ON BONE REGENERATION IN POROUS BIOCERAMICS

Studies in humans and rabbits using free form fabricated scaffolds

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Göteborgs Universitet kommer att offentligen försvaras i Hörsal A404 vid Avdelningen för Biomaterialvetenskap, Medicinaregatan 8b, våning 4, fredagen den 8:e juni 2007. kl.13.00 av

Johan Malmström
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Fakultetsopponent: Professor Fernando Jorge Monteiro, Biomaterials Laboratory, Porto University, Porto, Portugal

Avhandlingen baseras på följande delarbeten:

I J. Malmström, E. Adolfsson, L. Emanuelsson and P. Thomsen
Bone ingrowth in zirconia and hydroxyapatite scaffolds with identical macroporosity
J Mater Sci Mater Med, in press

II J. Malmström, E. Adolfsson, A. Arvidsson and P. Thomsen
Bone response inside free form fabricated macro porous hydroxyapatite scaffolds with and without an open microporosity
Clin Impl Dent Relat Res, in press

III J. Malmström, T. Jarmar, E. Adolfsson, H. Engqvist and P. Thomsen
Structure of the interface between bone and scaffolds of zirconia and hydroxyapatite
In manuscript

IV J. Malmström, C. Slotte, E. Adolfsson, O. Norderyd and P. Thomsen
Bone response to free form fabricated hydroxyapatite and zirconia scaffolds. A histological study in the human maxilla
In manuscript

ABSTRACT

The objective of the present thesis was to evaluate the effect of material chemistry and macro- and micro-porosity on bone regeneration in association with synthetic, porous ceramic materials. Ceramic scaffolds were designed and manufactured for experimental and human studies using free form fabrication (FFF), a technique which produces the object layer by layer using data from CAD files. The identical macroporous scaffolds of different chemistry and microporosity were created through control of the FFF and colloidal shaping processes.
The chemical composition of scaffolds was characterized by X-ray diffraction. Porosity was measured by Archimedes´ principle and the macroporosity of the scaffolds calculated from geometrical dimensions of the scaffold. Roughness of the macropores was investigated by scanning electron microscopy (SEM) and optical interferometry. The bone response to scaffolds made of zirconia and hydroxyapatite (with and without an open microporosity), inserted in rabbits and humans, were investigated at the light microscopical (LM) level. SEM, focussed ion beam microscopy (FIB) and transmission electron microscopy (TEM) were used for material-tissue interfacial analyses. A significantly greater bone ingrowth and direct bone contact were demonstrated inside macroporous scaffolds of hydroxyapatite compared to zirconia after 6 weeks in rabbit tibia and femur. The addition of open microporosity to hydroxyapatite provided an added, bone-promotive effect. Due to the FFF manufacturing process two different surface roughness values were obtained inside each macropore but no significant differences in bone contact were detected. The FIB technique to prepare intact samples for transmission electron microscopy was successfully applied on interfaces between bone and ceramic scaffolds. In zirconia a direct contact between the material and bone could be seen after 6 weeks in rabbit femur. For hydroxyapatite scaffolds, an apatite layer was demonstrated between the material and bone which was not present in the case of zirconia. The addition of micropores to the hydroxyapatite material reduced the width of the apatite layer from 200 nm to 100 nm. Furthermore, ingrowth of mineralized collagen fibrils could be detected inside the micropores. In the human study, the results from the two animal studies could be verified with respect to promotion of the bone response due to material and geometry, i.e. hydroxyapatite scaffolds were associated with a significantly greater bone regeneration than zirconia after 3 months in the human maxilla. Similar to observations in rabbit bone, a close contact was demonstrated between bone and hydroxyapatite and zirconia, respectively. In addition, ingrowth of bone was detected in the micropores of hydroxyapatite.
The FFF technique has enabled the production of ceramic scaffolds with controlled material properties, allowing systematic studies on the effects of material properties on bone regeneration in vivo. The results of the present studies show that bone ingrowth and bone contact is promoted in macroporous FFF ceramic scaffolds, in particular hydroxyapatite with an added open microporosity, hence providing FFF as a new, valuable research tool and a means to contribute to the clinical treatment of compromised bone conditions.

Keywords. bone regeneration, hydroxyapatite, zirconia, macroporosity, microporosity, free form fabrication, focused ion beam, scanning electron microscopy, transmission electron microscopy, rabbit, human

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Correspondence. Johan Malmström, Department of Biomaterials, Institute of Clinical Sciences, Sahlgrenska Academy at Göteborg University, Box 412, SE 405 30 Göteborg, Sweden, E-mail: johan.malmstrom@biomaterials.gu.se