Available online at www.sciencedirect.com
SCIENCE DIRECT®
Biomaterials 26 (2005) 3521–3526
Biomaterials
www.elsevier.com/locate/biomaterials

In vivo study of the effect of RGD treatment on bone ongrowth on press-fit titanium alloy implants

Brian Elmengaard[a,d,*], Joan E. Bechtold[b,c], Kjeld Søballe[a,d]

[a]*Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, Aarhus University Hospital, AKH, Norrebrogade 44, Bygn. 1A, DK-8000 Aarhus C, Denmark*
[b]*Orthopaedic Biomechanics Laboratory, Midwest Orthopaedic Research Foundation and Minneapolis Medical Research Foundation at Hennepin County Medical Center, Minneapolis, Minnesota*
[c]*University of Minnesota Departments of Orthopaedic Surgery and Biomedical Engineering*
[d]*Interdisciplinary Nanoscience Center (iNANO), University of Aarhus, Denmark*

Received 2 June 2004; accepted 20 September 2004

Abstract

Early bone ongrowth is known to increase primary implant fixation and reduce the risk of early implant failure. Arg–Gly–Asp (RGD) peptide has been identified as playing a key role in osteoblast adhesion and proliferation on various surfaces. The aim for this study is to evaluate the effect of RGD peptide coating on the bony fixation of orthopaedic implants, to justify its further evaluation in clinical applications. Sixteen unloaded cylindrical plasma sprayed Ti6Al4 V implants coated with cyclic RGD peptide were inserted as press-fit in the proximal tibia of 8 mongrel dogs for 4 weeks. Uncoated control implants were inserted in the contralateral tibia. Results were evaluated by histomorphometry and mechanical push-out test. A significant two-fold increase was observed in bone ongrowth for RGD-coated implants. Also, fibrous tissue ongrowth was significantly reduced for RGD-coated implants. Bone volume was significantly increased in a 0–100 μm zone around the implant. The increased bony anchorage resulted in moderate increases in mechanical fixation as apparent shear stiffness was significantly higher for RGD-coated implants. Increases in median ultimate shear strength and energy to failure were also observed. This study demonstrates that cyclic RGD coating increases early bony fixation of unloaded press-fit titanium implants.
© 2004 Elsevier Ltd. All rights reserved.

Keywords: Integrins; RGD peptide; Implant fixation; Osteoblasts; In vivo

1. Introduction

Total hip replacements generally enjoy high rates of success; however, the groups of young, physically active patients often outlive prostheses fixated by bone cement. For these patient groups, a non-cemented porous-coated titanium prosthesis has become a primary choice. For improved longevity of these implants, studies have shown that early bone ongrowth results in a stronger implant fixation and prevents formation of a fibrous tissue membrane at the interface [1]. A fibrous tissue membrane may in the long term prevent solid bony integration of an implant.

Strategies to improve implant longevity by enhancing early bone ongrowth include the use of different implant coatings to encourage bone growth directly at the implant surface.

Recently, the peptide Arg–Gly–Asp (RGD) has been suggested to increase osteoblast adhesion and subsequent proliferation to orthopedic implants [2,3]. The effects of RGD peptide on cell adhesion was first identified by Pierschbacher et al. [4]. The RGD sequence

*Corresponding author. Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, Aarhus University Hospital, AKH, Norrebrogade 44, Bygn. 1A, DK-8000 Aarhus C, Denmark. Tel.: +45 8949 4162; fax: +45 8949 4150.
E-mail address: brianelm@dadlnet.dk (B. Elmengaard).

0142-9612/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2004.09.039

binds to transmembrane proteins in the cell membrane known as integrins. Integrins are mediators of cell adhesion to extracellular matrix. More than 20 subtypes of integrins have been identified and nearly half of them recognize the RGD sequence [5].

Of relevance to bone biology the RGD peptide is found in several extracellular bone matrix proteins such as vitronectin, fibronectin, osteopontin and bone sialoprotein. Although the biological events after implantation of orthopaedic devices is not fully understood, the adsorption of RGD containing extracellular bone matrix proteins to the implant surface is likely to play a large role in osteoblast spreading and proliferation. Okamoto et al. have suggested that RGD peptide contributes to the osteoconductive effect of hydroxyapatite more than titanium. They found that extracellular proteins containing the RGD peptide adsorb more easily to the hydroxyapatite surface than on titanium [6].

Although RGD peptide has been studied extensively in vitro [3,7], few in vivo studies have been published [8,9]. No other studies have applied RGD peptide on a porous-coated titanium implant relevant to orthopaedic joint replacement therapy in a large animal model.

In this study, we use a cyclic RGD (Fig. 1) which interacts with the $\alpha_V\beta_3$ and $\alpha_V\beta_5$ integrin subunits, commonly associated with vitronectin, and developed to increase biointegration of metal implants [10,11]. Cyclic peptides have been shown to be more stable with regards to three-dimensional structure and resistance to enzymatic cleavage [12]. The integrin affinity and specificity to the RGD peptide is affected by both steric conformation and the amino-acid sequences flanking the RGD peptide [13,14].

The aim of this study is to investigate whether cyclic RGD coating will enhance the fixation of titanium implants in vivo. We examine the application of this cyclic RGD applied to a plasma spray titanium alloy (Ti6Al4 V) implant surface inserted in an unloaded cancellous bone site in the canine.

We evaluate the effect of RGD peptide coating with regards to tissue distribution and implant fixation. We hypothesize that RGD peptide-coated titanium implants inserted as press-fit will result in an increase in bone ongrowth at the bone–implant interface as measured histomorphometrically, and an increase in mechanical fixation as measured by push-out test.

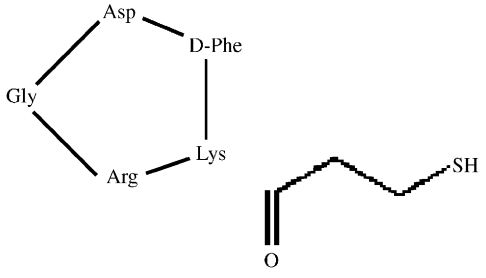

Fig. 1. Structure of cyclic RGD pentapeptide with spacer and thiol (-SH) anchor.

2. Methods

2.1. Implants and coating technique

Cylindrical plasma sprayed implants of titanium alloy (Ti6Al4 V) with a diameter of 6.0 mm and 10.0 mm of length (Biomet® Inc., Warsaw, IN, USA) were the substrate for application of cyclic RGD coating. Implants had in a pore size of 200–1000 μm at the substrate and the surface of the coating, respectively. The gross surface roughness of the plasma spray process (Ra) was 47 μm, with profile depth of 496 μm (determined using a roughness meter (Perthen, Hannover, Germany) with a stylus tip radius of 3 μm) [1].

The cyclic RGD peptide (-RGDfK[-beta-mercaptopropionyl]) with a thiol anchor was synthesized as described by Haubner et al. [11] according to Jonczyk et al. [15]. The implants were cleaned, autoclaved and thereafter suspended in a sterile filtrated 100 μM solution of the RGDfK peptide in PBS buffer at pH 8.3. A 100 μM solution of peptide have in an earlier study shown to promote cell adhesion to RGD-coated surfaces [2]. The implants was left in the suspension for 24 h and subsequently washed 3 times in PBS buffer followed by air drying in a laminar airflow chamber. All implants were sterilized using irradiation (35 kGy of Co-60 for 14 h, Risø National Laboratory, Roskilde, Denmark). The peptide coating procedure was performed by Biomet Merck BioMaterials GmbH, Darmstadt, Germany.

2.2. Animals and surgical procedure

Approval was obtained from our Institutional Animal Care and Use Committee prior to performing the study.

The 16 implants were inserted in the proximal tibia (Fig. 2) bilaterally in 8 skeletally mature mongrel dogs of average weight 21.0 ± 1.3 kg. The study design was paired. On the right side, RGD-coated implants were inserted. The contralateral titanium implants without RGD served as controls. The implants were inserted during general anaesthesia, using sterile technique.

In the proximal tibia, the implantation site was exposed through a medial approach, leaving the medial collateral ligament intact. The periosteum was removed only at the area of drilling 18 mm distal to the joint line. Initially a guide wire was inserted, followed by a 5.9 mm cannulated drill. Drilling was performed at 2 rotations per second to prevent thermal trauma to the bone. The implantation site was cleaned using isotonic saline with polymyxin B. The implant was incrementally inserted press-fit with repeated hammer blows. The overlying

Download English Version:

https://daneshyari.com/en/article/12732

Download Persian Version:

https://daneshyari.com/article/12732

Daneshyari.com