

Review

Titanium Surface Modification Techniques to Enhance Osteoblasts and Bone Formation for Dental Implants: A Narrative Review on Current Advances

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Abstract: Surface modifications for titanium, a material of choice for dental implants, can greatly alter the surface micro/nanotopography and composition of implants, leading to notable enhancements in their hydrophilicity, mechanical properties, osseointegration performance, and antibacterial performance, as well as their impacts on osteoblast activity and bone formation processes. This article aims to update titanium surface modification techniques for dental implants from the past to the present, along with their effects on osteoblasts and bone formation, by thoroughly summarizing findings from published studies. Peer-reviewed articles published in English consisting of in vitro, in vivo, and clinical studies on titanium dental implant surface treatments were searched in Google Scholar, PubMed/MEDLINE, ScienceDirect, and the Scopus databases from January 1983 to December 2023 and included in this review. The previous studies show that implant surface roughness, condition, and hydrophilicity are crucial for osteoblast adhesion and growth. While various techniques enhance osseointegration comparably, one of the most common approaches to accomplishing these properties is sandblasting large-grit acid etching surface treatment and coating with hydroxyapatite or chitosan. In conclusion, this review points out the efficacy of different subtraction and addition techniques in enhancing the surface properties of titanium dental implants, promoting favorable outcomes in terms of osteoblast activity and bone formation in various degrees. However, most existing studies predominantly compare treated and non-treated titanium, revealing a need for more comprehensive studies comparing the effects of various modification techniques. Moreover, further investigation of factors playing a role in the dynamic osseointegration process in addition to osteoblasts and their functions, as well as improved surface modification techniques for the treatment of compromised patients, is greatly required.

Keywords: surface treatment; sandblasting; acid etching; SLA; anodization; laser radiation



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1. Introduction

The current world population is undergoing a transition towards becoming a geriatric society. According to the World Population Prospects 2019, the data suggest that the percentage of people aged 65 and over would rise from 1 in 11 in 2019 to 1 in 6 by 2050 [1]. The most prevalent oral health concern among the elderly is tooth loss [2]. Replacement of missing teeth can be accomplished via various techniques; at present, dental implants are the most realistic alternative to natural teeth. Dental implants provide numerous advantages, such as enhanced oral health, improved pronunciation and chewing, preservation of adjacent teeth and bones, and an overall improvement in quality of life. Regarding the materials, metal alloys, including stainless steel, cobalt–chromium alloy, and titanium-based alloy, are typically utilized for dental implants [3–7]. Titanium alloys are widely acknowledged as the optimal materials for implants due to their ability to strike a balance between mechanical performance and biological compatibility, ensuring the success and longevity of medical implants [3]. The success rate of titanium dental implant surgery can exceed 90%, however,

there is still a failure probability of approximately 10% [8]. In order to reduce the failure rate, implant surface treatments play a crucial role in enhancing the healing process following implant placement, which is called “osseointegration”. Osseointegration is defined as the direct structural and functional connection between the living bone and the surface of a load-bearing implant [9]. This process can be divided into four overlapping phases: (1) Hemostasis phase; it occurs immediately after the extraction. It involves vasoconstriction, blood clot formation, and ion adhesion, primarily involving platelet cells; (2) Inflammatory phase; it can last from minutes to days after the extraction and is characterized by vasodilation, diapedesis, and pathogen elimination with the involvement of various inflammatory cells, such as neutrophils and proinflammatory (M1) macrophages; (3) Proliferative phase; it is crucial for primary stability, the initial interlocking between the alveolar bone and the implant body, which occurs roughly from days to weeks after the extraction. It is marked by the adhesion of various cells involved in tissue proliferation, including fibroblasts, endothelial cells, anti-inflammatory (M2) macrophages, and osteoblasts; and (4) Maturation phase, which occurs approximately 3 months to years after the extraction. During this phase, foreign body giant cells remove foreign bodies at the implant site, as well as osteoblasts and osteoclasts, which contribute to bone remodeling [10,11]. This ultimately leads to secondary stability, which refers to biological fixation achieved through continuing bone growth and remodeling around the implant surface [12]. There are three key variables that contribute to the achievement of secondary stability (Figure 1): (1) Osteogenesis: this process requires osteoblasts to adhere and grow on the surface of the implant; (2) Suppressing peri-implant inflammation: managing and reducing inflammation around the implant is essential; and (3) Antibacterial properties: enhancing the ability of the implant to resist bacterial growth is crucial [13]. The most important element for achieving these properties, as mentioned above, is the surface condition of the implants. Proper surface modification plays a significant role in improving the surface topography and composition of the implant. These modifications aim to provide suitable roughness, wettability, and antibacterial activity, thereby promoting the attachment of osteoblasts to the implant surface and facilitating a complete osseointegration process [13]. Our research question is whether the various established titanium surface treatment methods result in different physical, mechanical, and biological properties, and we expect that some approaches may potentially have more superior effects on promoting osseointegration than the others. Therefore, this review article aims to summarize various titanium surface modification techniques for dental implants from the past to the present, both conventional and novel, and compare their effects on osteoblasts and bone formation in in vitro, in vivo, and clinical studies.

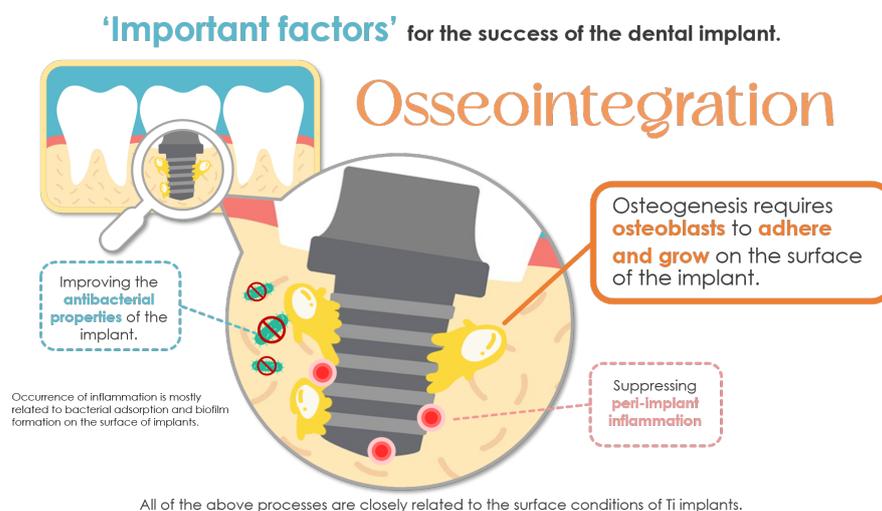


Figure 1. Important factors for the successful osseointegration following dental implant placement.

2. Materials and Methods

A literature search of electronic databases was conducted using Google Scholar, PubMed/MEDLINE, ScienceDirect, and the Scopus databases from January 1983 to December 2023. The search keywords, including combinations of terms such as “Titanium”, “Dental implants”, “Osteoblast”, “Anodization”, “Sandblasting”, “Acid etching”, “Laser radiation”, “HA coating”, “Chitosan” were used to search and obtain data about the surface modification techniques for dental implants on osteoblast and bone formation. Peer-reviewed articles published in English consisting of in vitro, in vivo, and clinical studies were included. These articles were categorized regarding the different methods of titanium surface treatments affecting osteoblast and bone formation, including sandblasting, acid etching, sandblasted large-grit acid-etching (SLA), anodizing, and laser radiation. Moreover, another set of keywords, including “implant success rate”, “implant surface”, “implant survival rate”, and “peri-implantitis” was used for a literature search regarding the clinical outcome of implants treated by various techniques. Non-English publications were excluded from this review.

3. Results

3.1. Titanium Surface Modification Techniques and Their Effects on Osteoblasts and Bone Formation In Vitro and In Vivo

The techniques for preparing the surface of dental implants can be broadly divided into two groups. The first group is the subtraction technique, which includes surface preparation methods such as sandblasting, acid etching, SLA, anodizing, and laser radiation. These technologies effectively modify the roughness, hardness, and oxidation of Ti. The other type is the addition technique. The titanium surface can be coated with different substances, which can significantly alter the surface composition and enhance its biological properties. Coating can be performed via several methods, such as plasma spraying, nanospray drying, sol-gel method, hydrothermal method, self-assembly method, 3D printing, and etc. [13]. In this review, various parameters will be employed in both in vitro and in vivo studies to serve as indicators of osteoblast activity and bone formation. For the in vitro studies, osteoblast morphology, proliferation, alkaline phosphatase (ALP), collagen calcium deposit, and etc., were determined. While, histology, bone-to-implant contact (BIC), and removal torque were mainly focused on the in vivo studies.

3.1.1. Subtraction Technique

Subtractive surface treatment refers to the processes that remove materials from the surface of dental implants to achieve desired surface characteristics. These methods typically involve mechanical, chemical, or electrochemical techniques to create a specific surface topography that can enhance osseointegration, resulting in a micro- or nanorough texture [14].

Sandblasting

Sandblasting is an essential surface treatment procedure used in dental implantology to improve the osseointegration of titanium implants. The procedure involves using compressed gas to propel microspheres and sharp-edge particles such as TiO₂, Al₂O₃, SiO₂, or hydroxyapatite (HA), onto the surface of titanium. This provides an uneven roughness that ranges from 0.3 to 3 μm, which is a major improvement compared to the average 0.04 μm roughness of polished titanium [15]. The heightened roughness leads to an expanded surface area and enhanced surface free energy, which enhances the attachment of cells and proteins and facilitates the formation of new bone tissue. The effectiveness of the sandblasting process is influenced by various factors, including the hardness, size, and speed of the microspheres, the distance and angle of the spray gun, the treatment time, and the pressure of the gas. These parameters play a crucial role in determining the final surface characteristics of the titanium implant.

- Surface Properties of Sandblasted Titanium

Although sandblasting enhances superior surface properties in various aspects, there are several pitfalls which should be aware of. For instance, grit-blasting process might potentially influence the adhesion of bacteria and the production of biofilms which needs to be carefully considered to achieve a balance between osteointegration promotion and biofilm inhibition [16]. Furthermore, different types and particle sizes of microspheres can result in contamination on the surface of the implant, potentially causing a local toxic or inflammatory response by the dissolution of Al_2O_3 ions into the surrounding bone tissue [17]. The surface preparation with the sandblasting technique also causes the titanium surface to have irregularities with sharp edges and become contaminated with residual particles. Consequently, this results in enhanced hydrophobicity of the implant surface, which inhibits the formation of a strong connection between the implants and bone tissue. This local release of remnants from blasting materials has been suggested to impair bone mineralization [18]. Osak et al. conducted experiments by subjecting titanium grade 4 (TiAl_6V_4) to sandblasting with Al_2O_3 , followed by ultrasonic treatment in acetone and ultrapure water to remove Al_2O_3 particle residues. The results revealed that when measuring the water contact angle, TiAl_6V_4 after mechanical polishing showed a value of 66° . After sandblasting, this angle increased significantly to 131° . This indicates that sandblasting changes the surface wettability of TiAl_6V_4 from intermediate wettability to hydrophobicity. Furthermore, the friction, attrition, and friction coefficient of TiAl_6V_4 in saliva were all diminished through sandblasting [19]. Although sandblasting can enhance the roughness of the Ti implant surface, it can also lead to uneven surface morphology and hydrophilic degradation. As a result, it is currently less commonly employed in clinical practice.

- In Vitro Studies of Sandblasting

Citeau et al. conducted a comparative analysis of various titanium surface treatments, including mechanical polishing (Tipolish), nitric acid passivation (Tipassiv), and biphasic calcium phosphate (BCP) grid-blasting (Tiblast). The study revealed that osteoblasts displayed enhanced adhesion capacities when cultured on rough and uneven surfaces of Tipassiv and Tiblast, as evidenced by their round form and the presence of massive pseudopodia. The existence of many dorsal microvilli, particularly when cells were cultivated on mirror-polished surfaces, indicated an increased level of cellular activity. To summarize, the findings indicate that cells exhibit more adhesion on the BCP grid-blasted surface while preserving their biological functionality. BCP grid-blasted discs caused an initial decline in cell viability and ALP activity, but this was completely restored in extended culture [20]. One possible reason for this temporary change in cell viability could be that osteoblasts are responsive not only to the roughness of the implant surface but also to its chemical composition. Titanium alloys that contain aluminum, such as Ti6Al4V, have a coating of aluminum oxides on their surfaces due to oxidation [21]. Grid blasting facilitates the creation of this layer, which arises from a chemical interaction between oxygen and metal [22]. The study findings indicate that aluminum oxide has the potential to cause cytotoxic effects on cells [18]. The decrease in osteoblastic activity may be associated with the liberation of trace elements [23] (Table 1).

- In Vivo Studies of Sandblasting

Gil et al. conducted an in vivo study showing that alumina exhibited beneficial effects on bone formation in different phases of implantation. In this study, alumina exhibited both bactericidal properties, reducing the attachment of germs to titanium surfaces, and significantly enhanced the proportion of BIC after 4 and 6 weeks of implantation. Furthermore, surfaces treated with alumina demonstrated decreased bacterial adherence for both *Lactobacillus salivarius* and *Streptococcus sanguinis* in comparison to clean surfaces [24]. The study demonstrates that TiO_2 -blasted implants, without any extra coating, display improved and expedited bone anchoring in comparison to machined implants. The initial greater BIC found with TiO_2 -blasted implants indicates that the surface roughness caused by TiO_2 blasting has a beneficial effect on implant stability. This is reinforced by the ele-

vated removal torque values observed for TiO₂-blasted implants, indicating a greater and more stable attachment in comparison to machined implants. The enhanced irregularity and augmented BIC seen on TiO₂-blasted surfaces underscore the potential advantages of surface modification techniques such as TiO₂ blasting in enhancing the functionality and durability of implants in orthopedic and dental applications [25]. There are several remarks that align with the findings of Ivanoff et al.'s study. This suggests the beneficial impact of utilizing implants treated with TiO₂ particles through blasting. Specifically, in the mandible, these implants exhibited significantly more BIC in comparison to turned implants. The increased bone presence within the threaded region demonstrates the beneficial effect of the roughened surface on the process of bone integration in mandibular applications. In contrast, no noticeable increase in bone quantity was noted for implants in the maxillae. These results collectively suggest that utilizing blasted implants with TiO₂ particles may offer enhanced osseointegration and load resistance, particularly in mandibular settings, presenting valuable insights for implantology practices [26] (Table 1).

Table 1. Descriptive data of sandblast technique.

Author, Year	Study Design	Method	Outcome
Gotfredsen et al., 1995 [25]	In vivo	Test group 1. TiO ₂ -blasted implants 2. TiO ₂ -blasted implants with HA coating Control group Machine implants	TiO ₂ -blasted implants had higher removal torque values than machined implants, indicating stronger anchorage.
Ivanoff et al., 2001 [26]	In vivo	Test group TiO ₂ -blasted implants Control group Turned implants	TiO ₂ -blasted implants had higher BIC compared to turned implants.
Citeau et al., 2005 [20]	In vitro	Test group 1. Tipassiv group (Tipassiv) 2. BCP grid-blasted titanium discs (Tiblast) Control group Mirror-polished titanium discs (Tipolish)	On Tiblast samples, MC3T3-E1 cells had a round shape, displayed dorsal microvilli, but exhibited only a few cytoplasmic extensions.
Gil et al., 2021 [24]	In vivo	Test group 1. Sandblasting with residual alumina 2. Sandblasting without alumina (due to cleaning process) Control group As-received lathed cut titanium samples	TiO ₂ -blasted implant with HA coating showed higher percentage of BIC after 4 and 6 weeks of implantation.

Acid Etching

The previous section revealed some disadvantages of sandblasting, such as the presence of contaminants on the implant's surface due to diverse sandblast particles, hydrophobicity, and the presence of imperfections with sharp edges on the sandblasted surface. Utilizing acetone and pure water alone may not adequately remove residual particles and optimize the sharp edges caused by sandblasting. Hence, acid etching as a treatment for the implant surface serves the dual purpose of eliminating residual particles and enhancing the surface properties of the implant, making it more suitable [27]. Typically, acid etching involves immersing the implant into solutions such as HCl, H₂SO₄, HNO₃, and HF to induce micropits through chemical reactions [15]. Acid etching is often used in conjunction with the sandblasting process; this combination is known as SLA, which provides superior properties compared to sandblasting alone [28].

- Surface Properties of SLA-treated Titanium

The SLA technique combines sandblasting and acid etching to create a surface with both macroroughness (from sandblasting) and micropits (from acid etching). The outer

layer of the titanium surface of the implants was analyzed using electron spectroscopy for chemical analysis. The machine and SLA implant exhibited different amounts of TiO_2 . Trace amounts of chlorine, calcium, silicon, phosphorus, and nitrogen were also detected. Implants that were sandblasted but not subjected to acid etching had remaining alumina particles, but the surfaces of implants that underwent SLA appeared to be free of such particles. The surface roughness measurements (Ra) were $0.75 \mu\text{m}$ for the machine implants and $2.15 \mu\text{m}$ for the SLA [29]. This combination results in an ideal roughness that is predicted to promote effective osseointegration [30]. Feng et al. utilized aluminum particles for sandblasting the surface of ultra-fine-grain titanium (UFG Ti). After undergoing sandblasting, the UFG titanium surface exhibited sharp edges and retained a significant amount of residual sand particles. Subsequently, the sandblasted UFG titanium was subjected to acid etching using a mixed solution of acids (37 wt% HCl/98 wt% $\text{H}_2\text{SO}_4/\text{H}_2\text{O}$, 2:1:1). The results showed more regular surface morphology and increased hydrophilicity of the UFG titanium. Furthermore, an increase in acid etching time led to an initial reduction in roughness, followed by a gradual increase later on [28]. Moreover, there are reports indicating that acid etching of titanium implants with a mixture of sulfuric acid and hydrogen peroxide in a ratio of 7:3 results in a significant increase in surface roughness and bone fusion. Additionally, the incorporation of silver nanoparticles has been shown to significantly enhance the antibacterial properties of the implant [31]. Kim et al. found that human osteoblasts exhibit excellent growth on the SLA surface, which offers a larger area for cell adhesion and proliferation [32].

- In Vitro Studies of SLA

SLA increases implant roughness, improving cellular adhesion and proliferation, particularly of osteoblast-like cells. The procedures also increase the rate and amount of bone formation on the implant surface [29]. Ramaglia et al. conducted an in vitro assessment of the biological characteristics of SaOS-2 human osteoblast-like cells cultured on two types of titanium surfaces: Smooth (S) and SLA. They examined cell morphology, adhesion, proliferation, expression of bone differentiation markers and ECM components, as well as the expression of specific integrin subunits. The findings indicated that the surface topography has the potential to affect the phenotypical expression of human osteoblast-like cells in a laboratory setting. The SLA titanium surface, specifically, caused a notable increase in Co I deposition and $\alpha 2$ - $\beta 1$ receptor expression compared to the smoother surface. This suggests that SaOS-2 cells are more likely to develop into mature osteoblasts on the SLA surface. The unique surface features of SLA titanium implants are expected to influence the biological behavior of osteoblasts during the repair of bone tissue [33]. The findings of this study support the experimental results from Orsini et al., demonstrating the non-cytotoxic cellular effects and overall biocompatibility of SLA implants. The observed irregular morphologies and numerous pseudopods in cells adhering to these surfaces, as revealed by scanning electron microscopy, suggest that the induced surface roughness through SLA plays a crucial role in influencing cell adhesion mechanisms. These morphological variations are indicative of enhanced initial cell anchorage, potentially contributing to improved osseointegration for SLA implants, further substantiating their viability for biomedical applications [29]. Kim et al. conducted experiments involving combined sandblast acid etching with anodization (Modi-ANO). The experimental results showed that the Modi-ANO surface exhibited higher initial MG-63 osteoblast-like cell adhesion and induced greater filopodia growth compared to the other groups. MG-63 cells also adhered more effectively to the Modi-ANO surface and developed more finger-like projections [34] (Table 2).

Table 2. Descriptive data of SLA technique.

Author, Year	Study Design	Method	Outcome
Orsini et al., 2000 [29]	In vitro	Test group SLA commercially pure TiAl ₆ V ₄ implants Control group Machined commercially pure TiAl ₆ V ₄ implants	Irregular cellular morphology and more pseudopodi for attachment in SLA-treated implants.
Li et al., 2002 [35]	In vivo	Test group SLA implant Control group MA (Machined acid-etch)	- Removal torque values (RTVs): RTVs of the SLA-surfaced implants were about 30% higher than those of the MA-surfaced implants, except at week 4 where the difference was not statistically significant. - Bone anchorage: The SLA surface achieved better bone anchorage than the MA surface.
Ramaglia et al., 2011 [33]	In vitro	Test group SLA-treated titanium disk Control group Smooth titanium disk	- SLA titanium surfaces promoted more mature osteoblastic phenotype in SaOS-2 cells compared to smooth surfaces. - Increased deposition of collagen I and expression of α 2- β 1 integrin receptor were observed on SLA surfaces. - SaOS-2 cells showed better adhesion, proliferation, and expression of bone differentiation markers on SLA-treated titanium disk.
Kim et al., 2015 [34]	In vitro In vivo	Test group - SLA group - ANO group - Modi-ANO group Control group Machined Titanium	In vitro The Modi-ANO group had the highest initial cell adhesion compared to SLA and ANO groups. In vivo - The Modi-ANO Ti implants had higher BIC (74.20%) compared to the machined (33.58%), SLA (58.47%), and ANO Ti (59.62%) implants. - The Modi-ANO implants showed better bone growth inside the screw threads of the implant than the other types.
Ortega et al., 2019 [36]	In vivo	Test group - SLA Titanium Dental implant (SA) Control group - Oxidized Titanium Dental Implants (OS)	- Both SA and OS implant surfaces showed good bone response and significant new bone formation after 12 weeks. - SA implants had a slightly higher BIC than OS implants, but the difference was not statistically significant.

- In Vivo Studies of SLA

The split-mouth study in miniature pigs conducted by Li et al. demonstrated that SLA outperformed machined and acid-etched surfaces (MA) in terms of implant stability. The surfaces treated with SLA exhibited a roughly 30% increase in removal torque values compared to the surfaces treated with MA. This superiority was consistently observed, except at the 4-week mark, where the difference was less noticeable. Moreover, SLA implants exhibited an interfacial stiffness that was more than 5% greater than that of MA implants, but this difference did not approach a level of statistical significance. In this experimental scenario, the overall data indicate that the SLA surface structure offers better bone anchoring compared to the MA surface [35]. Another in vivo study using a beagle

model revealed the BIC of Modi-ANO ($74.20\% \pm 10.89\%$) was much greater than that of machined ($33.58\% \pm 8.63\%$), SLA ($58.47\% \pm 12.89\%$), or ANO Ti ($59.62\% \pm 18.30\%$). In conclusion, this study demonstrates that Modi-ANO Ti implants produced by sandblasting, acid etching, and anodizing improve cell adhesion and bone growth as compared with machined, SLA, or ANO Ti implants [34]. Ortega et al. conducted a comparative study that examined implants with two distinct surfaces: One treated with sandblasting (SA) and another with an oxidized surface (OS). The implants were surgically placed into the femoral bones of rabbits. The histomorphometric study showed that the BIC was greater around the SA implants (53.49 ± 8.46) compared to the OS implants (50.94 ± 16.42); however, there were no statistically significant differences between them. After 12 weeks, both the SA and OS implant surfaces showed a favorable bone response, with considerable new bone growth. The study revealed that the SA surfaces exhibited a higher degree of roughness compared to the OS surfaces, which could potentially have an impact on the process of osseointegration [36] (Table 2).

- SLActive

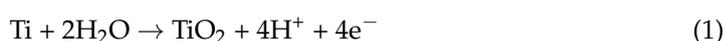
The SLA method has become increasingly popular due to its beneficial properties in surface preparation across different aspects. As a result, there have been developments in items that undergo surface preparation using SLA, and these products are readily accessible on the market. A noteworthy product is the offering by the company Straumann, which is branded as SLActive. SLActive is subjected to surface preparation procedures that are comparable to SLA. However, a crucial difference is that after the SLA process, SLActive is rinsed under nitrogen protection to avoid contact with air. Afterward, it is placed in a hermetically sealed glass tube filled with isotonic NaCl solution. Wennerberg et al. aggregated findings from a compilation of 15 *in vitro*, 17 *in vivo*, and 16 clinical studies. The results indicate that, in the early stages, the SLActive surface elicits more robust responses from cells and bone tissue compared to the SLA surface. Although the SLActive surface showed a stronger cell and bone tissue response than the SLA surface in the early stages, this difference diminished after 6–8 weeks. Clinical studies indicated that SLActive implants may have some early advantages, but long-term outcomes were similar to those of SLA implants. Notably, a study involving 248 SLActive implants reported a high survival rate of 98.8% over a 2-year period. In a case report, a patient with SLActive implants exhibited no implant failure and minimal bone loss after 20 months. Furthermore, an animal study revealed that SLActive implants demonstrated higher removal torque and interfacial stiffness in comparison to SLA implants [37]. This aligns with the research performed by Ozel et al., which indicated that one week after the implantation, there was an increase in stability for both SLA and SLActive surfaces. However, there were no notable disparities in stability noted between SLA and SLActive surfaces after 2 and 3 months [38].

Anodization

The anodizing process involves utilizing pure Ti as the anode and an inert material as the cathode, immersing them in an electrolyte, and inducing oxidation on the Ti surface through specific current and voltage conditions. This results in the formation of a stable and well-ordered TiO₂ layer with a porous structure. This surface characteristic enhances the adhesion and osteogenic differentiation of bone marrow mesenchymal stem cells, thereby promoting osseointegration. Moreover, the voids in the anodized TiO₂ surface can be utilized for carrying antibacterial drugs. Furthermore, it improves the material's antibacterial properties. Overall, anodizing proves to be a valuable technique for optimizing the biological and antimicrobial aspects of titanium surfaces in medical applications [39].

- Surface Properties of Anodized Titanium

The formation mechanism of nanostructures on Ti surfaces by anodic oxidation can be explained by the following two reactions:





The initial equation characterizes the process of oxide formation on a metal surface that has undergone anodization. The subsequent equation illustrates the chemical dissolution of the oxide through the formation of soluble fluoride complexes. During anodic oxidation, a thin layer of oxide is first generated on the surface of titanium. The oxide undergoes stresses as a result of the change in volume that occurs during the oxidation of Ti. Selective dissolution occurs as a result of distinct stresses. The pores formed initially exhibit irregularities as a result of non-uniform corrosion. The rate of dissolution and oxidation varies depending on the diameter of the pores. Through the process of anodization, the sizes of the pores become more consistent, leading to the creation of a nanopore. The thickness of the oxide film is greater at the wall of the pore compared to the bottom. As a result, the electrical field intensity at the bottom of the pore is significantly greater than that at the wall. This leads to a higher rate of consumption of TiO_2 toward the bottom of the pore, causing the pore to develop further towards the Ti substrate. As the pores deepen, the electric field in these metallic regions intensifies, which enhances the growth of oxide through the influence of the electric field and also leads to the dissolution of oxide. This process results in the formation of voids between the pores. Consequently, both empty spaces and cylindrical structures expand in balance, ultimately resulting in the creation of a tubular configuration, leading to the emergence of a nanotube-like structure [40]. The anodized oxide layer typically exhibits a rough and porous texture, with pore sizes ranging from a few hundred nanometers to a few micrometers, depending on the specific parameters used during the anodic oxidation process. It is important to note that the pores on the same anodized surface are not uniform in size. Studies have shown that factors such as current density, applied electrical potential, and the concentration of the electrolyte can influence the diameter of the porous layer [41,42]. The porous surface structure of anodized titanium has important implications for practical uses, especially in the field of biomedical implants. The surface properties are essential in determining the biocompatibility and successful integration of the implant with the surrounding tissue. The distinctive characteristics of anodized titanium, characterized by its porous structure, offer significant possibilities for greater performance and perhaps better results in the field of biomedical implant applications.

- In Vitro Studies of Anodization

Since the use of anodized titanium in orthopedic and dental implant applications, there have been several in vitro experiments and studies that have observed cells related to bone formation, such as osteoblasts, and various behaviors such as adhesion, morphological changes, functional alterations, proliferation, and differentiation when exposed to anodized titanium and its alloys. Many studies have indicated that the various behaviors of osteoblasts are largely influenced by factors such as surface properties, including composition, roughness, hydrophilicity, texture, and morphology of the oxide layer on titanium [43]. Li et al. have demonstrated that the transformation of titanium's hydrophobic nature into a hydrophilic surface through anodic oxidation results in nanostructures. The present study indicated a positive correlation between the level of surface roughness and the hydrophilic properties of titanium. Both roughness and hydrophilicity are recognized as two important characteristics that have an impact on osteoblast activities, including the accelerated formation of bone-like apatite, improved cell adhesion, and increased cell proliferation [40]. Similarly, Yao et al. stated that anodized titanium with nanotube-like structures has a significantly positive impact on osteoblast long-term functions. Through experiments comparing different titanium surfaces, it was observed that this specific surface modification exhibited the highest roughness and binding energy. Furthermore, it resulted in the highest calcium deposition by osteoblasts at day 21 of the study [44]. Zhu et al. performed tests investigating anodization under varying electrolytes and voltages. The researchers discovered that the surface roughness and wettability of the anodized titanium are dependent on the voltages applied and the electrolyte used. The cell culture experiments demonstrated

the absence of any negative effects on the cells and an enhancement in the attachment and growth of osteoblasts when exposed to the anodic oxides. Cells cultured on surfaces, including micro-pores, displayed irregular and polygonal growth patterns, along with an increased presence of lamellipodia. However, osteoblasts on the titanium surface employed as a control or on anodic oxides generated at low voltages exhibited prominent stress fibers and strong focal contacts. The ALP activity of the cells did not exhibit any correlation with the surface characteristics of the anodic oxides [43]. Anodization of titanium surfaces can have a beneficial impact on the behavior of bone cells. Surfaces that had phosphorus added exhibited accelerated bone cell development and differentiation in comparison to surfaces lacking phosphorus. Furthermore, the correlation between the surface texture and crystal arrangement of the anodized layers was associated with a higher rate of bone mineralization. The study found that the highest levels of mineralization were achieved by using a surface that combined phosphorus incorporation, an anatase phase oxide, low pore density, and high surface roughness, as it proved to be the most beneficial for bone formation [45]. Furthermore, the study revealed that the deposition of calcium phosphate and apatite-like crystals on the surface of titanium improved significantly when combining anodization with hydrothermal treatment [46] (Table 3).

Table 3. Descriptive data of anodization technique.

Author, Year	Study Design	Method	Outcome
Sul et al., 2002 [47]	In vivo	Test group - Group II: non-porous barrier structure; anodized up to 100 V; oxide thickness of approximately 202 nm. - Group III: porous structure, anodized up to 200 V; oxide thickness of approximately 608 nm. - Group IV: porous structure; anodized up to 280 V; oxide thickness of approximately 805 nm. - Group V: porous structure; anodized up to 380 V; oxide thickness of approximately 998 nm Control group Group I: non-porous barrier structure; turned surface implants; oxide film of approximately 17 nm	Removal torque (RT) values increased with oxide thickness, with significant differences between Group I and Groups III–V. Statistically significant differences in RT values when comparing Group II with Groups III–V Oxide properties, including thickness, micropore configurations, and crystal structures, significantly influence bone tissue response. No significant differences in RFA values among all groups after six weeks of implantation
		Test group - Anodized Ti surfaces treated with an electrolyte mixture for anodization. - Anodized Ti surfaces followed by a 2-h hydrothermal treatment. - Anodized Ti surfaces followed by a 4-h hydrothermal treatment Control group Control Ti surfaces without any treatment	Osteocalcin production was significantly higher on anodized and hydrothermally treated surfaces compared to the control. Osteoblasts on hydrothermally treated surfaces showed higher protein production than on the anodized surfaces. Anodized surfaces were porous, while hydrothermally treated surfaces had needle-like crystals rich in calcium and phosphorus.
Rodriguez et al., 2003 [46]	In vitro		

Table 3. Cont.

Author, Year	Study Design	Method	Outcome
Zhu et al., 2004 [43]	In vitro	<p>Group 1: pretreated Ti as a control (G-1); Group 2: pretreated Ti and anodized in 0.2 m H₃PO₄ till 200 V (G-2); Group 3: pretreated Ti and anodized in 0.2 m H₃PO₄ till 300 V (G-3); Group 4: pretreated Ti and anodized in 0.2 m H₃PO₄ till 350 V (G-4); Group 5: pretreated Ti and anodized in 0.03 m Ca-GP and 0.15 m CA till 140 V (G-5); Group 6: pretreated Ti and anodized in 0.03 m Ca-GP and 0.15 m CA till 200 V (G-6); Group 7: pretreated Ti and anodized in 0.03 m Ca-GP and 0.15 m CA till 260 V (G-7); Group 8: pretreated Ti and anodized in 0.03 m Ca-GP and 0.15 m CA till 300 V (G-8) (Ca-GP = calcium glycerophosphate, CA = calcium acetate)</p>	<p>Cells on anodized titanium surfaces exhibit a range of morphologies, including polygonal and polarized shapes.</p> <p>The number of fully spread cells is higher on anodized surfaces than on the control, indicating improved cell spreading.</p> <p>SaOS-2 cells cultured on anodized titanium surfaces showed no cytotoxicity and an increase in adhesion and proliferation.</p> <p>No statistical difference of ALP activity was found between the control and anodized surfaces.</p>
Yao et al., 2008 [44]	In vitro	<p>Test group 1. Anodized titanium (nanoparticle structure) 0.5% HF/10 V/20 min 2. Anodized titanium (nanotube-like structure) 0.5 HF/20 V/20 min</p> <p>Control group Unanodized titanium</p>	Osteoblasts secreted and deposited more calcium onto anodized titanium surfaces possessing nanotubes compared to unanodized titanium.
Li et al., 2014 [40]	In vitro	<p>Test group 1. Anodization was performed at 10 V for 1 h 1 M NaF solution (nano tube 70 nm) 2. Anodization was performed at 20 V for 20 min 1 M NaF solution (nano pore 25 nm)</p> <p>Control group Commercially pure Ti</p>	<p>Osteoblasts cultured on the anodized Ti surface exhibited a polygonal shape with many filopodia extending in all directions.</p> <p>Cell proliferation was about twofold on the anodized surface as compared to that on the polished surface.</p>
Sakshi et al., 2019 [45]	In vitro	<p>Test Group - Anodized specimens at 108 V in electrolyte A (A 108 V). - Anodized specimens at 180 V in electrolyte A (A 180 V). - Anodized specimens at 108 V in electrolyte B (B 108 V). - Anodized specimens at 180 V in electrolyte B (B 180 V) (Electrolyte A = 3.5 M sulfuric acid, 0.1875 M phosphoric acid, 0.75 M hydrogen peroxide, and 0.25 M oxalic acid; Electrolyte B = 5.6 M sulfuric acid)</p> <p>Control group Commercially pure titanium (CPTi) non-anodized specimens</p>	<p>ALP and osteocalcin assays revealed trends of early differentiation and maturation for phosphorus-incorporated oxides.</p> <p>Phosphorus incorporation into anodized titanium surfaces led to earlier osteoblast differentiation and maturation compared to non-phosphorus-containing surfaces.</p> <p>The combination of phosphorus incorporation, anatase phase oxide, low surface pore density, and high surface roughness resulted in the highest mineralization levels.</p>

- In Vivo Studies of Anodization

Sul et al. conducted an in vivo study involving the anodization of titanium to achieve oxide layer thickness ranging from 200 to 1000 nm. The experimental findings indicate that the oxide thickness of titanium implants significantly influences the bone tissue response. Specifically, implants with oxide thicknesses of approximately 600 nm, 800 nm, and 1000 nm exhibited stronger bone responses compared to those with oxide thicknesses around 17 nm

and 200 nm. This was measured by removal torque values six weeks after implantation. The removal torque values increased with the oxide thickness, showing significant differences between the control group (oxide thickness of 17 ± 6 nm) and the groups with thicker oxides. Additionally, resonance frequency analysis (RFA) did not reveal statistically significant differences among all groups, although there was a trend of increasing RFA with greater oxide thickness. These results suggest that specific oxide properties of titanium implants, such as thickness and micropore configurations, play a crucial role in the interaction with bone tissue [47]. Carvalho et al. discovered that dental implants with an anodized surface (AG) exhibited enhanced bone response after 2 weeks in comparison to machine surface implants and sandblasted implants. The anodized implants possessed a unique nanotopography and chemical composition that enhanced their bioactivity, resulting in improved early bone integration. However, at 6 weeks, differences in bone integration among the groups were not statistically significant. The anodized implants exhibited a higher degree of crystallinity and compatibility with bone tissue growth due to the presence of the anatase phase of TiO_2 . Generally, the anodizing approach employed in the study had a beneficial impact on the surface characteristics of the titanium implants, potentially improving their performance in clinical settings [48] (Table 3).

Laser Radiation

Laser radiation is utilized to prepare dental implant surfaces by directing a laser onto the surface of a titanium (Ti) implant, resulting in the melting or vaporization of the material due to its high energy. The process results in the creation of small cavities on the surface, and the properties of these cavities are affected by parameters such as the laser's type, energy, and direction. By manipulating laser parameters, it is possible to achieve several types of implant surface structures, allowing for accurate manipulation of the surface at the nanoscale. Significantly, laser machining minimizes surface contaminants [49]. The anodizing and laser structuring processes result in the creation of micro- and nanorelief on the surface of titanium oxide, specifically TiO_2 (rutile and anatase), Ti_2O_3 , and TiN. These alterations occur simultaneously. The thickness of the oxide layer ranges from a few nanometers to many microns [50,51]. Implants experience enhanced corrosion resistance due to the presence of titanium oxides [52].

- Surface Properties of Laser-Radiated Titanium

After laser surface treatment, titanium exhibits a modified surface with distinct topographical features and chemical composition. The laser processing conditions developed for Ti-6Al-4V titanium disks result in the formation of well-ordered, rough surfaces with subcellular to cellular period structures. Specifically, three different reliefs were created: "open grooves" (OG), "grid" (G), and "close grooves" (CG), each with varying depth and period of grooves. The surface composition analysis revealed a sandwich structure consisting of $\text{Ti} \rightarrow \text{TiO} \rightarrow \text{Ti}_2\text{O}_3\text{N}_x \rightarrow \text{TiO}_2$ (anatase) $\rightarrow \text{TiO}_2$ (rutile). Additionally, the wettability study demonstrated superhydrophilicity for all reliefs, with a contact angle (CA) of 0° . EDX-analysis showed a significant oxide increase on the laser-treated titanium surface, with the oxide percentage for the surface of OG, G, and CG reliefs varying within a ratio from 27.42 to 32.73 wt%. These changes in surface properties are crucial for cell attachment and proliferation, as evidenced by the *in vitro* verification showing that cells proliferated well on all reliefs, with the OG relief being the best for cell differentiation, alignment, and osteocalcin genesis [53].

- In Vitro Studies of Laser Radiation

Veiko et al. demonstrate that laser-assisted fabrication of titanium surfaces can significantly influence the behavior of human bone marrow mesenchymal stem cells (hMSCs). The study found that the laser-processed surfaces with "open grooves" (OG), "grid" (G), and "close grooves" (CG) topographies supported cell proliferation, with the OG relief showing the highest cell count at 266,500 cells/sample on day 20. The OG relief also promoted the best osteogenic differentiation, as indicated by the highest ALP activity and

osteocalcin expression. The cells on OG relief exhibited an even layer and fibroblast-like elongated shape from the first day after seeding, suggesting normal adhesion and favorable conditions for cell life-sustaining activity. In contrast, the G and CG reliefs showed lower cell counts and ALP activity, with cells having a rounded shape, indicative of incomplete adhesion. The study concludes that the continuous “open grooves” structures with subcellular to cellular periods are most beneficial for cell proliferation and osteogenic differentiation, which is critical for the early stages of osseointegration in implants [53] (Table 4).

Table 4. Descriptive data of laser radiation.

Author, Year	Study Design	Method	Outcome
Veiko et al., 2021 [53]	In vitro	Investigated cell behavior on three different laser-induced surface reliefs: open grooves (OG), grid (G), and close grooves (CG)	- Quantitative analysis showed the highest cell proliferation on the OG relief with 266,500 cells/sample on day 20. - The OG relief was found to be the most conducive for osteogenic differentiation, with the highest ALP activity and osteocalcin expression.
Veiko et al., 2022 [54]	In vivo	Test group I-topography (irregular structure) S-topography (slots) G-topography (μ -rooms-shaped grooves). Control group Machine surface	G-topography showed the highest BIC parameter and contained the highest number of mature osteocytes. Histological analysis indicated the best secondary stability and osseointegration for G-topography.

- In Vivo Studies of Laser Radiation

The in vivo study demonstrated that laser-structured dental implants with various topographies, specifically G-topography with μ -canals, S-topography with μ -cavities, and I-topography with an irregular structure, were successfully integrated into rabbit tibias. Histological analysis revealed that G-topography achieved the highest BIC parameter and contained the highest number of mature osteocytes, indicating superior secondary stability and osseointegration. RFA further supported these findings, showing that implants with laser-induced topographies had higher stability indices compared to untreated implants, with G-topography exhibiting the best results after three months. The study concluded that the G-topography, featuring periodic grooves commensurate with cell size, provided the most favorable environment for osteocyte integration and bone tissue formation [54]. The study investigated the effects of novel laser microtopographies on titanium dental implants and their influence on human osteoblast proliferation and bone deposition. The results showed that different titanium surface treatments led to varying degrees of osteoblast activity and bone matrix deposition. Specifically, the laser-treated L2 surface exhibited a more complex texture and significantly higher roughness parameters compared to SLA and L1 surfaces, which correlated with a higher level of osteoblast activity and bone matrix deposition on the L2 surface. Additionally, the study found that human adipose stem cells, when induced to osteogenic differentiation, displayed multilinkage differentiation capabilities, as evidenced by alizarin red stain and Oil Red O (ORO) assay. The expression of ALP, matrix extracellular phosphoglycoprotein (MEPE), and osteocalcin (OCN) was evaluated, revealing that L2 samples had a higher and faster increase in ALP and OCN levels compared to SBAE and L1 samples. Scanning electron microscopy further confirmed the presence of a multilayer network of osteoblast-like cells with several initial matrix deposition sites on the L2 surface. Energy-dispersive X-ray analysis (EDAX) confirmed the initial bone matrix deposition with the presence of calcium and phosphorous on the titanium surfaces. These findings suggest that the novel laser microtopography of the L2

surface may enhance osteoblast proliferation and bone deposition, which is crucial for the success of dental implants [55] (Table 4).

3.1.2. Additive Techniques

Additive dental implant treatment refers to the substances or surface modifications administered to the implant in order to improve its functionality, compatibility with living tissue, and integration with the surrounding bone. The dental implant's coating performs multiple functions, such as improving the healing process, diminishing the likelihood of infection, and enhancing the implant's long-term efficacy. The dental implant coating process comprises six primary techniques: Plasma spraying, nanospray drying, sol-gel, hydrothermal, self-assembly, and 3D printing [13]. Currently, a range of compounds are used to coat dental implants, including polyhydroxyalkanoates, calcium phosphate, carbon, bisphosphonates, hydroxyapatite (HA), bone-stimulating chemicals, bioactive glass, bioactive ceramics, collagen, and chitosan [56]. Among these particles, HA is one of the popular bioceramic substances often used as a coating material.

HA Implant Coating

- Mechanical and Chemical Properties of HA-coated Titanium

The plasma spraying technique is the most prevalent approach for placing the HA coating onto endosseous implants. The study conducted by Hung et al. examined the characteristics of the HA coating produced by plasma spray technology. The results showed that HA has an adhesive strength of around 41.44 MPa. The HA covering exhibited a thickness ranging from 47 to 130 μm . The crystallinity level was quantified at 54.88%, while the surface roughness (Sa) was estimated to be around 6.20 μm . There were no notable constituents of α -TCP and β -TCP phases. Modifying the hydrogen flow rate to a range of 6–14 L/min or reducing the powder feeding rate to 10 rpm during plasma HA spraying led to the total fusion of HA particles. As a result, the coatings exhibited enhanced adhesion strength, greater density, a more splatter-shaped appearance, and improved homogeneity [57]. The elevated temperatures in plasma spray induce the creation of the amorphous HA phase, leading to a greater rate of bio-dissolution compared to a coating with a high degree of crystallinity. The presence of the amorphous phase in a biological environment can induce the resorption, re-absorption, and degradation of the HA coating. This can lead to the disintegration of the coating, resulting in a decrease in both the strength of the binding between the coating and substrate as well as the fixation of the implant. Additionally, there is a potential danger of the separation and disintegration of the coating, resulting in the creation of small fragments [58]. Kuska et al. provided a report on the electrochemical deposition technology, emphasizing its various advantages. This approach enables precise manipulation of coating content and structure. In addition, the process operates at a low temperature, guaranteeing a uniform coating composition with a thin coating layer. The presence of an uneven surface (roughness) is seen as beneficial, and all these aspects contribute to the good biomedical characteristics of the coating [58].

- In Vitro Studies of HA Coating

Suwanprateep et al. conducted an experiment to evaluate the proliferation and calcification of osteoblasts on the surface of titanium coated with HA in comparison to uncoated titanium. The results indicated that titanium coated with HA demonstrated considerably greater osteoblast cell proliferation and cell calcification compared to the uncoated group on days 14 and 21 of the experiment [59]. Wang et al. performed HA-coated titanium through the micro-arc oxidation (MAO) and steam-hydrothermal treatment (SHT) processes. They found that Ti-M-H1 demonstrates the promotion of adhesion, spreading, and proliferation of osteoblasts, the cells responsible for bone formation. The material also enhances the secretion of ALP and collagen type I (Col-1), which are markers of osteoblast differentiation and bone matrix formation. Additionally, Ti-M-H1 increases the mineralization of the ECM, a critical step in the formation of new bone tissue. These properties suggest that Ti-M-H1

has a positive effect on osteogenesis *in vitro*, making it a promising material for bone regeneration applications [60]. Furthermore, experimental evidence has confirmed a similar finding to the work conducted by Park et al., indicating that titanium surfaces coated with HA have notably greater ALP activity than titanium surfaces without the coating. This suggests increased osteoblastic activity on the surfaces covered with HA. Furthermore, the surfaces coated with HA facilitate a higher level of cell migration compared to the titanium surfaces that are not coated. This indicates that the HA coating may improve the essential cellular responses necessary for bone healing and regeneration [61] (Table 5).

- In Vivo Studies of HA Coating

The *in vivo* study demonstrated that the sol-gel-derived HA coating on titanium implants significantly enhanced osseointegration. Mechanical testing revealed that the extraction torque required for HA-coated screws was substantially greater than for uncoated screws, indicating a stronger fixation to bone. This torque increased over time, suggesting progressive bone integration. Histological analysis corroborated these findings, showing faster bone healing around coated screws with no evidence of active inflammatory responses. The presence of bone fragments on the coated screws upon extraction further confirmed the strong bone-to-implant bonding. These results suggest that the HA coating produced by the sol-gel method could be a viable alternative to high-temperature plasma spray coatings, potentially reducing the risk of coating delamination and failure in clinical applications [59]. Jing et al. showed that the application of MAO to a novel titanium alloy (Ti-3Zr-2Sn-3Mo-25Nb) resulted in the formation of porous HA coatings. These coatings were found to greatly enhance bone ingrowth and enhance the mechanical properties of the bone-implant interface. When the HA-coated specimens were inserted into the medullary canal of beagles' proximal femur, they exhibited a greater level of BIC in comparison to the uncoated group. The results of mechanical testing, notably the pull-out test, demonstrated that the group with the HA coating exhibited a considerably greater maximum force at the interface between the bone and the implant at different time intervals after implantation (4, 12, and 24 weeks). This indicates a superior shearing strength in comparison to other groups [62]. Kuska et al. conducted a comparative study involving titanium implants with HA coatings and those with Al₂O₃ grit-blasted surfaces, both embedded into rabbit tibiae. The research revealed that HA-coated implants exhibited improved osseointegration compared to Al₂O₃ grit-blasted implants in rabbit tibiae. Surface characterization of the implants indicated that the HA coating had a microstructure with an arithmetical mean height (Sa) in the range of 0.71–1.04 μm and was free of contamination, while the control implants were enriched with corundum. The HA-coated implants demonstrated a statistically significant increase in the mean implant stability quotient (ISQ) and a decrease in the mean periosteal value (PTV), indicating better stability. Conversely, for the control implants, only the PTV showed a significant decrease over time. Scanning electron microscopy analysis revealed a uniform layer of rod-like HA crystals on the HA-coated implants, whereas the grit-blasted implants had a rough surface with irregular notches and sharp edges. Chemical analysis showed that the HA coating was the principal component of the electrodeposited layer with minimal impurities, while the grit-blasted surface contained Ti, O, and Al with carbon impurities. These findings suggest that the HA coating produced via the modified electrochemical method can enhance the osseointegration of titanium implants [63]. Faeda et al. demonstrate that the combination of laser ablation and subsequent chemical HA coating significantly enhances the biomechanical performance of titanium dental implants. The removal torque tests indicated that the HA-coated implants had a higher level of osseointegration compared to both the laser-modified surface (LMS) and machined surface (MS) implants. This suggests that the HA coating, when associated with laser-modified surfaces, provides a stable and bioactive surface that may promote faster bone healing and stronger bone-implant interaction. The results imply that such surface modifications could potentially reduce the healing time required after dental implant placement, which is a significant advantage in dental implantology. The study's findings support the use of laser ablation followed by chemical HA coating as a viable method to improve the biological

performance of dental implants [64]. Hermida et al. demonstrated that HA-coated implants (Group PA) had significantly greater bone ingrowth than non-coated implants (Group TI) at both 6- and 12-week post-implantation. The mean bone ingrowth was significantly different between the two groups, with the HA coated implants showing superior osseointegration. The SEM images and histomorphometric analysis confirmed that the HA coating facilitated a higher percentage of bone growth into the porous structure of the titanium surface, and this effect was consistent at various depths up to 0.9 mm from the surface [65]. Oliveira et al. demonstrated that nano-hydroxyapatite (NANO)-coated implants exhibited superior osseointegration compared to machined and double-acid-etched (DAE) surfaces. Gene expression analysis revealed that the NANO group had the best results in terms of RANK expression at 7 days in diabetic rats. Additionally, the levels of Runx2, Alp, Oc, and Opn suggested an increase in osteoblast proliferation, particularly in the early stages of osseointegration. Micro-CT analysis showed that the NANO group had statistically significant higher values for percent bone volume (BV/TV), bone surface/volume ratio (BS/BV), and lower total porosity (To.Po) across all evaluated time points and irrespective of systemic condition. These findings indicate that NANO-HA-coated implants promote new bone formation more effectively than machined or DAE surfaces, even in the presence of a diabetic condition [66]. In contrast, Zagury et al. conducted a study that compared implants made of titanium–aluminum–vanadium (TiAlV) with implants coated with HA. The histomorphometric analysis conducted in this study found no significant difference in the percentage of BIC between the HA-coated implants and the titanium–aluminum–vanadium (TiAlV) alloy screws. These findings indicate that the application of the HA coating using a biomimetic approach did not improve the level of contact between the bone and the implant, when compared to the conventional TiAlV implants in this specific investigation. The statistical analysis confirmed this discovery, demonstrating that there was no significant difference in osseointegration between the two categories of implants [67] (Table 5).

Table 5. Descriptive data of hydroxyapatite coating.

Author, Year	Study Design	Method	Outcome
Hermida et al., 2005 [65]	In vivo	Test group Porous titanium surface with HA coating. Control group Porous titanium surface without a solution deposited coating.	HA coated implants showed significantly higher bone ingrowth compared to non-coated implants at both 6 and 12 weeks.
Zagury et al., 2007 [67]	In vivo	Test group HA coated implants Control group Titanium–aluminum–vanadium (TiAlV) alloy implants	No significant difference in the percentage of BIC between HA-coated and titanium alloy implants. Histomorphometric analyses showed no statistically significant differences in osseointegration between the two groups.
Park et al., 2013 [61]	In vitro In vivo	Test group HA coating on titanium discs Control group Control group with uncoated titanium implants	In vitro - Higher ALP activity on HA-coated discs compared to titanium discs - Faster cell migration observed on HA-coated discs In vivo - Higher BIC percentage in HA-coated implants - Significantly increased height of bone regeneration in the HA-coated group

Table 5. Cont.

Author, Year	Study Design	Method	Outcome
Jing et al., 2015 [62]	In vitro	Test group HA coating with MAO Process Control group Uncoating titanium	- Histomorphometry indicated enhanced bone ingrowth in the HA-coated group. - The HA-coated group exhibited significantly higher maximum pull-out force at the bone-implant interface at 4, 12, and 24 weeks post-implantation. - HA-coated specimens showed improved BIC and mechanical performance compared to uncoated specimens.
Suwanprateeb et al., 2018 [59]	In vitro In vivo	Test group Coating sol with calcium to phosphorus molar ratios (Ca/P) of 1.67 using ammonium hydrogen Control group Uncoating titanium	In vitro - Osteoblast proliferation was significantly higher in the coated group compared to the uncoated group at day 14 and day 21. - Cell calcification increased significantly at days 14 and 21 in the coated group compared to the uncoated group In vivo The torques were approximately 2 times greater in the coated group in all timepoints
Kusha et al., 2019 [63]	In vivo	Test group Fourteen other implants were coated with HA using electrochemical deposition Control group Al ₂ O ₃ grit-blasted surfaces	- Increase in ISQ in the coated group - Decrease in PTV in the coated group
Oliveira et al., 2020 [66]	In vivo	Test group DAE (Double acid-etched) NANO (nano-hydroxyapatite coated) Control group Machine surface	- NANO surface implants showed higher gene expression levels of Runx2, Alp, Oc, and Opn, indicating increased osteoblast proliferation, especially in early osseointegration stages. - NANO group demonstrated higher percent bone volume (BV/TV), bone surface/volume ratio (BS/BV), and lower total porosity (To.Po) across all evaluated timepoints and systemic conditions.
Wang et al., 2021 [60]	In vitro In vivo	Test group Ti-M-H1; a titanium sample coated with nano-structured HA using MAO and steam-hydrothermal treatment (SHT) Control group Pure titanium	In vitro - Ti-M-H1 promoted osteoblast adhesion, spreading, and proliferation (validated by MTT assay). - Increased ALP, collagen secretion, ECM mineralization in Ti-M-H1. - Induced higher expression of osteogenic-related genes such as BMP-2, COL1, OCN, and RUNX2 in Ti-M-H1. In vivo Higher bone-to-implant interface and dendrite attraction were observed in Ti-M-H1, promoting osseointegration.

Chitosan Implant Coating

At present, dental implants are widely used in dentistry as replacements for lost teeth. One of the significant reasons leading to the failure of dental implants is peri-implant disease. Peri-implantitis is defined as the inflammation of the mucosa and the loss of bone tissue surrounding a dental implant, typically resulting from a bacterial infection.

Pathogenic bacteria can trigger the immune system, causing damage to the soft tissue and bone that support the implant [68]. The surface coating of implants with materials exhibiting crucial properties such as biocompatibility, biodegradability, osteoconductivity, and enhanced wound healing acceleration, along with anti-inflammatory attributes, holds significant implications for the success of implant treatments. Among the materials that encapsulate these essential properties, chitosan emerges as a promising candidate. Its unique combination of biocompatibility, biodegradability, osteoconductivity, antibacterial activity, and anti-inflammatory features makes chitosan a valuable material for improving the overall effectiveness and outcomes of implant treatments [69–71].

- Chemical Properties of Chitosan-Coated Titanium

Chitin, a plentiful natural resource on Earth, is typically obtained from crustaceans, insects, bacteria, and fungi. Chitosan, on the other hand, is the deacetylated version of chitin. It is made up of glucosamine and N-acetyl glucosamine units connected by $\beta(1-4)$ glycosidic bonds. The purity of chitosan is determined by its degrees of deacetylation and molecular weights. Chitosan is known for its ability to degrade naturally, its antibacterial properties, and its compatibility with living organisms. Chitosan is a heteropolysaccharide composed of hydroxyl groups that are reactive at locations C(2), C(3), and C(6), as well as an amino group and a linear polyamine. The presence of these groups is crucial for enabling chitosan to undergo modification processes, such as graft copolymerization. Consequently, it is employed to generate diverse advantageous frameworks for tissue engineering purposes. The chitosan that has undergone 100% deacetylation exhibits a highly crystalline structure, while chitosan with a degree of deacetylation below 100% displays a semi-crystalline character. Chitosan exhibits solubility in both organic and inorganic acids with a pKa value of 6.5. However, it is insoluble in solutions that are neutral or basic. The solubility of chitosan is determined by the quantity of unbound amino and N-acetyl groups present [72].

- In Vitro Studies of Chitosan Coating

Zhang et al. utilized chitosan as a coating in combination with HA and demonstrated that porous titanium implants showed no biological toxicity. Moreover, these porous implants were found to be superior to dense titanium in promoting the adhesion and proliferation of osteoblast-like MC3T3-E1 cells. The chitosan/hydroxyapatite (CSHA) coating applied to the porous titanium implants was shown to enhance both the proliferation and differentiation of MC3T3-E1 cells. These processes are crucial for bone regeneration and osseointegration [73] (Table 6).

- In Vivo Studies of Chitosan Coating

Takanche et al. demonstrated that Ch-GNPs/c-myb facilitated osseointegration in ovariectomized rats, which is a model for osteoporosis. The Ch-GNPs/c-myb complex promoted osteogenesis and inhibited osteoclastogenesis in MC-3T3 E1 cells. In vivo, Ch-GNP/c-myb-coated titanium implants increased the volume and density of newly formed bone in rat mandibles, as evidenced by micro-computed tomography. Immunohistochemical analysis revealed increased c-myb expression and upregulation of bone morphogenic proteins, osteoprotegerin, and EphB4, along with the downregulation of RANKL in the tissues surrounding the coated implants. Hematoxylin and eosin staining confirmed new bone formation around the Ch-GNP/c-myb-coated titanium implants. These findings suggest that c-myb delivered by Ch-GNPs supports dental implant integration even under osteoporotic conditions and may be applicable in the treatment of age-dependent bone destruction diseases [74]. These findings are further reinforced by results from an in vivo study, which are consistent with Zhang's research. This study revealed that the porous composition of the titanium implants promoted the proliferation of bone tissue within the pores, leading to successful osseointegration. Moreover, the study demonstrated that the titanium with the CSHA coating exhibited increased ALP activity, which is a reliable marker for osteogenic differentiation, in comparison to the uncoated titanium. Moreover, the ALP

activity exhibited by the porous titanium material surpassed that of the solid titanium material. This indicates that the combination of the porous structure and calcium silicate hydrate (CSHA) coating leads to a synergistic improvement in the process of osseointegration [73]. Kung et al. reported that chitosan–collagen composites have the potential to stimulate new bone formation around pure titanium implants in the subcutaneous tissues of rats. This suggests that these composites could enhance bone formation and the integration of implants in compromised conditions. Histological analysis showed active bone formation, as indicated by strong positive staining for osteopontin and ALP. Histomorphometric analysis revealed a slight increase in bone parameters for the 750 kDa chitosan group compared to the 450 kDa group, although this difference was not statistically significant. These findings suggest that the molecular weight of chitosan in the composites did not have a significant impact on bone formation in this study. The results support the potential future use of chitosan–collagen composites in clinical settings where bone regeneration is needed [75]. Furthermore, the surface coatings of chitosan or melatonin on titanium dental implants did not significantly affect peri-implant bone density (BD) when compared to the control group with a conventionally etched surface [76] (Table 6).

Table 6. Descriptive data of chitosan coating.

Author, Year	Study Design	Method	Outcome
Kung et al., 2011 [75]	In vivo	Test group - Implants wrapped with Col-I membrane containing 450 kDa chitosan - Implants wrapped with Col-I membrane containing 750 kDa chitosan Control group - Implants wrapped with plain Col-I membrane	- Strong positive staining for osteopontin and ALP indicated active bone formation in chitosan-coated group. - Chitosan–collagen composites induced new bone formation around the titanium implants in rats - Slight increase in bone parameters for the 750 kDa chitosan group compared to the 450 kDa group, though not statistically significant.
Takanche et al. 2018 [74]	In vitro In vivo	Test group Ch-GNP/c-myb-coated Ti implants Control group Pure titanium	In vitro - Increased expression of EphB4 and ephrinB2 suggested promotion of osteoblast differentiation and osteoclast suppression. - Ch-GNPs/c-myb promoted osteogenesis and inhibited osteoclastogenesis in MC-3T3 E1 cells. In vivo - Ch-GNP/c-myb-coated Ti implants increased bone volume and density in ovariectomized rat mandibles. - Immunohistochemical analysis showed upregulation of bone morphogenic proteins and osteoprotegerin. - Enhanced osseointegration of dental implants was observed via micro-computed tomography
Zhang et al., 2020 [73]	In vitro In vivo	Test group - Porous titanium implants without any coating. - Porous titanium implants with a CSHA composite coating. Control group - Dense titanium implants without any coating.	In vitro - Porous titanium implants supported better osteoblast adhesion and proliferation compared to dense titanium. - Porous titanium implants with CSHA coating showed improved higher ALP activity. In vivo Increased trabecular bone thickness and new bone tissue formation in implant pores were observed over time.

Table 6. Cont.

Author, Year	Study Design	Method	Outcome
López-Valverde et al., 2021 [76]	In vivo	Test group - Melatonin test group (MtG) - Chitosan test group (ChG)	Chitosan- and melatonin-coated titanium dental implants did not significantly affect peri-implant bone density (BD) when compared to the control group with a conventional etched surface.

3.2. Commercialized Dental Implants and Their Clinical Outcomes in Healthy Population

3.2.1. Turned (Machined) Surface

Adell et al. conducted a study involving 4636 standard Brånemark System fixtures (turned surfaces) in 759 totally edentulous jaws of 700 patients. The reported survival rates for osseointegrated implants showed that maxillary fixtures had rates of 89% at 5 years, 81% at 10 years, and 78% at 15 years, while mandibular fixtures exhibited higher rates of 97% at 5 years, 95% at 10 years, and 86% at 15 years [77] (Table 7).

3.2.2. HA-Coated Surface

Lee et al. conclude that HA-coated implants do not show compromised long-term survival when compared to uncoated titanium implants. The survival rates reported for HA-coated implants were similar to those for uncoated implants, with overall percentage survival rates ranging from 93.2% to 98.5% over periods of 4 to 8 years. Additionally, life-table analysis showed cumulative survival rates ranging from 79.2% to 98.5% over 5 to 8 years, with yearly interval survival rates consistently above 90%. The study found no evidence of a progressive or precipitous decrease in survival rates with increased years of follow-up, which suggests that resorption of the HA coating does not lead to late implant failure. These findings were based on a systematic review and meta-analysis of human clinical trials that met specific inclusion criteria [78] (Table 7).

3.2.3. Sandblasted Surface

In a comprehensive five-year clinical examination of 133 Astra Tech dental implants placed in 50 patients, Gotfredson et al. reported an impressive overall cumulative survival rate of 97.6%. While TiO₂-blasted implants exhibited a 100% survival rate, machined implants demonstrated a slightly lower rate of 95.1%, with no statistically significant difference between the two surfaces. Marginal bone loss was similar for both groups, with a mean loss of 0.21 ± 0.83 mm for machined implants and 0.51 ± 1.11 mm for TiO₂-blasted implants in the maxilla, and 0.22 ± 1.13 mm for machined implants and 0.52 ± 1.07 mm for TiO₂-blasted implants in the mandible, with no significant difference observed between the two surface types. The frequency of implants with signs of inflammation was comparable between the two groups throughout the study. Technical complications included persistent paresthesia in one patient, two fractured abutments, five loosened abutments, and twelve bridge screws that had loosened, all of which were addressed during the follow-up period. The study concluded that there were no significant differences in failure rate and marginal bone loss around implants with machined versus TiO₂-blasted surfaces [79] (Table 7).

3.2.4. Acid-Etched Surface

Ortega et al. reported a cumulative survival rate of 92.9% for dental implants with acid-etched surfaces over a follow-up period of at least 17 years. A total of 169 implants were placed in 48 patients, with 12 implants lost during the follow-up. The mean marginal bone loss was 1.91 mm, with a range from 1.1 to 3.6 mm. Complications were observed in 22 patients (48.8%), with peri-implantitis being the most frequent, affecting 18 implants (10.6%). Peri-implantitis was more common in patients with a history of periodontal disease and smokers. Technical complications with prosthetic restorations occurred in 12 patients (26.6%) over 24 implants (14.2%). The study concluded that early loading of acid-etched

implants is a clinically predictable treatment when appropriate selection criteria and clinical planning are applied [80] (Table 7).

3.2.5. SLA-Treated Surface

The retrospective study revealed a 10-year implant survival rate of 98.8% and a success rate of 97.0% for titanium dental implants featuring an SLA surface within a cohort of 303 partially edentulous patients. Among the 511 SLA implants, no instances of implant fractures were observed, six implants (1.2%) were lost, and two implants (0.4%) exhibited signs of suppuration during the 10-year examination. Seven implants (1.4%) had a history of peri-implantitis over the 10-year period but presented with healthy peri-implant soft tissues at the time of examination. The mean plaque index was 0.65, the mean sulcus bleeding index was 1.32, the mean probing depth was 3.27 mm, and the mean distance from the implant shoulder to the mucosal margin was -0.42 mm. The radiologic mean distance from the implant shoulder to the first BIC was 3.32 mm. The study concluded that the prevalence of peri-implantitis was low at 1.8% over the 10-year period in this cohort. It suggests that SLA implants represent a reliable option for long-term oral rehabilitation in partially edentulous patients. The findings emphasize the efficacy of SLA surface implants in preserving osseointegration and peri-implant health over an extended period, which is crucial for the long-term success of implant therapy [81] (Table 7).

3.2.6. Anodized Surface

Wennerberg et al. conducted a systematic analysis to compare the clinical performances of various implant surfaces over a period of 10 years. They found that oxidized surface implants had the highest cumulative survival rate (CSR), ranging from 96.6% to 99.2% [82]. Rocci et al. compared the immediate loading using TiUnite implants (anodized implants) to machined surface implants. The results indicated that all patients experienced healing with minor or no swelling. In the test group, 3 out of 66 TiUnite implants failed, leading to a cumulative success rate of 95.5% at both 1 and 9 years. In contrast, the control group saw 8 out of 55 machined implants fail, resulting in a success rate of 85.5%. The survival rate for implants in partial prostheses was 98.8%, and for single restorations, it was 92.2% in the test group. These rates were significantly higher than those in the control group, which were 87.8% for partial and 83.2% for single restorations. Smoking was found to significantly increase the failure rate of machined implants, but not TiUnite implants. Radiographic analysis showed an average marginal bone loss of 0.9 mm and 1.0 mm in the TiUnite and machined groups after the first year of loading, respectively. By the third year, this was reduced to 0.4 mm for test implants and 0.5 mm for control implants. At the 9-year examination, there was a negligible further loss in bone height, with some cases even showing slight bone gain for the test implants [83] (Table 7).

3.2.7. Laser-Radiated Surface

Guarnieri et al. conducted a study comparing short and standard laser-microgrooved implants supporting single and splinted crowns. The findings revealed that the cumulative survival rate (CSR) of short implants was 98%, compared to 100% for standard implants, with no statistically significant difference between the two. Marginal bone loss (MBL) over the observation period was also not significantly different, averaging 0.23 ± 0.6 mm for short implants and 0.27 ± 0.3 mm for standard implants. Peri-implant soft tissue parameters, such as plaque presence, the number of sites with bleeding on probing (BOP), probing depth, and mean mucosal recession, showed no statistical differences between short and standard implants. Moreover, when analyzing MBL in relation to crown/implant (C/I) ratio, implant length, location, type of antagonist, and type of prosthetic design (single or splinted), no statistically significant differences were found. Multivariate analysis and multiple linear regression models also indicated no statistically significant correlation between these variables and MBL [84] (Table 7).

Table 7. Clinical performances of the commercialized dental implants with different surface treatments.

Surface Modification	Implant Systems	Clinical Performance	
		Survival Rate	Success Rate
1. Turned surface	Brånemark System [®] , Southern Implant System [®] (Nobel Biocare, Kloten, Switzerland)	Maxillary 5 years; 89% 10 years; 81% 15 year; 78% Mandibular 5 years; 97% 10 years; 95% 15 year; 86% [77].	N/A
2. HA coating	Calcitek Integral [®] and Omnilock [®] (Zimmer, IN, USA), HA-coated (BioHorizons, Birmingham, AL, USA)	The overall percentage survival rate ranging from 93.2% to 98.5% over periods of 4 to 8 years [78]	N/A
3. Grit-blasting	MTX [®] and Inclusive [®] Tapered Implants (Zimmer, IN, USA)	100% survival rate [79]	N/A
4. Acid-etching	Osseotite [®] and NanoTite [®] (Zimmer, IN, USA)	The survival rate of 92.9% for dental implants with acid-etched surfaces over a follow-up period of at least 17 years [80]	N/A
5. SLA surface	SLA [®] and SLActive [®] (Straumann, Basel, Switzerland), TiOblast [®] (Dentsply Sirona, NC, USA)	10-year implant survival rate of 98.8% [81]	10-year implant success rate of 97.0% [79].
6. Anodization	TiUnite [®] Brånemark System (Nobel Biocare, Göteborg, Sweden)	The cumulative survival rate (CSR) ranging from 96.6% to 99.2% [82]	N/A
7. Laser microtextured surface	Laser-Lok [®] (BioHorizons, Birmingham, AL, USA)	The cumulative survival rate (CSR) of 98% in short implants [84]	N/A

3.3. Commercialized Dental Implants and Their Clinical Outcomes in Compromised Patients

While it is well established that most treated dental implants currently available on the market enhance the treatment outcome in the healthy population, this has remained elusive in compromised patients. The previous systematic review and meta-analysis concludes that dental implants placed in smokers had a 140.2% higher risk of failure compared to non-smokers, with statistically significant differences in implant failure rates for both the maxilla and mandible. Additionally, smokers exhibited a greater mean marginal bone loss (MBL) than non-smokers. However, this study found no clear influence of the follow-up time on the odds ratios (OR) of implant failure or the mean difference in MBL between smokers and non-smokers [85]. These findings are consistent with the study from Naseri et al., which indicated a statistically significant increase in the risk of dental implant failure with the number of cigarettes smoked per day, particularly for patients smoking more than 20 cigarettes daily. The risk ratio for implant failure was nearly doubled in this group compared to non-smokers. Additionally, for those who smoke 10 cigarettes a day, a higher failure rate was observed compared to lighter smokers and non-smokers. Several studies have shown that smoking is a significant risk factor for implant failure, regardless of the types of implant surface treatments [86]. Thus, further studies are greatly needed to determine the most effective dental implants with either established or novel surface treatment methods for smokers.

In addition to smoking, the previous study also concludes that dental implants in diabetic patients had a 77.7% higher risk of failure compared to non-diabetic patients, with a higher risk in type 1 than in type 2 diabetes. This study also found that the risk of implant failure was significantly increased in the maxilla but not in the mandible. Additionally, there was a 0.776 mm difference in MBL between diabetic and non-diabetic

patients, increasing with each additional month of follow-up. Also, the OR of implant failure and the mean difference of MBL between diabetic and non-diabetic patients were associated with follow-up time; longer follow-up time was correlated with the decreased OR for implant failure [87]. Moreover, Wegner et al. also reported that poorly controlled diabetes was associated with a higher risk of peri-implantitis and implant loss. However, the success rates of dental implant surgery in controlled diabetic patients were similar to those in healthy individuals. The use of perioperative anti-infective therapy, such as antibiotics and chlorhexidine, is also recommended to improve the success rate of implant placement [88]. Although the success rate of implant placement in controlled-diabetes patients is comparable to healthy individuals, previous studies suggest that improved surface modification techniques are still much needed to enhance osseointegration in patients with poorly controlled diabetes.

4. Current Limitations and Future Directions

While current approaches to surface modifications of titanium dental implants have shown to improve both success and survival rate in healthy patients, improved or novel methods are still vastly required to enhance osseointegration in compromised patients. As mentioned above, smoking, uncontrolled diabetes, and other systemic conditions may potentially hinder successful healing following dental implant placement by interfering with various phases of osseointegration. Additionally, several current implant manufacturing processes may also affect treatment outcomes. For instance, carbon contamination on dental implants can be observed during several stages of the production process, including machining and surface cleaning with carbon-contaminated silica powder. This might affect osseointegration by decreasing the surface energy and hydrophilicity of the implant surface, hence lowering the interaction between biomolecules and the bone-implant interface, which ultimately results in compromised healing. Moreover, the contaminated implant surfaces can intensify immunological reactions as well as accelerate the process of corrosion, resulting in the release of ions. These can potentially impact the development of bones, the longevity of implants, and can lead to toxicity or provoke allergic responses [89]. Thus, these current limitations are crucially needed to be addressed in future studies regarding the surface modifications of titanium dental implants.

The potential for future advancements in dental implant surface treatments is promising, driven by progress in materials sciences, nanotechnology, biotechnology, and digital dentistry. These breakthroughs aim to improve osseointegration, shorten healing periods, and increase the long-term success rate of dental implants. Some key anticipated trends include leveraging nanotechnology for precise surface modifications, developing bioactive coatings to stimulate bone regeneration and integration while reducing inflammation, and incorporating antimicrobial surfaces to decrease bacterial colonization and biofilm formation. Furthermore, investigations of immunomodulatory characteristics and biomimetic designs inspired by natural bone structures to improve tissue integration are now being considered. For instance, Kranz et al. highlighted the efficacy of coatings of gentamicin–tannic acid and ionic zinc in preventing bacterial colonization on plasma-chemically oxidized titanium surfaces. Their TiOB[®] SiOx Ag coating demonstrated exceptional biocompatibility and antimicrobial properties [90], which may be beneficial in compromised patients and bone areas that are prone to infection and inflammation. In addition, Veiko et al. conducted a study on titanium dental implant surface treatment using laser radiation techniques to adjust the topography of the implant surface to match the exact size of various cells. They found that G-topography featuring μ -rooms significantly enhances osseointegration and secondary stability by promoting a higher number of mature osteocytes and better BIC parameters [54]. Apart from the microsurface, dental implants can be designed at the macro scale to be specifically suitable for the different bone densities of each patient. The compatibility of the macrosurface characteristics of the implant with the bone density of each patient could potentially enhance biomechanical and biocompatibility, making it more specific and tailored to the individual characteristics of each patient [91]. Future

advancements may also include customized surface treatments designed to meet the specific needs of individual patients using CAD-CAM technology and digital dentistry. These approaches can design porous surfaces for titanium implants with specific and accurate pore sizes, which improve the various biomechanical properties of the implants to closely resemble the trabecular bone of individual patients. This subsequently leads to an enhanced biomechanical fit and biocompatibility of the implants compared to conventional surface treatments [92,93]. As these advancements progress, ensuring the regulated manufacturing standards and safety clinical protocols will be critical in assessing the long-term performance and biocompatibility of the novel implant surface treatments. Ultimately, the future of dental implant surface treatments holds great potential to transform the field, focusing on enhancing biocompatibility, expediting healing processes, and minimizing complications for better treatment outcomes, especially in patients with compromised conditions such as diabetes, smoking, osteoporosis, etc.

5. Conclusions

This review article summarizes the current titanium surface modification approaches for dental implants and compares their effects on osteoblasts and bone formation in *in vitro*, *in vivo*, and clinical studies. It shows that the frequently used parameters in *in vitro* biological tests include osteoblast morphology and proliferation, ALP, collagen, calcium deposition, and surface roughness. It can be observed that the various implant surface treatments mentioned in this review consistently involve increasing the surface roughness of the implant at different scales. When tested with osteoblasts, the implants prepared with current surface treatments exhibit similar positive effects on differentiation and function when compared to the non-treated surface. This may potentially explain why treated titanium implants, regardless of the techniques, tend to have higher success and survival rates compared to untreated implants in clinical studies. Additionally, it can be concluded that surface roughness plays a significant role both in terms of experimental outcomes *in vitro* as well as success and survival rate in clinical studies.

From the authors' perspective, surface preparation using SLA combined with coating with HA and chitosan is likely to provide the best treatment outcomes for patients. This is because the SLA-treated implant surface exhibits micro-roughness from sandblasting and nano-roughness from acid etching, resulting in the highest surface energy and hydrophilicity. Additionally, coating with HA, which has high biocompatibility, along with chitosan, which has antibacterial properties, potentially increases the chances of successful healing after implant placement. Nevertheless, this review mainly focuses on the bone formation process and osteoblast cells, both of which are just one aspect of osseointegration. Further studies/reviews are needed in the future to investigate other cells or factors impacting the success of osseointegration. Furthermore, current studies often compare treated implants with untreated ones, indicating the need for further studies that directly compare different surface preparations to determine the most effective methods. Last but not least, though conventional approaches have already been proven to ensure successful osseointegration in a healthy population, improved or novel techniques are still tremendously needed for superior surface properties and better treatment outcomes of implant placement in compromised patients.

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References

1. Lee, H.; Kim, D.; Jung, A.; Chae, W. Ethnicity, Social, and Clinical Risk Factors to Tooth Loss among Older Adults in the U.S., NHANES 2011–2018. *Int. J. Environ. Res. Public Health* **2022**, *19*, 2382. [CrossRef]
2. Petersen, P.E.; Yamamoto, T. Improving the oral health of older people: The approach of the WHO Global Oral Health Programme. *Community Dent. Oral Epidemiol.* **2005**, *33*, 81–92. [CrossRef] [PubMed]
3. Yan, X.; Cao, W.; Li, H. Biomedical Alloys and Physical Surface Modifications: A Mini-Review. *Materials* **2021**, *15*, 66. [CrossRef] [PubMed]
4. Lin, H.; Castillo, A.E.d.R.; González, V.J.; Jacquemin, L.; Panda, J.K.; Bonaccorso, F.; Vázquez, E.; Bianco, A. Effects of industrially produced 2-dimensional molybdenum disulfide materials in primary human basophils. *NanoImpact* **2023**, *29*, 100451. [CrossRef] [PubMed]
5. Yang, J.; Liu, C.; Sun, H.; Liu, Y.; Liu, Z.; Zhang, D.; Zhao, G.; Wang, Q.; Yang, D. The progress in titanium alloys used as biomedical implants: From the view of reactive oxygen species. *Front. Bioeng. Biotechnol.* **2022**, *10*, 1092916. [CrossRef] [PubMed]
6. Karabulut, G.; Beköz Üllen, N.; Akyüz, E.; Karakus, S. Surface modification of 316L stainless steel with multifunctional locust gum/polyethylene glycol-silver nanoparticles using different coating methods. *Prog. Org. Coat.* **2023**, *174*, 107291. [CrossRef]
7. Narayanan, D.; Liu, M.; Kuttolamadom, M.; Castaneda, H. Identification and development of a new local corrosion mechanism in a Laser Engineered Net Shaped (LENS) biomedical Co-Cr-Mo alloy in Hank's solution. *Corros. Sci.* **2022**, *207*, 110599. [CrossRef]
8. Accioni, F.; Vazquez, J.; Merinero, M.; Begines, B.; Alcudia, A. Latest Trends in Surface Modification for Dental Implantology: Innovative Developments and Analytical Applications. *Pharmaceutics* **2022**, *14*, 455. [CrossRef]
9. Brånemark, P.I. Osseointegration and its experimental background. *J. Prosthet. Dent.* **1983**, *50*, 399–410. [CrossRef] [PubMed]
10. Trindade, R.; Albrektsson, T.; Tengvall, P.; Wennerberg, A. Foreign Body Reaction to Biomaterials: On Mechanisms for Buildup and Breakdown of Osseointegration. *Clin. Implant. Dent. Relat. Res.* **2014**, *18*, 192–203. [CrossRef]
11. Pellegrini, G.; Francetti, L.; Barbaro, B.; Del Fabbro, M. Novel surfaces and osseointegration in implant dentistry. *J. Investig. Clin. Dent.* **2018**, *9*, e12349. [CrossRef] [PubMed]
12. Sawase, T.; Watanabe, I. Surface Modification of Titanium and Its Alloy by Anodic Oxidation for Dental Implant. In *Implant Surfaces and their Biological and Clinical Impact*; Springer Nature: Berlin/Heidelberg, Germany, 2015; pp. 65–76.
13. Sun, X.D.; Liu, T.T.; Wang, Q.Q.; Zhang, J.; Cao, M.S. Surface Modification and Functionalities for Titanium Dental Implants. *ACS Biomater. Sci. Eng.* **2023**, *9*, 4442–4461. [CrossRef] [PubMed]
14. Rupp, F.; Liang, L.; Geis-Gerstorf, J.; Scheideler, L.; Hüttig, F. Surface characteristics of dental implants: A review. *Dent. Mater.* **2018**, *34*, 40–57. [CrossRef] [PubMed]
15. Mandracci, P.; Mussano, F.; Rivolo, P.; Carossa, S. Surface Treatments and Functional Coatings for Biocompatibility Improvement and Bacterial Adhesion Reduction in Dental Implantology. *Coatings* **2016**, *6*, 7. [CrossRef]
16. Kligman, S.; Ren, Z.; Chung, C.-H.; Perillo, M.A.; Chang, Y.-C.; Koo, H.; Zheng, Z.; Li, C. The Impact of Dental Implant Surface Modifications on Osseointegration and Biofilm Formation. *J. Clin. Med.* **2021**, *10*, 1641. [CrossRef] [PubMed]
17. Gbureck, U.; Masten, A.; Probst, J.; Thull, R. Tribochemical structuring and coating of implant metal surfaces with titanium oxide and hydroxyapatite layers. *Mater. Sci. Eng. C* **2003**, *23*, 461–465. [CrossRef]
18. Esposito, M.; Hirsch, J.M.; Lekholm, U.; Thomsen, P. Biological factors contributing to failures of osseointegrated oral implants. (I). Success criteria and epidemiology. *Eur. J. Oral Sci.* **1998**, *106*, 527–551. [CrossRef] [PubMed]
19. Osak, P.; Maszybrocka, J.; Zubko, M.; Rak, J.; Bogunia, S.; Losiewicz, B. Influence of Sandblasting Process on Tribological Properties of Titanium Grade 4 in Artificial Saliva for Dentistry Applications. *Materials* **2021**, *14*, 7536. [CrossRef]
20. Citeau, A.; Guicheux, J.; Vinatier, C.; Layrolle, P.; Nguyen, T.P.; Pilet, P.; Daculsi, G. In vitro biological effects of titanium rough surface obtained by calcium phosphate grid blasting. *Biomaterials* **2005**, *26*, 157–165. [CrossRef]
21. Anselme, K. Osteoblast adhesion on biomaterials. *Biomaterials* **2000**, *21*, 667–681. [CrossRef]
22. Anselme, K.; Linez, P.; Bigerelle, M.; Le Maguer, D.; Le Maguer, A.; Hardouin, P.; Hildebrand, H.; Iost, A.; Leroy, J. The relative influence of the topography and chemistry of TiAl6V4 surfaces on osteoblastic cell behaviour. *Biomaterials* **2000**, *21*, 1567–1577. [CrossRef]
23. Xavier, S.P.; Carvalho, P.S.; Beloti, M.M.; Rosa, A.L. Response of rat bone marrow cells to commercially pure titanium submitted to different surface treatments. *J. Dent.* **2003**, *31*, 173–180. [CrossRef] [PubMed]
24. Gil, J.; Pérez, R.; Herrero-Climent, M.; Rizo-Gorrita, M.; Torres-Lagares, D.; Gutierrez, J.L. Benefits of Residual Aluminum Oxide for Sand Blasting Titanium Dental Implants: Osseointegration and Bactericidal Effects. *Materials* **2021**, *15*, 178. [CrossRef]
25. Gotfredsen, K.; Wennerberg, A.; Johansson, C.; Skovgaard, L.T.; Hjørting-Hansen, E. Anchorage of TiO₂-blasted, HA-coated, and machined implants: An experimental study with rabbits. *J. Biomed. Mater. Res.* **1995**, *29*, 1223–1231. [CrossRef]
26. Ivanoff, C.J.; Hallgren, C.; Widmark, G.; Sennerby, L.; Wennerberg, A. Histologic evaluation of the bone integration of TiO₂ blasted and turned titanium microimplants in humans. *Clin. Oral Implant. Res.* **2001**, *12*, 128–134. [CrossRef] [PubMed]

27. Giner, L.; Mercadé, M.; Torrent, S.; Punset, M.; Pérez, R.A.; Delgado, L.M.; Gil, F.J. Double acid etching treatment of dental implants for enhanced biological properties. *J. Appl. Biomater. Funct. Mater.* **2017**, *16*, 83–89. [[CrossRef](#)] [[PubMed](#)]
28. Feng, F.; Wu, Y.; Xin, H.; Chen, X.; Guo, Y.; Qin, D.; An, B.; Diao, X.; Luo, H. Surface Characteristics and Biocompatibility of Ultrafine-Grain Ti after Sandblasting and Acid Etching for Dental Implants. *ACS Biomater. Sci. Eng.* **2019**, *5*, 5107–5115. [[CrossRef](#)]
29. Orsini, G.; Assenza, B.; Scarano, A.; Piattelli, M.; Piattelli, A. Surface analysis of machined versus sandblasted and acid-etched titanium implants. *Int. J. Oral Maxillofac. Implant.* **2000**, *15*, 779–784.
30. Fernandes, D.J.; Marques, R.G.; Elias, C.N. Influence of acid treatment on surface properties and in vivo performance of Ti6Al4V alloy for biomedical applications. *J. Mater. Sci. Mater. Med.* **2017**, *28*, 164. [[CrossRef](#)]
31. Gaviria, J.; Alcudia, A.; Begines, B.; Beltrán, A.M.; Villarraga, J.; Moriche, R.; Rodríguez-Ortiz, J.A.; Torres, Y. Synthesis and deposition of silver nanoparticles on porous titanium substrates for biomedical applications. *Surf. Coat. Technol.* **2020**, *406*, 126667. [[CrossRef](#)]
32. Kim, H.; Choi, S.H.; Ryu, J.J.; Koh, S.Y.; Park, J.H.; Lee, I.S. The biocompatibility of SLA-treated titanium implants. *Biomed. Mater.* **2008**, *3*, 025011. [[CrossRef](#)] [[PubMed](#)]
33. Ramaglia, L.; Postiglione, L.; Di Spigna, G.; Capece, G.; Salzano, S.; Rossi, G. Sandblasted-acid-etched titanium surface influences in vitro the biological behavior of SaOS-2 human osteoblast-like cells. *Dent. Mater. J.* **2011**, *30*, 183–192. [[CrossRef](#)] [[PubMed](#)]
34. Kim, M.-H.; Park, K.; Choi, K.-H.; Kim, S.-H.; Kim, S.E.; Jeong, C.-M.; Huh, J.-B. Cell adhesion and in vivo osseointegration of sandblasted/acid etched/anodized dental implants. *Int. J. Mol. Sci.* **2015**, *16*, 10324–10336. [[CrossRef](#)] [[PubMed](#)]
35. Li, D.; Ferguson, S.J.; Beutler, T.; Cochran, D.L.; Sittig, C.; Hirt, H.P.; Buser, D. Biomechanical comparison of the sandblasted and acid-etched and the machined and acid-etched titanium surface for dental implants. *J. Biomed. Mater. Res.* **2002**, *60*, 325–332. [[CrossRef](#)] [[PubMed](#)]
36. Velasco-Ortega, E.; Ortiz-García, I.; Jiménez-Guerra, A.; Monsalve-Guil, L.; Muñoz-Guzón, F.; Perez, R.A.; Gil, F.J. Comparison between Sandblasted Acid-Etched and Oxidized Titanium Dental Implants: In Vivo Study. *Int. J. Mol. Sci.* **2019**, *20*, 3267. [[CrossRef](#)] [[PubMed](#)]
37. Wennerberg, A.; Galli, S.; Albrektsson, T. Current knowledge about the hydrophilic and nanostructured SLActive surface. *Clin. Cosmet. Investig. Dent.* **2011**, *3*, 59–67. [[CrossRef](#)] [[PubMed](#)]
38. Sayin Ozel, G.; Inan, O.; Secilmis Acar, A.; Alniacik Iyidogan, G.; Dolanmaz, D.; Yildirim, G. Stability of dental implants with sandblasted and acid-etched (SLA) and modified (SLActive) surfaces during the osseointegration period. *J. Dent. Res. Dent. Clin. Dent. Prospect.* **2021**, *15*, 226–231. [[CrossRef](#)] [[PubMed](#)]
39. Mühl, A.; Szabó, P.; Krafcsik, O.; Aigner, Z.; Kopniczky, J.; Nagy, A.; Marada, G.; Turzó, K. Comparison of surface aspects of turned and anodized titanium dental implant, or abutment material for an optimal soft tissue integration. *Heliyon* **2022**, *8*, e10263. [[CrossRef](#)] [[PubMed](#)]
40. Li, B.; Li, Y.; Li, J.; Fu, X.; Li, H.; Wang, H.; Xin, S.; Zhou, L.; Liang, C.; Li, C. Influence of nanostructures on the biological properties of Ti implants after anodic oxidation. *J. Mater. Sci. Mater. Med.* **2013**, *25*, 199–205. [[CrossRef](#)]
41. Chiesa, R.; Sandrini, E.; Santin, M.; Rondelli, G.; Cigada, A. Osteointegration of titanium and its alloys by anodic spark deposition and other electrochemical techniques: A review. *J. Appl. Biomater. Biomech.* **2003**, *1*, 91–107.
42. Delplancke, J.-L.; Winand, R. Galvanostatic anodization of titanium—I. Structures and compositions of the anodic films. *Electrochim. Acta* **1988**, *33*, 1539–1549. [[CrossRef](#)]
43. Zhu, X.; Chen, J.; Scheideler, L.; Reichl, R.; Geis-Gerstorfer, J. Effects of topography and composition of titanium surface oxides on osteoblast responses. *Biomaterials* **2004**, *25*, 4087–4103. [[CrossRef](#)] [[PubMed](#)]
44. Yao, C.; Slamovich, E.B.; Webster, T.J. Enhanced osteoblast functions on anodized titanium with nanotube-like structures. *J. Biomed. Mater. Res. Part A* **2007**, *85*, 157–166. [[CrossRef](#)]
45. Jain, S.; Williamson, R.S.; Janorkar, A.V.; Griggs, J.A.; Roach, M.D. Osteoblast response to nanostructured and phosphorus-enhanced titanium anodization surfaces. *J. Biomater. Appl.* **2019**, *34*, 419–430. [[CrossRef](#)]
46. Rodríguez, R.; Kim, K.; Ong, J.L. In vitro osteoblast response to anodized titanium and anodized titanium followed by hydrothermal treatment. *J. Biomed. Mater. Res. Part A* **2003**, *65A*, 352–358. [[CrossRef](#)] [[PubMed](#)]
47. Sul, Y.T.; Johansson, C.B.; Jeong, Y.; Wennerberg, A.; Albrektsson, T. Resonance frequency and removal torque analysis of implants with turned and anodized surface oxides. *Clin. Oral Implant. Res.* **2002**, *13*, 252–259. [[CrossRef](#)]
48. Villaça-Carvalho, M.F.L.; de Araújo, J.C.R.; Beraldo, J.M.; Prado, R.F.d.; Moraes, M.E.L.d.; Manhães Junior, L.R.C.; Codaro, E.N.; Acciari, H.A.; Machado, J.P.B.; Regone, N.N.; et al. Bioactivity of an Experimental Dental Implant with Anodized Surface. *J. Funct. Biomater.* **2021**, *12*, 39. [[CrossRef](#)]
49. Gaggli, A.; Schultes, G.; Müller, W.D.; Kärcher, H. Scanning electron microscopical analysis of laser-treated titanium implant surfaces—A comparative study. *Biomaterials* **2000**, *21*, 1067–1073. [[CrossRef](#)] [[PubMed](#)]
50. Milleret, V.; Lienemann, P.S.; Gasser, A.; Bauer, S.; Ehrbar, M.; Wennerberg, A. Rational design and in vitro characterization of novel dental implant and abutment surfaces for balancing clinical and biological needs. *Clin. Implant. Dent. Relat. Res.* **2019**, *21* (Suppl. 1), 15–24. [[CrossRef](#)]
51. Sul, Y.T.; Johansson, C.B.; Petronis, S.; Krozer, A.; Jeong, Y.; Wennerberg, A.; Albrektsson, T. Characteristics of the surface oxides on turned and electrochemically oxidized pure titanium implants up to dielectric breakdown: The oxide thickness, micropore configurations, surface roughness, crystal structure and chemical composition. *Biomaterials* **2002**, *23*, 491–501. [[CrossRef](#)]

52. Textor, M.; Sittig, C.; Frauchiger, V.; Tosatti, S.; Brunette, D. Properties and Biological Significance of Natural Oxide Films on Titanium and Its Alloys. In *Titanium in Medicine*; Springer: Berlin/Heidelberg, Germany, 2001; pp. 171–230.
53. Veiko, V.; Karlagina, Y.; Itina, T.; Kuznetsova, D.; Elagin, V.; Zagaynova, E.; Chernenko, G.; Egorova, E.; Zernitskaia, C.; Manokhin, S.; et al. Laser-assisted fabrication and in vitro verification of functionalized surface for cells biointegration. *Opt. Laser Technol.* **2021**, *138*, 106871. [[CrossRef](#)]
54. Veiko, V.; Karlagina, Y.; Zernitskaia, E.; Egorova, E.; Radaev, M.; Yaremenko, A.; Chernenko, G.; Romanov, V.; Shchedrina, N.; Ivanova, E.; et al. Laser-Induced micro-Rooms for Osteocytes on Implant Surface: An In Vivo Study. *Nanomaterials* **2022**, *12*, 4229. [[CrossRef](#)] [[PubMed](#)]
55. Mastrangelo, F.; Quaresima, R.; Canullo, L.; Scarano, A.; Muzio, L.L.; Piattelli, A. Effects of Novel Laser Dental Implant Microtopography on Human Osteoblast Proliferation and Bone Deposition. *Int. J. Oral Maxillofac. Implant.* **2020**, *35*, 320–329. [[CrossRef](#)] [[PubMed](#)]
56. Inchingolo, A.M.; Malcangi, G.; Ferrante, L.; Del Vecchio, G.; Viapiano, F.; Inchingolo, A.D.; Mancini, A.; Annicchiarico, C.; Inchingolo, F.; Dipalma, G.; et al. Surface Coatings of Dental Implants: A Review. *J. Funct. Biomater.* **2023**, *14*, 287. [[CrossRef](#)] [[PubMed](#)]
57. Hung, K.-Y.; Lo, S.-C.; Shih, C.-S.; Yang, Y.-C.; Feng, H.-P.; Lin, Y.-C. Titanium surface modified by hydroxyapatite coating for dental implants. *Surf. Coat. Technol.* **2013**, *231*, 337–345. [[CrossRef](#)]
58. Łukaszewska-Kuska, M.; Krawczyk, P.; Martyla, A.; Hędzielek, W.; Dorocka-Bobkowska, B. Hydroxyapatite coating on titanium endosseous implants for improved osseointegration: Physical and chemical considerations. *Adv. Clin. Exp. Med.* **2018**, *27*, 1055–1059. [[CrossRef](#)] [[PubMed](#)]
59. Suwanprateeb, J.; Suvannapruk, W.; Chokevivat, W.; Kiertkrittikhon, S.; Jaruwangsanti, N.; Tienboon, P. Bioactivity of a sol-gel-derived hydroxyapatite coating on titanium implants in vitro and in vivo. *Asian Biomed.* **2018**, *12*, 35–44. [[CrossRef](#)]
60. Wang, X.; Mei, L.; Jiang, X.; Jin, M.; Xu, Y.; Li, J.; Li, X.; Meng, Z.; Zhu, J.; Wu, F. Hydroxyapatite-Coated Titanium by Micro-Arc Oxidation and Steam-Hydrothermal Treatment Promotes Osseointegration. *Front. Bioeng. Biotechnol.* **2021**, *9*, 625877. [[CrossRef](#)]
61. Park, Y.-J.; Choi, K.-H.; Hahn, B.-D.; Lee, Y.-C.; Song, J.-Y.; Park, Y.-T.; Kim, S.-G. New bone formation between bare titanium surface and hydroxyapatite coating by the aerosol deposition technique in the nasal mucosal penetration model. *J. Craniofacial Surg.* **2013**, *24*, 632–635. [[CrossRef](#)]
62. Jing, W.; Zhang, M.; Jin, L.; Zhao, J.; Gao, Q.; Ren, M.; Fan, Q. Assessment of osteoinduction using a porous hydroxyapatite coating prepared by micro-arc oxidation on a new titanium alloy. *Int. J. Surg.* **2015**, *24*, 51–56. [[CrossRef](#)]
63. Łukaszewska-Kuska, M.; Krawczyk, P.; Martyla, A.; Hędzielek, W.; Dorocka-Bobkowska, B. Effects of a hydroxyapatite coating on the stability of endosseous implants in rabbit tibiae. *Dent. Med. Probl.* **2019**, *56*, 123–129. [[CrossRef](#)] [[PubMed](#)]
64. Faeda, R.S.; Tavares, H.S.; Sartori, R.; Guastaldi, A.C.; Marcantonio, E., Jr. Biological performance of chemical hydroxyapatite coating associated with implant surface modification by laser beam: Biomechanical study in rabbit tibias. *J. Oral Maxillofac. Surg.* **2009**, *67*, 1706–1715. [[CrossRef](#)] [[PubMed](#)]
65. Hermida, J.C.; Patil, S.; Dimaano, F.; Hawkins, M.; Colwell, C.W.; D’Lima, D.D. Solution Deposition of Hydroxyapatite on a Highly Porous Titanium Surface Enhances Osseointegration. *Key Eng. Mater.* **2005**, *284–286*, 215–218. [[CrossRef](#)]
66. de Oliveira PG, F.P.; de Melo Soares, M.S.; Silveira e Souza, A.M.M.; Taba, M., Jr.; Palioto, D.B.; Messoria, M.R.; de Souza, S.L.S. Influence of nano-hydroxyapatite coating implants on gene expression of osteogenic markers and micro-CT parameters. An in vivo study in diabetic rats. *J. Biomed. Mater. Res. A.* **2021**, *109*, 682–694. [[CrossRef](#)] [[PubMed](#)]
67. Zagury, R.; Harari, N.D.; Conz, M.B.; Soares, G.d.A.; Vidigal, G.M., Jr. Histomorphometric analyses of bone interface with titanium-aluminum-vanadium and hydroxyapatite-coated implants by biomimetic process. *Implant. Dent.* **2007**, *16*, 290–296. [[CrossRef](#)]
68. Jung, R.E.; Zembic, A.; Pjetursson, B.E.; Zwahlen, M.; Thoma, D.S. Systematic review of the survival rate and the incidence of biological, technical, and aesthetic complications of single crowns on implants reported in longitudinal studies with a mean follow-up of 5 years. *Clin. Oral Implants Res.* **2012**, *23* (Suppl. 6), 2–21. [[CrossRef](#)] [[PubMed](#)]
69. Hallmann, L.; Gerngross, M.D. Chitosan and its application in dental implantology. *J. Stomatol. Oral Maxillofac. Surg.* **2022**, *123*, e701–e707. [[CrossRef](#)] [[PubMed](#)]
70. Yuan, Y.; Chesnutt, B.M.; Haggard, W.O.; Bumgardner, J.D. Deacetylation of Chitosan: Material Characterization and in vitro Evaluation via Albumin Adsorption and Pre-Osteoblastic Cell Cultures. *Materials* **2011**, *4*, 1399–1416. [[CrossRef](#)] [[PubMed](#)]
71. Ueno, H.; Mori, T.; Fujinaga, T. Topical formulations and wound healing applications of chitosan. *Adv. Drug Deliv. Rev.* **2001**, *52*, 105–115. [[CrossRef](#)]
72. Balagangadharan, K.; Dhivya, S.; Selvamurugan, N. Chitosan based nanofibers in bone tissue engineering. *Int. J. Biol. Macromol.* **2017**, *104*, 1372–1382. [[CrossRef](#)]
73. Zhang, T.; Zhang, X.; Mao, M.; Li, J.; Wei, T.; Sun, H. Chitosan/hydroxyapatite composite coatings on porous Ti6Al4V titanium implants: In vitro and in vivo studies. *J. Periodontal Implant. Sci.* **2020**, *50*, 392–405. [[CrossRef](#)]
74. Takanche, J.S.; Kim, J.-E.; Kim, J.-S.; Lee, M.-H.; Jeon, J.-G.; Park, I.-S.; Yi, H.-K. Chitosan-gold nanoparticles mediated gene delivery of c-myc facilitates osseointegration of dental implants in ovariectomized rat. *Artif. Cells Nanomed. Biotechnol.* **2018**, *46* (Suppl. 3), S807–S817.
75. Kung, S.; Devlin, H.; Fu, E.; Ho, K.Y.; Liang, S.Y.; Hsieh, Y.D. The osteoinductive effect of chitosan-collagen composites around pure titanium implant surfaces in rats. *J. Periodontal Res.* **2010**, *46*, 126–133. [[CrossRef](#)]

76. López-Valverde, N.; López-Valverde, A.; Aragonese, J.M.; Martínez-Martínez, F.; González-Escudero, M.C.; Ramírez, J.M. Bone Density around Titanium Dental Implants Coating Tested/Coated with Chitosan or Melatonin: An Evaluation via Microtomography in Jaws of Beagle Dogs. *Coatings* **2021**, *11*, 777. [[CrossRef](#)]
77. Adell, R.; Eriksson, B.; Lekholm, U.; Brånemark, P.I.; Jemt, T. Long-term follow-up study of osseointegrated implants in the treatment of totally edentulous jaws. *Int. J. Oral Maxillofac. Implant.* **1990**, *5*, 347–359.
78. Lee, J.J.; Rouhfar, L.; Beirne, O.R. Survival of hydroxyapatite-coated implants: A meta-analytic review. *J. Oral Maxillofac. Surg.* **2000**, *58*, 1372–1379. [[CrossRef](#)]
79. Gottfredsen, K.; Karlsson, U. A prospective 5-year study of fixed partial prostheses supported by implants with machined and TiO-blasted surface. *J. Prosthodont.* **2001**, *10*, 2–7. [[CrossRef](#)] [[PubMed](#)]
80. Velasco-Ortega, E.; Jimenez-Guerra, A.; Monsalve-Guil, L.; Ortiz-Garcia, I.; Nicolas-Silvente, A.I.; Segura-Egea, J.J.; Lopez-Lopez, J. Long-Term Clinical Outcomes of Treatment with Dental Implants with Acid Etched Surface. *Materials* **2020**, *13*, 1553. [[CrossRef](#)] [[PubMed](#)]
81. Buser, D.; Janner, S.F.; Wittneben, J.G.; Brägger, U.; Ramseier, C.A.; Salvi, G.E. 10-year survival and success rates of 511 titanium implants with a sandblasted and acid-etched surface: A retrospective study in 303 partially edentulous patients. *Clin. Implant. Dent. Relat. Res.* **2012**, *14*, 839–851. [[CrossRef](#)] [[PubMed](#)]
82. Wennerberg, A.; Albrektsson, T.; Chrcanovic, B. Long-term clinical outcome of implants with different surface modifications. *Eur. J. Oral Implantol.* **2018**, *11* (Suppl. 1), S123–S136.
83. Rocci, A.; Rocci, M.; Rocci, C.; Scoccia, A.; Gargari, M.; Martignoni, M.; Gottlow, J.; Sennerby, L. Immediate loading of Brånemark system TiUnite and machined-surface implants in the posterior mandible, part II: A randomized open-ended 9-year follow-up clinical trial. *Int. J. Oral Maxillofac. Implant.* **2013**, *28*, 891–895. [[CrossRef](#)]
84. Guarnieri, R.; Di Nardo, D.; Gaimari, G.; Miccoli, G.; Testarelli, L. Short vs. Standard Laser-Microgrooved Implants Supporting Single and Splinted Crowns: A Prospective Study with 3 Years Follow-Up. *J. Prosthodont.* **2019**, *28*, e771–e779. [[CrossRef](#)]
85. Mustapha, A.D.; Salame, Z.; Chrcanovic, B.R. Smoking and Dental Implants: A Systematic Review and Meta-Analysis. *Medicina* **2021**, *58*, 39. [[CrossRef](#)] [[PubMed](#)]
86. Naseri, R.; Yaghini, J.; Feizi, A. Levels of smoking and dental implants failure: A systematic review and meta-analysis. *J. Clin. Periodontol.* **2020**, *47*, 518–528. [[CrossRef](#)] [[PubMed](#)]
87. Al Ansari, Y.; Shahwan, H.; Chrcanovic, B.R. Diabetes Mellitus and Dental Implants: A Systematic Review and Meta-Analysis. *Materials* **2022**, *15*, 3227. [[CrossRef](#)]
88. Wagner, J.; Spille, J.H.; Wiltfang, J.; Naujokat, H. Systematic review on diabetes mellitus and dental implants: An update. *Int. J. Implant. Dent.* **2022**, *8*, 1–21. [[CrossRef](#)] [[PubMed](#)]
89. Mtanis, T.; Biadsee, A.; Ormianer, Z. Assessing the Cleanliness of Dental Implants Using Scanning Electron Microscopy and Energy-Dispersive X-ray Spectroscopy Analysis-A SEM and EDS In Vitro Study. *J. Funct. Biomater.* **2023**, *14*, 172. [[CrossRef](#)]
90. Kranz, S.; Guellmar, A.; Voelpel, A.; Lesser, T.; Tonndorf-Martini, S.; Schmidt, J.; Schrader, C.; Faucon, M.; Finger, U.; Pfister, W.; et al. Bactericidal and Biocompatible Properties of Plasma Chemical Oxidized Titanium (TiOB((R))) with Antimicrobial Surface Functionalization. *Materials* **2019**, *12*, 866. [[CrossRef](#)] [[PubMed](#)]
91. Khaohoen, A.; Sornsuan, T.; Chaijareenont, P.; Poovarodom, P.; Rungsiyakull, C.; Rungsiyakull, P. Biomaterials and Clinical Application of Dental Implants in Relation to Bone Density-A Narrative Review. *J. Clin. Med.* **2023**, *12*, 6924. [[CrossRef](#)]
92. Zhang, J.; Chen, P.; Hu, F.; Chen, C.; Song, L. Porous structure design and properties of dental implants. *Comput. Methods Biomech. Biomed. Eng.* **2023**, *27*, 1–10.
93. Hudák, R.; Schnitzer, M.; Králová, Z.O.; Gorejová, R.; Mitrik, L.; Rajt'úková, V.; Tóth, T.; Kovačević, M.; Riznič, M.; Oriňaková, R.; et al. Additive Manufacturing of Porous Ti6Al4V Alloy: Geometry Analysis and Mechanical Properties Testing. *Appl. Sci.* **2021**, *11*, 2611. [[CrossRef](#)]

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