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Manufacturing of graded titanium scaffolds using a novel space holder technique

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ABSTRACT

To optimize both the mechanical and biological properties of titanium for biomedical implants, a highly flexible powder metallurgy approach is proposed to generate porous scaffolds with graded porosities and pore sizes. Sugar pellets acting as space holders were compacted with titanium powder and then removed by dissolution in water before sintering. The morphology, pore structure, porosity and pore interconnectivity were observed by optical microscopy and SEM. The results show that the porous titanium has porosity levels and pore size gradients consistent with their design with gradual and smooth transitions at the interfaces between regions of differing porosities and/or pore sizes. Meanwhile, the porous titanium has high interconnectivity between pores and highly spherical pore shapes. In this article we show that this powder metallurgy processing technique, employing the novel sugar pellets as space-holders, can generate porous titanium foams with well-controlled graded porosities and pore sizes. This method has excellent potential for producing porous titanium structures for hard tissue engineering applications.

1. Introduction

The development of implants for hard tissue engineering such as replacement of bone, teeth and joints is highly desired and has shown enormous success in orthopaedic surgery. Porous synthetic scaffolds are a highly promising new approach to repair and remodel damaged bone tissue, replacing techniques using autografts (bone harvested from patient) or allografts (donor bone) [1,2] as this technique can eliminate the potential disease transmission from donor to recipient through autogenous bone grafts [3]. Titanium and some of its alloys are considered to be the most attractive metallic materials for biomedical applications [4] due to their relatively low modulus, excellent strength-to-weight ratio, superior biocompatibility and corrosion resistance [5,6].

Solid titanium and its alloys currently used in biomedical implant applications have shown some limitations, such as lack of osseointegration [7] and mismatch between the mechanical properties of the bone and the implant [8]. Porous titanium structures have the potential to address these issues by providing a scaffold for bone cell ingrowth [9] and by more closely matching the mechanical properties of bone to alleviate stress-shielding effects [10]. However, structures with uniform porosity cannot satisfy all of the mechanical and biological requirements for implants due to their lack of flexibility in tailoring their mechanical behaviors, biocompatibility and osseointegration to that of the bone. More suitable designs could include porosity gradients to mimic that of the human bone, from a dense, stiff external structure (the cortical bone) to a porous internal one (the cancellous bone) with an appropriate degree of pore interconnectivity [11]. Wen et al. [12] developed titanium structures with porosity gradients with a solid core and highly porous outer shell using powder metallurgy technique. Thieme et al. [13] successfully manufactured titanium specimens using same method with graded porosities which matched the designed

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moduli. Titanium structures with graded porosities can be produced by various processes such as pressure filtration, solid free-form fabrication, multiple tape casting, etc. However, using these methods it is difficult to control pore interconnectivity and pore sizes [11].

In this study, a powder metallurgical process using sugar pellets as space holders is explored for the fabrication of graded porous titanium scaffolds with flexible porosity and pore size gradients. We demonstrated that titanium scaffolds can be manufactured with the predesigned graded porosities and pore sizes, while maintaining high levels of interconnectivity and spherical pore shapes for biomedical applications.

2. Materials and methodology

Titanium hydride-dehydride powder (>99.9% purity) with particle size of approximately 45 μm was used as a base powder due to its high sinterability. Spherical sugar pellets, (supplied by JF-Pharmaland Technology Development Co., Ltd, China) were used as the space holder. Three pellet size distributions, namely 0.212–0.355 mm, 0.3–0.425 mm and 0.425–0.5 mm, were chosen to generate porosity gradients in the compacts. Spherical pellets sized were chosen according to Loh et al.'s [14] review on the pore size and biocompatibility. Two different structures with gradient porosities were chosen to demonstrate the powder metallurgical process (as shown in Fig. 1).

With the help of a temporary mould to maintain shape during die filling, gradient structures were created as illustrated in Fig. 1(C). After removal of the mould, the sample was pressed at 400 MPa to acquire cylindrical green compacts of 15 mm in diameter and 10 mm in height. High compaction pressure of 400 MPa was employed to eliminate sample deformation during dissolution of the sugar pellet space holder. The space holder was dissolved by distilled water at temperatures of 70–80 °C with constant stirring using a magnetic stirrer. The dissolution time was 4 h and the water was changed twice to ensure thorough removal of the sugar pellets from the green compacts. Samples were then dried in an oven at 90 °C for 2 h. Sintering was carried out in a high vacuum furnace at 1300 °C for 2 h at a vacuum pressure of 10^{-5} Torr. In order to prevent contamination, all samples were placed on an Al_2O_3 ceramic disc for sintering. Samples were sectioned and polished for analysis of microstructure and surface morphologies. The porous structure and interconnectivity were evaluated by optical microscopy and SEM. The density and porosity of the sintered compacts was determined by the Archimedes method with oil impregnation. H-Galden ZT-180 was used instead of water to give more accurate results. The density of the sintered sample ρ and porosity $\boldsymbol{P_{Open}}$, were calculated using:

$$\boldsymbol{\rho = \frac{\rho_{HG} \times W_{Air}}{W_{Oil} - W_{HG}}} \tag{1}$$

$$\boldsymbol{P_{Open} = \frac{\rho_{HG}(W_{Oil} - W_{Air})}{\rho_{Oil}(W_{Oil} - W_{HG})}} \times 100 \tag{2}$$

where ρ_{HG} is the density of the H-Galden (1.69 g/mL at 21 °C), $\rho_{Oil}$is the density of the oil used (KS7470, density 0.885 g/mL), $W_{Air}$is the dry weight of the compact, $W_{Oil}$is the weight of the compact after oil infiltration, and $W_{HG}$is the weight of the oil infiltrated compact measured while immersed in H-Galden. The mechanical properties of the porous structures were measured with an Instron 5584 test machine. The properties are listed in Table 1. The elements of the specimen was determined with inductively coupled plasma optical emission spectrometry (ICP-OES), using Spectro-Arcos equipment. Carbon content was determined by carrier gas hot extraction using a LECO CS600 gas analyzer (see Table 2).

3. Results and discussion

Porous titanium foam with porosity gradients and high integrity were achieved, as shown in Fig. 2. Sintered compacts were sectioned in half to reveal the interior of the porous structures. The sintered compacts exhibit mechanically stable edges and surface, with little deformation and no degradation evident during the sugar pellet dissolution and sintering process. The interior porous structure of the sintered samples is presented in Fig. 3, as obtained by optical microscopy. Pore morphology and size can be clearly observed from the image. The space-holding particles have been completely removed. ICP-OES results showed that the residual carbon is only 0.01 wt%.

Image J was used to analyse the pore geometry after sintering. The sugar pellet space holders produced well-defined pore sizes which are reasonably spherical and uniform in shape. The porosity and pore size changes which are consistent with the predesigned models can be clearly observed and the transitions between regions of differing porosities are smooth with no traces of cracking. It is noted that slight deformation of the long cylindrical sample in Fig. 2(a) is observed due to the compact-and-sinter process. Higher compaction pressure would reduce the deformation.

Fig. 4 shows the SEM images of the pore structures and the interface between regions of differing porosities with a gradient of porosity. As shown in Fig. 4(a), the pores created by the sugar pellets are highly spherical and uniform in shape. Fig. 4(b) shows there is a high degree of interconnectivity between pores and that the pores have a relatively rough inner surface associated with the morphology of the sugar pellet space holders, especially at the interconnections. This rough surface is expected to increase the adhesion-attachment rate of cells for bone ingrowth [9]. Sugar pellets, which are comprised of sugar and starch, are materials considered to be very safe in the human body. After sintering, any residue from the space-holding materials will break down into carbon or form TiC particles which are considered harmless to human tissue [16]. However, it may influence the mechanical properties of the scaffolds. Inductively coupled plasma optical emission spectrometry (ICP-OES) results show that the residual C is only 0.01 wt%. Further studies are necessary to understand their influence on the properties and performance of the porous foam structures (see Fig. 5).

The main goal in the design and fabrication of an orthopaedic scaffold is to restore the function of the native tissue that is to be replaced. The ideal implant should be biocompatible, possess adequate mechanical properties to support the applied physiological load, be corrosion/wear resistant and finally show good bioactivity to ensure sufficient bonding at the material/bone interface. The manufacturing route demonstrated in this paper has been shown to produce porous titanium structures with highly spherical pore shapes, well-controlled pore size and porosity, and high interconnectivity [17]. The porous titanium scaffolds have excellent potential for hard tissue engineering applications. This powder metallurgical process using a sugar pellet as space holders can be used to fabricate graded porous structures that can facilitate bone ingrowth and effectively enable variation of the Young's modulus across the structures [18]. The elastic moduli of the porous samples is 18.5, 16.4 and 12.1 GPa for 30%, 40% and 50% porosity, respectively. This is consistent with the characteristics of natural bone, which typically has a stiffness of 0.1–20 GPa [1]. The yield strengths of the scaffolds, are 89.8, 176.5 and 202.3 GPa respectively, and with the exception of the one with 50% designed porosity, are superior to that of natural bone (130–180 MPa) [4]. In this regard, as the porosity and pore size can be well-controlled, we have planned FEM simulations to optimize the structural design to maximize the interaction between the implant and the surrounding bone. The techniques outlined in this work offer a stepwise improvement over other

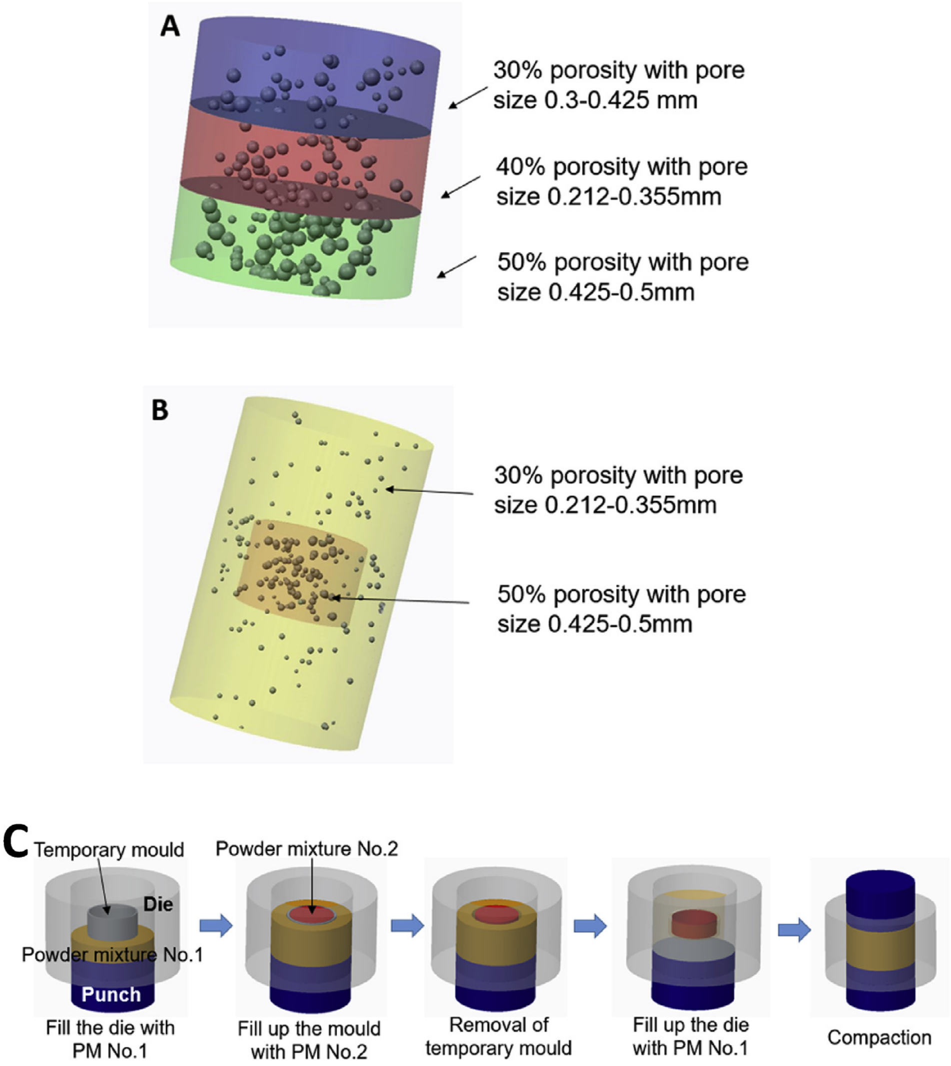

Fig. 1. Schematic of designed structures with porosity gradients: (A) a structure with three layers of different porosities, (b) a structure with differing interior porosity, and (C) the process of generate porosity gradient using temporary mould. PM No.1 and PM No.2 are two different kind of titanium and sugar pellets mixture to create gradients. For instance, 30% sugar pellets mixture with pore size 0.212–0.355 mm and 50% sugar pellets mixture with pore size 0.425–0.5 mm as shown in (b).

Table 1
Sintered titanium scaffold properties using sugar pellets as space holder.

Designed porosity using sugar pellets, %	30	40	50
Open porosity (%)	2.23	7.77	11.32
Open to total porosity ratio [15] (%)	11.09	28.79	35.52
Density (g/cm^3)	3.60	3.29	3.07
Elastic Modulus (E), (GPa)	18.5	16.4	12.1
Yield strength (σ_y), (GPa)	89.8	176.5	202.3

powder metallurgy based methods [12], which do not offer the same degree of control of the porosity, pore size and interconnectivity between pores. Thieme et al. reported a silicon-assisted liquid-phase sintering (LPS) to fabricate porous titanium structures with elastic modulus matching the targeted modulus of design, but the biocompatibility of these materials is still questionable and the pore sizes are too small to allow full growth of Harversian units [13]. The precise control of pore size and flexibility in pore gradients demonstrated in the present study can overcome the constraints imposed by the other fabrication methods as well as remove the requirement for surface coating/roughening processes [9] currently used to encourage material/bone bonding.

Powder sintering, employing spherical pharmaceutical sugar pellets as a new form of space holder material, has been shown to be an ideal processing technique as it allows customization of material properties and production of net or near-net shape components. It also allows easily adjustment of porosities, pore sizes and levels of interconnectivity between pores.

Table 2
Chemical analysis of the titanium powder and manufactured scaffold.

ICP-OES/LECO	Ti	C[b]	O[b]	N[b]
Titanium powder (wt%)	Balanced	<0.01	0.12	0.02
Scaffold with 50% porosity (wt%)	Balanced	0.01	0.27	0.30

[a] Analyzed by inductively coupled plasma optical emission spectroscopy (ICP-OES).
[b] Analyzed by a carrier gas hot extraction gas analyzer.

4. Conclusions

Porous titanium structures with graded porosity and varying pore sizes have been manufactured by powder metallurgy using sugar pellets as a space holder. It was demonstrated that pore sizes,

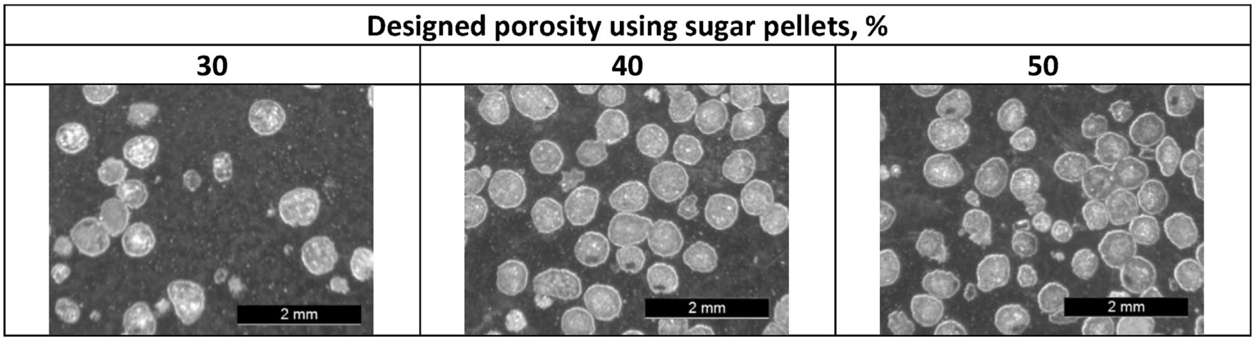

Fig. 2. Morphology of the porous structure.

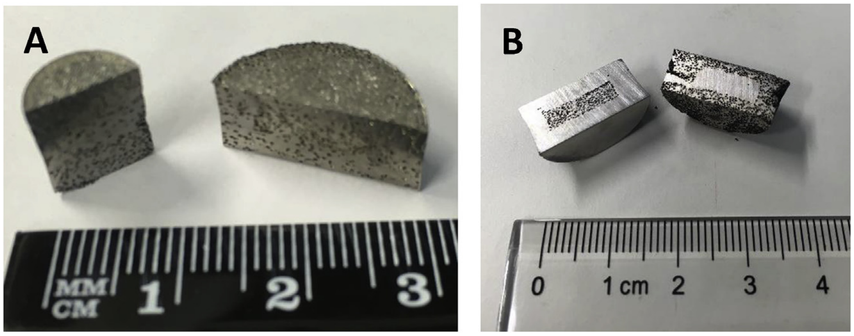

Fig. 3. Sintered titanium foam structures: (A) a porous structure with layers of differing porosities, and (B) porous structures with a solid shell/internal porosity and solid interior/porous shell.

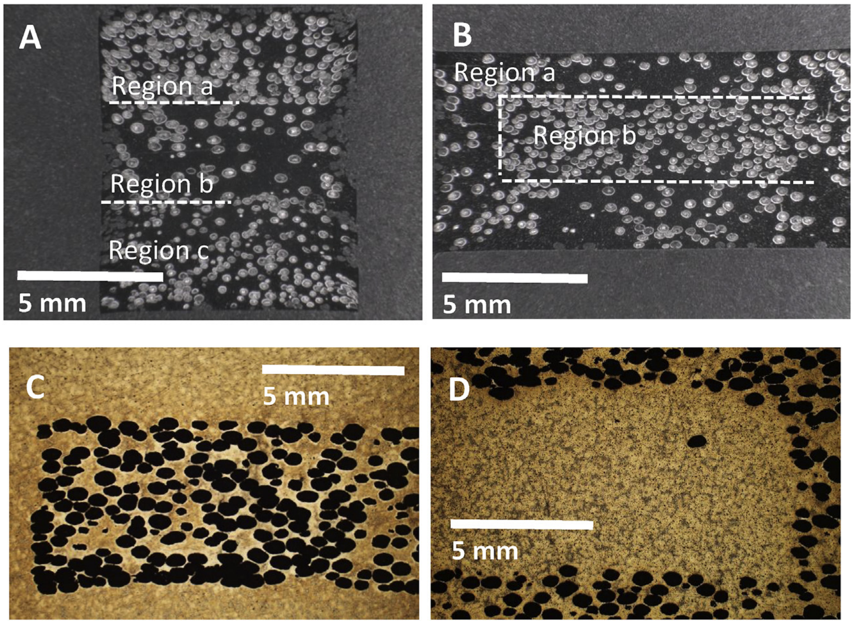

Fig. 4. Interface between regions of different porosities: (A) interfaces of regions with 60% porosity (0.3–0.425 mm pore size) (region a), 40% porosity (0.425–0.5 mm pore size) (region b) and 50% porosity (0.212–0.355 mm Pore size) (region c), (B) interface between regions with 40% porosity (0.425–0.5 mm pore size) (region a) and 60% porosity (0.3–0.425 mm) (region b), (C) interface between solid shell and porous interior with 50% porosity (0.3–0.425 mm pore size, and (D) interface between porous shell with 50% porosity (0.3–0.425 mm pore size) and solid core.

porosities and porosity gradients can be effectively controlled by varying the sugar pellets sizes, volume fractions and pressing order. The sintered titanium scaffolds with graded porosities have the potential to deliver optimized mechanical properties with excellent biocompatibility for hard tissue engineering applications. The techniques developed are highly flexible and can be applied to the manufacture of porous structures with varying porosities, pore sizes and geometries.

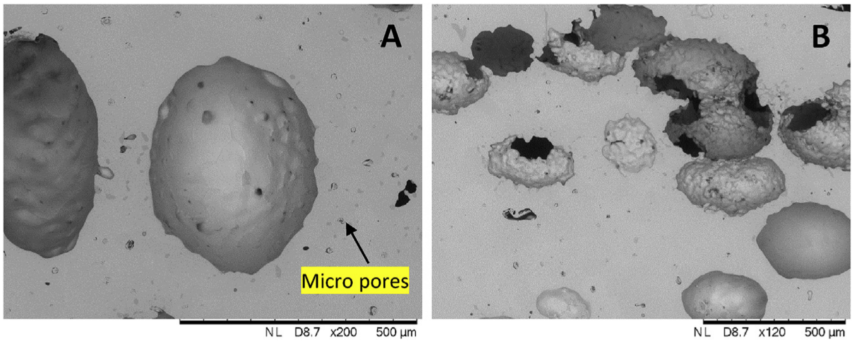

Fig. 5. SEM images of the porous titanium: (A) morphology of pores, including micro pores, (B) interconnectivity between pores.

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References

[1] P. Lichte, H.C. Pape, T. Pufe, P. Kobbe, H. Fischer, Scaffolds for bone healing: concepts, materials and evidence, Injury 42 (2011) 569–573, http://dx.doi.org/10.1016/j.injury.2011.03.033.
[2] S. Bose, M. Roy, A. Bandyopadhyay, Recent advances in bone tissue engineering scaffolds, Trends Biotechnol. 30 (2012) 546–554, http://dx.doi.org/10.1016/j.tibtech.2012.07.005.
[3] C. Myeroff, M. Archdeacon, Autogenous bone graft: donor sites and techniques, J. Bone Jt. Surg. Am. 93 (2011) 2227–2236, http://dx.doi.org/10.2106/JBJS.J.01513.
[4] C.N. Elias, J.H.C. Lima, R. Valiev, M.A. Meyers, Biomedical applications of titanium and its alloys, J. Min. Met. Mater. Soc. (2008) 46–49, http://dx.doi.org/10.1007/s11837-008-0031-1.
[5] Y. Li, C. Yang, H. Zhao, S. Qu, X. Li, Y. Li, New developments of ti-based alloys for biomedical applications, Mater. (Basel) 7 (2014) 1709–1800, http://dx.doi.org/10.3390/ma7031709.
[6] V.S. De Viteri, E. Fuentes, Titanium and titanium alloys as biomaterials chapter, Tribol. - Fundam. Adv. (2013) 155–182, http://dx.doi.org/10.5772/3427.
[7] J. Gallo, J. Vaculova, S.B. Goodman, Y.T. Konttinen, J.P. Thyssen, Contributions of human tissue analysis to understanding the mechanisms of loosening and osteolysis in total hip replacement, Acta Biomater. 10 (2014) 2354–2366, http://dx.doi.org/10.1016/j.actbio.2014.02.003.
[8] V. Goriainov, R. Cook, J.M. Latham, D.G. Dunlop, R.O.C. Oreffo, Bone and metal: an orthopaedic perspective on osseointegration of metals, Acta Biomater. 10 (2014) 4043–4057, http://dx.doi.org/10.1016/j.actbio.2014.06.004.
[9] S.K. Nishimoto, M. Nishimoto, S.-W. Park, K.-M. Lee, H.-S. Kim, J.-T. Koh, et al., The effect of titanium surface roughening on protein absorption, cell attachment, and cell spreading, Int. J. Oral Maxillofac. Implants 23 (2007) 675–680. http://www.ncbi.nlm.nih.gov/pubmed/18807564.
[10] B. Dabrowski, W. Swieszkowski, D. Godlinski, K.J. Kurzydlowski, Highly porous titanium scaffolds for orthopaedic applications, J. Biomed. Mater. Res. - Part B Appl. Biomater. 95 (2010) 53–61, http://dx.doi.org/10.1002/jbm.b.31682.
[11] X. Miao, D. Sun, Graded/gradient porous biomaterials, Mater. (Basel) 3 (2009) 26–47, http://dx.doi.org/10.3390/ma3010026.
[12] C.E. Wen, Y. Yamada, A. Nouri, P. Hodgson, Porous titanium with porosity gradients for biomedical applications, Mater. Sci. Forum 539–543 (2007) 720–725, http://dx.doi.org/10.4028/www.scientific.net/MSF.539-543.720.
[13] M. Thieme, K.P. Wieters, F. Bergner, D. Scharnweber, H. Worch, J. Ndop, et al., Titanium powder sintering for preparation of a porous functionally graded material destined for orthopaedic implants, J. Mater. Sci. Mater. Med. 12 (2001) 225–231, http://dx.doi.org/10.1023/A:1008958914818.
[14] Q.L. Loh, C. Choong, Three-dimensional scaffolds for tissue engineering applications: role of porosity and pore size, Tissue Eng. Part B. Rev. 19 (2013) 485–502, http://dx.doi.org/10.1089/ten.TEB.2012.0437.
[15] M.P. Albano, L.B. Garrido, K. Plucknett, L.A. Genova, Processing of porous yttria-stabilized zirconia tapes: influence of starch content and sintering temperature, Ceram. Int. 35 (2009) 1783–1791, http://dx.doi.org/10.1016/j.ceramint.2008.10.003.
[16] Y. Cheng, Y.F. Zheng, Characterization of TiN, TiC and TiCN Coatings on Ti–50.6 at.% Ni Alloy Deposited by PIII and Deposition Technique, 2006, http://dx.doi.org/10.1016/j.surfcoat.2006.07.216.
[17] Y. Chen, D. Kent, M. Bermingham, A. Dehghan-Manshadi, M. Dargusch, Manufacturing of biocompatible porous titanium scaffolds using a novel spherical sugar pellet space holder, Mater. Lett. 195 (2017) 92–95, http://dx.doi.org/10.1016/j.matlet.2017.02.092.
[18] N. Tuncer, G. Arslan, E. Maire, L. Salvo, Investigation of spacer size effect on architecture and mechanical properties of porous titanium, Mater. Sci. Eng. A 530 (2011) 633–642, http://dx.doi.org/10.1016/j.msea.2011.10.036.