*Applied Chemical Engineering (2024) Volume 7 Issue 1*
doi: 10.24294/ace.v7i1.2042

**REVIEW ARTICLE**

# Recent advancements in the surface treatments for enhanced biocompatibility and corrosion resistance of titanium-based biomedical implants

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## ABSTRACT

Titanium-based biomedical implants are widely used owing to their biocompatibility, corrosion resistance and mechanical strength. Although, they still face challenges such as poor osseointegration and implant failure caused by corrosion. To address these challenges, various surface treatments have emerged to enhance the biocompatibility and corrosion resistance of titanium implants. This review article presents a concise overview of the innovative surface treatments for enhanced corrosion resistance and biocompatibility of titanium-based biomedical implants. The surface treatment briefly discussed includes physical, chemical, and biological treatments, such as plasma spraying, anodization, electrochemical deposition, and biomimetic coating. Furthermore, this article also highlights the importance of surface treatments to enhance the biological performance of titanium-based implants. This review provides insights for researchers and clinicians in the field of titanium-based biomaterials and may contribute to the development of more effective and durable biomedical implants.

***Keywords:*** biomedical implants; surface engineering; titanium; alloys; biocompatibility; surface coatings

**ARTICLE INFO**

Received: 21 April 2023
Accepted: 2 June 2023
Available online: 26 January 2024

## 1. Introduction

Biomedical implants have become an essential part of modern medicine and have revolutionized the way we treat various medical conditions. These implants are used for a variety of purposes, including dental implants, joint replacements, cardiovascular devices, and neurostimulation devices. They are designed to substitute, support or enhance the functionality of various tissues or organs within the human body. The global demand for biomedical implants has been increasing rapidly over the years, due to the growing recurrence of chronic illness and the aging population. As per the World Health Organization (WHO), chronic diseases account for 60% of all fatalities and 43% of the worldwide impact of disease, making them a significant source of mortality and morbidity globally[1–3]. Additionally, by 2050, there will be 2 billion people in the world who are 60 years of age or older, which would result in an even greater need for biomedical implants. The utilization of biomedical implants is not limited to developed countries, but they are also used extensively in developing countries[4–7]. According to the Worldwide Footprint of Disease survey, low- and middle-income nations bear over 80% of the impact of non-communicable diseases worldwide. The use of biomedical implants in these countries is often restricted due to financial and healthcare infrastructure limitations. However, with the increasing affordability and accessibility of healthcare in these regions, the demand for biomedical implants is expected to rise significantly. Additionally, the international demand for biomedical implants, as per a study by Grand View Research, was estimated to be worth USD 87.6 billion in 2020 and is projected to increase at a CAGR of 7.8% from 2021 to 2028[8,9]. The rising incidence of chronic diseases, technological developments in implant materials and design, and the rising popularity of minimally invasive procedures are all cited as reasons for this trend. The global market for biomedical implants is dominated by the joint replacement category, with cardiovascular device, dental and hip implants coming in second and third. Due to the rising senior population and rising healthcare costs, the Asia Pacific sector is anticipated to see the largest market expansion. **Figure 1** illustrates the utilization of several biomedical implants in the vital parts of our body[10].

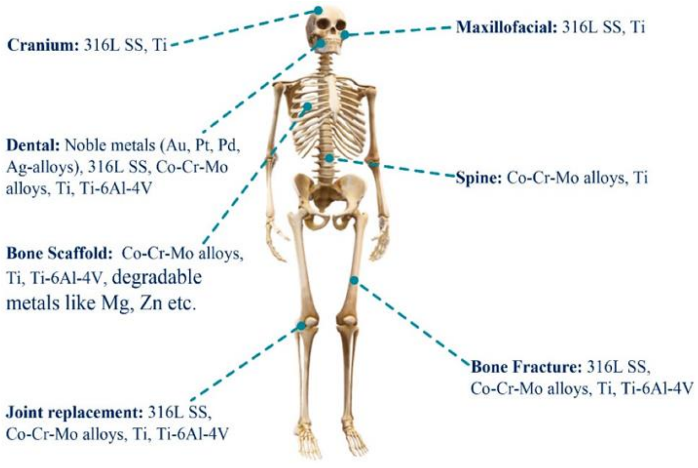

**Figure 1.** Versatile application of metallic biomedical implants. Reprinted with permission from the survey of Bai et al.[10] (Distributed under CCBY 4.0.).

Several metallic biomedical implants are used in various medical applications to restore function, support healing, and improve the quality of life for patients. Here are examples of metallic biomedical implants commonly employed:

- **Stainless steel implants:** Stainless steel implants, typically made of alloys such as 316 L stainless steel, are utilized in orthopedic and trauma surgeries. They are used in fracture fixation, joint replacements, spinal fusion, and bone reconstruction. Stainless steel implants offer good mechanical strength, corrosion resistance, and affordability.
- **Titanium-based implants:** Titanium and its alloys, such as Ti-6Al-4V, are widely used in biomedical implants due to their excellent biocompatibility, corrosion resistance, and mechanical properties. Titanium implants find applications in orthopedics, dental implants, cardiovascular interventions, ophthalmology, neurology, and cosmetic surgeries, as discussed earlier.
- **Cobalt-chromium implants:** Cobalt-chromium alloys, such as Co-Cr-Mo, are commonly employed in orthopedic implants, particularly for hip and knee replacements. These alloys offer excellent wear resistance, high strength, and good biocompatibility. Cobalt-chromium implants are known for their durability and longevity.
- **Nitinol implants:** Nitinol is a shape memory alloy composed of nickel and titanium. It exhibits unique properties, such as shape memory effect and superelasticity. Nitinol implants are used in various applications, including stents for vascular interventions, orthopedic implants, dental wires, and neurovascular devices. Nitinol’s ability to recover its shape and its biocompatibility makes it suitable for

implantable devices requiring flexibility and precise positioning.

- **Magnesium-based implants:** Magnesium and its alloys are emerging as potential materials for biomedical implants due to their biodegradability and biocompatibility. Magnesium implants are primarily explored in orthopedic and cardiovascular applications, where their temporary presence supports bone healing or vessel repair. However, extensive research is still underway to optimize their degradation rates and mechanical properties.
- **Gold implants:** Gold implants find use in specific medical applications. Gold is biocompatible and inert, making it suitable for implants in sensitive areas such as the eye. Gold implants are used in ophthalmology for certain procedures, such as eyelid weights for treating lagophthalmos (inability to close the eyelids completely).
- **Tantalum implants:** Tantalum is a biocompatible metal with excellent corrosion resistance. Tantalum implants are utilized in orthopedics, particularly for bone defect reconstructions and spinal fusion procedures. Tantalum's porous structures can promote bone ingrowth and facilitate implant integration.

These metallic implants demonstrate a wide range of characteristics, including mechanical strength, corrosion resistance, biocompatibility, and specific properties like shape memory or biodegradability. The choice of metallic implant depends on the specific application, patient requirements, and the implant's ability to support healing and provide long-term functionality. However, titanium-based implants are considered superior for several reasons. Firstly, they exhibit excellent biocompatibility, meaning they are well-tolerated by the human body and promote integration with surrounding tissues through a process called osseointegration. This reduces the risk of rejection or complications. Secondly, titanium is highly corrosion-resistant, with a natural oxide layer forming on its surface that protects it from corrosion in the body's environment. This ensures the longevity and structural integrity of the implant, minimizing the release of metal ions. Furthermore, titanium is radiolucent, meaning it does not interfere with medical imaging techniques, allowing for accurate evaluation without artifacts or distortions. The long-term stability of titanium implants has been extensively studied and validated, providing reliable outcomes and patient satisfaction. Overall, the combination of biocompatibility, corrosion resistance, strength, flexibility, imaging compatibility, and proven clinical success makes titanium-based implants a superior choice in many biomedical applications. Several potent researchers globally evaluate the recent advancements and enhanced characteristics of titanium-based biomedical implants by presenting their efficacious review articles. For instance, Sidhu et al.[11] presented notable findings in the realm of $\beta$-Ti alloy design, biological responses, strengthening mechanisms, and the creation of cost-effective implants with superior biocompatibility. They stated that the demand for low modulus-high strength implants has spurred the exploration of strategies involving the synchronization of $\beta$ stabilizer content and the incorporation of customized thermo-mechanical techniques. Additionally, the biological response of implants is recognized as a crucial factor in successful healing, emphasizing the significance of selecting optimal alloying elements. They mentioned that the design of $\beta$-Ti alloys involves tailoring the composition to enhance their mechanical properties and biocompatibility. By optimizing the content of $\beta$ stabilizers, such as niobium, tantalum, or molybdenum, the desired balance between strength and ductility could be achieved. Similarly, Sarraf et al.[12] presented their review article on commercially pure titanium and titanium alloys by discussing their exceptional mechanical tribological properties, corrosion resistance, biocompatibility, and antibacterial characteristics. They focused on the ability of titanium to promote osseointegration by establishing a direct bond with living bone without the need for additional adhesives is of paramount importance in producing robust metallic alloys for biomedical purposes. Furthermore, this review has investigated the potential applications of titania nanotubes in regenerative medicine and nanomedicine, such as localized drug delivery systems, immunomodulatory agents, antibacterial agents, and hemocompatibility. In conclusion, they stated that titanium and its alloys have proven to be highly valuable in the biomedical field, and continued research and advancements will undoubtedly expand their scope and potential, leading to improved patient outcomes and enhanced biomedical applications.

Furthermore, the utilization of titanium-based biomedical implants and surface modification of it globally could be idealized by the potent work being done in this field[13]. For instance, several potent researchers such as Hacioglu et al.[14] focused on the biomimetic coating of rough Ti6Al4V plates with bismuth + carbonate co-doped and pure hydroxyapatites (HAp). Herein, the survival rate of *Staphylococcus epidermidis*, a bacteria, was measured to assess the antibacterial properties of the coating. The structural analysis revealed that HAp nucleation commenced after four days of immersion, and nucleation progressed in parallel with the incubation period. The presence of co-dopants significantly influenced surface characteristics. The mechanical properties of the coatings were affected by the pretreatment procedure and dopants. All types of coatings exhibited critical load values above 100 mN before failure, with the highest value observed in the 0.3 mM co-doped coatings. The biological properties of the prepared coatings were evaluated using SaOS-2 cancerous bone cells. Among the co-doped samples, 0.1-C7 and 0.3-C7 exhibited the greatest reduction percentage. However, higher concentrations of dopants (up to 0.5 mM) led to increased toxicity and decreased cell proliferation. The antibacterial test results were consistent with the findings from the cell culture, indicating that 0.1-C7 and 0.3-C7 were the most effective antibacterial samples. Similarly, Kalyoncuoglu et al.[15] developed a biocompatible and antimicrobial surface for dental implants by coating Ti6Al4V with chitosan. The purpose was to create a smooth transmucosal region that promotes faster wound healing and increased bioactivity. In this experiment, the Ti6Al4V plates were prepared by abrasion and ultrasonic cleaning before being coated with chitosan. To mimic oral conditions, a subset of coated plates underwent treatment in a thermocycle apparatus. Lately, the behavior of fibroblastic cells was assessed using HGF-1 cells, and the antimicrobial effectiveness of chitosan was evaluated using *P. gingivalis*. The presence of C, H, and O elements in the EDS results confirmed the successful coating of Ti6Al4V plates with chitosan. The XRD patterns did not show significant differences between the coated and uncoated plates, but the characteristic bands of chitosan were observed in the FTIR patterns of both the coated and aged samples. The chitosan coating promoted fibroblast-cell attachment and proliferation while inhibiting bacterial growth. These findings demonstrate that chitosan is a biologically beneficial material suitable for coating the transmucosal regions of dental implants.

The hypothesis suggests that the development and application of new surface treatments for titanium-based implants can lead to improved biocompatibility, promoting better integration with surrounding tissues and minimizing adverse reactions. Additionally, these surface treatments are expected to enhance the implants’ corrosion resistance, ensuring their long-term performance and reducing the risk of implant failure or complications. The hypothesis assumes that these recent advancements in surface treatments have the potential to overcome existing limitations and further optimize the performance of titanium-based biomedical implants in clinical applications. Therefore, taking into the consideration of wide utilization of titanium-based biomedical implants, in this article, we aim to emphasize the utilization of Ti and its alloys in biomedical implants. In the preliminary stage, the author used renowned platforms such as ScienceDirect, PubMed, Elsevier, and Web of Science by using the keywords: biomedical implants, surface modification, corrosion, titanium, durability, and metals to search for potent articles. These articles were selected on the basis of quality and information provided in accordance with the advancement in the field.

## 2. Use of titanium and its alloys in biomedical implants

Owing to its unique biocompatibility, elevated strength-to-weight ratio, resistance to corrosion, and capacity to create a stabilized oxide film that facilitates osseointegration (the fusion of the implant with the bone tissue), titanium and its alloys have been broadly utilized in biomedical implants. The market for titanium-based alloys used in biomedical applications was estimated to be worth $10.6 billion globally in

2020 and is expected to increase to $16.6 billion by 2025, rising at a CAGR of 9.3% over the projected timeframe. The highest market share is accounted for by orthopedic implants made of titanium and its alloys[16–19]. This is a result of the rise in the desire for minimal intrusive surgical techniques and the incidence of orthopedic ailments including osteoporosis, osteoarthritis, and degenerative joint diseases.

Other applications of titanium-based alloys in biomedical implants include dental implants, cardiovascular implants, and ophthalmic implants. The utilization of titanium alloys in dental and hip implants has been increasing owing to their biocompatibility, strength, and durability. In terms of geography, North America and Europe are the largest markets for titanium-based alloys in biomedical applications, due to the context of the significant number of medical device manufacturers in these regions and the high incidence of orthopedic disorders. Due to the region's expanding demand for orthopedic and dental implants as well as the region's increasing acceptance of cutting-edge medical technology, the Asia-Pacific region is anticipated to develop at the highest CAGR during the projected period. **Table 1** shows the use of various types of titanium and titanium alloys in the biomedical implant in various implants.

**Table 1.** The use of various types of Titanium and titanium alloys in biomedical implants in various applications.

| Type of titanium/titanium alloy | Biomedical implant | Application | Properties |
|---|---|---|---|
| Ti-6Al-4V, Grade 2 titanium | Dental implants | Implant posts, abutments, crowns | Corrosion resistance, biocompatibility, high strength |
| Ti-6Al-4V | Spinal implants | Spinal fusion devices, pedicle screws, rods | High strength, low modulus of elasticity, biocompatibility |
| Ti-6Al-4V, Ti-6Al-7Nb | Knee implants | Femoral and tibial components | Corrosion resistance, biocompatibility, high strength |
| Ti-6Al-4V, Ti-6Al-7Nb | Hip implants | Femoral stems, acetabular cups | Corrosion resistance, biocompatibility, high strength |
| Ti-6Al-4V, Grade 2 titanium | Shoulder implants | Glenoid components, humeral components | Biocompatibility, corrosion resistance |
| Ti-6Al-4V | Pacemaker leads | Lead body | High fatigue strength, biocompatibility |
| Ti-6Al-4V | Vascular stents | Coronary, carotid, and peripheral artery stents | Biocompatibility, high strength, low profile |
| Ti-6Al-4V | Cochlear implants | Implant electrode arrays, receiver-stimulator packages | Corrosion resistance, biocompatibility |
| Ti-6Al-4V, Grade 2 titanium | Bone plates | Fracture fixation, spinal fusion | Biocompatibility, low modulus of elasticity, corrosion resistance |
| Ti-6Al-4V, Grade 2 titanium | Bone screws | Fracture fixation, spinal fusion | High strength, corrosion resistance, biocompatibility |
| Ti-6Al-4V | Ligament implants | ACL and PCL reconstruction devices | Biocompatibility, high strength |
| Ti-15Mo, Ti-6Al-7Nb | Dental implants | Implant posts, abutments, crowns | Biocompatibility, corrosion resistance |
| Ti-15Mo, Ti-6Al-7Nb | Spinal implants | Spinal fusion devices, pedicle screws, rods | Biocompatibility, low modulus of elasticity |
| Ti-15Mo, Ti-6Al-7Nb | Knee implants | Femoral and tibial components | High strength, biocompatibility |
| Ti-15Mo | Hip implants | Femoral stems, acetabular cups | Biocompatibility, high strength, low modulus of elasticity |
| Ti-13Nb-13Zr | Dental implants | Implant posts, abutments, crowns | High biocompatibility, low modulus of elasticity |
| Ti-13Nb-13Zr | Spinal implants | Spinal fusion devices, pedicle screws, rods | Biocompatibility, low modulus of elasticity |

**Table 1.** (*Continued*).

| Type of titanium/titanium alloy | Biomedical implant | Application | Properties |
|---|---|---|---|
| Ti-13Nb-13Zr | Knee implants | Femoral and tibial components | Corrosion resistance, biocompatibility |
| Ti-13Nb-13Zr | Hip implants | Femoral stems, acetabular cups | Low modulus of elasticity, biocompatibility |
| Ti-35Nb-7Zr-5Ta | Dental implants | Implant posts, abutments, crowns | Biocompatibility, high strength |

## 3. Properties of titanium and its alloys

Titanium is a chemical element having the symbol Ti and atomic number 22. It is a silvery-white, lustrous, strong, and lightweight metal featuring excellent corrosion resistance, a significant strength-to-weight ratio (which means that titanium is both strong and lightweight, making it advantageous in various applications where weight reduction and strength are important factors), and biocompatibility[20–22]. As a general guideline, titanium and its alloys typically have strength-to-weight ratios that are comparable or superior to other commonly used engineering and biomedical materials. For example, commercially pure titanium (Grade 2) has a tensile strength of approximately 370 MPa (megapascals) and a density of about 4.51 g/cm$^3$. This results in a strength-to-weight ratio of approximately 82 MPa/(g/cm$^3$). However, Titanium alloys, such as Ti-6Al-4V (Grade 5), are widely used and have even higher strength-to-weight ratios. Ti-6Al-4V has a tensile strength ranging from 900 to 1100 MPa, depending on the specific heat treatment, while its density is around 4.43 g/cm$^3$. This yields a strength-to-weight ratio of approximately 203 to 248 MPa/(g/cm$^3$). It's worth noting that the strength-to-weight ratio can vary among different titanium alloys and can be further optimized through alloying, heat treatment, and processing techniques. These variations allow engineers to tailor the material's properties to specific applications. These aforementioned characteristics make titanium and its alloys highly desirable for usage in a broad array of applications, such as biomedical implants. Some of the key characteristics of Ti and its alloys include:

- **Corrosion resistance:** Seawater, acids, and alkaline solutions are just a few of the situations in which titanium and its alloys display exceptional corrosion resistance. This is because a thin, persistent oxide coating forms on the material's surface, limiting additional corrosion.
- **Strength-to-weight proportion:** Because titanium and its alloys offer a significant strength-to-weight proportion, they are both robust and lightweight. Industries wherein weight reduction is crucial, such as those in the aircraft, automobile, and biomedical industries, are particularly attractive for using this characteristic.
- **Biocompatibility:** Because titanium and its alloys are biocompatible, they have no negative effects when used to implant medical devices in people. This property makes them highly desirable for use in biomedical implants, including orthopedic, dental, cardiovascular, and ophthalmic implants.
- **Ductility:** Titanium and its alloys are highly ductile, which means they can be easily formed into different shapes and sizes. The specific ductility of titanium and its alloys can vary depending on factors such as alloy composition, heat treatment, and processing conditions. However, in general, titanium alloys can exhibit elongations at fracture (ductility) ranging from 10% to 25% or more, depending on the specific alloy and conditions. This property makes them highly desirable for use in various manufacturing processes, including additive manufacturing or 3D printing.
- **Low thermal expansion:** Due to its limited thermal expansions, titanium and its alloys do not considerably expand and contract while subjected to temperature fluctuations. They are extremely suitable for usage in situations where dimensional consistency is important because of this characteristic.
- **Non-magnetic:** Titanium and its alloys are non-magnetic, which means they do not interfere with

magnetic fields. This property makes them highly desirable for use in applications where magnetic interference can cause problems, such as in MRI machines or other medical equipment.

## 4. Applications of titanium-based alloys in biomedical implants

The utilization of Ti-based alloys in biomedical implants has revolutionized the domain of medicine, enabling the creation of highly durable and long-lasting implants that are capable of fusing with the surrounding bone tissue. The most common applications of titanium-based alloys in biomedical implants are dental implants, orthopedic implants, cardiovascular implants, and ophthalmic implants.

- **Orthopedic implants:** Orthopedic implants are devices that are used to restore or repair injured or diseased joints and bones. The most common orthopedic implants made from titanium-based alloys include hip and knee replacements, spinal implants, and bone plates and screws. These implants are designed to withstand the stresses and strains of the body and to promote osseointegration with the surrounding bone tissue. Knee and hip replacements are the most typical types of orthopedic implants made from titanium-based alloys. These implants are designed to replace the damaged or diseased hip or knee joint and to restore the patient's movement and quality of life[23–25]. The utilization of Ti-based alloys in these implants encompasses transforming the terrain of joint replacement surgery, enabling the creation of highly durable and long-lasting implants that are capable of withstanding the stresses and strains of the body. Spinal implants made from titanium-based alloys are used to stabilize the spine and promote the fusion of the vertebrae. These implants are used to treat an array of spinal disorders, such as degenerative disc disease, spinal stenosis and herniated discs. The use of titanium-based alloys in spinal implants significantly progressed the domain of spinal surgery, enabling the creation of highly durable and long-lasting implants that are capable of withstanding the stresses and strains of the spine.
- **Dental implants:** Dental implants are prosthetics utilized to fill up tooth gaps. Dental implants, abutments, and dental crowns are the most typical dental implants created from titanium-based alloys. With a titanium-based implant that fuses with the surrounding bone tissue and a dental crown that is linked to the implant to form a natural-looking and functional tooth, these implants are made to replicate the structure of a natural tooth. The field of dental surgery has been transformed by the usage of Ti-based alloys in dental implants, enabling the development of extremely strong, long-lasting implants that can endure the strains and pressures of the mouth. The use of these implants has also eliminated the need for removable dentures, which can be uncomfortable and can interfere with eating and speaking.
- **Cardiovascular implants**: Cardiovascular implants are devices that are used to treat various heart and vascular diseases. Heart stents, valves and pacemaker leads are the most typical cardiovascular implants created from titanium-based alloys. These implants offer a secure and efficient treatment for a variety of cardiovascular illnesses since they are made to replicate the shape and operation of the normal heart and blood vessels. Heart valves made from titanium-based alloys are utilized to restore injured or disturbed heart valves. Heart valve dysfunction can be treated safely and effectively with these implants because they are made to replicate the anatomy and operation of the normal heart valve. Blockages in the coronary arteries are treated with stents constructed of titanium-based alloys, helping to reestablish blood flow to the heart. Pacemaker leads made from titanium-based alloys are used to regulate the heartbeat in patients with heart rhythm disorders.
- **Ophthalmic implants:** Ophthalmic implants are devices that are used to treat various eye disorders[26–28]. The most common ophthalmic implants made from titanium-based alloys include intraocular lenses (IOLs) and orbital implants. These implants offer a secure and efficient treatment for a variety of eye conditions since they are made to replicate the anatomy and operation of the native eye. Ti is used in combination with other materials for certain types of IOLs. Titanium is often used for the haptics or supporting arms of the IOL. The haptics is designed to keep the IOL securely in place within the eye's

capsular bag. Titanium is a biocompatible material that is lightweight, strong, and resistant to corrosion, making it suitable for this purpose. The combination of a titanium haptic and a different material for the optic, such as acrylic or silicone, is commonly used in some premium or specialized IOL designs. These implants offer a secure and efficient method of treating cataracts by mimicking the refractive qualities of the natural lens[29]. Orbital implants made from titanium-based alloys are used to replace the natural eye in patients with severe eye injuries or diseases.

## 5. Corrosion of titanium and titanium alloys being used in biomedical implants

Titanium and its alloys are broadly utilized in biomedical implants owing to their excellent biocompatibility, strength, and corrosion resistance. However, corrosion can still occur in certain environments, and it is a significant concern when it comes to the usage of such materials in implants. The corrosion resistance of titanium and its alloys is primarily due to the emergence of a thin, protective oxide film on the surface of the material[30–35]. This oxide layer is stable and non-toxic, and it provides significant corrosion resistance in several environments. However, this layer can be compromised under certain conditions, leading to localized corrosion. One of the primary factors that can lead to the corrosion of Ti and its alloys in biomedical implants is the availability of aggressive/corrosive ions in the body fluids. Chloride ions, which exist in high concentrations in the human body, can result in the breakdown of the oxide layer and cause localized corrosion[36–44]. The presence of other ions, such as fluoride and sulfate, can also contribute to corrosion. Another factor that can contribute to corrosion is the presence of crevices or gaps in the implant. These areas can trap fluids and create a localized environment where corrosion can occur. Additionally, mechanical stresses on the implant, such as those caused by bending or twisting, can also lead to localized corrosion[45–49].

**Table 2** shows the negative impact on biomedical implants due to the corrosion of titanium and titanium alloys.

To minimize the risk of corrosion, various surface treatments can be applied to titanium and its alloys. These treatments can modify the substrate of the material to enhance its corrosion resistance or to enhance the formation and stability of the protective oxide layer. For instance, surface passivation can be utilized to coat the material with a denser, more even oxide coating, improving corrosion resistance. Titanium and its alloys can also benefit from further surface treatments including anodizing, plasma spraying, and ion implantation to increase their corrosion resistance. The choice of the proper alloy composition, in conjunction with surface treatments, can significantly reduce the danger of corrosion. Ti-6Al-4V is one of the more corrosion-resistant titanium alloys, compared to commercially pure titanium. Therefore, the appropriate alloy composition must be selected based on the specific application and the conditions it will be exposed to.

**Table 2.** The negative impact on biomedical implants due to corrosion of titanium and titanium alloys.

| Negative impact | Description |
|---|---|
| Implant failure | Corrosion can lead to implant failure due to loss of structural integrity or mechanical properties of the implant. |
| Release of metallic ions | Corrosion can cause the release of metallic ions into the surrounding tissues, leading to adverse effects such as tissue damage, inflammation, and toxicity. |
| Implant loosening | Corrosion can cause implant loosening, which can lead to pain, discomfort, and instability in the joint or bone where the implant is placed. |
| Infection | Corrosion can create a rough surface on the implant, which can harbor bacteria and increase the risk of infection. |
| Allergic reactions | The release of metallic ions from corroded implants can trigger allergic reactions in some patients, leading to rash, hives, or other symptoms. |

## 6. Surface treatment of titanium and titanium alloys being used in biomedical implants

Titanium is a biocompatible substance that resembles bone in that it has a low modulus of elasticity. This characteristic lessens the impact of strain shielding and lowers the possibility of implant loosening. Additionally, in physiological conditions, titanium and its alloys demonstrate good corrosion resistance, which decreases the discharge of metallic ions and lowers the possibility of unfavorable responses. By varying the alloy composition, titanium and its alloys' mechanical characteristics could be modified, making them appropriate for a variety of biomedical purposes. For instance, dental implants frequently use pure titanium and its alloys, whereas orthopedic implants typically use high-strength titanium alloys like Ti-6Al-4V. Despite the excellent corrosion resistance of Ti and its alloys, the in vivo corrosion of these materials can occur, leading to implant failure. The composition of the implant material, the presence of impurities, and the implant design are only a few examples of the variables that might affect how easily titanium and its alloys corrode in physiological conditions. Pitting corrosion, localized corrosion and crevice corrosion are just a few examples of the different ways that titanium and its alloys can corrode. Metallic ions may be released as a result of the corrosion of titanium and its alloys, which may then result in unfavorable side effects such as inflammation, implant loosening, and bone resorption. Therefore, solutions for reducing corrosion have been developed to enhance the functionality and longevity of biomedical implants made of titanium. The corrosion resilience of titanium and its alloys in biomedical implants could be improved through surface modification techniques including mechanical methods (such as machining, grinding, polishing, blasting), chemical methods (such as chemical treatment, sol-gel, anodization, CVD, biochemical treatment) and physical methods (such as protective coatings, spraying, PVD, ion implantation and glow discharge plasma treatment) as shown in (**Figure 2**)[50].

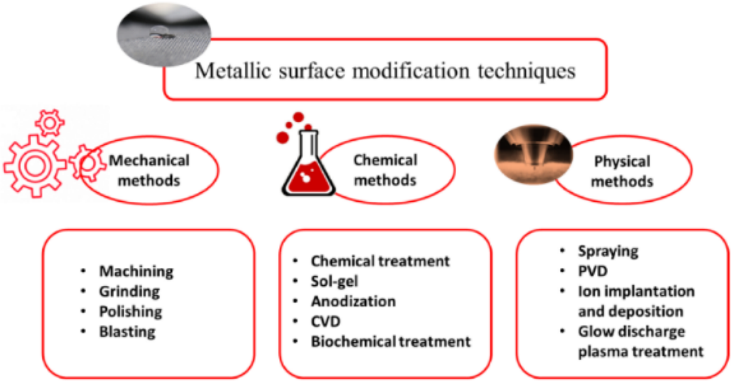

**Figure 2.** Metallic surface modification classification according to the type of technique. Reprinted with permission from the survey of Li et al.[50] (Distributed under CCBY 4.0.).

Mechanical methods involve the alteration of the surface of titanium and its alloys through processes such as machining, grinding, polishing, and blasting. Machining techniques can be employed to create precise shapes and dimensions on the implant surface while grinding and polishing processes refine the surface roughness and remove surface contaminants. Blasting techniques, such as sandblasting or grit blasting, involve the projection of abrasive particles onto the surface to create a controlled roughness or texture. The primary objective of mechanical methods is to optimize the surface topography, which plays a crucial role in promoting implant integration with surrounding tissues and reducing the risk of corrosion initiation. The creation of a suitable surface texture enhances the mechanical interlocking between the implant and bone, promoting osseointegration and improving the long-term stability of the implant. Chemical methods provide a diverse range of surface modification techniques for enhancing the corrosion resistance of titanium and its alloys. Chemical treatment involves the application of acids, alkalis, or other chemicals to clean the surface, remove contaminants, and promote the formation of a protective oxide layer. This oxide layer acts as a barrier against corrosive species, effectively reducing the corrosion rate. Sol-gel processes offer a method to deposit uniform and controlled coatings on the implant surface. A sol-gel solution is applied to the surface, followed by controlled chemical reactions and drying, resulting in the formation of a thin, dense, and uniform coating. Anodization is a widely employed technique that involves the controlled electrochemical oxidation of the titanium surface. This process generates a stable and thick oxide layer, known as a barrier or nanoporous oxide layer, which significantly improves corrosion resistance. Chemical vapor deposition (CVD) allows the deposition of thin films onto the implant surface. By introducing chemical precursors into a high-temperature environment, a chemical reaction occurs, leading to the formation of a dense and adherent coating. Biochemical treatments involve the application of biological agents or coatings to improve biocompatibility and corrosion resistance. This approach utilizes the natural properties of biomolecules or biological materials to enhance the performance of the implant surface.

Physical methods focus on the application of protective coatings or the modification of the surface through various physical processes. Protective coatings can be applied using techniques such as spraying or physical vapor deposition (PVD). In the spraying process, a protective material is applied as a powder or a solution onto the implant surface, forming a coating that acts as a physical barrier against corrosion. PVD techniques involve the deposition of thin films of protective materials through vaporization and condensation processes, resulting in coatings with improved corrosion resistance. Ion implantation is another physical method that modifies the surface by bombarding it with high-energy ions. This process alters the surface composition, creating a more corrosion-resistant layer. Glow discharge plasma treatment involves exposing the implant surface to a low-temperature plasma, which can modify the chemical composition and structure of the surface. This treatment can introduce desirable properties, such as improved corrosion resistance, wettability, or biocompatibility[51–54]. Furthermore, biological treatments involve modifying the surface of the material using biological materials or processes. One biological treatment method commonly used for titanium and its alloys are biomimetic coating. This entails coating the substance with a covering of calcium phosphate, a mineral found in bone, employing a liquid combining phosphate and calcium ions. The benefit of a biomimetic covering is that it could increase the material’s biocompatibility and encourage bone development around the implant. However, it may not provide better corrosion resistance, and the process could be sensitive to variations in the solution composition and processing conditions. Another biological treatment method is electrochemical deposition, which involves using an electrical current to deposit a layer of biologically active material, such as hydroxyapatite, onto the surface of the material. This can provide both improved biocompatibility and corrosion resistance. However, it may not provide a better adhesive linkage between the covering and the substrate, and the process can be time-consuming and require specialized equipment. Due to their capacity to repair and regenerate missing or injured bone tissue, implant materials have attracted a lot of attention in past years for use in bone tissue engineering applications. As implant materials, Ti and its alloys have been widely employed because of their superior mechanical and biocompatibility characteristics. However, implant failure and other complications might result from metal ions leaching from the implant site into the neighboring tissues. To address this issue, Ananth et al.[55] investigated various surface coatings for enhancing the biocompatibility and corrosion resilience of implant materials. One such coating investigated in this study was a bioglass-reinforced yttria-stabilized zirconia (YSZ) composite layer deposited on Ti6Al4V titanium substrates using the electrophoretic deposition (EPD) technique. The EPD technique involves the deposition of charged particulates onto a conductive surface in the presence of an electric field. In this case, YSZ was deposited as the base coating to inhibit metallic ion leaching from the substrate, followed by the deposition of the bioglass zirconia-reinforced composite as the second covering to enhance bone formation and implant fixation. The chemical, physical and biological characteristics of the bilayer system were studied, including its corrosion resistance, mechanical strength under load-bearing conditions, and biocompatibility in osteoblast cell culture. For three hours, the coverings were vacuum annealed at 900 °C to increase their mechanical and adhesive qualities.

The research discovered that the bioglass-reinforced YSZ bilayer system outperformed the monolayer YSZ covering over the Ti6Al4V implant substrate in terms of corrosion resistance and mechanical durability when subjected to load-bearing circumstances. The substantial bioactivity that the bilayer system generated suggests that it has relevance as an implant substrate for bone tissue engineering. The bioglass-reinforced YSZ composite coating was successfully deposited on the Ti6Al4V substrate using the EPD process. This study's findings have important implications for the development of implant materials and bone tissue engineering. The bioglass-reinforced YSZ bilayer system shows promise as a highly effective coating for enhancing the biocompatibility and corrosion resistance of implant components. This, in turn, can lead to improved implant success rates and reduced complications for patients. Additionally, the EPD technology used in this research is a potential technique for covering implant surfaces. It is a reasonably easy and economical method that may provide coatings with good uniformity and adherence. The EPD technique also allows for the deposition of coatings onto complex geometries, making it a versatile method for coating implant materials. In conclusion, the study highlights the potential of the bioglass-reinforced YSZ bilayer system for usage as an implant material and emphasizes the importance of surface coating for enhancing the corrosion resistance and biocompatibility of implant materials. The EPD technique used in this study is an effective and promising method for depositing coatings onto implant surfaces. Additional research is required to examine the bilayer system's long-term impacts in vivo and to improve the EPD method for coating other implant materials.

Similarly, in another study, Witkowska et al.[56] examined the modification of an amorphous carbon covering on NiTi alloy oxidized under glow-discharge conditions, produced via Radio-Frequency Chemical Vapor Deposition (RFCVD). The goal of the study was to suggest a short-term alteration that would alter the morphology and surface tension of the outermost amorphous carbon layer utilizing low-temperature oxygen plasma. The goal was to improve its performance in medical applications, particularly in cardiac applications. The amorphous carbon covering on NiTi alloy has the potential for usage in medical applications owing to its biocompatibility, corrosion resilience, and unique mechanical characteristics. However, the surface characteristics of the coating, including substrate energy, substrate roughness and wettability, can impact its biocompatibility and performance. Therefore, modifying the substrate attributes of the coating can potentially improve its functionality in medical applications.

According to the study, the application of low-temperature plasma changed the chemical constitution of the substrate layer's outer region and marginally increased interface abrasion at the nanoscale. Water and diiodomethane both saw an increase in contact angles of around 20% and 30%, respectively, while the surface free energy fell by about 11%. These results indicate that even brief exposure to low-temperature plasma could alter the surface characteristics of the carbon covering, possibly enhancing its functionality in medical applications. Atomic force microscopy (AFM) was used to assess the short-term oxygen plasma treatment's impact on the coating's surface morphology at the micro- and nanoscales. The measurements of surface topography in **Figure 3** showed that the hybrid process resulted in increased substrate abrasion at the microscale, while the nanoscale surface roughness was equivalent to the initial state of the NiTi alloy. The impact of short-term oxygen plasma treatment was different depending on the scale of measurement. In comparison to specimens that had an a-C: N: H+$TiO_2$ coating before to procedure, the plasma treatment produced specimens having a mildly reduced abrasive topography at the microscale. Surface abrasion was enhanced by the plasma treatment at the nanoscale, but the variations were minimal.

Previous studies[57–60] have demonstrated that some carbon structures, such as fibers and nanotubes, typically exhibit higher abrasion metrics, surface areas, and surface flaws after plasma treatment.

Nevertheless, other research[61–64] indicates that protracted therapy may have a reverse impact and cause flattening of the surface. In the present study, the short-term plasma treatment resulted in an increase in surface roughness at the nanoscale, which is consistent with previous research. The increase in roughness at the nanoscale could potentially improve the coating's cell adhesion properties, which is beneficial for medical applications. The contact angle measurements demonstrated that the plasma treatment enhanced the contact angles for water and diiodomethane, which suggests an increase in surface hydrophobicity. The increase in hydrophobicity is beneficial for reducing the risk of thrombosis and bacterial adhesion, which are common issues in medical applications. However, the decline in surface free energy also signals a drop in surface hydrophilicity, which can impact the biocompatibility of the coating. Overall, the research indicates that RFCVD-produced amorphous carbon coatings on NiTi alloys oxidized under glow-discharge conditions could be modified by short-term oxygen plasma treatment.

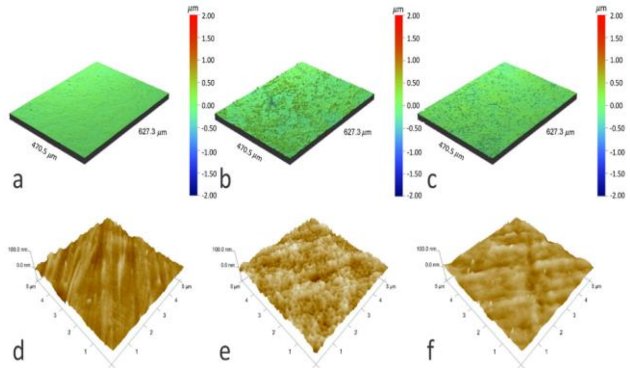

**Figure 3.** Optical profilometer scans (**a–c**) and AFM scans (**d–f**) of NiTi alloy substrate in preliminary phase(**a, d**), following glow-discharge oxidization and RFCVD procedure (**b, e**) and following glow-discharge oxidization and RFCVD procedure accompanied by short-term alteration using oxygen plasma (**c, f**). Reprinted with permission from the survey of Witkowska et al.[56] (Distributed under CCBY 4.0.).

Kim et al.[65] examined the utilization of a sol-gel technique to cover a titanium substrate using hydroxyapatite (HA) and a titania ($TiO_2$) buffer layer. The biocompatibility and osseointegration of titanium have been known to be enhanced by the HA coating for use in medical applications. The $TiO_2$ buffer coating, on the other hand, was included to strengthen the link between the HA stack and the Ti surface and to inhibit the Ti substrate from disintegrating. Sol, colloidal dispersion of solid granules in a liquid, was used during the sol-gel film formation. In this experiment, a solution of ethanol was used to create the sol in this instance by combining titanium tetraisopropoxide, calcium nitrate tetrahydrate, and ammonium hydrogen phosphate. The sol was then applied to the Ti substrate through a dip-coating process. The coated Ti substrate was then dried and heated at various temperatures to produce the desired HA/$TiO_2$ double-layer coating. To examine the effectiveness of the sol-gel covering method, various tests on the coated Ti substrate. The X-ray diffraction (XRD) technique was utilized to determine the phase content of the coating. The findings demonstrated that at 400 °C, the HA coating covered atop the $TiO_2$ exhibited a standard apatite phasing and that the stage strength improved above 450 °C. This shows that the HA coating was effectively produced and that its crystallinity was strong. Additionally, the bonding intensity of the HA/$TiO_2$ double-layer covering on Ti was significantly higher than that of the HA single-layer coating on Ti, reaching a maximum intensity of 55 MPa following heat treatment at 500 °C. The $TiO_2$ layer also increased the Ti substrate's resilience to corrosion. In light of this, it is possible for the HA/$TiO_2$ double-layer covering to offer more adherence and corrosion resilience than a solitary HA covering. Additionally, to evaluate the biological characteristics of the HA/$TiO_2$ double-layer covering, they also performed cell culture experiments using human osteoblast-like cells. These cells are responsible for bone formation and are often used in studies of biomaterials for orthopedic applications. The cells were cultivated on substrates with HA/$TiO_2$ coverings and their viability was evaluated to that of substrates with bare Ti and $TiO_2$ coverings. The outcomes demonstrated that the proliferation of the human osteoblast-like cells cultured over the HA/$TiO_2$ coated surface was comparable to that of the interfaces with a $TiO_2$ solitary coating and bare Ti. This suggests that the double-layer covering of HA/$TiO_2$ had no detrimental impact on cell development. On the HA/$TiO_2$ double coating, though, the alkaline phosphatase action of the cells was exhibited to a greater extent than on the $TiO_2$ solitary covering and bare Ti substrates. The enzyme alkaline phosphatase is crucial for the development of new bone, and the production of this enzyme is a sign of osteoblast differentiation. The HA/$TiO_2$ double-layer covering had an increased expression of alkaline phosphatase than the $TiO_2$ solitary covering and bare Ti substrates, which indicates that it can assist bone development more effectively.

In this study, Trivedi et al.[66] explored the development and characterization of Ti-Si-N nanocomposite covering over a Ti6Al4V substrate using magnetron sputtering at various power levels. The aim was to examine the substrate properties, structure, biocompatibility, and antibacterial characteristics of these coatings to determine their suitability for use as a surface alteration for orthopedic implants. To begin the study, the coatings were developed over the Ti6Al4V surface using magnetron sputtering at various power levels. The deposition was carried out using a Ti-Si-N target, and the power levels used were 20, 40, 60, 100, and 120 W. To investigate the biocompatibility, in vitro studies were conducted utilizing mouse bone marrow mesenchymal stem cells. These cells were chosen because they are commonly used in biocompatibility studies and are an important component of bone tissue. The viability and fluorescence results were obtained to evaluate the cytotoxicity and cell proliferation of the coatings. Furthermore, antibacterial studies were carried out using *Escherichia coli* microorganisms. This was done to examine the antibacterial properties of the coatings and their potential for preventing infections in orthopedic implants. The findings of the analysis revealed that the coverings accumulated at distinct power levels had varying substrate properties and structures. The coating accumulated at 120 W had a finer surface contrasted to the coverings that emerged at various power levels. It also showed optimal contact angle and good antibacterial properties. These findings suggest that the coating developed at 120 W is more suitable for orthopedic implants than the other coatings. In terms of biocompatibility, the viability and fluorescence results of the 120 W specimen affirmed its excellent biocompatibility contrasted to the coverings accumulated at 20, 40, 60 and 100 W power levels. This indicates that the 120 W coating is less toxic and more suitable for cell growth and proliferation, making it a suitable alternative for employment in orthopedic implants. In this experiment, osteogenic differentiation was also conducted to examine gene expressions. The findings showed that the coverings developed at different power levels had varying effects on the gene expressions of the cells. The 120 W coating was found to be more effective in promoting the expression of genes associated with bone formation, indicating its potential for use in orthopedic implants. With the help of this study, orthopedic implants will be developed that are more biocompatible and antimicrobial, which will ultimately enhance patient outcomes.

Yu et al.[67] research aimed to evaluate the effect of post-spray treatment on the in vitro and microstructure functions of plasma-sprayed HA coverings on Ti substrates. The study investigates the potential of spark plasma sintering (SPS) to increase the bioactivity of the plasma-sprayed covering by modifying its microstructure and composition. In this study, the researchers used plasma spraying to deposit HA coatings onto Ti substrates, which were then treated by SPS at different temperatures (500 °C, 600 °C, and 700 °C) and for different durations (5 and 30 minutes). The coverings were characterized using SEM and XRD to examine their substrate morphology, crystallinity, and phase composition pre and post in vitro incubation. The findings demonstrated that plasma-sprayed HA coatings subjected to a 5-minute SPS treatment displayed an enhanced fraction of beta-tricalcium phosphate ($\beta$-TCP) step with a preference for alignment in the (2 1 4) plane, and the material of $\beta$-TCP step enhanced with SPS temperature, reaching 700 °C. The HA concentration in the plasma spray coating was also improved by SPS treatment at 700 °C for 30 minutes. In vitro incubation of the HA coverings exposed in SPS for 5 minutes exhibited quick alterations in surface morphology, demonstrating that the SPS treatment increased surface activity. The coating subjected to SPS treatment at 700 °C for 5 minutes included the thickest apatite coating.

The SEM analysis revealed that the SPS-treated covering had a uniform and dense microstructure with good interfacial bonding to the Ti substrate. The SPS treatment also resulted in a more homogeneous distribution of particles and a reduction in porosity in the HA coatings. The XRD examination showed that the HA coatings treated by SPS had a higher degree of crystallinity and a more ordered crystal structure than the untreated coatings. Moreover, the SPS-treated coatings exhibited a higher content of HA and $\beta$-TCP phases and a minimal content of calcium oxide (CaO) phase, which is known to be less stable and less biocompatible than the HA and $\beta$-TCP phases. The in vitro incubation findings revealed that the SPS treatment enhanced the bioactivity of the HA coatings by promoting the emergence of apatite on their surfaces. The apatite layer thickened with SPS temperature and time, reaching its maximum thickness in the coating that was subjected to SPS at 700 °C for 5 minutes. The researchers hypothesized that the enhanced surface abrasion and crystallographic orientation of the $\beta$-TCP phase, which may encourage the nucleation and development of apatite on the covering surface, might be responsible for the enhanced bioactivity of the SPS-treated coatings. Using MC3T3-E1 osteoblastic cells, the study also assessed the cytocompatibility of the SPS-treated HA coatings. According to the results of the cell survival and proliferation tests, the SPS-treated coverings had no cytotoxic activity on the cells, and their rate of cell multiplication was comparable to that of the untreated coatings. The study also discovered that after the SPS treatment, the HA coatings' adhesive strength improved. The improvement in the interfacial connection among the HA covering and the Ti substrate was the reason why the HA coating treated at 700 °C for 30 minutes displayed the maximum adhesion strength. The SPS-treated HA coatings also showed improved corrosion resistance compared to the untreated coatings, which is a crucial quality of implant materials.

The study also investigated the in vitro functionality of the SPS-treated HA coatings. The findings showed that the substrate activity of the coatings was enhanced by the SPS treatment, leading to improved cell proliferation and differentiation. The study used MC3T3-E1 cells to examine cell viability, proliferation, and differentiation on the coatings. The cells were implanted onto the coatings, and they were then cultivated for up to 14 days. The results showed that the SPS-treated coatings supported higher cell proliferation and differentiation than the untreated coatings. The study also suggests that the SPS technique can be a promising approach for developing new implant materials with tailored surface properties for enhanced biological interactions. However, additional research is necessary to examine the long-term functionality of SPS-treated HA coatings in vivo and to assess their clinical viability for applications in bone regeneration and repair.

In the field of medical implants, biocompatibility is a viable point in the development and success of implantable devices. Titanium alloys are commonly utilized owing to their excellent biocompatibility, corrosion resistance, and mechanical properties. To assess the physiological stability and surface functionalization of the Ti-15Zr-4Nb alloy, a potential material for medical implants, Okazaki and Katsuda[48] carried out a study. Under rapid extraction circumstances, the authors tested three Ti-Zr alloys for biological safety. They evaluated the alloy's capacity to generate a hydroxyapatite coating, a sign of biocompatibility, using a simulated bodily fluid (SBF). According to the study, Ti-Zr alloys performed well in SBF tests that measured hydroxyapatite formation under both normal and accelerated extraction settings with no negative consequences. This indicated the Ti-Zr alloys' excellent biocompatibility and the potential for use in medical implants. To examine the long-term implantation effects of various metals and alloys, the authors performed a histopathological analysis in rats. The study found that bone formation occurred around Al, Zr, Nb, and Ni-Ti implants, whereas no bone was developed around bare V and Ni implants. This demonstrated the importance of appropriate material selection for medical implants to ensure good bone formation and biocompatibility. The study assessed the biocompatibility of the Ti-15Zr-4Nb alloy and used rabbits to examine how dental implant geometry affected morphometrical characteristics. The scientists evaluated the rate of bone growth on a plain surface to that on the threaded area of the Ti-15Zr-4Nb-4Ta dental implant (**Figure 4**). According to the study, bone growth on the threaded area occurred at a rate that was comparable to that of a flat surface. From this, it can be inferred that the Ti-15Zr-4Nb-4Ta dental implant has good biocompatibility and application possibilities. The study also looked at the maximum pullout characteristics of grit-blasted Ti-Zr alloys following implantation in rabbits. The maximal pullout loads of the grit- and shot-blasted Ti-Zr alloys grew linearly with the implantation duration, and the pullout load of the grit-blasted Ti-Zr alloy rods was greater than that of the shot-blasted ones. This demonstrated the outstanding mechanical qualities and long-term implantation resistance of the Ti-15Zr-4Nb alloy. The investigation also looked into the surface treatment of the Ti-15Zr-4Nb alloy using $Al_2O_3$ particulates. The surface abrasion and area ratio of leftover particles were evaluated to those of the grit-blasted Alloclassic stem surface by the researchers. The research reveals that the surface abrasion and area proportion of the Ti-15Zr-4Nb alloy amended using $Al_2O_3$ particles were identical to those of the Alloclassic stem surface, suggesting its prospective usage for prosthetic hip joint stems.

The Villanueva-Goldner staining optical micrographs in (**Figure 5**) depict the formation of the new bone surrounding the Ti-15Zr-4Nb implant. The threaded section exhibited a significant amount of new bone formation. Overall, the study suggests that Ti-15Zr-4Nb alloy is a biocompatible material that can be utilized for medical implants with appropriate surface modifications.

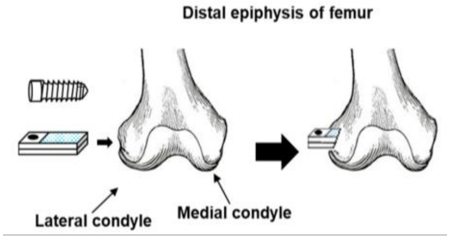

**Figure 4.** Representation in schematic form of rabbits' femurs after implantation. Reprinted with permission from the survey of Okazaki and Katsuda[48]. (Distributed under CCBY 4.0.)

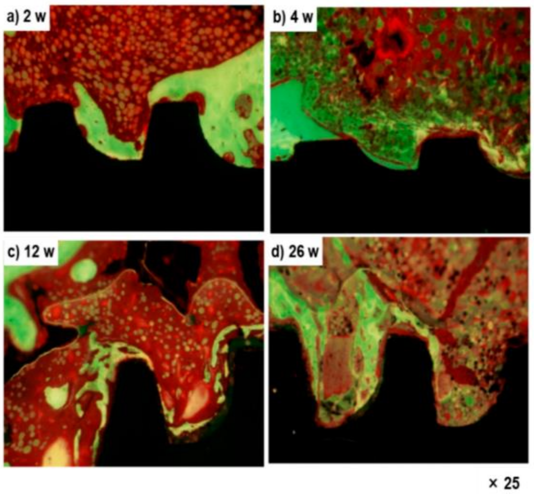

**Figure 5.** Optical micrographs of the new bone that has grown around a Ti-15-4-4 dental implant used in rabbits' femurs at **(a)** two, **(b)** four, **(c)** twelve, and **(d)** twenty-six weeks. Reprinted with permission from the survey of Okazaki and Katsuda[48]. (Distributed under CCBY 4.0.)

Owing to its improved mechanical qualities and low cytotoxicity, titanium and its alloys have gained popularity in the domain of orthopedic and dental implants. Pure titanium, on the other hand, lacks bioactivity and, as a consequence, does not promote bone formation, leading to poor osseointegration. Surface modification techniques have thus been developed to enhance the bioactivity of titanium implants in order to get around this restriction. One such method involves applying HA and fluor-hydroxyapatite (FHA) coatings utilizing the sol-gel method on a Ti substrate. In a study conducted by Kim et al.[68], the effect of $F^-$ incorporation into the apatite structure on the properties and behavior of the coatings was investigated. The study aimed to fabricate uniform and dense HA and FHA coatings on a Ti substrate using a sol-gel technique and evaluate the characteristics of the coatings, including their solubility, thickness, and cellular behavior. The results of the study revealed that both HA and FHA coatings were obtained with a uniform and dense structure, and the thickness of the coatings was approximately 5 μm. The solubility of the coatings was found to decrease with increasing $F^-$ incorporation, indicating that the solubility of the coatings can be tailored by functional gradient coating of HA and FHA. This is an essential finding as the dissolution rate of coatings plays a crucial role in bone formation and regeneration. A coating that dissolves too quickly can lead to an insufficient support structure for the growing bone tissue, while a coating that dissolves too slowly may impede bone growth, leading to poor osseointegration. In addition to the solubility of the coatings, the study also evaluated the cellular behavior of the coatings. While the alkaline phosphatase (ALP) function of the cells on all of the HA and FHA-coated specimens exhibited significantly greater expression rates relative to bare titanium, the findings demonstrated that the cell proliferation rate on the protective coating dropped marginally with growing $F^-$ incorporation. This implies that the sol-gel coating process enhanced cell function activity on the substrate.

The incorporation of $F^-$ into the apatite structure enhanced the mechanical characteristics of the coating. Although, the study did not evaluate the mechanical characteristics of the coverings. Therefore, future studies may investigate the impact of $F^-$ incorporation over the mechanical characteristics of the coverings. Overall, the study conducted by Kim et al.[68] provides insight into the use of sol-gel techniques for the deposition of HA and FHA coatings on a Ti substrate. The findings suggest that the sol-gel coating treatment could enhance the bioactivity of titanium implants, thereby enhancing bone formation and regeneration. This study serves as a basis for further research in the field of surface modification techniques for titanium implants.

The field of orthopedic surgery faces the challenge of bone defects, and three-dimensional scaffolds have developed as a promising solution for bone replacement. Among the potential materials, titanium alloys are favored owing to their low cytotoxicity and excellent mechanical characteristics. However, metal alloys have poor bioactivity, which can limit their efficacy in bone regeneration. One solution is to cover bioactive compounds over the substrate of the scaffold to enhance its bioactivity. In this context, a recent study conducted by Tsai et al.[23] aimed to develop and evaluate a modified titanium scaffold with improved bioactivity and mechanical properties for bone tissue engineering. The study focused on the fabrication of magnesium-calcium silicate (Mg-CS) and chitosan (CH) compounds onto a Ti-6Al-4V scaffold and assessing their physicochemical properties, mechanical testing, and cell behavior in vitro. In order to encourage bone-forming osteoblastic cells, the study sought to assess how the scaffold's surface composition interacted with stem cells. (**Figure 6**) depicts the results of the study's observation of cellular adhesion on the Mg-CS/CH-coated Ti-6Al-4V scaffolds following 6 and 24 hours of culture. The Mg–CS concentrations used in this study were 0%, 0.2%, and 0.5% (referred to as CS0, CS20, and CS50, respectively). The results revealed that cells cultured on the CS0 surface remained spherical with poor spreading behavior, while cells on CS50 exhibited higher levels of spreading into a polygonal morphology after 6 hours of seeding. On the Mg-CS/CH-coated Ti-6Al-4V scaffold, a convergence of the cell monolayer developed after 24 hours. Furthermore, the study found that CS50 released more Si ions, which stimulated Wharton's Jelly mesenchymal stem cells (WJMSCs) to secrete Col I and FN, promoting cell adhesion in the short term. Adhesion receptors were also found to form anchors and activate signaling pathways, regulating proliferation and differentiation processes. Even though the observed variation in cell adhesion was only temporary, it was believed to have an impact on how the ensuing osteogenesis differentiation pathway's proteins were expressed. It was discovered that the altered scaffold improved cellular behavior and matched the mechanical characteristics of genuine bone, enhancing osteogenesis and mineralization downstream.

The study's findings point to the modified scaffold as a potentially effective option for future bone tissue engineering scaffolds. The redesigned scaffold improved bone regeneration and ingrowth at critical-size bone lesions in rabbits, according to testing done in vivo. As a result, it seems possible to apply the suggested alteration as a potential bone tissue engineering scaffolds improvement. The work indicates the possibility of enhancing the bioactivity of titanium scaffolds for bone tissue creation by combining magnesium-calcium silicate and chitosan molecules. The research highlights the importance of designing scaffolds with the appropriate physicochemical properties to promote cellular behavior, leading to enhanced osteogenesis and mineralization downstream. The usage of *in vitro* and *in vivo* tests is also essential for evaluating the efficacy of modified scaffolds in bone tissue engineering. However, several challenges remain, such as the stability and durability of the modified scaffold over the long term and the compatibility of the modified scaffold with the host's immune system. Future research should also focus on identifying the optimal concentration of bioactive compounds that can enhance the scaffold's bioactivity without compromising its mechanical characteristics.

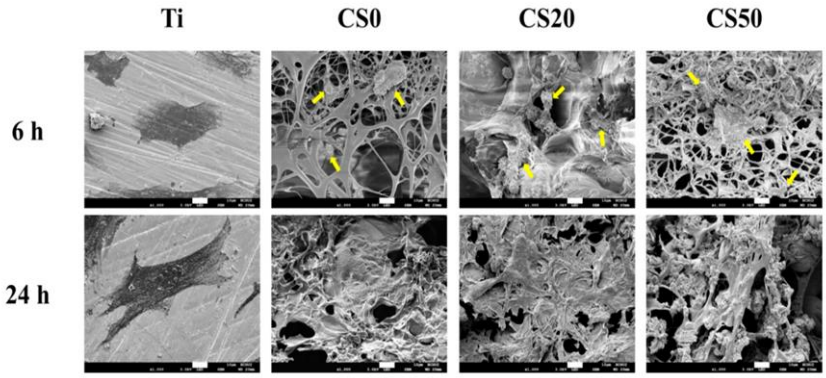

**Figure 6.** SEM images of WJMSCs attached over the Mg–CS/CH-covering Ti–6Al–4V scaffold surface following 6 h and 24 h. The yellow arrow refers to WJMSC. The scale bar is 10 μm. Reprinted with permission from the survey of Tsai et al.[23]. (Distributed under CCBY 4.0.)

## 7. Challenges and future outlooks

Despite the progress made in the development of substrate treatment techniques for titanium and its alloys used in biomedical implants, several challenges still need to be addressed to improve their performance. One of the major challenges is the accumulation of biocorrosion products that can lead to adverse biological responses. Surface solutions refer to various techniques or treatments applied to the surface of biomedical implants to improve their performance and reduce the risk of biocorrosion. While surface solutions can enhance the corrosion resistance of implants, it's important to note that they may not eliminate the risk of biocorrosion. However, they can significantly reduce the likelihood and severity of corrosion, thereby improving the lifespan and functionality of the implants. Therefore, more investigation is required to comprehend the mechanics underlying biocorrosion and create novel surface coatings that can lessen its consequences. The requirement for long-term strength and durability of the surface treatment presents another difficulty. The surface treatment of biomedical implants must be able to endure the hostile physiological environment throughout the duration of the implant because they are expected to function in the body for a long time. Long-term investigations are therefore required to assess the stability and toughness of surface treatments over time. In addition, the cost and feasibility of surface treatment methods remain a challenge. Some of the surface treatment methods can be expensive and require specialized equipment and expertise, which may limit their widespread adoption. Therefore, there is a need for the development of cost-effective and scalable surface treatment methods that can be easily implemented in clinical settings. The future outlook for surface treatment methods for titanium and its alloys utilized in biomedical implants is promising. Researchers are exploring new surface treatment methods, such as nanotechnology-based coatings and surface texturing, that can provide better biocompatibility, corrosion resistance, and tissue integration. Additionally, an interesting area of research that holds the ability to completely redefine the realm of biomedical implants is the development of smart surfaces that can react to changes in the physiological context, including pH and temperature. Overall, the difficulties and prospects of surface treatment techniques for titanium and its alloys used in biomedical implants emphasize the need for more investigation and advancement in this area. The development of new and improved surface treatment methods can significantly improve the performance and longevity of biomedical implants, leading to better patient outcomes and quality of life.

## 8. Conclusion

Due to its superior mechanical qualities, biocompatibility, and resistance to corrosion, titanium and its alloys have become the ideal material for biomedical implants. However, corrosion, wear, and inadequate tissue integration may have an impact on their long-term functionality in the physiological context. Therefore, techniques for improving the surface characteristics of titanium and related alloys have been devised in order to increase their biocompatibility, corrosion resistance, and tissue integration. In this article, we have discussed several chemical, physical and biological surface treatment techniques to enhance the corrosion resistance and biocompatibility of Ti-based biomedical implants. It could be concluded that the physical methods such as plasma spraying and laser ablation create rough surface textures that improve implant integration, while chemical methods such as anodization and electrochemical deposition create oxide layers or coatings that enhance corrosion resistance and biocompatibility. In order to encourage tissue fusion and healing, biological surface treatments like biomimetic coatings try to replicate the natural arrangement and function of tissues.

Despite the progress made in surface treatment methods, several challenges remain. Biocorrosion and the stability and durability of surface treatments over the long term are areas of concern that require further research. Additionally, the cost and feasibility of surface treatment methods need to be addressed to ensure widespread adoption in clinical settings. Looking ahead, nanotechnology-based coatings, surface texturing, and smart surfaces are promising areas of research that can lead to improved surface treatments for Ti and its alloys utilized in biomedical implants. Thus, continued research and innovation in surface treatment methods are essential to enhance the performance and longevity of biomedical implants and enhance patient outcomes and quality of life.

## Conflict of interest

The authors declare no conflict of interest.

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