Comparison of titanium coatings for cementless fixation in an ovine model

ABSTRACT

Novel coatings providing highly porous and roughened surfaces, as well as osteoconductivity, are continuously investigated in implants for uncemented fixation to achieve long-term clinical efficacy. However, comparative and dynamic investigations of the implant-bone integration process are lacking. This preclinical laboratory study compared the mechanical and histologic properties at the bone-implant interface between two state-of-the-art materials, one constituted by grit blasted titanium coated by hydroxyapatite (Ti + HA), and a coating made of titanium (MectaGrip®) on the same Titanium bulk, in an ovine model. Cylindrical implants with either material were placed under different gap conditions in cancellous bone, and in a line-to-line manner in cortical bone. At 4 and 12 weeks, push-out testing was conducted in the cortical samples to evaluate implant-bone mechanical properties, while histology was performed in cortical and cancellous samples to visualize bone ongrowth. Compared to grit blasted Ti + HA coating, MectaGrip®-coated implants showed significantly higher mechanical properties at the bone-implant interface at 12 weeks. Histology confirmed intimate implant-bone contact for both materials. Mechanical properties and osseointegration improved significantly with time for both materials. No adverse reactions were observed.

In conclusion, this preclinical evaluation in an ovine model showed that MectaGrip coating provides superior mechanical bonding than grit blasted Ti + HA coating, and that implant-bone integration is a dynamic process which takes more than 4 weeks to complete. MectaGrip® appears to offer a mechanically valid substrate for implant-bone integration in vivo, potentially improving the strength of implant fixation. These findings substantiate its use in joint arthroplasty.

BACKGROUND AND INTRODUCTION

The ultimate goal of most implantable devices is to restore impaired biological functions and achieve functional integration with the body. To achieve these objectives in the long-term, fixation between the implant and the host tissue is paramount [1]. While fixation has traditionally been achieved using bone cement, potential issues with thermonecrosis and toxicity have motivated the development of cementless fixation [2]. In this approach, fixation is achieved by osseointegration, consisting in the attachment of lamellar bone to the implants without intervening fibrous tissue [3]. The implant-bone interface represents a living system, where de novo bone formation and establishment of a biological and mechanical interlock take place [4]. Osseointegration is controlled by the surface properties and geometry of the implant, as well as by the loading conditions and surgical fit [5]. Adequate bone fixation of the implant surface has the potential additional benefits of reducing implant complications, such as subsidence, expulsion, nonunion, and micromotion [2], [6].

Restricting the analysis to the surface properties of the implants in uncemented fixation, coatings to obtain highly porous and roughened surfaces, as well as osteoconductivity, are continuously investigated [7].

Currently, porous and rough surfaces can be created by grit blasting or plasma spraying [8]. Grit blasting generates a textured surface by bombarding the implant with small abrasive particles, such as aluminum oxide. Plasma spraying involves mixing metal powders with a pressurized and ionized inert gas, thereby forming a high-energy flame: the flame is then sprayed onto the implant, creating a textured surface. Titanium and its alloys are utilized extensively in the production of porous mediums [9], with the first evaluations of porous metal surfaced titanium for orthopedic implants dating as far back as the 1970s [10].

With respect to osteoconductivity, hydroxyapatite (HA) is nowadays widely used: this is a calcium phosphate compound that is typically plasma-sprayed either directly on the implant, or over a porous coating [2]. HA is osteoconductive in that it enhances the growth of mineralized bone onto the implant. Like porous titanium, also HA coating has been extensively employed in orthopedics.

While the use of titanium and HA coating is widespread in orthopedic implants, comparative and dynamic investigations of the implant-bone integration process are scarce. Therefore, the objective of this study was to compare the osseointegration and implant-bone mechanical properties of two state-of-the-art materials, namely one constituted by grit blasted titanium coated by hydroxyapatite (Ti + HA), and a coating made of titanium (MectaGrip®) on the same Titanium bulk. MectaGrip® consists of a layer of commercially pure titanium deposited through the plasma spray technique, and was designed by Medacta International to enhance initial stability due to its high coefficient of friction and to provide a valid substrate for a mechanically efficient bond with bone. Implant-bone integrations under different gap conditions were evaluated in cancellous and cortical bone, using an established in vivo animal model.
Gathering data on the implant-bone integration process using established models could be instrumental in taking more evidence-based decisions in clinical practice.

MATERIALS AND METHODS

This laboratory study was conducted according to a protocol developed and validated at Surgical & Orthopaedic Research Laboratories of New South Wales University in Sydney, Australia. Both protocol and qualifications of the personnel involved in the study were reviewed and approved by the institutional Animal Care and Ethics Committee.

Implants

Cylindrical dowels (6mm x 25mm, Figure 1) of either grit blasted titanium + hydroxyapatite (Ti + HA) or titanium (MectaGrip©) on the same Titanium bulk, provided by the sponsor, were the implants used in the study. Before surgery, the surface features of the samples were qualitatively examined using a stereo-zoom microscope for macroscopic evaluation, and using an environmental scanning electron microscope (eSEM) for microscopic evaluation.

Study design

Skeletally mature adult male sheep (n=8, approx. 55-75 Kg) were used for comparative testing of the implants. Animals underwent a bilateral procedure using an established preclinical model\[1\], \[3\]–\[5\]: dowels were implanted into the cancellous bone of the distal femur and proximal tibia under 3 different gap conditions (press fit, line-to-line, 1 mm gap and 2 mm gap), as well as in the cortical bone of the tibial diaphysis in a line-to-line manner (Figure 2). Samples were evenly distributed across the two implant groups.

The animals were euthanized at 4 weeks (n=4) and at 12 weeks (n=4). Upon harvesting, the surgical sites were examined for signs of adverse reaction or infection. The harvested bones were X-rayed in the anteroposterior and lateral views to determine implant placement and any adverse bony reactions.

Subsequent sample processing differed according to the location of the implants. Cancellous sites were isolated using a saw including the implant and surrounding bone and were fixed in cold phosphate buffered formalin. These samples underwent histological analysis only. Cortical sites were isolated using a saw and split in half perpendicular to the implant long axis: the medial portion was used for mechanical testing followed by histology, whereas the lateral portion was processed for histology only.

The medial portion of cortical implants was tested for implant-bone interface shear strength (MPa) using a standard push-out test. Shear strength can be defined as the resistance of a material against a force (shear load) that tends to produce a sliding failure along a plane parallel to the direction of the force. Specimens were displaced at 0.5 mm/min using a calibrated servohydraulic testing machine (MTS Mini Bionix®, MTS Systems Inc., Minneapolis, Minnesota, USA) (Figure 3). The linear portion of the load-deformation curve resulting from the push-out test was used to determine the maximum push-out force (i.e. peak load, N) and the energy to failure (Nmm) necessary to rip the implant from the bone, as well as the stiffness of the bone-implant interface (N/mm)(Figure 4). Post-processing of force-displacement data was performed using an in-house script written for MatLab (Mathworks, Inc., Natick, MA, USA).
3. Set up for mechanical testing of cortical bone samples.

4. Typical load versus displacement graph. The peak load is the highest point on the curve. The area under this point (depicted in blue) is the energy necessary to rip the implant from the bone. Stiffness is the gradient of the linear portion of the curve (represented by the green line).
**Histological analysis and histomorphometry**

Two thin (~15-20 micron) sections were cut along the long axis of each embedded implant (cortical and cancellous) for histological evaluation. Sections were stained with methylene blue and basic fuchsin for examination under a light microscope (Olympus, Japan) for bone organization, general tissue response, presence of inflammatory cells or local particulate at the implant-bone interface.

Furthermore, digital images were taken at the bone-implant interface to determine the percentage of direct bone contact with the implant, where 0% indicated no contact and 100% indicated complete contact (Figure 5). Digital image analysis was performed with an in-house script written for MatLab.

**RESULTS**

**Pre-operative testing**

Surface macroscopic and microscopic appearance of grit blasted Ti + HA and MectaGrip® implants are shown in Figure 6.

**Adverse events**

Surgery was completed without incidents. No evidence of infection or adverse events were encountered during this study. Radiographic review found no evidence of fracture or adverse bony reactions at any site in neither time point.

**Mechanical testing**

A significant effect was detected for both factors, time and surface coating. With respect to time, a significant increase in all mechanical parameters between week 4 and week 12 was present for the MectaGrip® group, whereas in the grit blasted Ti + HA group this was true for all parameters except energy to failure, which did not increase significantly. With respect to surface coating, significant differences emerged for shear strength and peak load at 12 weeks: both parameters were significantly higher in the MectaGrip® group than in the grit blasted Ti + HA group. No significant differences were present at 4 weeks in any mechanical parameter. Values are shown in Figure 7.

**Statistical analysis**

Sample size was determined based on previous experiments and power calculations. Mechanical and histomorphometric data was analyzed using a two-way analysis of variance (ANOVA) with post hoc tests for pairwise comparisons to assess the influence of time and surface coating on each parameter. Significance level was set at $p<0.05$. 

**Example of bone ongrowth analysis.** Ongrowth occurs when bone grows onto a roughened surface. The green line defines the areas of direct implant-bone contact, while the red line defines the areas with no direct implant-bone contact. Images were taken with Scanning Electron Microscopy (SEM).
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Mechanical parameters. * indicates p value <0.05.

Histological analysis and histomorphometry

Qualitative assessment of histological images demonstrated direct bone contact with the implants on both cancellous and cortical sites. This effect, already present at 4 weeks, was marked at 12 weeks (Figure 8).

The percentage of contact between the implant and bone was confirmed quantitatively with histomorphometric analysis with an increase from 62% (grit blasted Ti + HA) and 61% (MectaGrip©) at 4 weeks to 88% (grit blasted Ti + HA) and 83% (MectaGrip©) at 12 weeks. No difference emerged between the two coatings.

DISCUSSION

This study compared the preclinical results of two state-of-the-art materials: one constituted by grit blasted titanium coated by hydroxyapatite (Ti + HA), and a coating made of titanium (MectaGrip©) on the same Titanium bulk, using an established in vivo animal model.

Both coatings demonstrated new bone formation at 4 weeks that continued to progress at 12 weeks through the roughed domains of the implant. Sound osseointegration results with time were confirmed by both histology and mechanical tests.
At 4 weeks, the MectaGrip® bone-implant interface appeared stronger than the one of grit blasted Ti + HA coating, since all mechanical parameters were higher for the former, albeit not significantly. This effect was confirmed and even enhanced at 12 weeks, where MectaGrip® showed significantly higher shear strength and peak load compared to grit blasted Ti + HA. Shear strength, which depends on the amount and strength of surrounding new bone[6], is particularly relevant since, in femoral stems, shear loads are the most critical to compensate for. These findings demonstrate that MectaGrip® coating provides superior mechanical bonding than grit blasted Ti + HA coating. MectaGrip® appears therefore to offer a mechanically valid substrate for implant-bone integration in vivo, potentially improving the strength of implant fixation. Other laboratory studies demonstrated that porous titanium implants outperformed titanium grit blasted implants with HA coating[7]. The excellent performance of MectaGrip®, coupled with HA coating, is also proven at the clinical level by the anatomically-shaped Minimax femoral stem, developed by Medacta International and launched on the market in 2007 for use in total or partial hip arthroplasty for primary or revision surgery. Minimax features in the Regional Register of Orthopaedic Prosthetic Implantology (R.I.P.O)[8], with a survival rate of 98.3% (CI 96.9-99.1) at 5 years after surgery and with preliminary data revealing a 94.2% (CI 87.7-97.3) survival rate at 10 years after surgery (data from a manufacturer ad hoc R.I.P.O report obtained in October 2018).

Another important finding of this study concerns the time necessary to obtain early stabilization and osseointegration. For both materials, in fact, the mechanical bonding with the surrounding bone improved significantly between 4 and 12 weeks. This demonstrates that, even in an optimal situation represented by healthy young animals with a well-healing bone bed, one month is not enough for bone ongrowth to take place. This becomes even more relevant when considering the less optimal situation represented by elderly patients. It is also recognized that good osseointegration depends on additional factors, such as post-operative treatments, amount of movement and load, as well as on the patient’s condition and cooperation. It is therefore of utmost importance to consider, in post-operative rehabilitation protocols, the time necessary for stabilization and osseointegration, and to protect patients from excessive strain of the bone-implant interface in the early phases of the rehabilitation.

The limitations of this study are those typical of preclinical models: in fact, the model does not provide a direct comparison to the complex load bearing that is encountered in patients following a joint arthroplasty, and it has a limited sample size and number of time points[5]. However, the use of an established ovine model does provide a reproducible means to evaluate the performance of different materials and coatings in uncemented fixation.

Future clinical studies should investigate the initial stability and osseointegration of cementless implants by addressing, together with the coating of the stem, also the effect of additional factors including the geometry of the implant, patient age, activity level, bone type, and deformities[2]. To reach this objective it is important that investigators consistently report clinical findings as well as all radiographic osseous changes. In this way, more definitive conclusions can be drawn about which stem to use for each patient, and realize an evidence-driven personalized medicine.
References


The current paper is based on the study of W.R. Walsh et al. “Evaluation of implant fixation in an ovine model – Medacta Arthroplasty fixation surfaces”.
Study Report available on内部 files.