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Bone ingrowth in porous titanium implants produced by 3D fiber deposition

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Abstract

3D fiber deposition is a technique that allows the development of metallic scaffolds with accurately controlled pore size, porosity and interconnecting pore size, which in turn permits a more precise investigation of the effect of structural properties on the in vivo behavior of biomaterials.

This study analyzed the in vivo performance of titanium alloy scaffolds fabricated using 3D fiber deposition. The titanium alloy scaffolds with different structural properties, such as pore size, porosity and interconnecting pore size were implanted on the decorticated transverse processes of the posterior lumbar spine of 10 goats. Prior to implantation, implant structure and permeability were characterized. To monitor the bone formation over time, fluorochrome markers were administered at 3, 6 and 9 weeks and the animals were sacrificed at 12 weeks after implantation. Bone formation in the scaffolds was investigated by histology and histomorphometry of non-decalcified sections using traditional light- and epifluorescent microscopy. In vivo results showed that increase of porosity and pore size, and thus increase of permeability of titanium alloy implants positively influenced their osteoconductive properties.

Keywords: Osteoconduction; Porous Ti6Al4V; Scaffold; 3D fiber deposition

1. Introduction

At present, most widely used clinical therapies for bone replacement and regeneration employ autologous and allogeneic bone grafts. It is well known that autologous bone graft is considered to be the golden standard in spinal fusions, i.e. for achieving a bony bridge between transverse processes. However, treatments with both autografts and allografts exhibit a number of limitations. The harvest of the autologous graft requires an additional invasive surgical procedure that may lead to donor site morbidity, chronic post-operative pain, hypersensitivity and infection [1–5]. Another important drawback of the use of autograft is the limited availability. Unlike autologous bone, allogeneic grafts are widely available and do not require an additional surgery on the patient. However, allogeneic bone has to undergo processing techniques such as lyophilization, irradiation or freeze-drying to remove all immunogenic proteins in order to avoid any risk of immunogenic reaction [6]. In turn, these processing techniques have a negative effect on osteoinductive and osteoconductive potential of the allograft [7], which consequently decreases its biological performance as compared to autografts [8].

Therefore, the use of synthetic biomaterials for orthopedic reconstructive surgery as a means of replacing autografts and allografts is of increasing interest and the

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large number of scientific reports confirm this trend. Calcium-phosphate-based biomaterials, such as ceramics and cements and polymeric biomaterials are attractive as they can be produced in such a way that they mimic the mineral composition and/or the porous structure of bone. However, although ceramics show excellent corrosion resistance and good bioactive properties, porous ceramic structures, as they are available today, are limited to non-load-bearing applications, due to their intrinsic brittleness. Likewise, porous polymeric systems are deemed to be ductile with insufficient rigidity and inability to sustain the mechanical forces present in bone replacement surgery.

Metals have so far shown the greatest potential to be the basis of implants for long-term load-bearing orthopedic applications, owing to their excellent mechanical strength and resilience when compared to alternative biomaterials, such as polymers and ceramics. Particularly, titanium and its alloys have been widely used in orthopedic and dental devices because of their excellent mechanical properties and biocompatibility [9].

Several factors have shown their influence on bone ingrowth into porous implants, such as porous structure (pore size, pore shape, porosity and interconnecting pore size) of the implant, duration of implantation, biocompatibility, implant stiffness, micromotion between the implant and adjacent bone etc. [10–22]. The architecture of a porous implant has been suggested to have a great effect on implant integration by newly grown bone [23,24]. However, up to now, porous structures of most metallic implants are not very well controlled due to their production techniques, involving porogens and replication methods [25,26]. These techniques mostly result in porous structures with a certain pore size range, rather than structures with an accurately defined pore size.

Recently, rapid prototyping, such as fused deposition modeling and 3D printing, has been employed to fabricate 3D scaffolds with accurately designed structure [27,28], which allowed investigation of architectural influences on tissue regeneration. However, these studies focused on porous scaffolds made of ceramics and polymers [12,29,30], while very little is known about porous titanium scaffolds with precisely controlled pore structure.

Because there is hardly consensus regarding the optimal pore size for effective bone ingrowth, researchers have created scaffolds with pore sizes between 150–300 μm and 500–710 μm to promote bone formation [31]. A minimum pore size of 100–150 μm is generally considered acceptable for bone ingrowth [20,32–35].

3D porous Ti6Al4V scaffolds were successfully fabricated in our group by a rapid prototyping technology, named 3D fiber (3DF) deposition [36]. 3DF deposition, being a layer-by-layer manufacturing technique, can be used to manufacture prototypes in which each layer may have a different fiber diameter, thickness, fiber space and fiber orientation. This technique, therefore, provides a possibility to develop scaffolds with well-controlled pore size, porosity and interconnecting pore size. The advantage of scaffolds produced by 3DF is that they permit parametric analyses to be conducted, which is essential in investigations of how scaffolds perform as a function of their physical characteristics.

In the present study, implants with different pore size, porosity and interconnecting pore size were fabricated by 3DF technique. Influence of the structural characteristics on the bone ingrowth was screened by using the well-established multi-channel cage model [37–40] that was adapted to use on the transverse process of the goat lumbar spine.

2. Materials and methods

2.1. Implants

Five different porous TI6Al4V scaffolds made by 3DF deposition were used in this study. The preparation procedure of these scaffolds was described earlier [2]. In short, Ti6Al4V slurry (80 wt% of Ti6Al4V powder with a mean particle diameter of 45 μm (AP&C Inc., Canada) in 0.5% aqueous water methylcellulose solution), is forced through the syringe nozzle by using a 3D-bioplotter machine (Envisiontec, GmbH, Germany). The slurry is plotted on a stage as a fiber, which rapidly solidifies by drying, and the scaffold is fabricated by layering a pattern of fibers. After deposition, the obtained Ti6Al4V scaffolds were dried for 24 h at RT, and sintered under high vacuum at 1200 °C for 2 h. By varying spacing and fiber lay-down pattern, 5 different Ti alloy scaffolds (low porosity (3DFL), middle porosity (3DF), high porosity (3DFH), double-layered (3DFDL) and gradient porosity (3DFG)) were produced as is specified in Table 1.

2.2. Cage

A cage design and its fabrication were described previously [40]. In brief, polyacetal cages were designed for fixation to the transverse process of the goat lumbar spine. Each cage consisted of two sidewalls, two end pieces, four stainless steel machine screws for cage assembly and two self-tapping bone screws to attach the cage to the transverse process. Three scaffolds ($4 \times 7 \times 8\,mm^3$) were plugged into a cage and separated by thin

Table 1
3D fiber deposition conditions for different implants

Implant	Fiber spacing (μm)	Lay down angle	Layer thickness (μm)
3DFL	200	0/45	320
3DF	500	0/45	320
3DFH	800	0/45	320
3DFDL	500	0/0/45/45	320
3DFG	800→200(bottom to top)	0/90	320