DENTAL MATERIALS 33 (2017) 198–208

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.intl.elsevierhealth.com/journals/dema

Simple additive manufacturing of an osteoconductive ceramic using suspension melt extrusion

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ARTICLE INFO

Article history:
Received 15 June 2016
Received in revised form
23 November 2016
Accepted 29 November 2016

Keywords:
Ceramic
Bone implant
Additive manufacturing
Tricalcium phosphate
3D printing
Implant

ABSTRACT

Objective. Craniofacial bone trauma is a leading reason for surgery at most hospitals. Large pieces of destroyed or resected bone are often replaced with non-resorbable and stock implants, and these are associated with a variety of problems. This paper explores the use of a novel fatty acid/calcium phosphate suspension melt for simple additive manufacturing of ceramic tricalcium phosphate implants.

Methods. A wide variety of non-aqueous liquids were tested to determine the formulation of a storable 3D printable tricalcium phosphate suspension ink, and only fatty acid-based inks were found to work. A heated stearic acid-tricalcium phosphate suspension melt was then 3D printed, carbonized and sintered, yielding implants with controllable macroporosities. Their microstructure, compressive strength and chemical purity were analyzed with electron microscopy, mechanical testing and Raman spectroscopy, respectively. Mesenchymal stem cell culture was used to assess their osteoconductivity as defined by collagen deposition, alkaline phosphatase secretion and de-novo mineralization.

Results. After a rapid sintering process, the implants retained their pre-sintering shape with open pores. They possessed clinically relevant mechanical strength and were

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http://dx.doi.org/10.1016/j.dental.2016.11.012

chemically pure. They supported adhesion of mesenchymal stem cells, and these were able to deposit collagen onto the implants, secrete alkaline phosphatase and further mineralize the ceramic.

Significance. The tricalcium phosphate/fatty acid ink described here and its 3D printing may be sufficiently simple and effective to enable rapid, on-demand and in-hospital fabrication of individualized ceramic implants that allow clinicians to use them for treatment of bone trauma.

1. Introduction

Bone trauma is a common condition that is treated at most hospitals and which may occur due to a number of reasons such as accidents, falls, violence, surgery, infection, degenerative diseases and cancer resection [1,2]. Some bone defects and fractures are treated with titanium mini-plates and screws as bone heals on its own. However, permanent implants may be required to replace pieces of resected or destroyed bone that are either too large to heal on their own or where the restoration of a particular anatomical feature is critical to the aesthetic or functional outcome [3]. The current paper focuses on this type of implant. Autologous bone may be used for such implants but tissue harvesting results in increased morbidity and increased time of surgery. Implants made from non-resorbable materials are common alternatives, but, depending on the type of defect and type of implant, such materials are at risk of infection and rejection and may stress shield surrounding bone, generate wear debris and loosen over time. Furthermore, non-resorbable implants cannot be repaired and remodeled by the body and often need to be replaced in young growing patients. Degradable (resorbable) implant materials may solve these problems [4]. Ceramic calcium phosphate-based implants are an established alternative to non-resorbable implant materials and autologous bone and have been used clinically for many years [5]. Tricalcium phosphate (TCP) is especially interesting as it slowly biodegrades and is remodeled to true bone to which it contributes calcium and phosphate. To accelerate new bone formation, bone forming cells such as mesenchymal stem cells (MSCs) are often added to implants [6–8].

To further improve the use of resorbable, tricalcium-based implants, the use of three dimensional (3D) printing has evolved to a level at which such techniques can actually contribute to more predictable reconstructions. 3D printing, a method of additive manufacturing, is a computer-assisted manufacturing method where an object is built layer-by-layer using a digital object model also known as a CAD model. It has recently been applied to the fabrication of bone implants as it can be used to produce individualized implants that recapitulate patient anatomy especially when used in conjunction with patient scanning data and virtual surgical planning [9,10]. 3D printing also enables the formation of bone-forming pores with specific diameters and direction within the implant. TCP can be 3D printed using different methods, including stereolithography [11], selective laser sintering [12], binder ink jetting [13–15], and robocasting. Robocasting, also known as direct writing and extrusion printing, is an additive manufacturing technique where an "ink" is deposited by a computer-controlled extruder onto a build platform [16]. Robocasting is an attractive technique for in-hospital 3D printing due to its simplicity, low-cost, low-maintenance and its capability to use any material and combinations of several different materials in one print [17]. Several previous studies have used robocasting to produce calcium phosphate implants that have successfully supported osteogenesis in vitro and in vivo [18–22]. Recently, a number of simple-to-operate and low-cost (under $ 10,000) robocasting capable 3D printers have become commercially available; these include the Biobot's Biobot [23], Cellink's Inkredible [24], and Hyrel's System 30M [25]. The simplicity and pricing of these 3D printers could enable low-cost and on-demand 3D printing of individualized implants locally at hospitals. This also requires an ink that is equally low-cost and simple to prepare and handle.

Most publications concerning robocasting describe inks that are complex aqueous powder suspensions that contain multiple additives and which often take several hours to prepare. Aqueous suspension may also suffer from problems such as detrimental influence from their pH and uneven dehydration during printing. Strategies for improving robocasting such as using inks that gel independently of pH [26] or by printing into an oil bath [27] are therefore of great interest. However, all water-based prints must be fully dehydrated before sintering as the boiling water produced in the process would otherwise introduce cracks in the final ceramic. This dehydration step typically takes one or more days. Aqueous formulations may also support chemical reactions such as oxidation, hydration or recrystallization of the powder, resulting in a non-usable ink; this precludes extended storage and requires fresh inks to be prepared for each print. The need for fresh inks, the complexity and time required to prepare such inks and the extended post-printing dehydration time present a significant obstacle to rapid, local, on-demand printing of implants in hospitals.

Long aliphatic chains efficiently lubricate surfaces, and molecules that contain such chains are often used as lubricants. Stearic acid, for example, lowers inter-particle attraction and granular shear strength [28]. This paper investigates the use of such lubricants to create a new calcium phosphate implant fabrication method that relies on a simple-to-prepare, two-component, non-aqueous robocasting ink. Our aim was to develop a simple and inexpensive individualized implant production method that could be implemented