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Recent Advances in Manufacturing and Surface Modification of Titanium Orthopaedic Applications

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Abstract

Implant failure is a common problem in orthopedic applications, which causes pain and stress for patients, prolonged antibiotic therapy, increased time and cost of hospitalization, and revision surgery. Selecting the optimum porous structure, manufacturing process and surface modification approach is crucial to reduce the rate of implant failure. The design of porous structures in orthopedic implants plays an important role in vascularization, diffusion of nutrients, and in the relationship between implants and osteoblasts. Common techniques for porous design are computer aided design (CAD), image based design, implicit surface design, and topology optimization. Metal-based additive manufacturing methods such as electron beam melting (EBM), selective laser melting (SLM) and selective laser sintering (SLS) have been extensively developed for fabrication of porous structures on Titanium. Several chemical surface modification methods are used, such as acid etching, anodization, and coatings, to improve mechanical properties, biocompatibility, increase surface roughness, and to promote osseointegration and bone regrowth. This paper reviews the design and manufacturing of porous implant material via additive manufacturing techniques, as well as recent advances in surface modification, to achieve biocompatible surfaces. The outcome of this research will provide an effective strategy for manufacturing, and surface modification of titanium orthopedic implants.

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Keywords: Porous structure, Additive manufacturing, Surface modification, biocompatibility

1. Introduction

Commercially pure (CP) Titanium and the Ti-6Al-4V alloys, are commonly used for orthopedic implants (Niinomi, 1998; Niinomi, Narushima, & Nakai, 2015) including hip joint implants, stents, screws, heart valves, bone plates and thigh bone implant, due to the excellent mechanical (tensile strength, light weight, and low density), physical and biological (excellent corrosion resistance, and enhanced biocompatibility) (Lütjering & Williams, 2007). Titanium implants possess greater mechanical properties and stiffness compared to natural bone, which results in stress shielding, leading to implant resorption, and failure in the body. In order to solve this problem, the Titanium implant should be fabricated with a porous structure (Wang et al., 2016), facilitating vascularization (Kumar et al., 2016), enhancing osseointegration, bone growth, transport of

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nutrients, metabolic waste (Wang et al., 2016), eliminating stress shielding, and increases biocompatibility and implant lifetime (Yan, Hao, Hussein, & Young, 2015). The design of porous structures are based on computer aided design (CAD) (Wettergreen et al., 2005), magnetic resonance imaging (MRI)/computer tomography (CT) images (Bucklen, Wettergreen, Yuksel, & Liebschner, 2008), implicit surface design (Giannitelli, Accoto, Trombetta, & Rainer, 2014), and topology optimization (Challis, Guest, Grotowski, & Roberts, 2012).

Although traditional manufacturing methods of porous Titanium, such as powder metallurgy, plasma spray, and electron beam evaporation, are controlled by changing process variables, obtaining the porous structure is not feasible by traditional methods (Banhart, 2001; Ryan, Pandit, & Apatsidis, 2006). Hence, in the last decade, additive manufacturing techniques, such as EBM, SLM, and SLS, have been developed to fabricate porous structures on Titanium (Kumar et al., 2016; Lin et al., 2016).

Once the porous structure has been imparted, surface modification techniques are used to enhance biocompatibility, increase osseointegration, biological performance and improve the interaction between the implant and bone. Methods such as acid etching, anodization, and various organic and inorganic coating methods are commonly used. These are used to increase surface roughness and wettability, increase the interaction between the implant and body tissue, and improve mechanical properties. The methods discussed here are primarily chemical, however physical and mechanical methods of surface modification are also used to improve mechanical and biological performances.

In this paper, recent advances in the design, and manufacturing processes of porous structures in orthopedic implants will be introduced. Following this, the latest methods of surface modification, will be discussed. Finally, future research directions will be presented. Fig1 illustrates the process of design, manufacture and surface modification of Titanium implants.

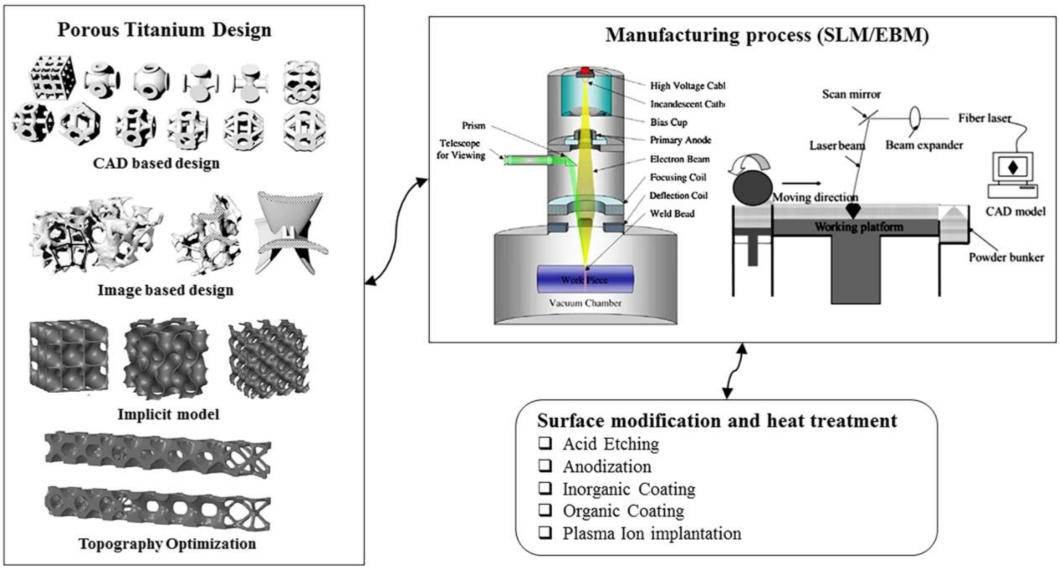

Fig 1. The process of Design, Manufacturing and surface modification of Titanium Implants (Bucklen et al., 2008; Chang, 2015; Giannitelli et al., 2014; Radman, Huang, & Xie, 2013; Wang et al., 2016; Wettergreen et al., 2005; Zhang, Wei, Cheng, Li, & Shi, 2014)

2. The porous structure of Titanium implants

Titanium implants used in the human body require similar characteristics to prevent implant failure, and ensure bone fixation. Therefore, an efficient approach to unify the mechanical properties of bone and implants is through manufacturing porous structures in Titanium implants (Kumar et al., 2016). In order to design porous Titanium implants, important outputs including biological features (permeability, flow perfusion properties), and mechanical characteristics (stiffness and strength) should be taken into consideration. The porous structure is fabricated based on various design methods including CAD, integrated by Finite Element Analysis (FEM), image based, implicit designs, and topology optimization. Square holes, cross beams, truncated octahedrons, hollow spheres, curved connectors, hollow corners, fire hydrants, 4 spheres, and rhombicuboctahedrom (RCO), are the most common structures designed using CAD (Wettergreen et al., 2005). Image based design (based on MRI and CT imagining) is able to design porous structures from real bone (Murr et al., 2010). One of the principle challenges in designing the structure is to simultaneously optimize biological functionality, permeability, and stiffness. Topology optimization, based on mathematical methods, and multi objective optimization (Shahali, Yazdi, Mohammadi, & Iimanian, 2012), are an efficient tools which allow optimum biocompatibility and mechanical functionality to be reached, using trial and error approaches (Bendsoe & Sigmund, 2013). Furthermore, bidirectional evolutionary structural optimization (BESO) has the ability to successfully optimize the structure, based on maximum bulk or shear modulus, according to desired constraints (X. Huang, Radman, & Xie, 2011).

3. Additive manufacturing of porous structures

Additive manufacturing, as known as rapid prototyping and 3D printing, can manufacture and fabricate different structures, based on a solid model from CAD, and involves building the model layer by layer (Chang, 2015; Wohlers & Gornet, 2011). Additive manufacturing can be classified as binder jetting, direct energy deposition, material extrusion, sheet lamination and vat photo polymerization. New techniques are able to manufacture metals, based on direct energy deposition and powdered base systems. EBM, SLM and SLS are used to manufacture models using common metals, such as Stainless Steel, and Titanium from powder (Chang, 2015). The powder is melted using electrons or lasers, and the layer is solidified. The process is then repeated for subsequent layers, forming the model (Chang, 2015). In this section, the effect of different structures and manufacturing process variables on the biocompatibility of Titanium implants is presented.

3.1 Electron beam melting (EBM)

During the EBM process, electrons are boiled off by a heated tungsten filament. The speed of the stream of electrons is low, therefore two magnetic sources are applied, in order to focus and arrange the speed of the electrons. The first magnetic source concentrates the beam to the ideal diameter (Chang, 2015). The second source bounces off the concentrated beam, to the target on the powder bed. Kinetic energy is quickly changed into thermal energy, by contact between the elections and metal powder. Due to the high energy in EBM, this process is an efficient method for manufacturing high density and strength models, for orthopaedic applications (Bandyopadhyay & Bose, 2015; Chang, 2015). EBM is also advantageous in fabricating porous Titanium to assist in bone regrowth and shear stress, in comparison to traditional processes like plasma sprayed Titanium (Bertollo, Da Assuncao, Hancock, Lau, & Walsh, 2012).

3.1.1. Effect of EBM fabricated porous structures and size on bone ingrowth

Geometry and size of porous structures have an impact on bone bonding and bone regrowth. . It has been found that porous structures produced via EBM resulted in higher bioactivity and mechanical stability in bone fixation, in comparison to CP Titanium, and Ti-6Al-4V. This shows the impact that EMB has on bone bonding and regrowth. This has potential advantages for weight bearing orthopaedic implants, such as acetabular cups (Hara et al., 2016). Similarly it is shown that EBM samples with a surface roughness of less than 0.5 μm produced the ideal biocompatibility, in comparison to solid Ti-6Al-4V (Springer, Harrysson, Marcellin-Little, & Bernacki, 2014).

3.1.2. Effect of EBM parameters and porous structure on mechanical properties

Fatigue life, wear and stress shielding are the most common reasons for Titanium implant failure (Hosseini, 2012). It was shown that by optimizing two important parameters, buckling and bending deformation, high fatigue strengths are viable through EBM. The growth of the fatigue crack in the struts contributed more to the fatigue damage of the meshes, while increasing the bending component. The compressive fatigue strength increased with increased buckling deformation on the struts of the structure (Zhao et al., 2016). Moreover, increasing surface roughness and decreasing truss thickness, as well as the density of the porous structure, leads to a decline in fatigue (Jamshidinia, Wang, Tong, Ajlouni, & Kovacevic, 2015).
Higher surface hardness (8 Gpa) and good wear resistance is achieved on gum alloys via EBM, due to high cooling rates and precipitation of the α'' phase. The re-melting depth increases with increasing line energy density, and scanning speed. Shallow melting areas on the surface are attainable at low line energy densities and scanning speeds of 3m/s (Chen et al., 2015).
Mechanical properties and microstructures of porous β-type Titanium have been investigated by EBM and SLM. Due to the high temperature and slow cooling rate in EMB, the structure includes $\alpha+\beta$ phases increasing the elastic modulus to 1.34 Gpa. The lower temperatures and high cooling rates in the SLM process produces β phases, decreasing the elastic modulus to 0.095 Gpa. As a result of higher initial temperature and energy density in EBM, the melt pool width is 128 μm, compared to 146 μm in SLM. The spot size generated by SLM is 5 times smaller than EBM, leading to a deep hole generated by radiation reflection. Spherical shape defects generated during EBM occur due to continuous scanning and conical defects have been caused by interrupted conical melt pools. Lower pulling back pressure, and high surface tension in deep holes cause 10 times more defects in SLM than EBM (Y. J. Liu et al., 2016). In fact, microstructure differences in EBM are affected by dwell time, whereas mechanical behaviour is not affected by microstructure (Galarraga, Lados, Dehoff, Kirka, & Nandwana, 2016).

3.2 Selective laser melting (SLM)

Focused laser beams have been applied in SLM processes to bind powders together, layer by layer, to fabricate high complexity and high density parts. The SLM technique possesses a lower laser point size (<100 μm), and focused energy, which enhances accuracy. One drawback is the poor surface quality that is produced (Brinksmeier, Jawahir, Meyer, Yasa, & Kruth, 2011). SLM, integrated with CT data, and CAD/CAM software, has the ability to manufacture and reconstruct complex implants with porous structures, mimicking human bone (Habijan et al., 2013).

3.2.1 Effect of SLM parameters on mechanical properties

The space between scan lines is one of the important parameters in SLM, and has a great impact on pore characteristics and mechanical properties. The increase of scan spacing leads to a reduction of mechanical strength and young modulus in SLM, of Ti-6Al-4V. In order to fabricate the best interconnection between pores, the diameter of pores must be 3 times more than the size of the powder, showing that the ideal pore size is varied from 250 to 450μm (Zhang et al., 2014). An 80 - 95% porosity in Ti-6Al-4V TPMS structures are fabricated by SLM, with a Young's modulus of 0.12 - 1.25 Gpa, and is compliant with trabecular bones. At a 5 – 10% porosity the Young's modulus of cortical bone is the same as the TPMS structure of Ti-6AL-4V fabricated by SLM (Yan et al., 2015).

3.2.2 Effect of SLM fabricated porous structures and size on bone ingrowth

Recent research shows that the pore size of Titanium implants manufactured by SLM has considerable influence on bone ingrowth. The optimal pore size is considered the by 600 μm, which provides high mechanical properties, biocompatibility and bone fixation (Taniguchi et al., 2016). The structure of TPMS surfaces is one of the most useful designs for biocompatible scaffolds. Two structures including gyoid and diamond, with porosity percentages of 80-90%, and pore sizes of 560-1600 μm and 480-1450 μm, were fabricated by the SLM process. Dimensional accuracy between 3D μ-CT and original CAD models of Ti-6AL-4V, shows the excellent fabrication capability of the SLM method (Yan et al., 2015).

3.2.3. Effect of SLM parameters on defects

There are two main parameters in the SLM process: scan speed and laser power. The ratio of laser power to scan speed is called linear energy densities (LED). The lower liquid viscosity and high thermal stress at minimum scan speed (100 mm s^{-1}), and maximum LED (900 J m^{-1}), shows micro balling and cracks. At higher scan speeds (400 mm s^{-1}), balling effects and disordered liquid solidification are produced. Hence, for obtaining the best porous structure, parameters including scan speed and laser power should be optimized. A scan speed of 200 and 300 mm s^{-1}, and LED of 300 and 400 J m^{-1}, should be selected (D. D. Gu et al., 2012).

3.3. Selective laser sintering (SLS)

Unlike EBM and SLM, SLS is able to fuse powder under low temperatures, allowing SLS to be used to fabricate complex structures using polymers (polyethylene, polyetheretherketone, polyamide, polycaprolactone and polyvinyl alcohol), polymer bio-ceramic composites, Ti-10Mo, NiTi and Titanium silica (F. Xie, He, Lu, Cao, & Qu, 2013).

3.3.1 Effect of SLS parameters on mechanical properties and bone ingrowth

Scanning speed, layer thickness, laser power, and laser hatch spacing control the outcomes of the SLS process. Bone scaffolds made of a mixture of Titanium and Silica, with a 2:1 ratio, can be efficiently fabricated by the SLS method. The process variables for fabricating Titanium implants reported a laser power of 15 KW, 16 KHz frequency, and scanning velocity of 100 mm/s within 3 hrs. After post-curing with a temperature of 900 ^{0}C for 120 minutes, the strength of Titanium implant 142 Mpa. Laser energies lower than 12 W and higher than 28 W, are not suitable for sintering Titanium powder. Cell culture study results show that optical density (OD) increased from 0.1 to 2.4 after 7 days. Hence, sintered and post heat treated Titanium implants are ideal for bone-ingrowth (Mitsuishi et al., 2013). The holding time in the SLS process affects pore size and mechanical behaviour. When the holding time is increased to 6 hrs, pore size and porosity were reduced to 50 μm and 40%, respectively (F. Xie et al., 2013).

Porous NiTi, enhance the bioactivity of implants, and can be effectively manufactured by SLS. In comparison with organic porous Titanium, the structure of Nitinol surfaces involves a nano-fractal pattern range of 140 – 460 nm. The size of the nano-structure increases to 140 nm, while laser power increased and scanning speed reduced (Shishkovsky, Morozov, & Smurov, 2007).

4. Chemical methods of surface modification

Chemical treatments of the surface are performed to improve biocompatibility, osseointegration, blood compatibility, and wear and corrosion resistance (Kulkarni, Mazare, Schmuki, Iglic, & Seifalian, 2014). This is done through the use of processes such as acid etching, anodization, and plasma spraying are used to increase surface roughness, modify topography, induce wettability, and modify chemical composition (Kulkarni et al., 2014; X. Liu, Chu, & Ding, 2004).

4.1. Acid etching

Currently one of the most common methods for the chemical treatment of implants is acid etching, which cleans and removes oxide scales and contaminants, as well as increases surface roughness of the implant material (Jemat, Ghazali, Razali, & Otsuka, 2015; Nanci et al., 1998). This increases the surface energy and surface area of the implant, providing increased bone to implant contact, resulting in a higher micromechanical retention, in comparison to smooth surfaces (Kulkarni et al., 2014).

Acid etching with strong acids, such as hydrofluoric acid (HF), nitric acid (HNO_3), sulphuric acid (H_2SO_4), are used to modify the titanium oxide layer. This reaction increases the surface roughness, bioactivity, cell growth, adhesion, and osseointegration of the implant (Bagno & Di Bello, 2004; Jemat et al., 2015; Kirmanidou et al., 2016).

There have been many studies that act as evidence to support the fact that the increased surface roughness, obtained via acid etching, increases cell adhesion to the implant, as well as bone formation (Jemat et al., 2015; Rupp, Scheideler, Rehbein, Axmann, & Geis-Gerstorfer, 2004; Wong, Eulenberger, Schenk, & Hunziker, 1995).

4.2. Electrochemical anodization

Electrochemical anodization is used to improve mechanical properties of the implant, fabricate required surface topographies, and improve corrosion resistance, bioactivity and bone conductivity (Kirmanidou et al., 2016). The process involves connecting the metallic implant to the positive pole of an electrical circuit, and immersing it into an electrolyte solution, containing oxidizing agents. The surface of the implant is oxidized, thickening the TiO_2 layer to a maximum of 40 μm.

4.2.1. Thickening of the oxide layer

The Titanium oxide layer increases the wear and corrosion resistance, as well as improves cell adhesion, and bonding to the implant (Kirmanidou et al., 2016; X. Liu et al., 2004). It is thought that the anatase and rutile phases present in the layer have the ability to form hydroxyapatite (HA), a naturally occurring compound found in bone, which promotes bone regrowth and improves osseointegration (Kulkarni et al., 2014; Leeuwenburgh, Wolke, Jansen, & Jonge, 2008). Anodization, and heat treatment modifies crystal and microstructures of the oxide layer, leading to an increase in HA, thus, increasing osseointegration (Cho et al., 1995; Li et al., 1992; Sul et al., 2009).

4.2.2. Effect of process parameters

Changing process parameters of the anodic reaction leads to different properties in the oxide layer formed. Changing the voltage of the anodic reaction has an effect on the resulting thickness of the oxide layer. At higher voltages, the porosity and pore sizes of the oxide layer in increased, due to the dielectric breakdown. Low anode voltages result in a thin, compact oxide film, while higher voltages produce thick and porous films (Kirmanidou et al., 2016; Kuromoto, Simao, & Soares, 2007).

The choice of acid also affects the final surface. A study conducted by Xie et al. 2010, found reactions which used H_2SO_4 and H_3PO_4 were found to produce a maximum pore size of 1 μm, which were evenly distributed and well separated. Samples which used CH_3COOH resulted in a much more heterogeneous surface, with larger grooves and craters (approximately 200 μm). Fibroblast cells were also tested on this surface, showing increased adhesion on this surface (L. Xie et al., 2010).

The use of alkaline electrolytes has also been tested, with reactions using alkaline electrolytes showing a lower oxide layer growth rate, compared to acidic electrolytes. In addition, increasing concentration of the electrolyte and temperature, decreased the anodic forming rate (Kirmanidou et al., 2016; Sul et al., 2001; Sul et al., 2009).

4.3. Coatings

Coatings improve mechanical properties, and osseointegration, by enhancing bone regeneration at the interface of the implant and surrounding tissue. Coatings imitate organic and inorganic components in bone, establishing similarity between bone and the foreign implant material, allowing early and strong fixation of the implant (Leeuwenburgh et al., 2008).

4.3.1. Inorganic coatings

Calcium phosphates (CaP) have a similar mineral phase to bone, with the most abundant phase being HA (Leeuwenburgh et al., 2008). Coating implants with this compound, increases signalling of cells at the implant interface (Kulkarni et al., 2014). CaP ceramics have excellent bioactivity properties, forming a chemical bond between the material and tissue. The interaction between the implant and body fluids forms a carbonate apatite layer on the surface of the implant, which is chemically and microstructurally similar to that of bone, enhancing the healing process. However, CaP is too brittle to be used as an implant directly and is therefore used as a coating on metal, combining the excellent mechanical properties of metal, with the biological properties of ceramic (Leeuwenburgh et al., 2008). While plasma spray coating is the most common method of application, other processes such as magnetron sputtering, pulsed laser deposition and sol-gel deposition, are also used.

4.3.1.1. Plasma spray coating

In this process, a plasma flame is used to aim powdered HA at the implant surface, which solidifies on the surface as a coating (Duan & Wang, 2006). High deposition rates, and its ability to coat large areas, make this method popular. The use of this method has also been found to induce nucleation and increase the growth of apatite on the implant surface (Y. W. Gu, Khor, Pan, & Cheang, 2004; Jemat et al., 2015). Studies have shown that HA coated implants possess excellent bioactivity after 4 weeks immersion in a simulated body fluid solution, with properties decreasing after 56 days. The initial properties are due to the fact that HA coated implants exhibit higher bone to implant contact, and accelerates the formation of bone, due to the porous surface which promotes cell proliferation (Darimont, Cloots, Heinen, Seidel, & Legrand, 2002; Fouda, Nemat, Gawish, & Baiuomy, 2009; Y. W. Gu et al., 2004).

There are a number of drawbacks associated with the process. The coating can only be applied to areas within direct sight, meaning that it is difficult to coat irregular shapes in a uniform fashion (Duan & Wang, 2006). The strength of HA coatings decreased after long immersion times in simulated body fluids, due to the degradation of the intermolecular bonds in the coating, indicating that long term performance of HA coatings is a concern (Duan & Wang, 2006; Jemat et al., 2015). In addition, phase changes of the CaP powder are unpredictable, due to the high temperature differences, which may cause unwanted phases in the coating. There is also poor control over the final morphology and coating thickness, which may have adverse effects on the rate of bone regrowth (Leeuwenburgh et al., 2008).

4.3.2. Organic biomolecule coatings

Organic biomolecule coatings are used to immobilize organic proteins, enzymes and peptide chains onto the surface of the implant, to improve bone regeneration, and tissue response. (Leeuwenburgh et al., 2008). Organic coatings can be applied by methods such as immobilization and physical deposition.

4.3.2.1. Physio-chemical adsorption

Physical adsorption involves fully immersing the implant into a bioactive peptide-containing solution, under mild conditions (Kulkarni et al., 2014; Leeuwenburgh et al., 2008), allowing the molecules to be physically entrapped and adsorbed onto the surface coating, improving tissue reaction to the foreign material. The mild conditions mean that there is little disruption to biomolecules. It has been found that certain process parameters, such as temperature, pH, and solvent, have an effect on biolinkage. Biomolecules are usually incorporated onto coatings made from poly (D, L-lactide), ethylene vinyl acetate, and collagen (Leeuwenburgh et al., 2008). While this method is effective way in which biomolecules desorb from the surface is uncontrolled, and can be displaced from adsorption sites. In addition, this method does not ensure controlled deposition, which is needed for initiating interactions with biological issue (Kulkarni et al., 2014; Leeuwenburgh et al., 2008).

4.3.2.2. Covalent binding

This method is widely used to bind biomolecules to the surface of material, through covalent bonding, in order immobilize peptides, enzymes and adhesive proteins on to the surface of Titanium implants. During the process, the Titanium surface is derived into reactive groups, which react with biomolecules present on the surface, to form covalent bonds, immobilizing the biomolecule. This process does not allow control over the surface density of biomolecules, which affect the biological response of the body to the implant. It is also more complicated in than other immobilization techniques, however, it allows very high surface loading, and low protein loss (Kulkarni et al., 2014; Leeuwenburgh et al., 2008). While this method has been widely used, results on the exact parameters which optimize cell and tissue response is still lacking.

4.3.2.3. Peptide inclusion

Immobilizing peptide sequences onto Titanium surfaces promotes cell adhesion. By immobilizing peptide chains, and extracellular matrix proteins onto the surface, the cellular processes and responses can be regulated. This influences cell adhesion, proliferation, migration, morphological change, gene expression and cell survival, through intracellular signalling (Kulkarni et al., 2014; Leeuwenburgh et al., 2008). These peptide and protein components simulate an interface that is similar to naturally occurring interfaces, improving the acceptance of the implant into the body. Peptide sequences can be produced artificially, allowing control over composition, and giving the ability to reduce the number of undesired cellular interactions. Cellular attachment has known to be increased by immobilizing proteins, such as fibronectin and vitronectin, in this manner (Leeuwenburgh et al., 2008).

4.3.2.4. Ion implantation

Ion implantation is a common physical process involving the bombardment of ions, in an electric field, into the surface layer of the substrate in a vacuum environment. High purity layers can be produced, with the ability to control concentration and impurity depth distribution with high accuracy (Jemat et al., 2015; Leeuwenburgh et al., 2008; Rautray, Narayanan, Kwon, & Kim, 2010). The process is conducted below critical temperatures, which allows modification of the material surface without affecting the mechanical properties of the bulk material (Mändl & Rauschenbach, 2002).
The main application for ion implantation has been to improve Titanium implants, for increased integration with bone. This technique can be used in conjunction with HA coatings, enhancing the precipitation of HA in solution. Improved smooth muscle cell adhesion, and survival have been observed after using ion implantation. (Rautray et al., 2010). It is found that implanting Oxygen via plasma ion implantation can enhance the stability of the oxide layer on Titanium. Similarly, implanting Cobalt ions into Titanium alloys improves osseointegration (Braceras et al., 2002; Jemat et al., 2015). The process also has the ability to improve blood compatibility and antibacterial properties on polymer substrates (N. Huang et al., 2004).
An advantage of ion implantation is that there is no sharp interface between the implant material layer and the substrate, and therefore adhesion issues do not occur. Corrosion resistance, as well as wear resistance, has also been found to improve by using ion implantation (Rautray et al., 2010). The major disadvantage to this process is that it required vacuum conditions. (Lu, Qiao, & Liu, 2012).

6. Future direction of Study

1. Due to the high energy in EBM and SLM as additive manufacturing techniques, more attention should be focused on investigation and optimizing of defects which affect mechanical properties of the structure.
2. Artificial intelligent optimization methods, including genetic algorithms, can be applied to topology optimization in order to achieve groups of optimized solutions.
3. The methods of chemical surface modification mentioned here are only short term solutions, as the effect of these coatings, and oxide layers, are often masked by proteins in the body, or displaced from the implant surface. A possible future direction of study is to investigate how the life of these coatings can be extended.
4. While the methods of surface modification explained in this paper are successful in improving properties, there is very little in the way of antibacterial properties. A current line of study is using a chemical hydrothermal method to fabricate a nano-pillar texture on Titanium substrates, in order to reduce bacterial adhesion in orthopedic implants.
5. Investigation and modelling of the effects of changing hydrothermal process parameters, on the final morphology and antibacterial properties of the substrate, are also currently being tested.

5. Conclusion

In this review paper, recent advances in design, manufacturing and surface modification of Titanium orthopedic implants have been reviewed, and the following conclusion have been made:

1. Several methods for the design of porous structures have been studied, including CAD based design, image base design, implicit design, and topology optimization. Topology optimization based on the design of functionally graded material (FGM) and bidirectional evolutionary structural optimization (BESO) is the best technique to successfully design porous structures.
2. EBM and SLM and was developed for fabricating porous Titanium and its alloys, due to its use of high temperatures compared to SLS. The EBM process has better performance and produces fewer defects in CP Titanium, compared to SLM due to its clean process environment under vacuum condition.
3. Several methods of chemical surface modification have been presented, including acid etching and anodization, and organic and inorganic coating methods. These methods are used to improve mechanical properties, surface roughness, and corrosion and wear resistance, and increase and enhance osseointegration, cell adhesion, and bone regeneration.
4. Anodization and acid etching are the most commonly used techniques. Coatings, such as CaP and HA coatings, are used in making the implant surface mimic biomolecules found in bone, reducing the body's reaction to the foreign material, and increasing cell adhesion and bioactivity.

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