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Brief communication

Evaluation of a new press-fit in situ setting composite porous scaffold for cancellous bone repair: Towards a "surgeon-friendly" bone filler?

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ABSTRACT

In this study, a composite porous material obtained by coating a poly(ester urethane) foam with a calcium phosphate cement is proposed as novel cancellous bone filler with easy handling, in situ hardening and press-fitting properties. The coating can be applied to the foam in the surgical theater, allowing refinement of scaffold shape to the needs of the ongoing surgery. An innovative experiment was developed in order to determine the setting curve of the composite scaffold as well as the time of manipulation available to the surgeon without risk of material damage. This composite material is soft and can be press-fit in a cavity without damaging the scaffold in the first 5 min after coating application. The composite scaffold hardens quickly (22 min) and, once the cement has set, its compressive strength and fracture energy are increased by over an order of magnitude as compared to the initial poly(ester urethane) foam. This set of interesting properties makes calcium phosphate cement-coated elastomeric scaffolds a new promising strategy for cancellous bone filling.

1. Introduction

The treatment of traumatic and post-traumatic skeletal complications (e.g. delayed unions, non-unions), defects due to bone removal (e.g. bone tumors, congenital diseases) or low bone quality (e.g. osteoporosis, osteopenia) usually requires bone fillers to plug the bone defect. Auto- or allograft bone is still regarded as the gold standard, but in several cases (elderly patients, critical-sized bone defects) synthetic bone fillers are necessary [1,2]. Usual requirements for synthetic cancellous bone fillers are: easy handling, low likelihood of extravasation and three-dimensional porous structure for bone ingrowth, bioresorbability, osteoconductivity and adequate strength during bone healing. Current fillers only partially meet these needs. For example, sintered porous ceramics are osteoconductive, but brittle. Bone cements are injectable, but may extravasate in damaged tissue and most of them are not macroporous. Biodegradable polymeric implants seldom favor bone ingrowth. Therefore, a composite approach could lead to bone fillers with improved mechanical and biological properties.

Previous studies on composite bone fillers have included polymer coating of ceramic scaffolds, biomimetic calcium phosphate coating deposition, interpenetrating network fabrication and sol–gel techniques [3–6]. Even though these composite materials showed improved mechanical strength and toughness, they lack in adaptive capacity and have either easy handling or high mechanical strength.

Calcium phosphate cements (CPCs) are adaptive materials as they undergo a hardening process over time: just after preparation they behave as a viscous paste and can be molded or injected in a cavity. After a certain time they start to harden, and once the hardening process is completed, CPCs appear as microporous solids. This microporosity can be advantageous for both cell attachment and nutrient diffusion, but macroporosity is essential for vascularization and new bone ingrowth [7]. Therefore, several strategies aiming to create macroporous cements have been developed in recent years, involving for example addition of albumen [8], mannitol [9], biodegradable particles [10] or fibers [11] and meshes [12] to the cement paste. A moldable micro- and macroporous paste obtained by mixing calcium phosphate granules with fibrin glue has also been reported [13]. However, none of these materials possesses press-fitting characteristics in the early stage evolving over time to a rigid scaffold.

To our knowledge, the composite scaffolds we present here are the first to demonstrate these press-fitting abilities with evolving mechanical properties that enable them to meet the changing requirements during the different phases of orthopedic surgery. This was obtained by the coating of a biodegradable elastomeric poly(ester urethane) foam with a calcium phosphate cement. On the one hand, poly(ester urethane) (PU) foams possess an elastomeric behavior which allows easy handling and ability to press-fit the foam in the cavity to be filled [14]. On the other hand,

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calcium phosphate cements harden over time (meaning that a cement paste can be injected or shaped in the early stage of cement setting, while after setting it will behave like a brittle solid). Because the elastomeric foam allows a good control of the cement location, contrast agents (e.g. $BaSO_4$) for later radiographic localization of the cement [15] become unnecessary.

Moreover, the composite PU foam–CPC can be press-fit in the cavity (prior to cement hardening) to ensure tight contact with native bone. The chemical composition and the mechanical properties of CPCs are close to those of cancellous bone. Additionally, CPCs have shown an osteoconductive behavior [16–18]; hence, it is expected that a CPC coating will improve osteoconductivity of PU foams as well.

An overview of the proposed preparation and insertion of this composite in a bone defect is shown in Fig. 1. After cutting of the PU foam to the desired shape and preparing the cement paste, the foam can be infiltrated with the required amount of cement. The cement paste is homogenously distributed in the foam by hand, after which the composite is ready to be inserted in the bone cavity. Hardening process takes place in situ and starts a few minutes after insertion.

Hence, the main advantages of each constituent (e.g. easy handling and press-fitting for PU, in situ hardening and osteoconductivity for CPCs) are conserved in the composite and properties unachievable for a single material (e.g. an open porosity in a CPC without the use of porogens and a hardening property for PU) are obtained with the composite scaffold.

In the following sections, the preparation methods and the characterization of the microstructure, setting and compressive behavior of the porous composite are reported and discussed.

2. Materials and methods

2.1. Poly(ester urethane) foam and calcium phosphate cement processing

Poly(ester urethane) was synthesized as already reported by a one-step polycondensation reaction of hexamethylene-1,6-diisocyanate with 1,4,3,6-dianhydro-D-sorbitol, 3,7,11-trimethyl-2,6,10-dodecatrien-1-diaminobutane amide and poly(ε-caprolactone) diol [19]. Porous PU scaffolds (90% porosity, 0.8–2 mm pores size) were obtained by a salt-leaching phase inverse method using sodium phosphate heptahydrate as porogen [19]. Cylinders 15 mm diameter and 30 mm height were obtained by laser-cut from the foams and used for dynamic measurements of scaffold hardening and unconfined compression experiments.

An α-tricalcium phosphate (α-TCP)-based cement was prepared by rapid quenching of a 2:1 molar mixture of monetite (Aldrich, C7263) and calcium carbonate (Aldrich, C4830), based on the works of Ginebra et al. [20]. Briefly, powders were heated in alumina crucibles at a rate of 5 °C min^{-1} until 1300 °C, followed by a dwell of 15 h prior to quenching in air. Cement particles then underwent a two-step milling process: 1 h with agate balls (5–10 mm size, balls/powder ratio by weight = 2) and 2 h with zirconia balls (2 mm size, balls/powder ratio by weight = 4). Milling was performed in an agate jar using a planetary ball mill (Fritsch, Pulverisette 7) at 300 rpm and ethanol (>98% purity) was used as cooling fluid. After milling, cement powder was composed of 60% α-TCP and 40% β-TCP; particle size distribution was centered on 5 μm.

2.2. Cement paste preparation and PU foam infiltration

Setting liquid consisted of a deionized water solution containing 2.5 wt.% of disodium hydrogen phosphate dihydrate (Sigma–Aldrich, S7907) and 1.5 wt.% of citric acid monohydrate (Aldrich, 27490) [20]. For paste preparation, the liquid-to-powder ratio (L/P) was set to 0.6 ml g^{-1}. Cement paste was prepared by adding the setting liquid to the cement powder, followed by helicoidal hand-mixing of the paste with a spatula for 30 s. The mixing procedure was repeated after a 30 s delay after which an appropriate amount of cement paste was weighed and introduced in the PU foams. The latter were manually homogenized to ensure a good cement distribution in the whole volume of the scaffolds. The quantity of cement paste to be introduced was calculated so that the volume occupied by the cement paste was 25% and 50% of the total volume of the scaffold.

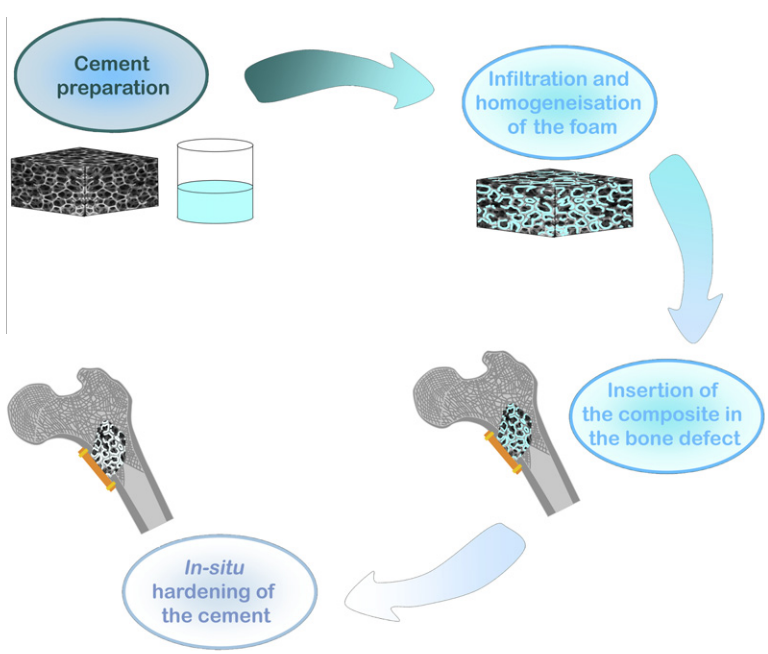

Fig. 1. schematic overview of the composite scaffold preparation and insertion in a bone cavity. A fixation plate might be added to ensure sufficient stability during the healing process.