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Osseointegration and biocompatibility of titanium implants

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Abstract

Orthopedic implants are a growing field of modern medicine at which titanium is at the forefront. Titanium offers favorable surface modification, phase control, and mechanical properties. A challenge of orthopedic implants is the osseointegration and biocompatibility of the implant. The following pages review recent advancements in improving the osseointegration and biocompatibility of titanium implants with bone.

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1. Introduction

A biomaterial is any substance (synthetic or natural) that is used for any period of time, as a whole or as a part of the system, that is able to treat/augment any tissue, organ, or body function [1]. Biomaterials are selected to replace, connect, or stimulate growth based on biocompatibility, biodegradability (toxicity), and osseointegration. Biocompatibility is the mutually accepted co- existence of a biomaterial and natural tissues which undergo growth and sustainability [2]. Titanium and its alloys have been researched extensively as a material suitable for orthopedic implants. Titanium has lesser to benign toxicity, chemical inertness, and mechanical strength similar to bone; however, there are still some faults of the material [6]. As a result, there has been much research investigating specific phases, chemical stability, and surface modifications of titanium to improve osseointegration of implants.

Osseointegration is the functional and mechanical connection of living, natural bone to the load bearing implant, titanium in this case [6]. This property is critical for the stability of the implant and must be a property of any material considered for implants. Titanium and titanium- based alloys are unique in their properties of osseointegration. Properties are observed at the interface of the tissue and the implant. It is also important to note that osseointegration is a time dependent healing process [6]. The interface of tissue and implant raises a series of questions in addition to osseointegration, like the concern of stress shielding (reduces the density of surrounding bone when the implant has higher load bearing capacity) [7]. This is a result of Wolff's Law; bones will adjust and adapt based on the applied load to the bone in a healthy person or animal.

Biocompatibility of titanium implants will be investigated for the purpose of aiding corrupted bone including mechanical and surface chemistry properties.

2. Composition and Phase

Metals, in general, are not specifically biocompatible in their pure form especially without coating [8]. This is because the metal ions have a net positive charge. Cell membranes and DNA in the body have a net negative charge. This causes the disassociated metal ions from the implant to become attracted to and often form a bond with DNA and cell membranes, making them inactive. The inhibition of proteins like DNA causes injury to organs in the respiratory, nervous, and reproductive systems [8]. Metals alloys are less susceptible to the disassociation of positive metal ions. For example, the covalent bonds from the carbon atoms, in steel alloys, limit the disassociation of ions [4]. For this reason, carbon fiber composites are becoming more common as implants.

Similarly, different phases and alloys of titanium are being investigated which have more favorable biocompatibility and promising mechanical properties. The β-phase of titanium significantly increases the compatibility and functionality with the human body. This phase has favorable chemical and physical properties. The chemical environment of an implant, before integration, tends to be salty and maintain a pH (blood and interstitial fluid) of 7.35 to 7.45 [11]. Once the implant is placed in the patient, the pH drops to ~5.2 in the hard tissue; recovery to a pH of ~7.4 takes up to two weeks [11]. This general rule in pH change presents a high chance of degradation of material and corrosion at the surface. β-phase titanium (and alloys) have shown the best response to this environment.

Ti-35Nb-7Zr-5Ta, with β-phase titanium, is an example of an alloy with a porous coating system and favorable properties. This alloy shows favorable adhesion to substrate due to its composition and porosity. The porosity allows for cells to migrate and adhere to the implant directly (through the voids). Bone is constantly changing due to changes in environment, including the scaffold nature. The porous nature of bone tissue allows for cell migration and proliferation of osteoblasts and mesenchymal cells [12]. The porosity of Ti-35Nb-7Zr-5Ta can mimic this behavior contributing largely to its biocompatibility. The alloys porosity contributes to the mechanical properties of the material-- interlocking and webbing between hard tissue that also mimics natural bone [12]. The minimum pore size to regenerate mineralized bone is ~100 micrometers and can be achieved with different processing techniques.

In addition to the lesser cytotoxicity in the β-phase titanium, the mechanical properties also prove to be suitable for implants. The Youngs modulus and other properties of this phase are closer to human bone. For a material to have good biocompatibility, the mechanical properties cannot be vastly different than what the implant is replacing/aiding [9]. If the mechanical properties of the implant are much greater than the bone, there will be a large stress accumulation on the interface of the implant and bone and lead to fracture, failure, or stress shielding. The β-phase of titanium has a modulus of 55-60 GPa and human bones typically fall between 25-30 GPa. This is an entire order of magnitude closer to bone than titanium which exceeds 100 GPa. This advancement has several benefits towards the goal of biocompatibility and osseointegration [9]. The mechanical properties of β-phase titanium offer better biocompatibility than conventional implants like stainless steel and cobalt-chromium alloys [12].

Titanium alloys like Ti-6Al-4V are biocompatible with oral and dental tissues, in the short term. However, there is still risk in Al and V atoms posing a cytotoxicity threat to the patient. A common method to overcome this threat is to coat the titanium alloys in with a ceramic, polymer, or calcium phosphate layer. Titanium and its alloys by itself have very favorable low corrosive properties. This property lessens the threat of disassociating positive ions, however, coatings can reduce this risk even more.

3. Surface Modification

The surface properties of implants dominate the process of osseointegration, aside from internal mechanical properties. A successful implant needs agreement between the collagen/fibroblastic matrix and implant [8]. Additionally, the strength of the implant should increase dramatically within twelve weeks of surgery. The mechanical surface properties dictate the potential stress distribution and corrosion, both properties are accounted for with titanium. Wear and surface roughness also play roles in osseointegration. These topographic properties are also good for titanium implants. High degrees of surface roughness and differences in surface chemistry discourage osseointegration [8]. These factors also influence the surface energy of the material [8]. Generally, smaller the grain size of material the greater the surface energy of the material. This is more favorable for cell adhesion and therefore osseointegration. This is supported by the mimicking of bone surfaces. A nanostructured implant surface has shown to increase the degree of osseointegration and shorten the time, with dimensions between 1-100 nm [6]. These surfaces mimic the surface of naturally occurring bone and tissue.

There is still a concern in the long run of biocompatibility of any implant metal, including titanium. The low corrosion properties of titanium already put it ahead of several other alternatives [10]. The main concern of Ti-6Al-4V is long term degradation of the material of Al and V ions having potential health consequences. Some of these health consequences can be avoided by altering the alloy by adding up to 6 wt. % of copper, however, this will enhance the mechanical properties of the material and change the desired/targeted moduli of the implant.

4. Conclusions

New advancements in research have investigated the biocompatibility of titanium alloys due to favorable phase control and surface modification. A Ti-35Nb-7Zr-5Ta, with b-phase titanium with accurate surface porosity and chemistry seems to be the best answer to the titanium problem. This phase and alloy have the lowest value Youngs modulus and the most coherent surface chemistry (unaltered). Ti-6Al-4V offers similar mechanical properties, however, the long- term threat of toxicity remains a risk to patients' health. A variety of coatings could be utilized to minimize this threat; however, additional materials used in implants all bring consequences. A polymer or ceramic coating raises issues of adhesion to the implant and natural tissue. There are remaining research areas in improving the osseointegration of titanium-based alloys for orthopedic implants.

Conflict of Interest

No conflict of interest to be declared.

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