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Toward 3D printed bioactive titanium scaffolds with bimodal pore size distribution for bone ingrowth

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Abstract

Inkjet 3D printing as a versatile rapid manufacturing method was utilized for making titanium scaffolds with customized pores and geometry. A suitable binder/powder/solvent system was employed to make titanium printable and the parts were subjected to a firing process for strengthening. Mechanical stiffness of the part was tailored by varying printing and sintering parameters to meet that of the bone. Since titanium is inherently bioinert, the bioactivity of the parts was enhanced by surface modification of internal channels by electrochemical deposition of hydroxyapatite or hydrothermal treatment to form titania on the surface.

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1. Introduction

Additive manufacturing (AM) is a collection of techniques for mouldless free form fabrication of 3D components by computer controlled sequential delivery of energy and/or material to specified points in space to produce the component [1-3]. Although additive manufacturing is a well-known technology for concept modeling and visualization, utilizing of this technology for manufacturing functional parts is currently a very new topic. New technologies provide this opportunity to rapidly manufacture functional parts, with the same or even superior properties to that of bulk products. Currently, AM techniques for metals are paving the path toward applications in the near-net shape fabrication of complex geometries with tailored mechanical properties for biomedical, automation and aerospace sectors [3-5]. Biomedical sector is looking for some unique advantages in additive manufacturing techniques, such as customizing shape and geometry of implants, manipulating with pore size and its geometrical distribution, modifying mechanical properties by creating porous structures and patient oriented designs [3,6-9].

Metals have so far shown the greatest potential to be the basis of implants for long-term load-bearing orthopaedic applications, owing to their excellent mechanical strength and resilience when compared to alternative biomaterials, such as polymers and ceramics. Particularly, titanium and its alloys have been widely used in orthopaedic and dental devices because of their excellent mechanical properties and biocompatibility. In order to perform like natural bone, bone implants should match the mechanical properties of natural bone. The mismatch of the mechanical properties could result in "stress shielding" when the mechanical properties of the implant is in excess of the properties of bone.

Bone tissue scaffolds must provide initial sufficient mechanical strength and stiffness to oppose contraction forces, and later for the remodelling of tissue. In regenerating load-bearing bone tissues, additional issues relating to the scaffolds' mechanical properties have to be resolved [10].

With the advent of electron beam melting (EBM), direct metal laser sintering (DMLS), selective laser melting (SLM), selective laser sintering (SLS), laser engineered net shaping (LENS) and laser aided additive manufacturing (LAAM) processes direct replication of metallic structures has become a reality [10]. Creating pores in the CAD design is one of the strategies to manipulate the stiffness of implants. The range of materials used with these advanced manufacturing technologies has also increased over time, broadening the spectrum of applications [5,10-12].

Currently stainless steel, titanium and its alloys have been successfully manufactured using the above techniques. Although these technologies are capable to make precise components with properties close to that of bulk material, the high capital cost of the equipment prevents these technologies to find an appropriate position in small and medium manufacturing industries. Inkjet 3D printing is one of the rapid manufacturing techniques which can provide some unique advantages over other AM technologies for metals [1]. In this technique instead of using laser or electron beam to melt the powder, an ink cartridge, print a binder layer by layer on top of a powder bed. The parts can be subsequently sintered in a furnace to obtain necessary strength. Much lower capital cost of the equipment and capability to control sintering process via the subsequent thermal cycle are some advantages of the inkjet 3DP method. Although precision of the parts out of inkjet 3DP is not as good as SLM or EBM, for biomedical applications the precision of the parts is not that critical. So, inkjet 3DP is a suitable technique for low cost rapid manufacturing of metallic components for biomedical applications.

Although titanium is a biocompatible material, it is not considered as bioactive and in case of bone tissue engineering or implant stabilization titanium material has no or little effect on fast growing and good attachment of cells to the implant. Surface modification technologies can alleviate this problem and promote bone adhesion and cell ingrowth [13]. Currently, most surface modification techniques such as HA coating, or biomimmetic coatings are done on plane substrates using techniques such as plasma spraying, Sol-gel, electrochemical deposition, hydrothermal treatment and electrophoretic deposition.

Although titanium can be rapidly manufactured using additive manufacturing techniques, modifying the surface or internal channels of scaffold or porous material can be utilized in order to push the technology one step further.

In this work, a feasibility study on manufacturing of titanium scaffolds using inkjet 3D printing method is presented. By optimization of process, porous titanium parts with mechanical properties close to that of bone are obtained. The surface and internal channels of scaffold is coated by TiO_2 and HA by using a hydrothermal treatment and electrochemical deposition respectively.

2. Experimental

2.1. 3D printing of titanium

A schematic of 3D printing process for manufacturing functional components has been shown in Fig.1. The process starts with preparation of powder material. In this stage, Titanium powder with spherical shape and certain particle size is dry mixed with PVA, a water soluble polymer. The mixing is carried out using a ball mill mixer or vibratory mill for 8-10 hr. Zirconia balls with diameter of 20 mm are used to facilitate the mixing process. After preparation of powder mixture, the parts were created using a ZPrinter 310 Plus. A view of the machine has been shown in Fig.1. The CAD files were created using an Autocad or SolidWorks software package and converted to an STL file to feed into machine using the company software. The depositing binder used was Deionized water which is dispersed through a printhead provided by HP. In 3D printing process, a print head travels over a bed of loose powder upon which it prints the cross-sectional data. The powder is distributed accurately and evenly across the build platform by using a feed piston and platform, which rises incrementally for each layer. The layer thickness we used in this research was adjusted to 0.1 mm. A roller mechanism spreads powder fed from the feed piston onto the build platform. This process repeats until the whole model built up completely. After printing completed, the samples are left overnight in powder bed in order to get enough strength. Then the parts are taken out and put in an oven at 50-70°C for at least 1 hr. The samples are taken out for de-powdering. The samples are put in a tube furnace for debinding and sintering in Argon environment at a temperature between 1000 to 1350°C for 2 hours. Debinding and sintering profile has been shown in Fig.1.

Using the above techniques, titanium scaffolds with interconnected porosity were prepared and characterized using scanning electron microscopy and mercury porosimetry. Young's modulus of the scaffolds was measured in the compression mode using printed cylinders or cubical scaffolds.
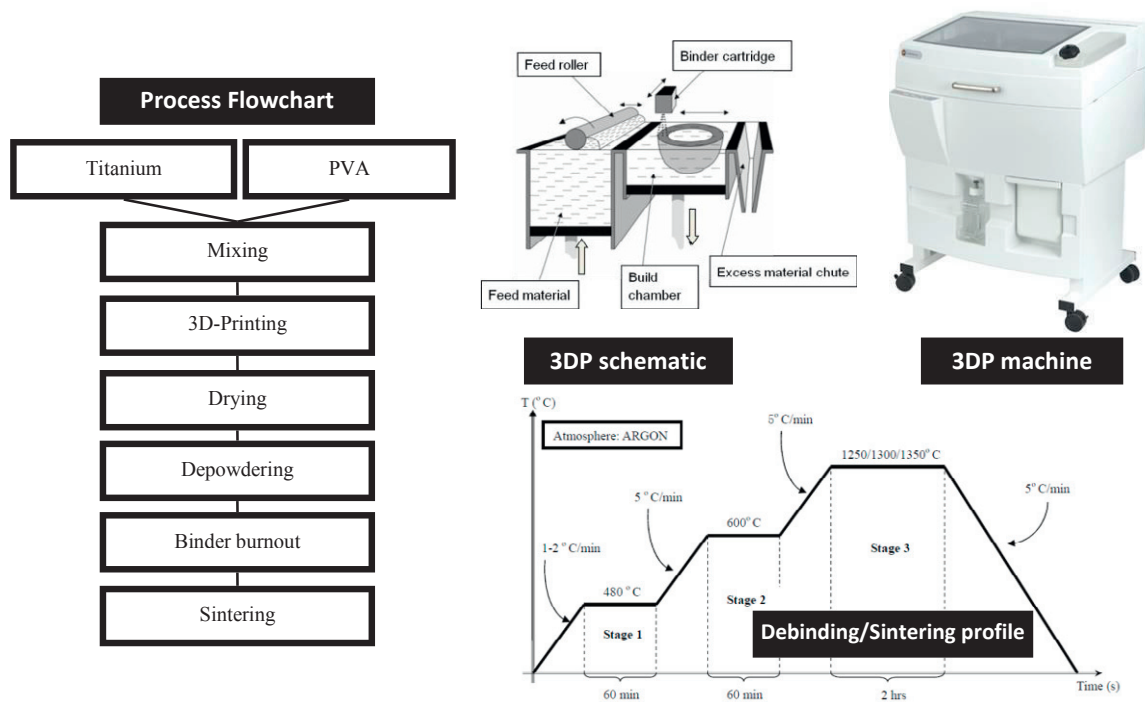
Fig.1.3D printing process flowchart, equipment, principles and sintering profile.

2.2. Surface modification

For improvement of bioactivity of scaffolds, the surface and the internal channels were modified using two techniques. Firstly, the samples were coated with TiO_2 by intentionally transforming a thin layer of titanium to titanium oxide by hydrothermal treatment. In this process, the samples were soaked in an oxidizing solution containing hydrogen peroxide (3 vol%) in an autoclave vessels with PTFE liner while the temperature is controlled by leaving the autoclave in a convection oven. After this treatment, hydroxyapatite was coated on TiO_2 using constant voltage electrochemical deposition. The electrolyte contains calcium nitrate, $Ca(NO_3)_2$, and ammonium hypophosphate, $NH_4H_2PO_4$, in Ca/P molar ratio of 1.67. The pH and temperature of solution were controlled during the process. A platinum mesh was used as anode. The deposition time was 30 min. After completion of electrochemical deposition, the coating was converted to HA using alkaline treatment. For this purpose, the samples were soaked into sodium hydroxide solution for 2 hr. The coated titanium samples were rinsed with distilled water and dried at room temperature in air. The phase and morphology of the coating layer was confirmed using Field Emission SEM (JEOL) and XRD (Bruker).

3. Results and discussion

3.1. Physical and mechanical properties of porous 3DP titanium

Fig.2 shows two typical titanium scaffolds before and after sintering and also the SEM image of the structure. It's obvious that printed parts contain a bimodal pore size. In other word, two types of porosity can be distinguished easily in the samples, i.e. pores by design and pores by process. Pores by design can be manipulated with the CAD model and the pores by process are due to the binder content, sintering temperature, debinding profile and some other factors. However, there are some process limitations which prevent us from freely controlling these pores. Although pores by design can be played with the CAD file, strength of the parts during handling and depowdering must be considered. The resolution of print head is below 50 micron. However, the smallest achievable designed pore size is around 600μm after sintering. Thickness and length of the struts also play an important role in handling strength of the parts.
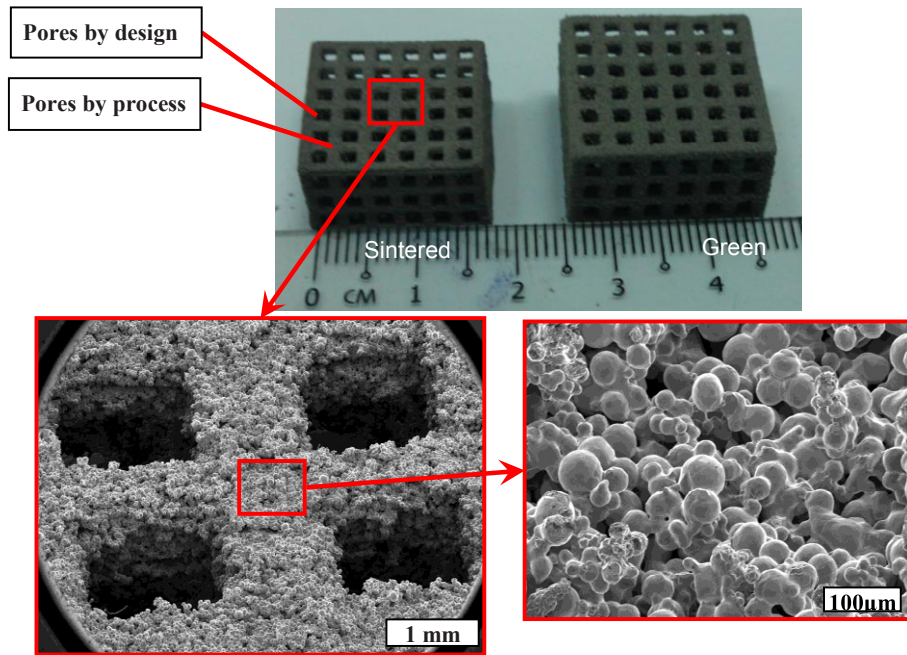
Fig.2. Images of 3D printed titanium cages with two types of pores, i.e. pores by process and pores by design (Binder content in printing feedstock: 10wt%, sintering temperature: 1250˚C).
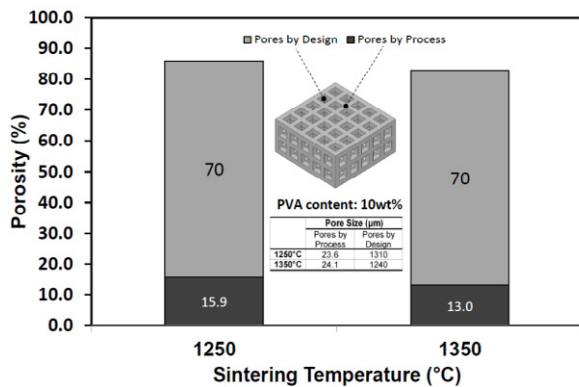

Fig.3. Porosity characterization of two typical scaffolds sintered at different sintering temperatures.

Fig.3 shows porosity content of two scaffolds sintered at different temperatures obtained from mercury porosimetry and geometrical calculations. The total porosity is above 80%, 70% due to pores by design and 13-16% due to pores by process. The higher the sintering temperature, the lesser the porosity by process. However, the percentage of pores by design is not affected by the sintering temperature. According to dimensional measurement of large pores and mercury porosimetry on small pores, the size of the pores is 23-25μm and 1200-1400 μm for pores by process and pores by design respectively. These values are slightly influenced by sintering temperature. The original pore size and wall size of scaffold in the CAD model were 2 and 1 mm respectively. After sintering a linear shrinkage of 14-18% was observed which depends on the sintering temperature and binder content. The wall size of the scaffold is a little bit bigger than what was designed in the CAD model and consequently pores by design are also smaller. It is due to bleeding of ink solution into larger areas when depositing on the powder bed.

According to intrusion volume in mercury porosimetry, 88 and 90% of pores by process are interconnected for sintering temperatures of 1250 and 1350°C respectively. 10 to 12% of the pores become closed after sintering. Presence of interconnected pores on the surface can help cell adhesion as well as nutrient flow to the bone which grows in the larger pores.

Stiffness of scaffold is also an important issue for bone tissue engineering and bone implants. The higher Young's modulus of implant means that nearly all of the load-bearing function is transferred to the metal prosthesis. Consequently, bone surrounding or grown in the implant is subjected to negligible mechanical stress, a situation known as "stress shielding." Since inappropriately un-stress-stimulated cells and tissues are dysfunctional and absorbed by the body, the bone holding the implant in place softens, leading to loosening of the implant. To avoid this problem the stiffness of the scaffold can be manipulated by different processing parameters. Herein, 3D printing provides a platform to carefully control the scaffold stiffness by playing with the CAD model and sintering parameters.
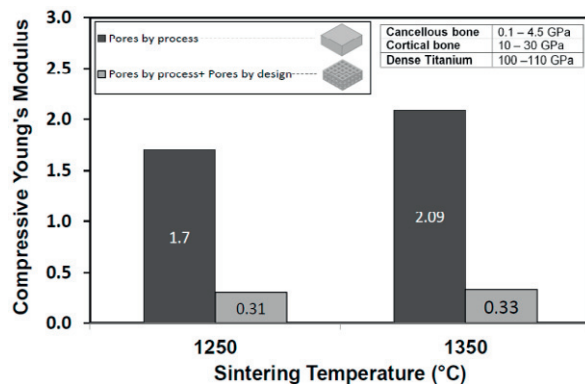
Fig.4. Compressive Young's modulus of scaffolds in two different sintering temperatures.

Fig.4 shows compressive young's modulus of typical scaffolds sintered at two different temperatures. The measurements were done on 3 samples and an average was obtained. As it can be seen, the young's modulus of both type of porous titanium, e.g. one with pores by process and one with pores by process and pores by design, falls in the range of cancellous bone modulus, which is quite promising for bone tissue engineering. The modulus is much less than the stiffness of dense titanium, which is around 100-110 GPa. Increasing the

sintering temperature can play a role in strengthening the wall material and introducing pores by design can help to tailor mechanical stiffness.

3.2. Surface modification results

Although pore structure and mechanical properties of scaffolds are important for bone tissue engineering, the properties of material surface for cell adhesion and grow is vital for bone ingrowth as well [13]. Pores provide the necessary path for bone to grow in, while surface property of the walls and internal channels have to support and encourage the cells to grow in via proliferation. Otherwise the scaffold will become useless and will be rejected by the body. Titanium is inherently not a bioactive material. In this work, 3D printed titanium scaffolds was coated with a more hydrophilic titanium oxide coated by hydrothermal treatment followed by hydroxyapatite precipitation using electrochemical deposition. This method of coating has already been found in literature for coating of dense titanium parts [14-16]. However, in this work these methods are utilized on 3D printed porous titanium parts. The SEM micrographs of the coating in different stages have been shown in Fig.5.
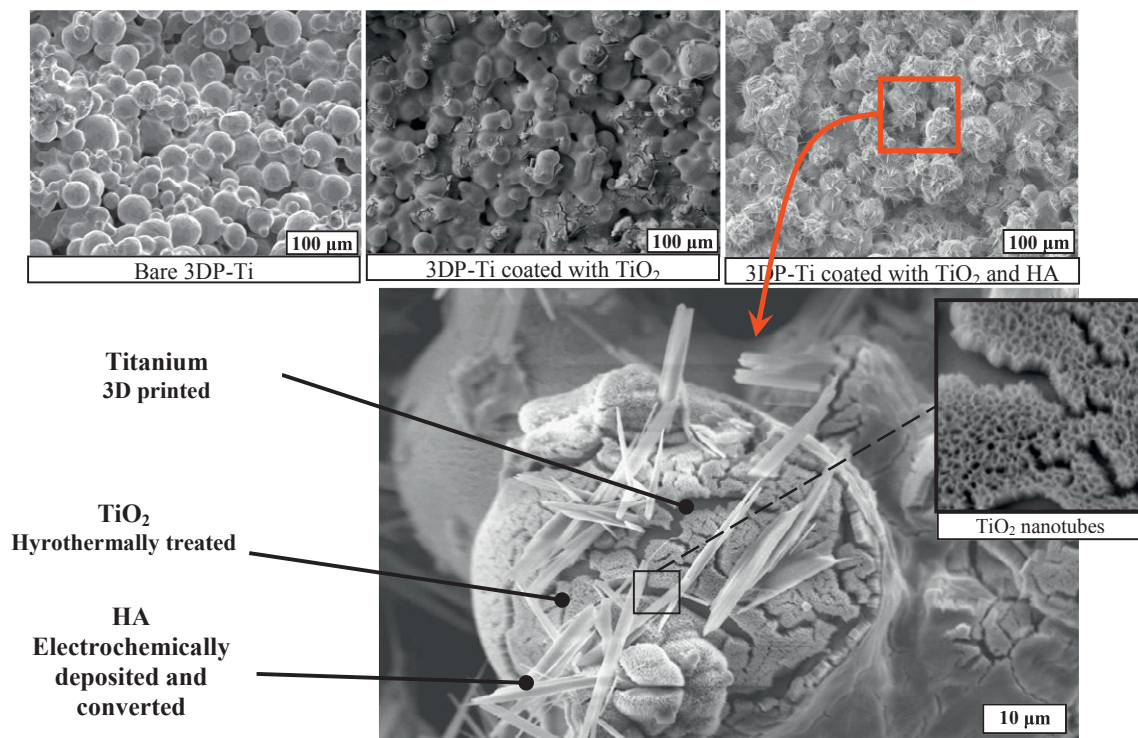

Fig.5. SEM micrographs of 3D printed titanium scaffolds coated with Titanium Oxide and Hydroxyapatite using hydrothermal treatment and electrochemical deposition respectively.

Titanium oxide nanotubes are observed on titanium with a thickness of 0.5 to 1μm. However, due to difference in coefficient of thermal expansion the Titania coating cracks during cooling from treatment process. Hydroxyapatite flakes are distributed evenly on titanium oxide layer. Titanium oxide nanotubes provide the necessary path for charge transfer during electrodeposition.

XRD patterns of coating (Fig.6) obviously confirm presence of titanium oxide and hydroxyapatite. No brushite peaks are observed in this material which shows fully conversion of brushite to hydroxyapatite via the alkaline treatment.
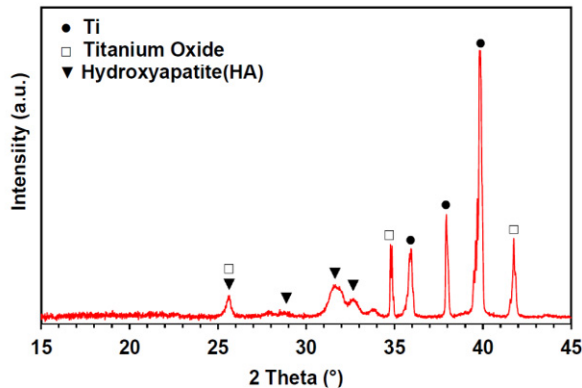

Fig.6. XRD pattern of scaffolds coated with titanium oxide and hydroxyapatite.

4. Conclusion

Inkjet 3D printing method was utilized for manufacturing of titanium scaffolds with above 80% porosity and bimodal pore size distribution, i.e. pores by process (20-30μm) and pores by design (1200-1400μm). The compressive young's modulus of the bone can be affected by sintering temperature and pore size of the scaffold. In a typical prototype the scaffolds stiffness falls in the range of the young's modulus for cancellous bone.

In order to enhance cell proliferation and adhesion, hydrothermal treatment was utilized to convert a thin layer of titanium surface to titanium oxide. Hydroxyapatite was coated on titanium oxide using electrochemical deposition followed by alkaline treatment. The properties of surface are showing uniform and relatively continuous coating of titanium oxide and evenly distribution of hydroxyapatite needles on titania nanotubes.

For further validation of 3D printed products, bioactivity testing and animal model testing is necessary to investigate cell proliferation behavior.

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