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# Improving the strength and biocompatibility of porous titanium scaffolds by creating elongated pores coated with a bioactive, nanoporous $TiO_2$ layer

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ABSTRACT

This paper reports a novel way of improving the mechanical properties and biocompatibility of porous Ti scaffolds using a combination of the modified sponge replication method and anodization process. The use of a stretched polymeric sponge as a novel template allowed the creation of elongated pores in a porous Ti scaffold, which, accordingly, led to a high compressive strength of $24.2 \pm 2.08$ MPa at a porosity of approximately 70 vol%. Furthermore, the surfaces of the Ti walls were coated successfully with a bioactive nanoporous $TiO_2$ layer using the anodization process, which enhanced the biocompatibility remarkably, as assessed by the attachment of MC3T3-E1 cells.



## 1. Introduction

Porous titanium (Ti)-based scaffolds are attracting increasing interest in bone tissue engineering, because they can provide a favorable environment for bone ingrowth with outstanding mechanical properties [1,2]. Therefore, considerable effort has been made to develop new manufacturing methods for producing porous Ti scaffolds [1]. Among these methods, the sponge replication method can achieve high porosity and good interconnections between pores [3–6], which is quite beneficial to the bone ingrowth and vascularization of newly formed tissue [7]. However, it is still needed to improve the mechanical properties and biocompatibility of the porous Ti scaffolds produced using this method and still preserve their high porosity for practical applications.

Therefore, we herein demonstrate the utility of a combination of the modified polymeric sponge replication method and anodization process, which can create elongated pores to improve the compressive strength of porous Ti scaffolds [8] and a bioactive, nanoporous $TiO_2$ coating layer to enhance their biocompatibility [9], respectively. The fabricated samples were characterized by the pore structures, crystalline phases, chemical composition, and compressive strength. The preliminary osteoblastic activity of the samples was also evaluated using *in vitro* cell tests.

## 2. Experimental procedure

Porous Ti scaffolds with elongated pores were produced using a stretched polymeric sponge as a novel template in the modified sponge replication method. The as-received polyurethane sponges (15 pores per inch, Jeil Urethane Co., Korea), $7 \times 35 \times 17$ mm in size, were stretched to an elongation of 50% and then heat-treated at 200 °C for 2 h in an oven [8]. The resulting sponges were then coated with a titanium hydride ($TiH_2$ ) slurry prepared using $TiH_2$ powder (Alfa Aesar, Ward Hill, MA, USA), according to the procedure described elsewhere [6]. The $TiH_2$-coated sponges were heat-treated at 800 °C for 3 h to remove the polymeric sponges and convert $TiH_2$ to Ti metal, which was followed by sintering of the Ti walls at 1300 °C for 2 h in a vacuum. This dip-coating/heat-treatment procedure was repeated up to three times to reduce the porosity of the sample.

The surfaces of the Ti walls were coated with a bioactive, nanoporous $TiO_2$ layer using an anodization process. Anodization was carried out in an electrolyte solution containing 2 vol% D.I. water and 0.3 wt.% ammonium fluoride ($NH_4F$, Sigma-Aldrich, USA) in ethylene glycol ($C_2H_6O_2$, Sigma-Aldrich, USA) [10] at an applied voltage of 60 V for 30 min using a DC power supply (Model-EV243, Consort NV Co., Turnhout, Belgium) at room temperature. The anodized samples were then cleaned ultrasonically with D.I. water.

The resulting porous Ti scaffolds were evaluated using several analysis techniques. The porosity of the samples was calculated by measuring their weight and dimensions. The interior porous structure of the sample was examined using a micro-computed tomography scanner (Skyscan 1173, Skyscan, Kontich, Belgium). The pore structures and the level of densification of the Ti walls were also characterized by field emission scanning electron microscopy (FE-

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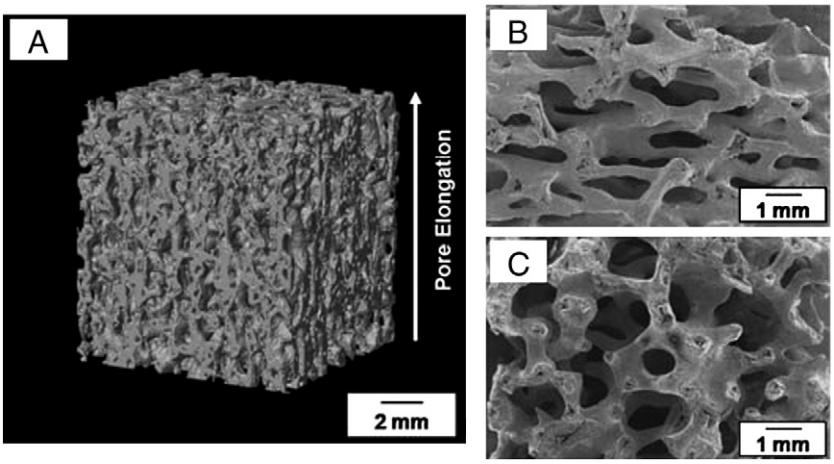


**Fig. 1.** Typical 3-dimensional reconstructed μ-CT image of the porous Ti scaffold with the elongated pores (A), SEM micrographs of the sample showing the pore structure developed parallel (B), and normal (C) to the direction of pore elongation.

SEM, JSM-6701F, JEOL Techniques, Tokyo, Japan). The crystalline phases and chemical compositions were examined by X-ray diffraction (XRD, M18XHF-SRA, MacScience Co., Yokohama, Japan) and energy dispersive spectroscopy (EDS) attached to the scanning electron microscope, respectively. The possible secondary elements, such as oxygen, hydrogen, carbon, and nitrogen, were more closely examined by an elemental analyzer (EA1110, CE Instrument, Italy). The compressive strengths of the samples with dimensions of approximately $10\times10\times15$ mm were measured using a screw driven load frame (Instron 5565, Instron Corp., Canton, MA, USA) at a crosshead speed of 5 mm/min. The samples were compressed either parallel or normal to the direction of pore elongation. Five samples were tested to obtain the mean and standard deviation.

The biocompatibility of the porous Ti scaffold with a nanoporous $TiO_2$ coating layer was examined by *in vitro* cell tests using a pre-osteoblast cell line (MC3T3-E1; ATCC, CRL-2593, USA), according to the procedure described elsewhere [11]. For comparison, the porous Ti scaffold without a nanoporous $TiO_2$ coating layer was also tested. The cells were seeded on the samples at a density of $5\times10^4$ cells/ml and cultured in a humidified incubator with 5% $CO_2$ at 37 °C. The morphology of cells attached to the samples after 3 h culture was observed by confocal laser scanning microscopy (CLSM, FluoView FV1000, Olympus Inc., Japan).

## 3. Results and discussion

The use of a stretched polymeric sponge as a novel template in the modified sponge replication method allowed the creation of elongated pores in a porous Ti scaffold. Fig. 1(A) shows a typical reconstructed 3-dimensional μ-CT image of the sample produced using three dip-coating/heat-treatment cycles. Elongated pores were formed well throughout the sample without noticeable large defects and resembled the original pore structure of the polymeric template. The construction of elongated pores was examined more closely by scanning electron microscopy (SEM), as shown in Fig. 1(B) and (C). Elongated and slightly distorted pores were formed parallel (Fig. 1(B)) and normal (Fig. 1(C)) to the direction of elongation, respectively. The Ti walls were densified well without significant differences between the layers.

The chemical composition of the sample was evaluated by EDS. Strong peaks associated with Ti were observed (data not shown here). In addition, the possible secondary elements, such as oxygen, hydrogen, carbon, and nitrogen, were more closely examined by an elemental analyzer, as summarized in Table 1. The oxygen and hydrogen contents were much lower than the critical values which can deteriorate ductility of Ti metal [12]. However, a considerable amount of carbon was detected, which was presumably due to the carbon contamination during thermal decomposition of the polymeric sponge.

The porosity of the sample decreased from $84\pm0.2$ vol% to $70\pm1.8$ vol% with increasing number of dip-coating/heat-treatment cycles from 1 to 3 times, as summarized in Table 2. In addition, the compressive strengths of the samples with various porosities were measured to evaluate their potential applications as a bone scaffold, as summarized in Table 2. The sample with a porosity of ~84 vol% showed a high compressive strength of $7.0\pm0.54$ MPa, when compressed parallel to the direction of pore elongation, which was much higher than that ($2.7\pm0.42$ MPa) of the sample compressed normal to the direction of pore elongation. The compressive strength increased further to $24.2\pm2.08$ MPa with decreasing porosity to ~70 vol%. This value is a factor of ~1.3 higher than that of a porous Ti scaffold with similar porosity but isotropic pores produced using a conventional polymeric sponge [6]. This improvement was attributed primarily to the construction of elongated pores, as is often the case with aligned porous materials [8,12–14]. However, the sample exhibited a sign of embrittlement, as shown in Fig. 2 [12,15], which was presumably due to the incorporation of carbon in the Ti walls (Table 1).

The creation of a bioactive, nanoporous $TiO_2$ coating layer on the Ti walls using an anodization process was examined by SEM, as shown in Fig. 3(A). Nanoporous $TiO_2$ (i.e. $TiO_2$ nanotubes with the mean size of approximately 45 nm) were formed uniformly throughout the

**Table 1**
Oxygen, hydrogen, carbon, and nitrogen concentration of the porous Ti scaffold.

| Elements | Oxygen | Hydrogen | Carbon | Nitrogen |
|---|---|---|---|---|
| Concentration [ppm] | 115 | 502 | 4858 | 155 |

**Table 2**
Measured porosities and compressive strengths of the porous Ti scaffolds produced using various numbers of dip-coating/heat-treatment cycles (one, two, and three times).

| Samples | One time | Two times | Three times |
|---|---|---|---|
| Porosity [vol%] | $84\pm2.0$ | $77\pm1.9$ | $70\pm1.8$ |
| Compressive strength [MPa] | $7.0\pm0.54$ ($2.7\pm042$)* | $14.8\pm2.23$ | $24.2\pm2.08$ |

*: Compressive strength was measured normal to the direction of pore elongation.