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The influence of sintering conditions on microstructure and mechanical properties of titanium dioxide scaffolds for the treatment of bone tissue defects

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In this study the attempts to improve mechanical properties of highly-porous titanium dioxide scaffolds produced by polymer sponge replication method were investigated. Particularly the effect of two-step sintering at different temperatures on microstructure and mechanical properties (compression test) of the scaffolds were analysed. To this end microcomputed tomography and scanning electron microscopy were used as analytical methods. Our experiments showed that the most appropriate conditions of manufacturing were when the scaffolds were heat-treated at 1500 °C for 1 h followed by sintering at 1200 °C for 20 h. Such scaffolds exhibited the highest compressive strength which was correlated with the highest linear density and the lowest size of grains. Moreover, grain size distribution was narrower with predominating fraction of fine grains 10–20 μm in size. Smaller grains and higher linear density suggested that in this case densification process prevailed over undesirable process of grain coarsening, which finally resulted in improved mechanical properties of the scaffolds.

Key words: *ceramic scaffolds, porosity, titanium dioxide, bone tissue engineering, mechanical properties, polymer sponge replication*

1. Introduction

One of the most pressing issues in modern medicine is treatment of bone defects caused by various diseases or injuries. Although bones have a very good regenerative potential, extensive defects often require a supporting structure for their healing process [1]. There are several methods for the treatment of bone defects: autografts, allografts, application of demineralized bone matrix, bone morphogenetic proteins and stem cells [2]. Although transplanting human tissues seems to be a very good solution, there is a serious risk of immunogenicity or disease transmission when allografts are applied. Use of autografts may be harmful to the patient and may cause infection around donor place. On the other hand, therapy with stem cells or growth factors is much more complex and requires further investigation [3], [4]. Therefore, there is a growing interest in manufacturing porous implants for bone tissue regeneration.

Ceramic materials can be processed into porous scaffolds whose morphology, mechanical parameters and chemical composition resemble those of mineral part in bone tissue [5]. Bioactive materials like hydroxyapatite (HAp) or resorbable tricalcium phos-

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phate (TCP) are often used for scaffold manufacturing [4], [6]. Nowadays, researchers turned their attention also to titanium dioxide (TiO_2). It is a biocompatible and non-resorbable material that has the ability to directly bond to bone tissue [7]–[9].

An ideal ceramic scaffold for bone defect treatment should be biocompatible and it should bind directly to the bone (non-degradable implant) or be replaced by a new bone tissue (degradable implant). In terms of microstructure it should be highly porous, with open porosity and pore size greater than 100 μm, preferably 300–400 μm, otherwise vascular tissue cannot grow into the scaffold [4], [10], [11]. Another important parameter is a high interconnectivity which enables cells migration into the implant [5], [12], [13]. On the other hand, scaffolds should withstand loads carried by bones or inflicted by implantation procedure. Combining good mechanical properties with high porosity for ceramic scaffolds is a difficult challenge due to the presence of pores and defects which cause stress concentration. One way to achieve this is to design such a microstructure that will assure the most appropriate mechanical properties (e.g. highest compressive strength, fracture toughness) by reducing its grain size [14]–[16].

Many years of practise in manufacturing ceramics proved that microstructure, particularly grain size and its homogeneity, strongly depends on sintering conditions – temperature, time and pressure [17]. As porous scaffolds cannot be sintered under the increased pressure, the easiest way to control grain growth is to apply different temperatures and time regimes. Long sintering time and high temperature provide good consolidation and densification, but also lead to coarsening and excessive grain growth and consequently to decrease in mechanical strength [18], [19]. From the economic point of view prolonged heat-treatment conditions are also disadvantageous. It is not possible to minimize temperature during the whole process of sintering, but instead of one-step sintering, a two-step procedure can be used [20], [21]. The first – higher temperature step, supplies energy to initiate neck growth and consolidation of the powder, while the second – less energetic step allows densification of material progress and prevents abnormal grain growth [15], [21], [22].

The aim of this study was to manufacture titanium dioxide scaffolds using the polymer sponge replication method in various two-step sintering conditions. Two different temperatures were applied in the first step and two in the second step of a two-step sintering procedure and microstructure (scanning electron microscopy (SEM) and micro-computed tomography (μCT)) as well as mechanical properties of the scaffolds were assessed. Additionally, a statistical analysis was performed in order to find a correlation between microstructure parameters and compressive strength of TiO_2 scaffolds.

2. Materials and methods

2.1. Materials

TiO_2 powder (Kronos 1171, Kronos Titan GmbH, Leverkusen, Germany), polyurethane foams (60 ppi, Bulbren S Eurofoam GmbH, Wiesbaden, Germany), sodium hydroxide (1 M NaOH) and hydrochloric acid (0.1 M HCl and 1 M HCl; POCh, Gliwice, Poland) were used in the experiments.

2.2. Sample preparation

TiO_2 porous scaffolds were manufactured by the polymer sponge replication method. Cylindrical polyurethane sponges (12 mm both in height and in diameter) were cut, cleaned with detergent, washed in UHQ-water (produced in PS PureLab system), then dried for 48 h.

TiO_2 powder (350 g) was soaked in 400 ml 1 M NaOH and then washed 6 times in UHQ-water. The powder was later rinsed with 550 ml of 0.1M HCl and again washed with UHQ-water (until pH between 3.4 and 3.5 was achieved). Excess water was removed, TiO_2 paste was spread on filter paper and dried for 24 h at 37 °C. Then it was broken into small pieces and sieved in order to collect particles <100 μm.

The ceramic slurry was prepared by gradual addition of 65 g cleaned TiO_2 powder to 25 ml of UHQ-water. TiO_2 powder was mixed with UHQ-water at 1000 rpm speed (Digital Programmable Omni Macro ES Homogenizer, Omni International, United States of America). First, approximately one-half of 65 g of the powder was added and stirred for 10 min. Afterwards the rest of the powder was added thereto and stirred for 15 min. To avoid the problem of the particle aggregation and to control the viscosity, the pH of the slurry was kept below 1.5 throughout the stirring by adding small portions of 1 M HCl (total volume of 2 ml). Stirring was continued for 2.5 h at a speed of 5000 rpm and the temperature of the slurry was kept at 15 °C.

Polyurethane sponges were coated with titanium dioxide by thorough immersion in the slurry. Excess slurry was removed by squeezing the sponges between two sheets of polyurethane foam. This is a very important stage of manufacturing process as it is essential to ensure that only a thin layer of slurry evenly covers the entire surface of the polymer sponge without any pore blockage.

The samples were placed on a ceramic plate and allowed to dry at room temperature for 24 h. Removal of the polymer material was performed by burn-out procedure. The samples were heated at a rate of 0.5 °C/min up to 450 °C and kept at that temperature for 1 h. Then they were cooled at a rate of 5 °C/min and submitted to two-step sintering. Four different batches were sintered: the first step of sintering was performed for 1 h at 1500 °C or 1600 °C, while the second step for 20 h at 1100 °C or 1200 °C. Heating rate was 3 °C/min. The scaffolds were cooled down at a rate of 5 °C/min.

2.3. Scanning electron microscopy (SEM)

Observation of the microstructure of the cross-section of the scaffolds produced was carried out using scanning electron microscope (SEM, Nova Nano SEM 200, FEI Company Europe, acceleration voltage 18 kV). Before the examination the samples were sputtered with carbon layer and imaged at 350× and 1000× magnifications.

The measurements of the grain diameters were performed with the use of ImageJ software (Broken Symmetry Software). For size determination 1000-fold magnification images of flat surfaces of the scaffolds were used. Final diameter was estimated as an average of two perpendicular grain diameters. For each batch 80 grains were evaluated.

2.4. Micro-computed tomography (μCT)

The TiO_2 scaffolds (10 samples from each batch) were placed upright on a holder and scanned using the imaging system 1172 micro-CT (Skyscan, Kontlich, Belgium). The study was conducted with a resolution of 6 μm/voxel, 100 kV accelerating voltage, 100 μA current, with 0.5 mm aluminium filter. The samples were rotated by 180° about the vertical axis, performing three images every 0.4° of rotation. Images of the samples were then reconstructed using the software SkyScan (NRecon). Imaging analysis of the reconstructed axial bitmap was performed using the standard SkyScan software (CTAN and CTvol). In order to avoid potential defects at the boundary sample analysis area was narrowed to a cylinder (5 mm in diameter and 2.5 mm in height) selected in the centre of the sample. It was assumed that the samples were homogenous throughout the entire volume, therefore reducing the volume of interest (VOI) should not have a significant impact on the results of the scan of the entire sample.

Micro-CT reconstructions allowed the calculation of microstructural parameters such as porosity, surface area-to-volume ratio, pore size, strut thickness, structure linear density, degree of anisotropy and the fractal dimension.

2.5. Compressive strength

The mechanical compression test of the same samples, previously submitted to μCT, was conducted in order to measure the compressive strength of the scaffolds prepared (ZwickRoell, Ulm, Germany) in accordance with DIN EN ISO 3386, at room temperature, using a pressure sensor in a range of 0–1 kN. The initial load was 0.5 N and the speed of displacement of the head was 100 mm/min until failure.

2.6. Statistics

For comparison of different data groups, a one-way analysis of variance (one-way ANOVA) test was performed followed by Tuckey's post hoc test. Normality assumption and equal variance were verified by setting the p-value to 0.05 using the Shapiro–Wilk and Levene median tests, respectively. A correlation study between mechanical strength and microstructure parameters (obtained from μCT reconstructions) was performed with a bivariate regression analysis, Spearman Rank Order correlation, using the computer software SigmaStat version 3.5 (Symantec, St. Louis, USA). The results were interpreted as follows: low correlation, if $0.1 < |y| < 0.3$, the average correlation if $0.3 < |y| < 0.5$ and the high correlation if $0.5 < |y| < 1$. When R values are less than zero, there is a negative correlation, while greater than zero – a positive correlation. Unless stated otherwise the

results were presented as mean ± standard deviation (SD).

3. Results

The polyurethane sponge, template coated with the slurry and the final product – sintered scaffold are presented in Fig. 1. The decrease in volume of the sintered scaffolds was clearly visible. Both heights and diameters of all samples were measured before and after sintering and percentage shrinkage was calculated (Table 1). There was no significant difference between shrinkage of the samples treated at different temperatures.

Table 1. Shrinkage after sintering and compressive strength of TiO_2 scaffolds

Scaffolds batch number	Sintering temperatures 1st step/2nd step	Shrinkage [%]	Compressive strength [MPa]
1	1500 °C/ 1100 °C	22.83 ± 0.29	0.67 ± 0.09^{ns}
2	1500 °C/ 1200 °C	22.54 ± 0.41	$0.69 \pm 0.04^{3,4}$
3	1600 °C/ 1100 °C	23.10 ± 0.31	0.52 ± 0.09^{2}
4	1600 °C/ 1200 °C	23.13 ± 0.39	0.51 ± 0.03^{2}

* Statistical significance $p < 0.05$ according to one-way ANOVA in comparison with a certain experimental group of scaffolds is indicated by the number of that group in the superscript, ^{ns} – not significant, mean ± SD.

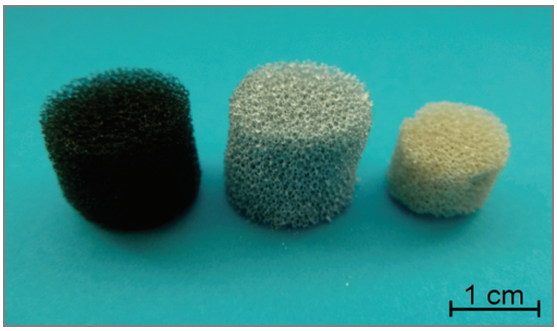

Fig. 1. Samples at different manufacturing stages: polyurethane template (left), template coated with TiO_2 slurry (centre) and scaffold after sintering (right)

Mechanical test results are shown in Table 1. The compressive strength of the TiO_2 scaffolds was found to range from 0.51 MPa to 0.69 MPa. The samples sintered at 1500 °C during the first step and at 1200 °C during the second step had significantly higher compressive strength than both samples sintered at 1600 °C.

The μCT and SEM examinations were employed to visualise microstructure of manufactured scaffolds. 3D visualisations of the scaffolds are shown in Figs. 2A–D, followed by SEM images of their cross-sections at 350× (Fig. 2E–H). The pictures show that the samples were highly porous with circular and oval pores of 400 μm in size, and their microstructure was very similar to that of natural cancellous bone. There was very little blockage of the pores, so the polymer template was well replicated.

Figures 2I–L show cross-sections of the struts at 1000× magnification, where it is possible to observe triangular voids resulting from the burn-out of polyurethane foam. In the pictures recorded at this magnification the grains are clearly visible.

Figures 2 M–P show grain diameters histograms of each type of the scaffolds. Based on them it can be concluded that the samples sintered in the first step at 1500 °C have smaller and more homogenous grain distribution than the samples sintered at 1600 °C. For those batches grain size distribution (Fig. 2 M, N) was fairly narrow with a dominance of grains between 10 and 20 μm, and oversize grains occurred rarely. In the batches sintered at 1600 °C (Figs. 2 O, P) grain size distribution was shifted towards larger grains (>40 μm).

Additionally, μCT reconstructions were used to determine parameters characterising the morphology and architecture of the scaffolds produced (Table 2). All the scaffolds had the same porosity (around 90%) and pore size (around 400 μm); no significant differences were found according to ANOVA. The other parameters, e.g., surface area-to-volume, strut thickness, degree of anisotropy and fractal dimension of the struts did not differ either. In order to evaluate the correlations between the parameters of the scaffold microstructure and compressive strength calculations using the Spearman rank correlation coefficient were performed (Table 2, last column). Strong correlation was found between compressive strength and: porosity (negative correlation), intersection surface, linear density and fractal dimension (positive correlations). Medium correlation was found between compressive strength and surface area-to-volume ratio (negative correlation) and strut thickness (positive correlation).

Figure 3 shows a relationship between grain size and compressive strength of the scaffolds. It can be found that the scaffolds sintered at 1500 °C during the first step have much smaller grains and exhibited higher compressive strength than those sintered at 1600 °C.

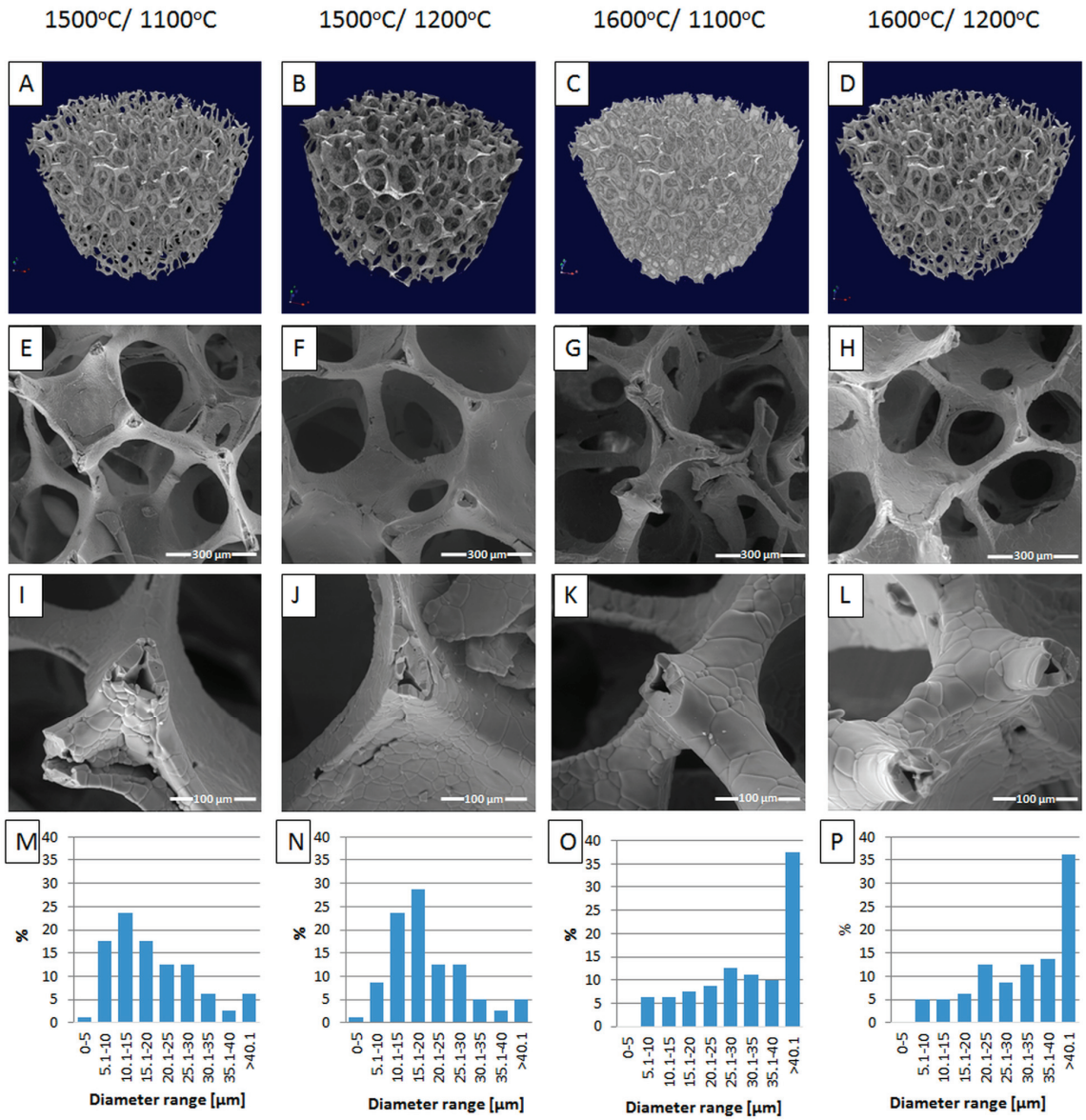

Fig. 2. Micro-CT models (A–D), SEM images (E–I) at magnification 350× (E–H) and 1000× (I–L) and histograms presenting size of the grains (M–P) of TiO_2 samples sintered at different temperatures: 1500 °C/1100 °C (A, E, I, M), 1500 °C/1200 °C (B, F, J, N), 1600 °C/1100 °C (C, G, K, O) and 1600 °C/1200 °C (D, H, L, P)

Table 2. Structural parameters of TiO_2 scaffolds and correlation between them and compressive strength, mean ± SD; * $p < 0.05$, ** $p < 0.01$

Parameter	Unit	1500 °C/1100 °C	1500 °C/1200 °C	1600 °C/1100 °C	1600 °C/1200 °C	Spearman correlation
Porosity	%	89.9 ± 0.5	89.1 ± 0.3	90.0 ± 0.4	89.3 ± 0.7	–0.67**
Pore size	µm	432 ± 5	428 ± 5	434 ± 4	411 ± 11	–0.21
Intersection surface	mm^2	7.4 ± 0.4	7.7 ± 0.3	7.2 ± 0.4	8.0 ± 0.5	0.61**
Surface-area to volume ratio	1/mm	65.4 ± 1.3	63.3 ± 1.5	62.8 ± 1.3	64.4 ± 1.2	–0.47**
Strut thickness	µm	49.7 ± 1.0	51.9 ± 0.9	52.1 ± 1.4	53.1 ± 1.1	0.38*
Linear density	1/mm	2.00 ± 0.06	2.07 ± 0.04	1.89 ± 0.04	1.99 ± 0.09	0.79**
Degree of anisotropy		1.36 ± 0.02	1.37 ± 0.03	1.34 ± 0.02	1.41 ± 0.02	0
Fractal dimension		2.40 ± 0.01	2.42 ± 0.01	2.40 ± 0.01	2.41 ± 0.01	0.7**

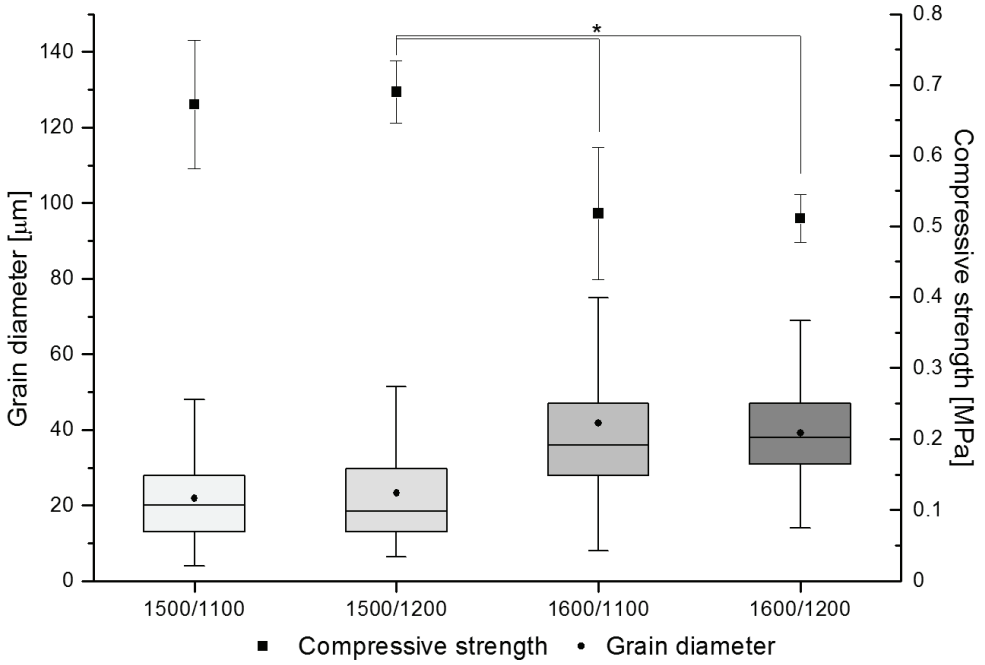

Fig. 3. Merged graph presenting grain size and compressive strength of the scaffolds sintered at different conditions. Data of grain size are presented as box and whiskers plot featuring median, interquartile range and minimum/maximum; mean values are presented as dots. Data of compressive strength are presented as mean ± SD, * $p < 0.05$ according to one-way ANOVA

4. Discussion

This study demonstrates that polymer sponge replication method is a very effective technique for manufacturing highly porous TiO_2 scaffolds for bone tissue engineering. Polyurethane template was pyrolised during the burn-out, leaving well preserved ceramic structure. After two-step sintering it was possible to obtain the scaffolds with porosity of about 90% and the size of pores of about 400 μm. Such microstructure parameters were similar to those of the scaffolds sintered previously by one-step procedure at 1500 °C for 20 h [23]. The experiments performed on mini pigs revealed that the aforementioned scaffolds were found to provide a favourable microenvironment for bone in growth [7]. This is in accordance with other literature findings that the morphology and size of the pores are the key factors influencing cellular growth and tissue regeneration. If the pores are too small, the cells cannot penetrate the scaffold, as well as nutrients and metabolites and finally vascularization is hindered. Pores with the pore size greater than 300 μm are considered optimal for cell in growth [12], [24]. Therefore, we may hypothesise that our scaffolds obtained in two-step procedure, at least from the microstructure point of view, will also be appropriate for bone tissue engineering applications.

The compressive strength of the scaffolds described in this study was found in the range from 0.51 to 0.69 MPa and was at the lower limit of the strength of healthy human trabecular bone. For example, compressive strength of trabecular bone originating from human mandible has been reported to be in the range from 0.2 to 10 MPa [25]. It was also similar to the value of TiO_2 scaffolds reported in the previous study obtained by one-step sintering at 1500 °C for 20 h [26]. In our case the strongest correlation was found between compressive strength and porosity (negative correlation) as well as compressive strength and linear density (positive correlation) of the scaffolds produced.

Our experiments showed that the most appropriate conditions of manufacturing were when the scaffolds were heat-treated at 1500 °C for 1 h followed by sintering at 1200 °C for 20 h. Such scaffolds exhibited the highest compressive strength which was correlated with the highest linear density and the lowest size of grains. Moreover, grain size distribution was narrower with predominating fraction of fine grains in the range 10–20 μm. Smaller grains and higher linear density suggested that in this case densification process prevailed over undesirable process of grain coarsening. In

the case of the scaffolds heat-treated at 1600 °C for 1 h followed by sintering at 1100 °C or 1200 °C for 20 h the energy provided to the system was much higher and resulted in excessive grain growth.

To sum up, it was found that the two-step sintering procedure at 1500 °C for 1 h followed by sintering at 1200 °C for 20 h provides TiO_2 scaffolds with relatively small gain size, high densification and improved mechanical properties. Such results also suggest that it may be possible to further improve mechanical properties of the highly porous TiO_2 scaffolds by performing the sintering at lower temperatures and shorter time regimes.

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References

[1] AMINI A.R., LAURENCIN C.T., NUKAVARAPU S.P., *Bone tissue engineering: recent advances and challenges*, Crit. Rev. Biomed. Eng., 2012, 40(5), 363–408.

[2] NANDI S.K., ROY S., MUKHERJEE P., KUNDU B., DE D.K., BASU D., *Orthopaedic applications of bone graft & graft substitutes: a review*, Indian J. Med. Res., 2010, 132, 15–30.

[3] DU C., LI N., GAO N., YAO C., WANG S., BU L., *A preliminary study on the application of bone marrow stromal cell sheet on the formation of functional tissue-engineered bone in dogs*, J. Oral Maxillofac. Surg., 2013, 71, 1531–1531.

[4] HANNINK G., ARTS J.J.C., *Bioresorbability, porosity and mechanical strength of bone substitutes: What is optimal for bone regeneration?*, Injury, 2011, 42(2), 22–25.

[5] HENCH L.L., *Bioceramics: from concept to clinic*, Am. Ceram. Soc. Bull., 1993, 72, 93–98.

[6] AL-SANABANI J.S., MADFA A.A., AL-SANABANI F.A., *Application of calcium phosphate materials in dentistry*, Int. J. Biomater., 2013, DOI:10.1155/2013/876132.

[7] TIAINEN H., WOHLFAHRT J.C., VERKET A., LYNGSTADAAS S.P., HAUGEN H.J., *Bone formation in TiO2 bone scaffolds in extraction sockets of minipigs*, Acta Biomater., 2012, 8, 2384–2391.

[8] SABETRASEKH R., TIAINEN H., LYNGSTADAAS S.P., RESELAND J., HAUGEN H., *A novel ultra-porous titanium dioxide ceramic with excellent biocompatibility*, J. Biomater. Appl., 2011, 25, 559–580.

[9] JOKINEN M., PÄTSI M., RAHIALA H., PELTOLA T., RITALA M., ROSENHOLM J.B., *Influence of sol and surface properties on in vitro bioactivity of sol-gel-derived TiO_2 and TiO_2-SiO_2 films deposited by dip-coating method*, J. Biomed. Mater. Res., 1998, 42, 295–302.

[10] HOLLISTER S.J., *Porous scaffold design for tissue engineering*, Nat. Mater., 2005, 4, 518–524.

[11] REZWAN K., CHEN Q.Z., BLAKER J.J., BOCCACCINI A.R., *Biodegradable and bioactive porous polymer/inorganic composite scaffolds for bone tissue engineering*, Biomaterials, 2006, 27, 3413–3431.

[12] KARAGEORGIOU V., KAPLAN D., *Porosity of 3D biomaterial scaffolds and osteogenesis*, Biomaterials, 26, 5474–5491.

[13] WILL J., MELCHER R., TREUL C., TRAVITZKY N., KNESER U., *Porous ceramic bone scaffolds for vascularized bone tissue regeneration*, J. Mater. Sci. Mater. Med., 2008, 19, 2781–2790.

[14] TRUNEC M., CHLUP Z., *Higher fracture toughness of tetragonal zirconia ceramics through nanocrystalline structure*, Scripta Mater., 2009, 61, 56–59.

[15] RAHAMAN M.N., *Ceramic Processing and Sintering*, CRC Press, 2003.

[16] KNUDSEN F.P., *Dependence of mechanical strength of brittle polycrystalline specimens on porosity and grain size*, J. Am. Ceram. Soc., 1959, 42, 376–387.

[17] LAY K.W., [in:] *Sintering and Related Phenomena* (Kuczynski G.C.) 65–80, Springer, U.S., 1973.

[18] HE Z., MA J., *Densification and grain growth during interface reaction controlled sintering of alumina ceramics*, Ceram. Int., 2001, 27, 261–264.

[19] SHAW N.J., *Densification and coarsening during solid state sintering of ceramics: A review of the models*, II – *Grain growth*, Powder Metall. Int., 1989, 21, 31–33.

[20] MAZAHERI M., ZAHEDI A.M., HAGHIGHATZADEH M., SADRNEZHAAD S.K., *Sintering of titanianoceramic: Densification and grain growth*, Ceram. Int., 2009, 35, 685–691.

[21] CHEN I.W., WANG X.H., *Sintering dense nanocrystalline ceramics without final-stage grain growth*, Nature, 2000, 404, 168–171.

[22] WANG X.H, DENG X.Y, BAI H.L, ZHOU H, QU W.G, LI L.T., *Two-step sintering of ceramics with constant grain-size*, II: *$BaTiO_3$ and Ni–Cu–Zn ferrite*, J. Am. Ceram. Soc., 2006, 89, 438–443.

[23] TIAINEN H., WIEDMER D., HAUGEN H.J., *Processing of highly porous TiO_2 bone scaffolds with improved compressive strength*, J. Eur. Ceram. Soc., 2013, 33, 15–24.

[24] MURPHY C.M., HAUGH M.G., O'BRIEN F.J., *The effect of mean pore size on cell attachment, proliferation and migration in collagen–glycosaminoglycan scaffolds for bone tissue engineering*, Biomaterials, 2010, 31, 461–466.

[25] MISCH C.E., QU Z., BIDEZ M.W., *Mechanical properties of trabecular bone in the human mandible: Implications for dental implant treatment planning and surgical placement*, Journal of Oral and Maxillofacial Surgery, 1999, 57, 700–706.

[26] TIAINEN H., LYNGSTADAAS S.P., ELLINGSEN J.E., HAUGEN H.J., *Ultra-porous titanium oxide scaffold with high compressive strength*, J. Mater. Sci. Mater. Med., 2010, 21, 2783–27.