can be achieved by nano-scale modification. However, the variations in the size of nano-scale structures are not necessarily crucial in certain surface modification methodologies. Nevertheless, it is imperative to exercise caution when drawing definitive conclusions about the superior surface modification approach. This is due to certain investigations being confined to in vitro experiments, lacking comprehensive in vivo and clinical evaluations, rendering it scientifically unsound to unequivocally proclaim any particular surface modification method as the preeminent choice. Future research can focus on the following directions: firstly, more long-term clinical trials are needed to evaluate the long-term stability and effectiveness of these surface modification technologies. Secondly, exploring the combination of different surface modification methods to achieve synergistic effects may further improve the performance of the implant. In addition, in-depth research on how surface modification affects the interaction between implants and surrounding tissues, including cellular behavior and tissue reactions, is crucial for optimizing implant design. Finally, with the advancement of nanotechnology and biomaterials science, the development of new surface modification methods, such as nanostructured coatings or intelligent responsive materials, may bring innovation to the field of implant surface modification.

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