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New depowdering-friendly designs for three-dimensional printing of calcium phosphate bone substitutes

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ABSTRACT

Powder-based three-dimensional printing (3DP) is a versatile method that allows creating synthetic calcium phosphate (CaP) scaffolds of complex shapes and structures. However, one major drawback is the difficulty of removing all remnants of loose powder from the printed scaffolds, the so-called depowdering step. In this study, a new design approach was proposed to solve this problem. Specifically, the design of the printed scaffolds consisted of a cage with windows large enough to enable depowdering while still trapping loose fillers placed inside the cage. To demonstrate the potential of this new approach, two filler geometries were used: sandglass and cheese segment. The distance between the fillers was varied and they were either glued to the cage or free to move after successful depowdering. Depowdering efficiency was quantified by microstructural morphometry. The results showed that the use of mobile fillers significantly improved depowdering. Based on this study, large 3DP scaffolds can be realized, which might be a step towards a broader clinical use of 3D printed CaP scaffolds.

1. Introduction

Powder-based three-dimensional printing (3DP) is a versatile method to produce synthetic scaffolds and bone graft substitutes. It allows an outstanding flexibility in geometry and material [1]. Freedom in choice of materials also allows the use of calcium phosphate (CaP) biomaterials [2–7]. Furthermore 3DP provides geometrical flexibility for virtually unlimited shapes and structures, at least from a theoretical point of view. Due to the absence of typical constraints of traditional production methods, any geometry that contains features within the range of 3DP resolution is feasible. In theory, these great advantages make powder-based 3DP perfectly suitable for building up complex shaped scaffolds and bone graft substitutes. This is especially appealing, as biocompatibility of 3DP scaffolds has already been demonstrated by successful in vivo applications [8–11].

However, considering the literature, it is obvious that in practice the scaffolds produced by powder-based 3DP do not reflect the great geometrical flexibility of this method. Typically 3DP is used to produce rather simple and small objects such as cubes and cylinders with a rather simple and regular inner architecture [8,10,12–18]. Even in the case of more complex structures, e.g. custom-made 3DP models, the inner structures of such structures are predominantly isotropic and typically limited to simple cylindrical bores in a homogeneous body [19,20].

In our previous work, a moisture-based 3DP method was proposed to enhance the accuracy of the method [21]. Moisture was used to stabilize the powder bed just before printing and thus improve 3DP accuracy. The accuracy was quantified by looking at outer dimensions of simple solid bodies and roughness values on the outside of a printed pyramid structure. However, the critical inside part of the printed porous objects was neglected. In 3DP, the solid is created by the reaction of a liquid selectively sprayed onto a powder bed. After printing, the hardened object is embedded in the powder bed and all non-hardened areas, including pores and cavities, are filled with loose powder. Once the printed object is cleared from the surrounding powder in the build volume of the printer, the final and most critical step of powder clearance is still to come, where the loose powder within the printed object's pores and cavities must be removed. If this critical step, also referred to as depowdering, cannot be accomplished, the printed porous object is of no use.

To our knowledge, depowdering of 3DPCaP scaffolds has not been studied and published in depth yet. Depowdering is particularly difficult when the pores and pore interconnections are small and/or when the object is large. As a result, 3D printed porous objects are limited to small dimensions and large pores. Furthermore the 3DP resolution is limited. For example, it has been

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reported that macropores smaller than 500 μm currently cannot be achieved using 3DP [1]. Even though it is still unclear what the optimal pore size for vascularization and cell proliferation is [22], most authors agree that an adequate range should probably be between 50 and 1000 μm [6,23,24]. Considering this conflicting requirement, there is a clear need for new approaches within powder-based 3DP. Especially the need for large scaffolds and at the same time a pore size and porosity range not only controllable at the periphery but especially in the middle of the scaffold is a challenging task.

Therefore, the present study aims at improving the depowdering step by exploiting 3DP versatility. Specifically, scaffolds consisting of two distinct parts are printed at once: the outer part consists of a stiff but porous CaP cage whose windows are large enough to enable depowdering while still trapping the inner part consisting of loose fillers.

2. Material and methods

2.1. Powder

The printing experiments were performed with a custom-made α-TCP (α-tricalcium phosphate, α-$Ca_3(PO_4)_2$) powder. This powder was produced according to a published procedure [25]. In summary, a 0.45:1 M blend of calcium carbonate ($CaCO_3$, Merck, Germany, catalogue No. 102076) and monetite (GFS Chemical, USA, catalogue No. 1548) powder was mixed and calcined at 900 °C (Nabertherm, Germany). After sieving (AS 200, Retsch, Switzerland) the calcined powder was sintered at 1400 °C and quenched in air. This sintered powder was finally milled and sieved to get the desired particle range used in this study. The phase composition obtained by this procedure was >95 wt.% α-TCP, as verified by powder X-ray diffraction (XRD).The properties of this powder have been published previously [21]. For the given powder a particle size distribution of $d_{10} = 9$ μm; $d_{50} = 21$ μm; $d_{90} = 37$ μm, specific surface area of 0.28 $m^2\,g^{-1}$, a bulk density of 974 $kg\,m^{-3}$, a tapped density of 1399 $kg\,m^{-3}$ and finally a flowability ffc (flow factor) of 5.3 was found.

After every printing cycle the unreacted powder was dried in a preheated oven at a temperature of 200 °C for 1 h. It was then sieved with a jet sieving device and a cyclone (e200 LS, Alpine, Germany) and the fraction of particles smaller than 45 μm was reused for further printing. The legitimation of powder recycling was given in detail in our previous work [21]. Our previous study has indeed revealed that the recycled powder did not deteriorate in terms of printing characteristics compared to the original α-TCP powder.

2.2. 3D printer and printed specimens

All samples were printed using a commercial but customized 3D printer (ZPrinter 310 Plus, ZCorporation, USA) as described previously [1]. A constant layer thickness of 50 μm was used for all experiments. A custom-made moisture unit was used to apply 5 s of moisture from a water nebulizer (USV 3002, Schulte, Germany) on every layer in order to stabilize the powder bed via liquid bridges [21] just before printing. In 3DP, the solid is created by the reaction of a liquid selectively sprayed onto this powder bed. In our case, 10 wt.% phosphoric acid solution (Carl Roth, Germany) was used as reaction liquid [14,26]. Phosphoric acid partially dissolved α-TCP powder particles, and these two compounds precipitated locally, resulting in calcium phosphate (CaP) phases of brushite (DCPD, $CaHPO_4{\cdot}2H_2O$) and monetite (DCP, $CaHPO_4$), known for their excellent in vivo behavior [27–31]. Although different definitions for the term "binder" exist, in this paper we refer to the phosphoric acid solution as "binder". The local dissolution of powder particles and precipitation of new crystals resulted in an entanglement and thus local binding between previously unbound particles occurred.

Original silicon tubes were replaced by chemically inert PTFE tubes in order to reduce any material degradation due to the use of phosphoric acid in the 3D printer. Furthermore the original polymeric fluid container was replaced by an inert glass container.

Prior to the present study, a systematic analysis of printer settings had been performed with the aim of defining the most adequate binder/volume ratios (defined as saturation). Values of 45% for the shell and 90% for the core saturation were defined. The optimization was done by printing benchmark samples with concavities (Fig. S1) and different potential bone filler designs with convexities (Fig. S2). The printed samples were analyzed macroscopically using imaging software (Image Access 11 Premium, Release 11.3, Imagic, Switzerland).

Various scaffold designs were printed to assess the ability of the new design parameters proposed in this study to improve depowdering. The new design consisted of a cylindrical cage filled with various connected or loose fillers (Fig. 1). The walls included windows with a width of 2 mm preventing the fillers from escaping but allowing the removal of loose powder. The scaffolds varied according to the following parameters: (i) two different shapes of filling objects, namely sandglass (SG, Fig. 1a–c) structures and cheese segments (CS, Fig. 1d–f); (ii) different filler distances, i.e. far, near and glued; and (iii) mechanical properties after post-hardening regimes in 10% phosphoric acid compared to no post-hardening. Filler distances of 0.25/0.5 and 0.5/1 mm for near/far distance were tested for SG and CS fillers, respectively. A summary of experiments and definition of nomenclature can be found in Table 1.

The rationale for the design of the fillers was based on three criteria. First, the fillers had to have a certain printing stability. In other words, the filler geometry had to be chosen such that lateral or rotational motions were minimized during printing. Fillers presenting a flat and large base (e.g. SG and CS) were preferred to spherical designs due to their inherent stability [21]. Second, since osteoinduction is predominantly found in concavities [32], preference was given to filler designs resulting in multiple concavities between their neighbors after depowdering, e.g. SG. Finally, large empty spaces are generally considered to favor soft tissue ingrowth. So the CS geometry was chosen to fill out most of the inner volume.

All specimens were drawn with the CAD software NX 7.5 (PLM Software, Siemens, Germany) and imported into the 3D printing software in the STL (stereolithography) file format.

2.3. 3DP sample characterization

2.3.1. X-ray diffraction

The crystalline composition of pre-printed powders, as well as pre- and post-hardened printed objects, was determined by XRD. XRD was performed using a powder diffractometer (CubiX^3, PANalytical, Netherlands) with graphite-monochromated Cu$K\alpha$ radiation in the range 4–60° 2θ. The quantitative phase composition was determined by Rietveld refinement using the software BGMN (http://www.bgmn.de) version 4.2.20 [33]. Structural models were taken from Mathew et al. [34] for α-TCP, from Dickens et al. [35] for monetite, and from Curry and Jones [36] for brushite. No other phases were identified in the diffraction patterns.

2.3.2. Mechanical testing

The compression strength and diametral tensile strength of printed bulk cylinders were determined before and after post-hardening. Four cylinders were tested for every group using a static