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Diametral compression behavior of biomedical titanium scaffolds with open, interconnected pores prepared with the space holder method

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ABSTRACT

Scaffolds with open, interconnected pores and appropriate mechanical properties are required to provide mechanical support and to guide the formation and development of new tissue in bone tissue engineering. Since the mechanical properties of the scaffold tend to decrease with increasing porosity, a balance must be sought in order to meet these two conflicting requirements. In this research, open, interconnected pores and mechanical properties of biomedical titanium scaffolds prepared by using the space holder method were characterized. Micro-computed tomography (micro-CT) and permeability analysis were carried out to quantify the porous structures and ascertain the presence of open, interconnected pores in the scaffolds fabricated. Diametral compression (DC) tests were performed to generate stress-strain diagrams that could be used to determine the elastic moduli and yield strengths of the scaffolds. Deformation and failure mechanisms involved in the DC tests of the titanium scaffolds were examined. The results of micro-CT and permeability analyses confirmed the presence of open, interconnected pores in the titanium scaffolds with porosity over a range of 31–61%. Among these scaffolds, a maximum specific surface area could be achieved in the scaffold with a total porosity of 5–55%. DC tests showed that the titanium scaffolds with elastic moduli and yield strengths of 0.64–3.47 GPa and 28.67–80 MPa, respectively, could be achieved. By comprehensive consideration of specific surface area, permeability and mechanical properties, the titanium scaffolds with porosities in a range of 50–55% were recommended to be used in cancellous bone tissue engineering.

1. Introduction

In recent years, bone tissue engineering has been increasingly studied as an alternative approach to healing critical-size bone defects (Bose et al., 2012; Burg et al., 2001; Lichte et al., 2011; Vats et al., 2003). With this approach, a new functional bone tissue is formed and developed to repair or reconstruct bone defects. For this purpose, a synthetic porous material, namely a scaffold with open, interconnected pores, is designed and fabricated to provide mechanical support and to guide the formation and development of new bone tissue at the defect site (Bose et al., 2012; Karageorgiou and Kaplan, 2005; Lichte et al., 2011). With open, interconnected pores, the transport of nutrients, oxygen and metabolic waste during bone tissue regeneration is effectively facilitated, and so is cell migration during tissue development (Bose et al., 2012; Karageorgiou and Kaplan, 2005; Karande et al., 2004). Titanium is often chosen as one of the preferred biomaterials for bone tissue engineering scaffolds owing to its excellent biocompatibility and mechanical properties (Fujibayashi et al., 2004; Geetha et al., 2009; Singh et al., 2010a).

So far, the space holder method has been preferably used in the fabrication of titanium scaffolds with high porosity and open, interconnected pores for bone tissue engineering (Arifvianto and Zhou, 2014; Dunand, 2004; Ryan et al., 2006; Singh et al., 2010a). With this method, temporary space-holding particles are utilized as a pore former in the titanium matrix. Firstly, titanium powder particles and space-holding particles are mixed and compacted to produce a green body or a scaffold preform. Afterwards, space-holding particles are removed, leaving new pores behind in the scaffold green body. Finally, sintering is carried out to achieve permanent bonding between titanium powder particles and the final form of the scaffold. In principle, with the right choices of the starting materials and fabrication process parameters, open, interconnected pores can be produced by adjusting the volume fraction of space-holding particle to make sure that multiple links between these particles are achieved within the scaffold (Arifvianto and Zhou, 2014).

As rightly pointed out by other researchers (Ryan et al., 2006; Singh et al., 2010a), elastic modulus and compressive strength are the critical parameters of the scaffold that must be ensured prior to its clinical use

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for bone tissue engineering. A scaffold with an elastic modulus higher than that of the host bone tissue may fail to induce bone regeneration due to stress shielding (Ryan et al., 2006; Singh et al., 2010a). On the other hand, a scaffold with adequate strength and fracture resistance can aid in the healing of the defect in the load-bearing skeletal tissue (Imwinkelried, 2007; Ryan et al., 2006). In general, the mechanical properties of a scaffold decrease with increasing porosity (Dabrowski et al., 2010; Esen and Bor, 2007; Gligor et al., 2013; Imwinkelried, 2007; Kim et al., 2013; Li et al., 2013; Mansourighasri et al., 2012; Mondal et al., 2012; Wen et al., 2001; Wen et al., 2002). Therefore, it is necessary to search for a trade-off between these two opposite parameters in order to meet the requirements of scaffolds for bone tissue engineering.

In most cases, the elastic modulus and compressive strength of a scaffold material are determined by performing uniaxial compression (UC) tests (Li et al., 2013; Singh et al., 2010b). In order to obtain comparable results, specimens with standardized dimensions are required, such as those specified in the ISO 13314:2011 standard. According to this standard, the specimen of a porous or cellular metallic material subjected to uniaxial compression tests with a loading direction parallel to its height should have a height-to-diameter ratio (H/D) between 1 and 2. With the space holder method, however, scaffolds with such a high H/D ratio could not be produced without a region with a low green strength that is prone to collapse during the removal of space-holding particles to create macro-pores in the scaffold green body (Ozkan and Briscoe, 1997). In the case of a green body prepared with a single-action die press, its H/D ratio must be kept low in order to ensure a homogeneous green density distribution and to minimize the presence of a region with a low green strength, relative to the rest of the powder compact body (Ozkan and Briscoe, 1997). Considering this limitation, an alternative method to determine the mechanical properties of disc-shaped scaffolds should be used.

In the last few decades, diametral compression (DC) tests have been applied in a number of studies to determine the mechanical properties of powder compacts or grain compacts with low H/D ratios or disc shapes (Fell and Newton, 1970; Jonsén et al., 2007; Kamst et al., 1999; Ozkan and Briscoe, 1997). Although the method was originally used for rock specimens, a standard for the DC tests has been established, such as that specified in ASTM D3967-08. DC tests have also been used to determine the mechanical properties of porous ceramic biomaterials (Almirall et al., 2004; Pilliar et al., 2001). With increasing use of numerical analysis in recent years, stress distributions inside disc-shaped specimens during DC tests have been revealed (Es-Saheb et al., 2011; Procopio et al., 2003). However, the use of DC tests to determine the elastic moduli and compressive strengths of porous titanium scaffolds and sintered metallic materials has rarely been reported in the open literature. In contrast to UC tests (Esen and Bor, 2007; Li et al., 2013), it is still not confirmed whether the stress-strain diagrams derived from DC tests are applicable to indicate the deformation behavior and failure of porous metallic materials under compressive loads.

The present research was aimed to establish the correlations between the diametral compression behavior, space-holder volume fraction and geometric parameters of the scaffolds prepared by using the space holder method. Porous structures and open, interconnected pores within the scaffold interior were ascertained by performing micro-computed tomography (micro-CT) analysis and permeability tests. The elastic moduli and yield strengths of the scaffolds with various porosities were determined from the stress-strain diagrams obtained from the DC tests. In addition, the porous structures of the scaffolds after compression to a number of predetermined strains were characterized in order to establish the deformation and failure mechanisms involved in the DC tests of the porous titanium scaffolds. In the end, the scaffolds with balanced elastic modulus, yield strength and optimum porosity that could meet the requirements for bone tissue engineering were recommended.

2. Materials and methods

2.1. Scaffold preparation

In this research, titanium scaffolds were prepared by mixing a spherical titanium powder (TLS Technik, Germany) with rectangular carbamide particles (Merck, Germany) for 3 h by using a roller mixer (CAT, Germany). The median particle diameters (D_{50}) of the titanium and carbamide powders were 70.32 ± 1.61 µm and 399.23 ± 4.85 µm, respectively, as determined by using a Mastersizer laser diffractometer (Malvern, UK). To produce a set of highly porous titanium scaffolds, carbamide volume fractions in the titanium/carbamide powder mixture were selected to be 50 to 80%. Prior to mixing, a polyvinyl-alcohol (PVA) binder solution was first blended with the titanium powder in order to minimize the segregations of titanium and carbamide powders due to their dissimilar characteristics. The volume fraction of PVA was 3%. The green bodies of the scaffolds were produced by compacting the titanium/carbamide powder mixtures in a single-action uniaxial die press at pressures of P = 100–220 MPa, which were the critical compacting pressures determined in a previous study (Arifvianto et al., 2015). To generate macro-pores, carbamide particles in the scaffolds were removed by immersing the green bodies in 250 ml demineralized water for varied periods of time (Arifvianto et al., 2014). Finally, the scaffold preforms were sintered in a tube furnace (Carbolite, UK) at 1200 °C for 3 h under a flowing argon atmosphere, after heating at a rate of 10 °C/min. By using this procedure, titanium scaffolds with a diameter of 12 mm and a height of 3–4 mm were prepared for subsequent characterization. Prior to characterization, both the top and bottom surfaces of the sintered disk-shaped specimens were ground using a Struers LaboPol-21 manual grinding machine with fine-grade sandpaper (2000 grit) and flowing water for 3–5 min until smooth surfaces were obtained.

2.2. Micro-computed tomography (Micro-CT) analysis

The porous structures of the titanium scaffolds were characterized by using X-ray micro-computed tomography (micro-CT) (Nanotom, Phoenix X-rays, The Netherlands) with an image resolution of 10 µm. In addition, the influence of compressive strain during the DC tests on the porous structure characteristics of the scaffold was investigated. Prior to micro-CT, the sample was first cleaned by sonication in ethanol for 5 min. Quantitative analysis of the porous structure was performed by using the open-source ImageJ 1.50i software (Ferreira and Rasband, 2012) with BoneJ plugin (Doube et al., 2010) on the 3D model of the scaffold with dimensions of 2.5 × 2.5 × 2.5 mm, which was chosen by cropping the volume of interest at the core of the scaffold. Prior to the quantitative analysis, an auto local thresholding using the Bernsen method and a radius of 30 was applied on the 3D model of the scaffold.

By using the BoneJ software, a set of geometrical parameters describing the characteristics of a scaffold could be determined, i.e., (i) porosity (p), (ii) the specific surface area of the matrix framework (*SSA*), (iii) the connectivity density of pores that are formed from the space previously occupied by space-holding particles (*Conn.D.*), (iv) the thickness of the matrix framework (*Th.Ti*) and (v) the spacing of the space occupied by space-holding particles in the scaffold preform (*Th.Sp.*).

2.3. Permeability tests

To ascertain the presence of open, interconnected pores in the scaffolds, gas permeability tests with air as the working fluid were carried out at room temperature. A gas permeameter (Ruska, USA) was used to determine the pressure drop (ΔP) of the air that flew steadily through the scaffold. As shown schematically in Fig. 1, a diametrically-sealed sample was placed by press-fitting into a cylindrical rubber holder with its circular area facing the air inflow. The intrinsic