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Characterization of the porous structures of the green body and sintered biomedical titanium scaffolds with micro-computed tomography

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ABSTRACT

The present research was aimed at gaining an understanding of the porous structure changes from the green body through water leaching and sintering to titanium scaffolds. Micro-computed tomography (micro-CT) was performed to generate 3D models of titanium scaffold preforms containing carbamide space-holding particles and sintered scaffolds containing macro- and micro-pores. The porosity values and structural parameters were determined by means of image analysis. The result showed that the porosity values, macro-pore sizes, connectivity densities and specific surface areas of the titanium scaffolds sintered at 1200 °C for 3 h did not significantly deviate from those of the green structures with various volume fractions of the space holder. Titanium scaffolds with a maximum specific surface area could be produced with an addition of 60–65 vol% carbamide particles to the matrix powder. The connectivity of pores inside the scaffold increased with rising volume fraction of the space holder. The shrinkage of the scaffolds prepared with >50 vol% carbamide space holder, occurring during sintering, was caused by the reductions of macro-pore sizes and micro-pore sizes as well as the thickness of struts. In conclusion, the final porous structural characteristics of titanium scaffolds could be estimated from those of the green body.

1. Introduction

In recent years, porous titanium has become a material of choice for scaffolds to be used in bone tissue engineering owing to its excellent biocompatibility and corrosion resistance [1–4]. As noted by Karageorgiou and Kaplan [3], the porous architecture of the scaffold plays a critical role in bone tissue regeneration. A highly porous structure with open, interconnected pores are generally required to allow the migration and proliferation of osteoblasts and mesenchymal cells, and also to stimulate vascularization in the newly formed bone tissue within the scaffold [3,5]. With the new bone tissue growing on the internal surfaces of the porous scaffold, mechanical interlocking between the implant and host bone tissue can be achieved, leading to a great stability of the implant. In addition, mismatch in elastic modulus between the implant and host bone tissue can be avoided by controlling the porosity of the scaffold and thereby implant failure due to stress shielding can be minimized [4,5].

The space holder method has been considered as one of the viable techniques for the fabrication of titanium scaffolds. With this technique, the porous structure of the titanium scaffold is generated by a space-holding powder that acts as a pore former in the titanium matrix [6–22]. Firstly, the titanium matrix powder is mixed with a pre-determined amount of space holder volume fraction to obtain a desired composition. The powder mixture is then compacted to produce a green body, i.e., a scaffold preform. Afterwards, space-holding particles are removed to generate macro-pores in the green body of the scaffold. Finally, the porous green body is sintered to achieve permanent bonding between titanium powder particles and the final form of the scaffold [4,5,23]. Despite its capability of producing highly porous metallic scaffolds, the space holder technique has not been widely accepted for the fabrication of titanium scaffolds, mainly because of its complexity. Optimization of multiple processing parameters to control the porous structure of the scaffold remains a challenge. So far, only a few studies concerning the optimization of scaffold processing conditions have been conducted [13,18,20,24–27].

Laptev et al. [13] and Tuncer et al. [20] tried to link the physical properties of the green body with those of the sintered titanium scaffolds prepared with the space holder method. By calculating the relative density, Laptev et al. noticed that the green body was densified to some extent during sintering, as indicated by an increase in the relative density of the scaffold [13]. This result was confirmed by the measured axial and radial shrinkages of the green body during sintering [13]. Owing to the irregular porous structure prepared with the space holder method, however, the work conducted by Laptev and his co-workers [13] did not reveal detailed spatial changes in the interior of the scaffold as a result of sintering. Obviously, to understand the shrinkage phenomena that occurred during the sintering of titanium scaffolds prepared with the space holder method, 3-dimensional (3D) analysis is needed.

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Tuncer et al. utilized micro-computed tomography (micro-CT) to analyze the changes of the 3D porous structure from the green body to the titanium scaffold as a result of sintering [20]. In their study, pore wall thickening and slight decreases in the sizes of macro-pores created by the space holder, accompanied by the overall shrinkage of the green body during sintering, were reported [20]. Despite the precise quantitative and qualitative analysis of the 3-dimensional (3D) porous structure of the scaffold [28], the micro-CT study conducted by Tuncer et al. [20] did not provide information on the shrinkage occurring during sintering with representative geometrical parameters, such as pore interconnection and specific surface area both of which are actually of critical importance for the explanation of the shrinkage mechanisms as well as for bone tissue regeneration inside the scaffold [28]. As mentioned earlier, pore interconnection is needed to provide access for the transport of nutrients, oxygen and metabolic waste through the scaffold as well as to facilitate cellular activities, e.g. cell migration, for the growth of new bone tissue [28,29]. Also needed is a high ratio of surface area to volume to enhance cellular attachments for bone tissue ingrowth [28].

On the basis of the understanding of the structural evolutions throughout the scaffold fabrication with the space holder method, it was hypothesized that the final porous structure of titanium scaffold product prepared with this method could be estimated from the titanium and space-holding powder arrangements in the green body. To test this hypothesis, the porous structures of both the green body and the sintered titanium scaffolds prepared with the space holder method were quantitatively characterized. Micro-CT and image analysis were performed to determine the porosity and geometrical parameters of the green body containing carbamide space-holding particles and the sintered titanium scaffolds in order to establish the mechanisms involved in the structural changes from the green body to the final scaffold products. In this connection, the water leaching process for the complete removal of the space holder material from the green body and the sintering process that resulted in shrinkage were examined.

2. Materials and Methods

2.1. Scaffold Preparation

Titanium scaffolds were prepared by mixing a spherical grade 1 titanium powder (TLS Technik, Germany) and a cubical carbamide powder (Merck, Germany) as the matrix and space holder materials, respectively. The mean and median diameters of both the powders determined from five samples by using a Mastersizer X laser diffractometer (Malvern, UK) are presented in Table 1.

The compositions of the mixtures (x) were established by using Eq. (1):

$$x = \frac{m_{sh}/\rho_{sh}}{m_m/\rho_m + m_{sh}/\rho_{sh}} \quad (1)$$

where m_m and m_{sh} are the masses of the titanium powder and carbamide space-holding particles added to the matrix, respectively, and ρ_m and ρ_{sh} are the theoretical densities of titanium (i.e., 4.5 g cm^{-3}) and carbamide (i.e., 1.32 g cm^{-3}), respectively. In this research, m_m and m_{sh} were adjusted to produce titanium scaffold preforms with $x = 40$, 50, 60, 70 and 80 vol%. Mixing of the titanium and carbamide powders was carried out with a roller mixer (CAT, Germany) operating at 80 rpm. A dry cylindrical glass bottle having an inner diameter of 40 mm and a length of 52 mm was used as the mixing container. To prevent the mixture from segregating, the titanium powder was first blended with a 6 wt% polyvinyl-alcohol (PVA) binder solution for 1 h prior to 3 h mixing with the dry carbamide powder. The binder solution was prepared by dissolving 6 wt% PVA particles (Alfa Aesar, Germany) in water at 80–90 °C.

Compaction of titanium/carbamide powder mixtures was conducted with a uniaxial powder press (Carver, USA). At this step, approximately 1.3 g powder mixture was cold-compacted in a 13 mm diameter die (Carver Inc., USA) and at uniaxial compressive pressures of 260, 220, 180, 140 and 100 MPa for preparing titanium scaffold preforms with 40, 50, 60, 70 and 80 vol% carbamide particles, respectively [26]. The removal of carbamide particles from the scaffold preforms was performed with the water leaching technique. Detailed procedures and methods for characterizing the water leaching behavior of carbamide are presented in Subsection 2.3. The porous green body was then sintered at 1200 °C for 3 h.

Table 1
Sizes of titanium and carbamide powder particles.

Particle size parameter	Titanium	Carbamide
Particle mean diameter, D_m (μm)	71.47 ± 1.47	415.62 ± 5.66
Particle diameter (50 vol% of the sample particles below this size) D_{10} (μm)	55.28 ± 1.06	285.55 ± 5.42
Particle diameter (50 vol% of the sample particles below this size, i.e., the median particle diameter), D_{50} (μm)	70.26 ± 1.29	396.94 ± 5.04
Particle diameter (90 vol% of the sample particles below this size), D_{90} (μm)	89.50 ± 2.69	573.52 ± 9.16

2.2. Characterization of Porous Structure of the Green Body and Sintered Scaffolds

3D structures of titanium scaffold preforms and sintered scaffold products were characterized by using X-ray micro-computed tomography (micro-CT) (Nanotom, Phoenix/X-rays, The Netherlands). With this technique, a set of 2-dimensional (2D) radiographs of a projected structure with carbamide particles or a projected porous scaffold with an image resolution of 10 μm were generated. A 3D model of the structure with dimensions of 2.5 × 2.5 × 2.5 mm was then constructed by cropping a stack of radiographs and analysed quantitatively by using the open-source ImageJ 1.50i software [30] with BoneJ plugin that was originally intended for the characterization of the trabecular structure of bone tissue [31].

Quantitative analysis was performed by applying auto local thresholding using the Bernsen method (radius = 30). An additional series of image processing steps were followed for the analysis of macro-pores, i.e., median filter application (with a radius of 3 pixels) and purification to eliminate micro-pores and isolated small pores in the 3D model of the scaffold.

Both ImageJ and BoneJ plugin have been used in other studies, for instance, in the investigation of bone histomorphometry [32] and the porous structures of tissue engineering scaffolds [29]. By using BoneJ, a set of structural parameters describing the characteristics of scaffold preforms or scaffolds could be determined, i.e., (i) porosity (p), which is derived from the ratio of the framework volume and the total volume of the 3D model (BV/TV); (ii) the connectivity density of the pores that are formed from the space occupied by space-holding particles ($Conn.D.$); (iii) the specific surface area of the matrix framework (SSA), which is derived from the surface area of the framework (BS) divided by the total volume of the 3D model (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 ($Th.Sp.$). All these structural parameters were determined in triplicate and plotted against the volume fraction of the carbamide space holder embedded in the titanium matrix.

Observation of the morphologies of macro- and micro-pores in the titanium scaffold was carried out by using a JSM-6500F field emission scanning electron microscope (JEOL, Japan). Prior to the characterization, the sample was first ground to expose the interior of the scaffold and cleaned by sonication for 5 min in ethanol.