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Bone formation in TiO_2 bone scaffolds in extraction sockets of minipigs

Hanna Tiainen, Johan Caspar Wohlfahrt, Anders Verket, S. Petter Lyngstadaas, Håvard J. Haugen *

Department of Biomaterials, Institute for Clinical Dentistry, University of Oslo, P.O. Box 1109 Blindern, NO-0317 Oslo, Norway

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ABSTRACT

The osteoconductive capacity of TiO_2 scaffolds was investigated by analysing the bone ingrowth into the scaffold structure following their placement into surgically modified extraction sockets in Gottingen minipigs. Non-critical size defects were used in order to ensure sufficient bone regeneration for the evaluation of bone ingrowth to the porous scaffold structure, and sham sites were used as positive control. Microcomputed tomographic analysis revealed 73.6 ± 11.1% of the available scaffold pore space to be occupied by newly formed bone tissue, and the volumetric bone mineral density of the regenerated bone was comparable to that of the native cortical bone. Furthermore, histological evidence of vascularization and the presence of bone lamellae surrounding some of the blood vessels were also observed within the inner regions of the scaffold, indicating that the highly interconnected pore structure of the TiO_2 scaffolds supports unobstructed formation of viable bone tissue within the entire scaffold structure. In addition, bone tissue was found to be in direct contact with 50.0 ± 21.5% of the TiO_2 struts, demonstrating the good biocompatibility and osteoconductivity of the scaffold material.

1. Introduction

Due to the innate capacity of bone to remodel, bone tissue has natural potential to regenerate thus allowing the spontaneous repair of small bone lesions. However, in many cases the defect is too severe or the local environment is not optimal for adequate self-repair of the damaged or missing tissue [1,2]. Bone grafts or bone graft substitutes are generally required to assist the healing of such critical size, or non-healing, bone defects [3].

Bone transplants contain all the necessary elements for stimulating bone regeneration, and therefore have been favoured in current clinical practice for restoring damaged, diseased or resorbed bone tissue [4–7]. Scarcity of viable graft material, donor site morbidity, resorption of the graft material and possible immunogenic reactions associated with allografts are all shortcomings that limit the use of auto- and allogenic transplants in tissue reconstruction [8–10]. Scaffold-based solutions, which aim at promoting the natural regenerative capacity of bone tissue with the aid of a porous scaffold, offer an alternative solution for supporting bone growth in large bone defects [11,12]. Several natural and synthetic materials have been used in developing bone scaffolds with various pore structures [13–18]. However, regardless of the chosen material or pore architectural design, a bone scaffold should provide both an appropriate three-dimensional (3-D) microenvironment to promote osteogenesis and adequate mechanical stability for the defect site [2,19].

Titanium dioxide (TiO_2) is a highly biocompatible ceramic material with good osteoconductive properties [20–22]. Osteoconductivity is an important feature for scaffolds that are intended to integrate with bone as this property promotes direct contact between bone tissue and scaffold material [23,24]. Rutile TiO_2 has been studied as a promising scaffolding material for inducing bone formation from the surrounding tissue in the restoration of large bone defects [25–28]. The present authors have reported the fabrication of non-resorbable ceramic TiO_2 scaffolds with pore architectural properties well matched for those required for a bone scaffold, namely high porosity, appropriate pore size distribution and well-interconnected pore volume [26,28]. These scaffolds were also shown to be biocompatible and to promote adhesion of murine osteoblasts and human mesenchymal stem cells (hMSC) onto the entire scaffold surface in vitro [25,26,29].

However, increased porosity and pore size are known to have a detrimental effect on the mechanical strength and consequently reduce the mechanical integrity of the scaffold structure. Due to the inherently higher compressive strength of ceramic TiO_2 in comparison to other common osteoconductive scaffold materials, such as calcium phosphate ceramics (CaP), bioactive glass and CaP/polymer composites, TiO_2 can be expected to provide better mechanical strength to the scaffold structure at high interconnected porosities. Compressive strength values of approximately 2.5 MPa were reported for ceramic TiO_2 scaffolds at an overall porosity of ~85% [28], and this strength is also retained after implantation due to the non-resorbable nature of TiO_2. The compressive strength values reported for CaP and CaP/polymer composite scaffolds at similar porosities are generally well below

* Corresponding author. Tel.: +47 22 85 23 50; fax: +47 22 85 23 51.
E-mail address: h.j.haugen@odont.uio.no (H.J. Haugen).

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