



## Influence of the pore generator on the evolution of the mechanical properties and the porosity and interconnectivity of a calcium phosphate cement

Marco A. Lopez-Heredia<sup>a</sup>, Kemal Sariibrahimoglu<sup>a,1</sup>, Wanxun Yang<sup>a,1</sup>, Marc Bohner<sup>b</sup>, Daiki Yamashita<sup>c</sup>, Aliz Kunstar<sup>d</sup>, Aart A. van Apeldoorn<sup>d</sup>, Ewald M. Bronkhorst<sup>e</sup>, Rosa P. Félix Lanao<sup>a</sup>, Sander C.G. Leeuwenburgh<sup>a</sup>, Kiyoshi Itatani<sup>c</sup>, Fang Yang<sup>a</sup>, Phil Salmon<sup>f</sup>, Joop G.C. Wolke<sup>a</sup>, John A. Jansen<sup>a,\*</sup>

<sup>a</sup> Department of Biomaterials, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

<sup>b</sup> RMS Foundation, Bettlach, Switzerland

<sup>c</sup> Department of Materials and Life Sciences, Faculty of Science and Engineering, Sophia University, Tokyo, Japan

<sup>d</sup> Department of Tissue Regeneration, Faculty of Technological Sciences, MIRA—Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands

<sup>e</sup> Department of Preventive and Curative Dentistry, Radboud University Nijmegen Medical Centre, The Netherlands

<sup>f</sup> SkyScan NV, Kontich, Belgium

### ARTICLE INFO

#### Article history:

Received 23 May 2011

Received in revised form 9 July 2011

Accepted 11 August 2011

Available online 30 August 2011

#### Keywords:

Porous calcium phosphate cements

Porogen

Mechanical properties

Interconnectivity

### ABSTRACT

Porosity and interconnectivity are important properties of calcium phosphate cements (CPCs) and bone-replacement materials. Porosity of CPCs can be achieved by adding polymeric biodegradable pore-generating particles (porogens), which can add porosity to the CPC and can also be used as a drug-delivery system. Porosity affects the mechanical properties of CPCs, and hence is of relevance for clinical application of these cements. The current study focused on the effect of combinations of polymeric mesoporous porogens on the properties of a CPC, such as specific surface area, porosity and interconnectivity and the development of mechanical properties. CPC powder was mixed with different amounts of PLGA porogens of various molecular weights and porogen sizes. The major factors affecting the properties of the CPC were related to the amount of porogen loaded and the porogen size; the molecular weight did not show a significant effect per se. A minimal porogen size of 40  $\mu\text{m}$  in 30 wt.% seems to produce a CPC with mechanical properties, porosity and interconnectivity suitable for clinical applications. The properties studied here, and induced by the porogen and CPC, can be used as a guide to evoke a specific host-response to maintain CPC integrity and to generate an explicit bone ingrowth.

© 2011 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.

## 1. Introduction

Injectable calcium phosphate cements (CPCs) are excellent materials for bone-grafting procedures. CPCs adapt to the bone defect, are biocompatible, osteoconductive and have a composition similar to that of natural bone [1,2]. On the other hand, their degradation behavior is poor when delivered as a solid and is controlled via a layer-by-layer mechanism, which hampers the bone-remodeling process [3,4]. Increasing the porosity and interconnectivity of CPCs allows transport of body fluids within the CPC scaffolds, enhances their degradation and also improves the possibility that proteins and cells will colonize the CPCs [5]. Several methods to obtain porous CPCs have already been studied [6,7]. One of the more common methods to increase the porosity of CPCs is by including degradable pore-generating microparticles, known

as porogens [8,9]. Relevant material properties, such as porosity and interconnectivity, can be affected by the amount, size and type of polymer used to prepare the microparticles [10,11]. Poly(D,L-lactic-co-glycolic acid) (PLGA) is a biodegradable material that can be used for such a purpose [12]. PLGA degrades via a nonenzymatic hydrolytic mechanism and is a porogen, which can be loaded with drugs or proteins [13,14]. PLGA microparticles can be produced by a water-in-oil-in-water (W/O/W) double-emulsion technique [15–17]. Several parameters, i.e. amount of solvent, temperature, emulsification and agitation, affect the size and morphology of PLGA microparticles produced by this technique [18–22]. Increasing the porosity reduces the mechanical properties of the material, which can have an effect on the final clinical application [23]. This has been confirmed by finite-element and mathematical models [24–26]. These approaches permit the calculation of the expected stress and Young's modulus. Porosity on calcium phosphate (CaP) materials is categorized as follows [27]: macroporosity (330–100  $\mu\text{m}$ ), mesoporosity (100–10  $\mu\text{m}$ ) and microporosity (10  $\mu\text{m}$ –30 Å).

\* Corresponding author. Tel.: +31 (0) 243614920; fax: +31 (0) 243614657.

E-mail address: [j.jansen@dent.umcn.nl](mailto:j.jansen@dent.umcn.nl) (J.A. Jansen).

<sup>1</sup> These persons contributed equally to this study.