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A bioactive titanium foam scaffold for bone repair

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Abstract

While titanium has been clinically successful as an orthopedic or dental implant material, performance problems still persist related to implant–bone interfacial strength and mechanical modulus mismatch between titanium and tissue. We describe here the preparation of a titanium foam as a better mechanical match to tissue with surfaces attractive to bone cells through deposition of an organically-modified apatite layer (organoapatite). In a rotating bioreactor, these organoapatite-coated foams are successfully colonized by preosteoblastic cells. Finite element analyses suggest that ingrown tissue in these systems may improve both implant performance and tissue formation through load-sharing and stress distribution. The novel metal–ceramic–polymer hybrid materials described here hold great promise for bone tissue engineering.

Keywords: Porous titanium; Organoapatite; Hydroxyapatite; Bioreactor; Osteoblasts; Finite element model; Stress-shielding

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1. Introduction

Titanium (Ti) and its alloys continue to be utilized extensively for skeletal repair and dental implants. Titanium's excellent strength-to-weight ratio, toughness, and most importantly, the biocompatibility and corrosion resistance of its naturally forming surface oxide have led to widespread clinical success [1–4]. There are, however, unresolved technical problems associated with using titanium as an implant material. The bioinert character of its protective surface oxide does not readily form a strong interface with surrounding tissue. Furthermore, the relatively high stiffness of titanium, as compared to surrounding bone, can lead to problems of stress-shielding and subsequent implant loosening.

One approach to resolving the interface problem involves coating titanium surfaces with hydroxyapatite, the principal mineral in bones and teeth. Methods such as plasma spraying [5,6], sol–gel [7], electrophoretic deposition [8], and even solution phase apatite growth [9,10] have all been explored. Mechanical evaluation of extracted hydroxyapatite-coated implants has shown evidence of increased interfacial strength compared to implants with bare titanium surfaces [11–13]. Stupp et al. [14–16] previously developed materials known as organoapatites (OA) which incorporate 2–3% poly-(L-lysine) into the mineral hydroxyapatite. The inclusion of these macromolecules into the mineral phase mimics some natural biogenic minerals containing small amounts of occluded proteins that regulate crystal formation and also toughen otherwise brittle matrices [17–19]. Previous in vivo work showed that organoapatite

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promotes not only bone apposition, but also interfacial resorption and bony replacement [16]. We have developed a method to grow OA on titanium-based implant surfaces, with the expectation that it may serve as an agent to encourage new bone growth at the implant interface before being resorbed and recycled [20]. The organoapatite coating is grown out of solution onto a double layer of oppositely charged poly(amino-acids) bound to titanium's natural oxide surface. This growth process offers a number of significant advantages over current coating procedures. The solution-phase nature of the growth allows for the coating of interior surfaces of porous structures, unlike directionally restricted methods such as plasma spraying. Furthermore, methods such as plasma spraying, sol–gel, and electrophoresis may produce highly crystalline coatings, which are difficult to resorb. The low density, nanocrystalline character of OA is expected to be more susceptible to natural remodeling processes, critical to maintaining the body's natural tissue. The deposition of organoapatite on titanium surfaces has been shown to enhance their colonization by bone cells [21].

A second approach to enhancing implant interfacial strength utilizes a porous implant surface, created by plasma spraying or surface sintering titanium powder or wires onto a solid implant surface [22–24]. Such systems rely on bone ingrowth into the shallow porous surface layer to stabilize the implant. An improvement on this concept is to use a titanium foam presenting porosity not only at the implant surface but throughout the entire structure. This scheme may allow for a greater degree of bony infiltration, while also reducing the stiffness of the foam as compared to that of solid titanium, thereby addressing the stress shielding problem. Stress shielding refers to the condition whereby fully dense titanium, which is significantly stiffer than bone, shields surrounding tissue from stresses, resulting in interfacial resorption and implant loosening. As reviewed recently [25], three-dimensionally porous titanium can be produced by various sintering methods, including partial sintering of powders [26,27] or wires [28], or by sintering of powders around a temporary space-holding phase [29,30], but the resulting structure is relatively weak, due to the small necks connecting the individual powder particles. An alternative foaming method for Ti alloys was developed by Kearns et al. [31,32]. Micron-size bubbles of pressurized inert argon gas are entrapped within a titanium matrix during consolidation of titanium powders by hot isostatic pressing (HIPing). Upon subsequent exposure to elevated temperatures and ambient pressure, these bubbles expand by creep of the titanium matrix, resulting in formation of a titanium foam with up to approximately 50% porosity. As compared to foams produced by powder sintering, these foams exhibit higher strength because of the more rounded pore shape and full density of struts [33].

In this work, we report on the synthesis of hybrid titanium foams in which porous surfaces have been modified by osteoconductive organoapatite layers. We study the in vitro colonization of the foams by bone cells and also predict the hybrid material's mechanical interactions with ingrowing tissue through finite element (FE) modeling.

2. Methods and materials

The foaming process was previously described by Davis et al. [34]. Spherical CP-Ti powders (−100 mesh size) with median size of ~130 μm were packed to approximately 70% density in a steel can. The can was evacuated, back-filled with 3.3 atm Ar, sealed, and then subjected to HIPing at 890 °C and 100 MPa for 125 min. Cubic specimens with approximately 6 mm edges were cut from the consolidated billet, encapsulated in evacuated quartz capsules and introduced in a preheated furnace at 960 °C and foamed for a total of 24 h. Total specimen porosity was determined by Archimedes density measurements on samples sealed with a thin layer of vacuum grease in distilled water. Density measurements were also performed using helium pycnometry on unsealed specimens, allowing for measurement of closed porosity.

Foamed titanium was cut with a diamond-coated abrasive saw into samples 4 mm × 4 mm × 1 mm, and 1 mm diameter holes were drilled through the samples for skewering in a bioreactor. These substrates were cleaned ultrasonically for 15 min each in reagent-grade dichloromethane, reagent-grade acetone, and de-ionized water. Pores clogged by metal smearing during cutting were opened by etching in a 0.25% HF, 2.5% HNO_3 solution for 45 min. Samples were then repassivated in 40 vol.% HNO_3 solution for 30 min, and rinsed with de-ionized water. The processes for sample pretreatment and growth of organoapatite were adapted from previous work [20,21] for application with the titanium foam. Foam samples were suspended in a Teflon sample holder and pretreated for 22 h in poly(L-lysine) (pLys) at pH 7.4, followed by 20 h in poly(L-glutamic acid) (pGlu) at pH 7.4. Organoapatite precipitation was conducted by combining 500 mL each of 15 mM calcium hydroxide and 9 mM phosphoric acid solutions with 400 mL of 1 mM poly(L-lysine) at 37 °C and pH 7.4 Collected precipitate was partially dissolved by addition of HCl. Pretreated samples were then introduced to the partially dissolved organoapatite and the OA was reprecipitated by the dropwise addition of 3 M NaOH restoring pH to 7.4. After several hours, samples were rinsed with de-ionized water and dried under vacuum. Non-adherent precipitate was rinsed and vacuum desiccated for later analysis.

Surface analysis of the OA-coated foam substrates was performed on gold/palladium-coated samples by