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In vivo biomechanical stability of osseointegrating mesoporous TiO_2 implants

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ABSTRACT

Mesoporous materials are of high interest as implant coatings to receive an enhanced osseointegration. In this study, titanium implants coated with mesoporous TiO_2 thin films have been evaluated both in vitro and in vivo. Material characterization showed that, with partly crystalline TiO_2 (anatase), long-range-ordered hydrophilic mesoporous thin films with a pore size of 6 nm were obtained. Evaluation of the mechanical resistance showed that the films were robust enough to withstand the standard implantation procedure. In vitro apatite formation was studied using simulated body fluids, showing that the pores are accessible for ions and that formation of apatite was increased due to the presence of the mesopores. An in vivo study using a rabbit model was executed in which the removal torque and histomorphometry were evaluated. The results show that the biomechanical stability of the TiO_2 coating was unaffected by the presence of mesopores and that osseointegration was achieved without any signs of inflammation.

1. Introduction

The main focus in the development of implants for improved osseointegration is on the modification of specific surface properties. Properties that are suggested to affect osseointegration are surface topography, surface chemistry and physical properties such as surface charge and energy [1–3]. Topographical modifications on different length scales (macro-, micro- and nanometer) have been identified to be of importance in obtaining good osseointegration of implants [4]. Whether the nanotopography alone promotes osseointegration has recently been discussed, though a conclusion is yet to be reached concerning its actual effects [5]. In vitro studies have demonstrated that different nanostructures enhance the protein adsorption [6], and that osteoblasts are influenced by the surface nanotopography [7,8]. Webster et al. [9] found an increased osteoblast adhesion on nanostructured titania, alumina and hydroxyapatite compared to their non-nanostructured counterparts. In vivo studies have demonstrated favorable results in terms of bone healing around implants coated with nanosized calcium apatite particles compared to non-treated titanium [10–14]. Histological evaluation has shown that significantly more bone formation was seen on the nanoparticle coated implants compared to non-treated titanium implants [4,11]. Also, torque removal tests have shown that the nanoparticles resulted in increased tissue integration to the nanotreated implants compared to conventional titanium implant screws [12]. Gene expression analysis of tissues around nanostructured calcium phosphate implants has been performed and compared with those of uncoated implants in a rabbit model [15]. After 2 weeks of healing, alkaline phosphatase (ALP) expression was significantly higher, and runt-related transcription factor 2 and tumor necrosis factor-α expressions were significantly lower for the coated than for the uncoated implants. After 4 weeks of healing, ALP and osteocalcin were significantly up-regulated in the coated group, indicating enhanced mineralization of the bone around the implant compared to the control.

Porous nanostructures have an additional property of interest, since they have the ability to serve for drug-delivery purposes. For example, a sustained release can be obtained from mesoporous materials (with a size range of 2–50 nm [16,17]), such as mesoporous silica. It has been shown that the release rate can be tuned depending on the material properties [18–23], and that they possess a high drug-loading capacity [24,25]. A recent approach is to use mesoporous materials for local drug delivery from the implant surface for increased bone regeneration [23,26,27]. An example of this has been shown by Xia et al. [28], who reported a sustained in vitro release from a mesoporous TiO_2-coated implant of the antibacterial drug cephalothin. However, no in vivo studies using mesoporous TiO_2 have been reported.

In this study, titanium implants coated with a thin layer of mesoporous TiO_2 have been evaluated and compared to nonporous TiO_2 coatings. The mesoporous TiO_2 thin films were formed using the evaporation-induced self-assembly (EISA) method, which

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