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Hierarchically structured titanium foams for tissue scaffold applications

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ABSTRACT

We present a novel route for producing a new class of titanium foams for use in biomedical implant applications. These foams are hierarchically porous, with both the traditional large (>300 μm) highly interconnected pores and, uniquely, wall struts also containing micron scale (0.5–5 μm) interconnected porosities. The fabrication method consists of first producing a porous oxide precursor via a gel casting method, followed by electrochemical reduction to produce a metallic foam. This method offers the unique ability to tailor the porosity at several scales independently, unlike traditional space-holder techniques. Reducing the pressure during foam setting increased the macro-pore size. The intra-strut pore size (and percentage) can be controlled independently of macro-pore size by altering the ceramic loading and sintering temperature during precursor production. Typical properties for an 80% porous Ti foam were a modulus of ~1 GPa, a yield strength of 8 MPa and a permeability of 350 Darcies, all of which are in the range required for biomedical implant applications. We also demonstrate that the micron scale intra-strut porosities can be exploited to allow infiltration of bioactive materials using a novel bioactive silica–polymer composite, resulting in a metal–bioactive silica–polymer composite.

1. Introduction

Titanium alloys possess a combination of mechanical properties that make them suitable for use in biomedical engineering, including high specific strength, a modulus lower than steel or cobalt alloys and corrosion resistance [1–4]. More importantly for bioengineering, titanium is very stable in a body fluid environment [2]. Titanium alloys have already been used extensively as a biomaterial in applications such as prostheses [4,5] and more recently as a foam structure for applications such as spinal fusion devices [6–8]. These porous implant structures, termed scaffolds, offer several advantages over monolithic implants. An interconnected pore structure can allow tissue in-growth and vascularization [9]. Rough surfaces provide sites for better biological cell attachment [6,9]. If the permeability is matched to bone, they also provide pathways for nutrient supply to the ingrowing tissue, hence increasing implant durability by improving the efficacy of osteointegration [10]. The presence of porosity and reduced density lowers the effective Young's modulus, reducing "stress-shielding" [11].

Porous titanium structures are currently produced through multi-step powder metallurgical (PM) routes, as reviewed by Singh et al. [12]. Examples of these techniques include: space-holder or sacrificial template methods [13–18]; polymer replication [19]; controlled expansion of entrapped argon gas in a Ti preform at high temperature and pressure [20]; freeze casting [21]; laser processing [22]; and rapid prototype methods, including selective electron beam melting [23]. All of these techniques require expensive Ti powders as their starting material and in general yield a single scale of porosity. A second level of porosity is possible through incomplete sintering, forming either interconnected or more frequently closed porosities, on the scale of tens of microns, within the walls. The reactivity of titanium when producing finer particles and sintering them is so high that the contamination levels, including oxygen, are unacceptable [3].

In this study we explore the use of the Fray, Farthing and Chen (FFC) Cambridge process [24] to produce titanium foams. This technique provides a means of producing a near net shape metal product directly from an inexpensive metal oxide precursor. During the FFC Cambridge process a TiO_2 cathode is progressively reduced and deoxidized in a molten calcium chloride salt. At the cathode the titanium oxide is reduced to titanium and the oxide ions dissolve into the calcium chloride. These oxide ions migrate to a carbon anode, where they undergo an electrochemical reaction with the carbon anode to yield CO/CO_2. Since its discovery, significant research has focused on applying this technique to the production of titanium and its alloys [25–30]. A study conducted for the US Department of Energy in 2004 identified more than a dozen emerging technologies for Ti extraction [31]. However, only the FFC Cambridge process lends itself to the production of Ti foams via the reduction of a porous TiO_2 precursor. This process (see Fig. 1) also has other benefits, such as the ability to produce conventional or unique alloys by blending the relevant oxides [25].

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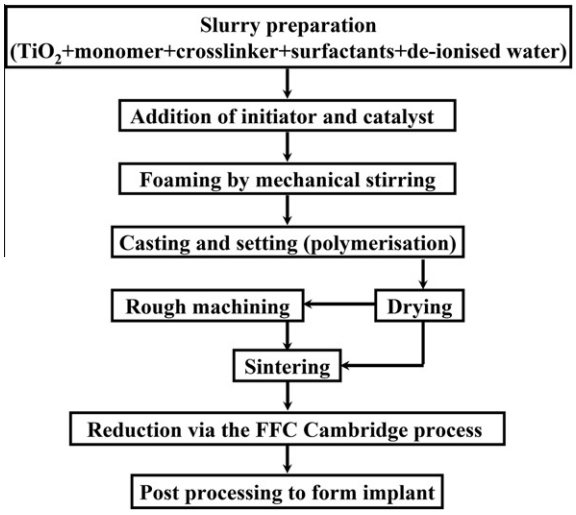

Fig. 1. Overview of metallic titanium foam production.

To the authors' knowledge there has been only one prior attempt to produce titanium foams via the FFC Cambridge process [32]. In that study Centeno-Sánchez et al. [32] produced the ceramic precursor using a space-holder technique. Whilst the level of interconnectivity, mechanical properties and permeability were not analyzed, this study demonstrated that reduction of a porous ceramic precursor was possible. Due to the limitations of the space-holder technique [33] the pore walls were irregular in thickness. Alternative methods for producing the porous ceramic precursor are required.

One such technique involves the preparation of a slurry mix, mechanical foaming and setting by gelation (e.g., in situ polymerization). Although not previously applied to TiO_2, this technique, termed "gel casting", has been shown to be an effective method in other ceramic systems [33] for producing highly interconnected open foams.

In this study, we present a novel route for the production of titanium foams with interconnected pore networks. We develop a method for gel casting of a TiO_2 foam precursor, which was then reduced using the FFC Cambridge process. Using a variety of two-dimensional (2D) and three-dimensional (3D) characterization techniques, in combination with physical and mechanical testing, the evolution of both the microstructure and properties was tracked.

This characterization will show that the hierarchical porosity in these Ti foams can be tailored to match the mechanical and physiological requirements. Large, highly interconnected pores in the range 100–800 μm were produced with independently varied microporosities within their walls on a scale of 0.5–5 μm. Sound walls can also be produced, although the novelty of the process is the controlled micron scale porosity, which has not been achieved via other routes. Further, we demonstrate that the tailorable fine intra-strut porosity allows infiltration with a bioactive glass–polymer composite.

2. Materials and methods

New titanium foams were produced by reducing a titanium oxide foam using the FCC Cambridge process. The titanium oxide foam was produced using the gel cast foaming process, which dictated the macro-pore structure of the final foam. The titanium foams were then characterized using scanning electron microscopy (SEM) and X-ray micro-computed tomography (μCT). Mechanical and fluid transport properties were also assessed.

2.1. Gel casting of the precursor foam

A gelling system based on methacrylamide (monomer), *N*,*N*′-methylenebysacrylamide (cross-linker) and ammonium persulfate (initiator) was employed in this work to make the precursor titania foam. The standard composition in Table 1 corresponded to a slurry composition loaded with maximum possible titania while keeping the remainder of the reagents unchanged. A slurry with a low ceramic content (~34 wt.% TiO_2, compared with the standard ~48 wt.%) was used to investigate the effect of ceramic loading on pore wall characteristics and on foam integrity. All the reagents were from Sigma–Aldrich. Initial TiO_2 powder particle size plays an important role in determining the rheology of water-based slurry systems. The oxide particles had a d_{50} (defined as median diameter when ranked by weight percent) of 0.93 μm when measured by laser diffraction (CILAS 1064 Laser Particle Size Analyzer).

The reagents were mixed in the order listed in Table 1, with the initiator (in the form of a solution; 0.52 g/ml) and catalyst being added immediately prior to foaming by vigorous agitation for 60 s. The foamed suspension was cast into 60 ml autoclavable straight edge polymethyl pentene molds (NalgeneLabware, UK). The molds were sealed with screw-caps and allowed to gel at room temperature for 24 h. The gelled foams were 44 mm in diameter and varied from 20 to 40 mm in height. Drying of the foam was carried out at 60 °C for at least 18 h, followed by a similar time at 100 °C. Differential scanning calorimetry (Fig. 2a) was used to determine the appropriate sintering schedule for the dried precursor (Fig. 2b). It was found that accelerated drying and decomposition of the polymer occurred over a range of temperatures from 100 °C to 700 °C. Therefore, selection of the initial ramp rate to the sintering temperature was critical in order to avoid crack formation. Heating at 0.5 °C min^{-1} to 350 °C, followed by a 1 h hold, was found to be appropriate for removal of the majority of the polymer without cracking. The samples were then ramped at 3 °C min^{-1} to the sintering temperature (950–1450 °C) and held for 3 h, followed by a furnace cool.

A series of samples was produced using these base conditions with the individual processing conditions varied.

2.2. Reduction of the precursor foam via the FFC Cambridge process

A schematic of the experimental set-up used for the reduction of the samples is shown in Fig. 3a. The cell design was essentially the same as used in previous investigations [26,34,35] except for improved sealing (replacement of silicone bungs with brass pipe fittings) where the electrodes entered the retort (Fig. 3b). The current design is able to ensure a stable airtight seal whilst still allowing movement of current collectors, keeping their separation constant.

The reduction cell consisted of a programmable vertical tube furnace housing an Inconel® (Inconel 601) reaction vessel with a

Table 1
Ingredients used in gel casting of titania foams.

Material (function)	Amount (g or ml)	
	Standard	Low loading
TiO_2 powder (main component)	33	14
Methacrylamide (monomer)	6	6
N,*N*′-methylenebysacrylamide (cross-linker)	2	2
Distilled water (carrier)	23	14
Triton X-100 (surfactant)	0.1	0.1
Dispex (surfactant)	2 drops	2 drops
N,*N*,*N*′,*N*′-tetramethyl ethylene diamine (TEMED) (catalyst)	2	3
Ammonium persulfate (APS) solution (initiator)	3	2

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