

Developing a novel femoral stem in hip arthroplasty

An innovation process using a weight-bearing animal model

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Abbreviations and terms

CI: Confidence interval

CNC technique: Computer numerical control technique.

CP: Calcium phosphate

CPT: Commercially pure titanium

HA: Hydroxyapatite

PMMA: Polymethyl methacrylate, typically used as bone cement

RSA: Radiostereometric analysis

SSI: Surgical site infections

TiCap: CP over a coating of porous, commercially pure titanium

TiAl6V4: Alloy consisting of 90% titanium, 6% aluminium and 4% vanadium

TPS: Titanium plasma spray

UHMWPE: Ultra-high-molecular-weight polyethylene, typically used in acetabular cups

Uncemented/cementless: Implants designed for bone ingrowth/ongrowth without the use of cement

1 Scientific environment

This project was performed at the Department of Orthopaedic Surgery, Stavanger University Hospital, while I was working as a registrar in a 50 per cent research and 50 per cent clinical position from 2004 to 2008, as a registrar from 2008 to 2011, and later as a consultant surgeon. I was a PhD candidate and received scientific supervision at the Department of Surgical Sciences and later at the Department of Clinical Medicine, University of Bergen. I also received supervision from staff at the Department of Clinical Dentistry–Biomaterials.



Stavanger University Hospital
Stavanger Hospital Trust

2 Acknowledgements

My introduction to research occurred during my medical training at the University of Bergen, where the seed was sown by Professor Dagfinn Øgreid. I collaborated with him to write my first scientific paper and was afforded the opportunity to attend scientific meetings. I later started my orthopaedic career at Kysthospitalet in Hagavik, where I met Professor Einar Sudmann. He suggested the topic for a project that later led to my dissertation. Dr. Ole Dankert Lunde was my first employer and the surgeon who performed the first 2 goat operations prior to the initiation of my role in the project. He also assisted in the first operations that I performed on goats.

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In the second study, I had the good fortune of relocating to Høyland, Sandnes, after becoming acquainted with Professor Martha Ulvund, Norwegian University of Life Sciences (NMBU). She and her excellent staff have helped me more than they know. I am especially grateful to Garman Auklend and Asbjørn Haga, who took care of the animals on a day-to-day basis.

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3 Abstract

Introduction:

To address the growing incidence of hip replacement revision, this project aimed to find a stem that would fulfil three criteria. First, solid osteointegration and long survival of the implant. Second, easy removal, if deemed necessary. Third, little or no bone loss at the time of revision to facilitate the implantation of the revision stem.

Methods:

A stem of our own design was implanted in two animal series. Study 1 was performed in 2006, and 12 goats were operated upon. Study 2 was performed in 2008 and included 35 goats. In both studies, the goats were observed for 6 months, and full weight-bearing was permitted. After the goats were euthanised, the stems were randomised to drilling or no drilling of the area of osteointegration and tested biomechanically for differences in pull-out force. In Study 1, the implants were coated with calcium phosphate (CP); in Study 2, hydroxyapatite (HA) was used instead. Histological analysis was performed in both studies.

Results:

A significantly lower pull-out force was observed in Study 2 after drilling in the area of osteointegration (mean, 1526 N vs. 2033 N, $p = 0.028$). The calcium phosphate coating was inferior in performance to hydroxyapatite regarding bone apposition and pull-out force (CP mean, 174 N vs. HA 1526 N, $p = 0.003$). No correlation of the bone apposition evaluated by histology and pull-out force was observed. In addition, there were no signs of inflammation.

Conclusion:

A significant effect of drilling longitudinally orientated grooves in a femoral stem in goats to reduce pull-out force was observed. The hydroxyapatite coating appears preferable to calcium phosphate on TiAl6V4-loaded implants with respect to bone apposition and pull-out force. Bone growth towards the femoral stem was not correlated with the pull-out force of the implant.

4 List of publications

- I. Harboe K, Enoksen CH, Gjerdet NR, Sudmann E. Development of a femoral stem providing strong anchorage and facilitated removal. An experimental study in goats. *Vet Comp Orthop Traumatol.* 2012; 25(2):95-101.
- II. Harboe K, Gjerdet NR, Sudmann E, Indrekvam K, Søreide K. Retention force and bone-growth in two differently coated femoral stems after 6 months of loading in a goat model. *J Orthop Surg Res.* 2014;9:69
- III. Harboe K, Ellingsen CL, Sudmann E, Gjerdet NR, Søreide K, Indrekvam K. Can bone ongrowth predict retention force of a femoral stem? An experimental weight-bearing hip implant model in goats. Accepted for publication. *BMC Musculoskeletal Disorders*, April 2015.

5 Introduction

A total hip arthroplasty consists of a femoral stem and acetabular cup and is the end-stage treatment for hip arthrosis (Figure 1). This condition can be caused by several factors, such as hip dysplasia or Calvé-Legg-Perthes disease, and can also occur in the posttraumatic period. Most commonly, it is of an idiopathic in nature, meaning no firm cause-effect can be established. Arthrosis is characterised clinically by pain during movement or at rest and decreased range of motion, and the diagnosis is confirmed by radiography of the pelvis. The radiographic image typically shows a decrease in the joint space, subchondral sclerosis, osteophytes, and possibly subchondral cysts (Figure 2). The radiographic findings are not necessarily correlated with the patient's symptoms; commonly, the clinical symptoms, including nightly pain, should dictate the need for an operation when conservative management is no longer sufficient. Conservative management consists of analgesics (i.e., paracetamol and NSAIDs), partial weightbearing, physiotherapy and reassurance of the patient about the cause of the hip pain.

A total hip arthroplasty (THA) consists of a femoral stem and an acetabular cup fixed to the bone with bone cement (Polymethyl methacrylate, PMMA) or bone apposition (i.e., uncemented). The stem can be modular with a separate stem, neck and head. The most common variants possess modular heads, without a modular neck. If the head is fixed to the stem, the stem is called a monoblock. Modularity can allow a correction of offset (ie. distance from the center of rotation of the cup to the long axis of the femur), leg length and anteversion (ie. the direction of the femoral neck in relation to the acetabular cup) after the implantation of the femoral stem. The acetabular cup can be made of ultra-high-molecular-weight polyethylene (UHMWPE) and cemented directly into the acetabulum. With uncemented cups, there is a metal cup backing with different inserts (e.g., UHMWPE, ceramic, or metal).

In Norway, there is a trend towards cement fixation of the acetabular component and uncemented fixation of the femoral component, called a reverse hybrid (1).

The operation is performed using different approaches. The most common approaches in Norway are the direct lateral (transgluteal), posterior, and anterior (typically named mini invasive or muscle sparing) (1). One seeks to restore the normal biomechanical parameters of the hip, i.e., leg length, offset and range of motion. The operation should be planned using templates, and using computer-based systems to achieve these aims is now common (2).

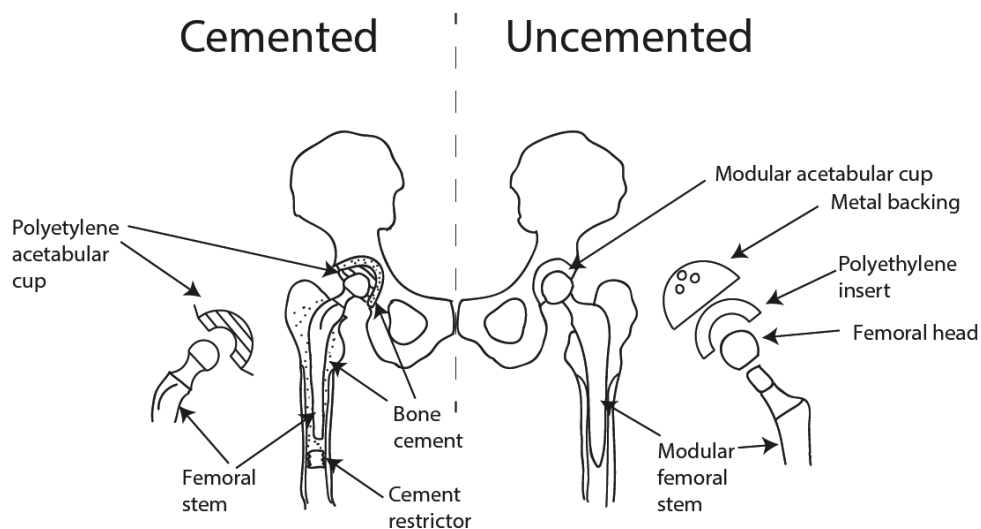


Figure 1. Basic principles of a total hip arthroplasty. Cemented components vs. uncemented (adapted and used with permission from Geir Hallan).

The goal after the operation is a pain-free and normally functioning hip joint. The patient should immediately load the extremity. The duration of the hospital stay varies but has gradually been reduced. In the 1990s, patients at Stavanger University Hospital were hospitalised for 3-4 weeks. With the addition of standardised patient treatment and early mobilisation (“Fast track surgery”/”Rapid recovery”), the stay is 3-4 days and occasionally less. Most patients are satisfied with the operation (3), and the operation is highly cost-effective (4).

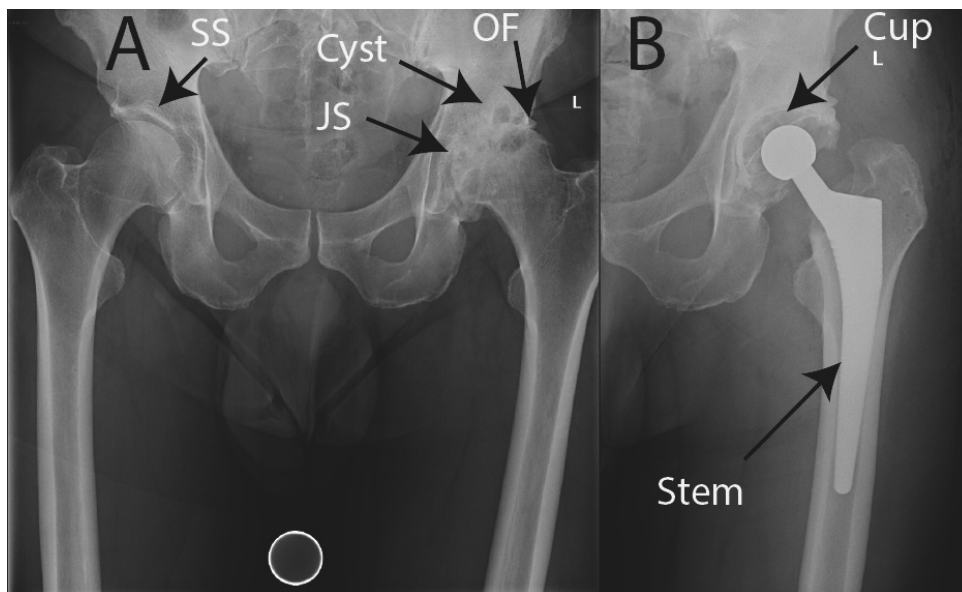


Figure 2 A: Total hip arthroplasty. Pre-operative picture. JS = reduced joint-space. Cyst = subchondral cyst. OF = osteophyte. SS = subchondral sclerosis. B: Stem = uncemented femoral stem. Cup = cemented acetabular cup.

5.1 History of total hip arthroplasty.

The history of treatment for hip arthrosis is long, and a brief overview of the development of total hip arthroplasty is outlined below.

5.1.1 Early efforts to treat arthrosis

Hip arthrosis has been described in bones found from early in human history (5) and has been difficult to treat using conservative methods. The end stage of the arthrosis was ankylosis (bony fusion of the femur to the pelvis) with poor function but with little pain from the joint. Starting in the 1700s, the surgical option was to excise the affected joint, and by keeping the remaining joint space in motion, a pseudarthrosis was created. This surgery was performed without any anaesthesia, and as one would

expect, the procedure was associated with a mortality rate of 50%. After some time, the joint pseudarthrosis usually healed, and the range of motion was lost. The next technique used was interpositional arthroplasty, a fascia lata interposition that was reported by Murphy (6). Jones used a strip of gold foil to replace the lost cartilage of the femoral head (7). In 1891, Glück attempted to use ivory as a joint replacement but was unsuccessful (8). Smith-Petersen introduced a cast prosthesis of cobalt chromium molybdenum (CoCrMo) alloy (Vitallium) in 1937 after first using glass as the cast material, which broke under the load (9). Moulded Vitallium was the best solution to date and was used until the Charnley® was introduced. The longest reported survival of a Smith-Petersen hip prosthesis was 56 years (10). The Judet brothers used an acrylic polyethylene hemi-arthroplasty with limited success (11). Vitallium was also used by Thompson and Moore in the first stems that were fixed with any success to the femoral canal (12). The Ring stem, with its metal-on-metal articulation, was introduced in 1962. It performed well (13) and later served as an inspiration for the new generation of metal-on-metal models. One of the most recent models is the Birmingham Hip Resurfacing® (BHR) model (14). Weber implanted the rotation endo-prosthesis starting in 1967 (15).

Sir John Charnley introduced modern total hip replacement in November 1962 with the “low friction arthroplasty” (16). This total hip replacement was implanted in 379 patients and after 4 years of follow-up, was noted to have a low incidence of loosening and reduced postoperative pain. The cup was made from UHMWPE, after first using polytetrafluoroethylene (Teflon) with poor results. This model set the reference standard for all other total hip replacements that were later developed. Until 2006, the Charnley® stem was still the most commonly used stem in Norway (1). Not long after Charnley, Ling and Gee in Exeter, England, started their work on the triple tapered Exeter® stem, and it has been implanted since 1970. The present Exeter® design is still in use, with good results, and is the most commonly used cemented stem in Norway (1).

The most commonly used uncemented femoral stem in Norway is the Corail® AMT stem, with a survival of above 97% after 20 years of follow-up (17). The articulation

has moved from UHMWPE to highly cross-linked polyethylene with either ceramic or cobalt chromium heads as a result of lower wear properties. A shift from almost only cemented total hip replacements to a situation in which uncemented femoral stems are combined with cemented cups, in the so-called reverse hybrid total hip replacement, has occurred (1). This was encouraged by the poor results of uncemented cups.

See the timeline in Figure 3.

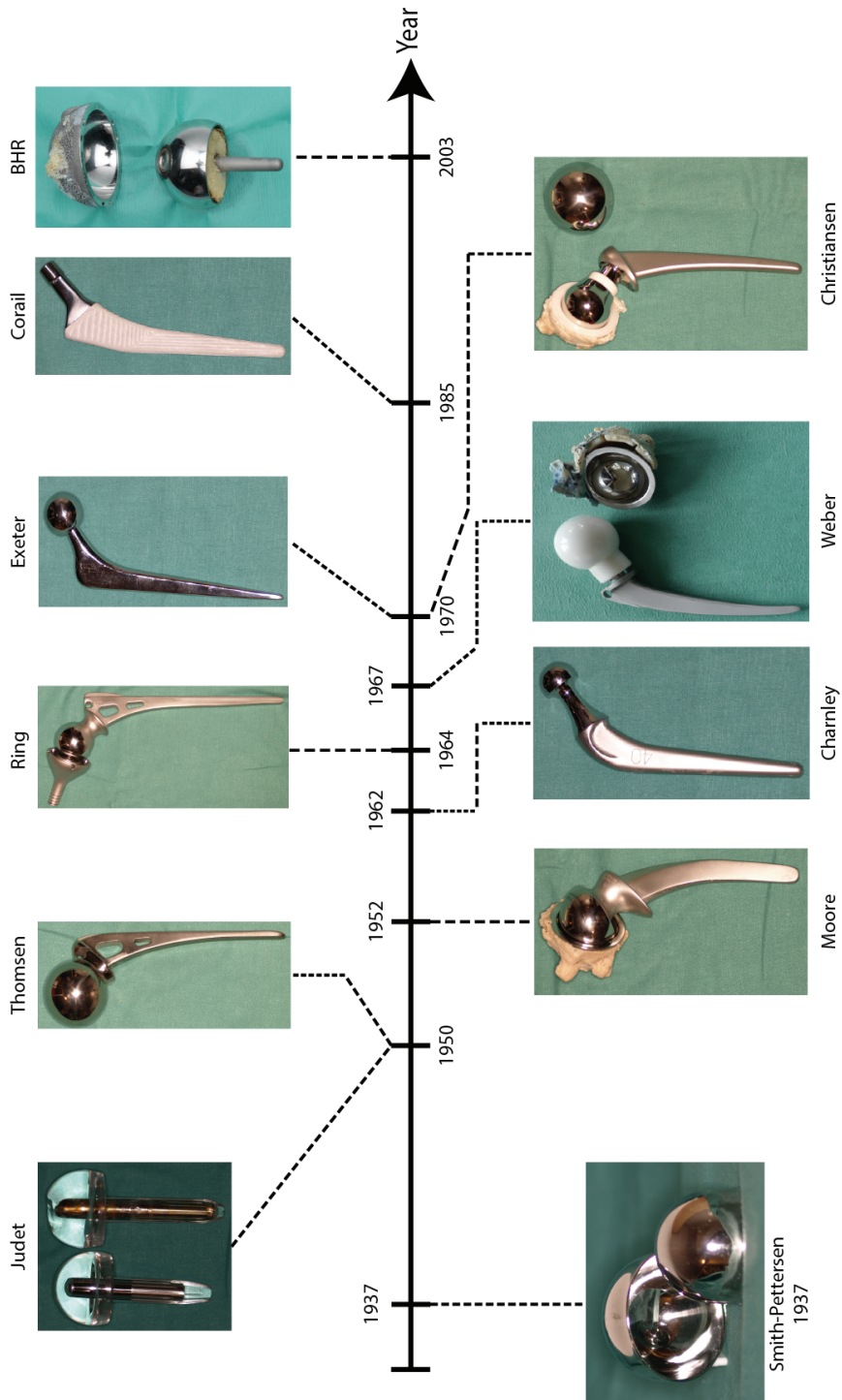


Figure 3. Timeline of selected implants.

5.1.2 Brief history – total hip replacements in Norway and Stavanger

The first total hip replacement in Norway was performed at Hospital Sofies Minde in Oslo in 1969. The procedure was conducted using a Weber prosthesis that had a polyethylene prosthetic head with a metallic cup and stem, and this prosthesis performed poorly, with breakage of the polyethylene head (18). In 1972, the first Charnely prosthesis was inserted in Ålesund, and later the same year, the Charnley was introduced at Sandnes Hospital after the staff had visited Dr. Charnely in Wrightington. In the beginning at Sandnes, there were some problems with infections, similar to Wrightington. From the model of use in Wrightington, the operative cage (green house) was introduced, with laminar airflow, operating suites and an exhaust for the surgeon's breath (Figure 4). The hospital later became the reference hospital for the Charnley prosthesis in Norway, and many orthopaedic surgeons have undergone their training in the use of the Charnley total hip replacement at Sandnes hospital.



*Figure 4. Sandnes Hospital, around 1977. Green house with exhaust suits.
(Photo: Finn Stokke)*

In 1973, total hip replacements were also performed at Kysthospitalet in Hagevik. Both the Charnley and Kristiansen prostheses were used. The latter prosthesis used an articulation of a polyoxymethylene (Delrin) plastic inserted into the collum of the stem and into the head of the prosthesis. This polymer was said to be self-lubricating but soon was a disaster in the clinical setting (19, 20). Professor Sudmann and his colleagues suggested the establishment of a national joint registry to monitor poorly performing prostheses, which later became the Norwegian Arthroplasty Registry (NAR) (21-24).

In NAR, all primary and later secondary procedures in all joint replacements are registered (Figure 6). Registered variables include the date of the operation, side of the body that is operated upon, reasons for the operation/reoperation, surgical approach, bone loss at revision, type of implant used, antibiotic prophylaxis, American Society of Anesthesiologists (ASA) score, per-operative complications and more. These registrations are completed and sent to the NAR in Bergen. An annual report is available (1). The registrations in NAR have been validated and found to be of high quality (25).

5.3 Revisions

A revision can be defined as a replacement of one or more components of the total hip arthroplasty (Figure 5). The revision operation is usually more technically demanding and time consuming than the primary operation (26).

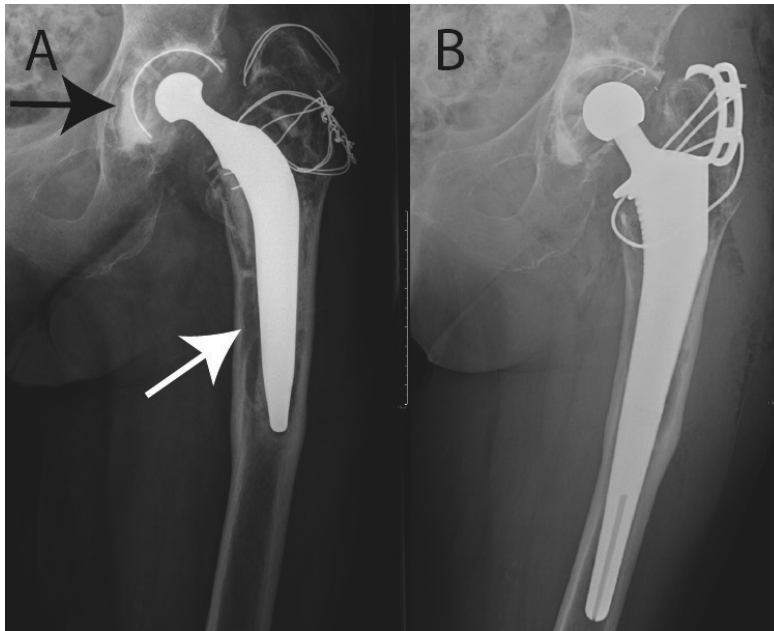


Figure 5. Revision. A: Black arrow shows osteolysis at the acetabular cup. White arrow shows osteolysis at the femoral stem. B: Uncemented revision stem and cup.

5.3.1 Revision burden

Regardless of the success of the modern total hip replacement, the relative number of revisions has remained nearly constant at 14-15% (1). However, the total number of implant operations is increasing rapidly; therefore, the actual number of revisions is increasing in conjunction.

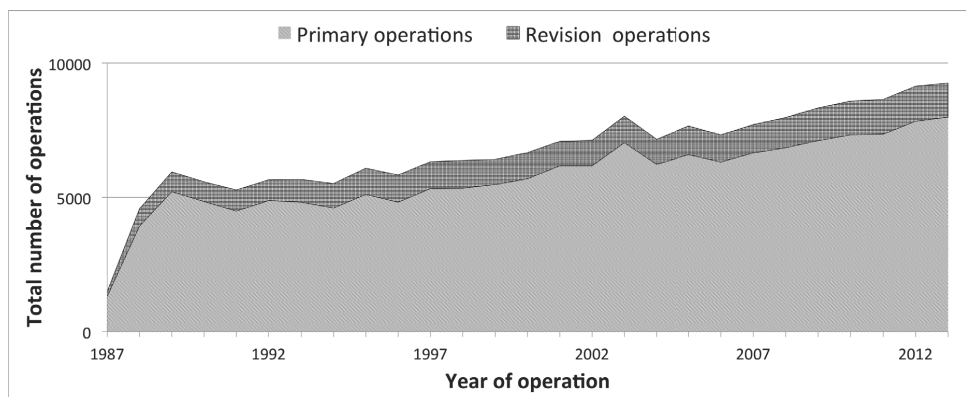


Figure 6. Number of total hip arthroplasties registered in Norwegian Arthroplasty Registry 1987-2013 (from 2014 annual report (1))

5.3.2 Reasons for revision

The reasons for revisions are many (Table 1). The clinical diagnosis of aseptic loosening is the most common, and can be attributed to different factors. Particle debris from wear on the polyethylene that leads to osteolysis (resorption of bone) has been considered an important factor (27). Osteolysis, as observed with the Charnley prosthesis, typically occurs in the calcar region, with consequent breakage of the cement mantle at the level of the stem tip (28). A change in design can have an effect, as seen in the cemented titanium-based stem (Titan®) after the year 2000, for which a 4.7-fold increase risk of revision was observed (29).

The improved diagnostics of infections have possibly moved some of the causes for revision from aseptic loosening to late infection. However, there is also a trend towards increased septic loosening and infection without loosening (30). In particular, the increased risk for infection in uncemented implants is concerning. The patient population increasingly has more comorbid conditions that can also contribute to the increased rate of infection (30). Since the time of Charnley's first series, the use of laminar airflow in the operating theatre has been considered to be an adjunct to prevent surgical site infections (SSI), but recent literature appears to contradict this

assumption. The effect is not great and in some reports is shown to increase the risk of SSI (31, 32).

Table 1 Reasons for revisions in 2013 (from 2014 NAR annual report (1))

Reasons for revisions in 2013	
Missing	7
Other	121
Previous Girdlestone procedure	11
Plastic wear	55
Femur osteolysis w/o loosening	42
Acetabular osteolysis w/o loosening	52
Pain	141
Peri-implant fracture	130
Deep infection	275
Luxation	205
Femoral loosening	311
Acetabular loosening	434

Implant fractures occur infrequently compared with the early days of prosthetic surgery, but there remain other implant failures hampering the total hip replacement procedure. In recent years, metal-on-metal articulations have been associated with the formation of pseudotumours (33, 34), and fretting corrosion on the connection of the modular neck to the stem causes adverse local tissue reactions (35, 36). Ceramic on ceramic articulations may induce severe squeaking and could lead to a revision (36).

The treatment of osteoporosis with antiresorptive drugs, such as alendronate, has the significant effect of reducing the incidence of new fractures. However, there is some concern about the issue of atypical femoral fractures that can occur in an intact femur or with a previously implanted femoral stem (37).

The risk of revision (38) can be predicted by a poor early Oxford hip score (ranges from 0-100, where 100 is best) (39). If patients have a score lower than 27, they are predicted to have a 15-fold higher risk of revision compared with patients with scores of 42-48. In an outpatient setting, this tool can be used to screen patients for revision risk after 6 months and 5 years.

5.3.3 Revision techniques and challenges

Revisions present the surgeon with an extra challenge when removing the implant because it is important that most of the bone stock be preserved to support the replacement implant. Few publications have reported these issues (40), although these problems remain a part of everyday practice in revision hip surgery. Several methods have been developed to address these difficulties (41-44), but none have supplied an optimal solution.

Cemented stems can often be removed from the proximal end without too much difficulty. The removal of all the cement, however, can be challenging. Many methods are available. The most basic methods include the use of osteotomes to make small fractures in the cement mantle, high speed burrs, ultrasound and reverse cutting tools (45). The aim is to remove the cement mantle with minimal loss of host bone.

Uncemented stems can also be extracted from the proximal end with consecutive burring using K-wires along the stem, long chisels, and slap-hammer disimpaction. In cases where this action is not sufficient, a posterior longitudinal split osteotomy to slightly increase the diameter of the femur has been described, allowing disimpaction of the stem (46). The femur is reinforced with cerclages before the new stem is implanted.

When the above-mentioned methods do not suffice, extended trochanteric osteotomy is a well-established method of gaining access to the femur when removal from the proximal end (47-49) (i.e., the area of the stem beneath the collar) is not possible. Surgeons would typically use a saw on the lateral part of the femur and make a longitudinal cut until the end of the stem, thereafter making several burr holes on the medial side. In the end, the femur is opened with an osteotome, making the fracture controlled and gaining access to the femoral canal. After removal of the stem and (in the case of a cemented implant) when the cement is extracted, the bony "lid" is fastened with wires, and the new implant can be inserted. Obviously, this can lead to extensive damage to the bone stock and weakening of the proximal femur, which is needed for the new stem (50). The patient will need to exercise restricted weight-

bearing for the next 6-8 weeks, while the osteotomy heals. There are few problems with the healing of the osteotomy (51-53).

After the successful removal of the stem and the cement in cases of cemented implants, one is left with the issue of bone loss. Paprosky introduced the most common classification of femoral bone loss in a revision setting (Ranges from I to IV, where IV is the worst) (54-56).

The different types of bone loss require a progression of the extent of the effort into restoring bone stock. In the case of only minimal bone loss, medium length uncemented revision stems perform well (57). To overcome the more severe grades of bone loss, a surgeon can use long-stemmed uncemented implants (58) or the impaction grafting technique, which has a survival rate above 90% at 15 years, even in the presence of Paprosky grade III bone loss (59).

Long modular uncemented stems have evolved, and the survival of these stems is comparable to re-cementing a revision stem (without impaction grafting) and requires less operating time (60). Compared with impaction grafting, the uncemented modular stem also performs adequately (58).

These challenges led to the development of the current project, which aimed to address these difficulties with a new stem design that minimises bone loss, should there be a need for revision.

6 Study aims

This study aimed to explore the possibility of developing a femoral stem that is well fixed to bone and easy to remove (if deemed necessary), with minimal bone-loss. Testing was performed in a load-bearing setting using goats as the animal model.

6.1 Specific aims

To test the concept of the unlocking procedure, facilitating removal of the well-fixed femoral stem.

To biomechanically compare the different coatings used during the development of the femoral stem.

To evaluate the bone apposition on the loaded femoral stem by applying a new scoring procedure.

7 Material and methods

The experiments were based on a large animal model using goats in two animal cohorts and were termed Study 1 and Study 2. The observation period was six months under clinical loading conditions. Novel femoral stems, as described below, were implanted.

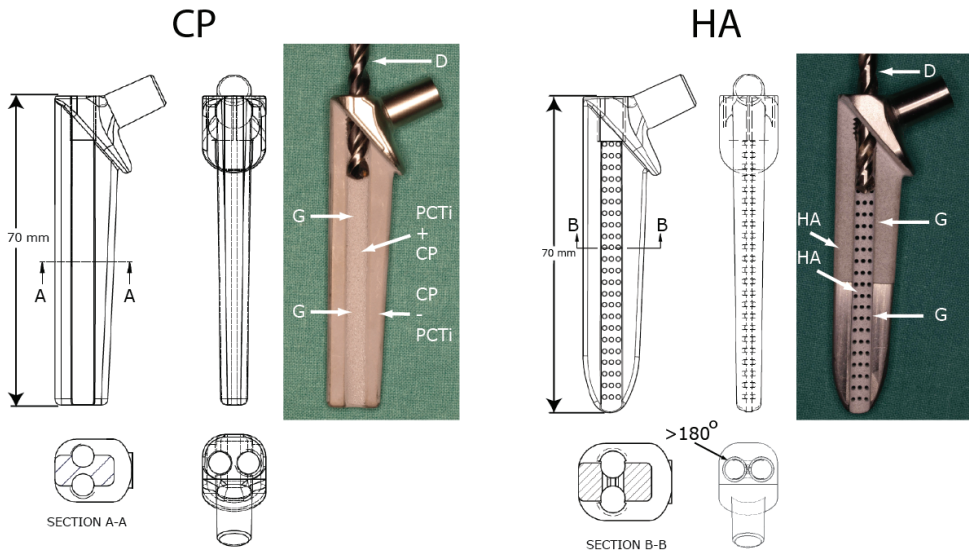


Figure 7. CP coated stem: Front, side and top view. Far right, stem with drill bit. Calcium phosphate coated area (CP). Porous, commercially pure titan with calcium phosphate in groove (PCTi + CP). Drill bit (D). Groove (G). (in Paper 2, PCTi was called TPS)

Hydroxyapatite (HA)-coated stem: Front, side and top view. Note on top view that the grooves are more than 180 degrees to prevent drill bit from going astray. Far right, stem with drill bit. HA-coated area (HA). Drill bit (D). Groove (G). Transverse canals are one millimetre in diameter.

Table 2. Overview of implants used in Papers I, II and III.

Paper	Study	Material	Surface				Groove Design	Stem	
			Roughness	Treatment	Coating	Coated Area		Length	Sizes
II	1	TiAl6V4	1.5 μ m	Grit blasted	Calcium-phosphate	All area below the collar	Porous commercially pure titanium	70 mm	1
I, II, III	2	TiAl6V4	3-7 μ m	Grit blasted	Hydroxy-apatite	Groove and 50% of area beneath the collar	69 transverse 1 mm canals	70 mm	2

7.1 Implants

The implants were manufactured using a CNC machining technique (Aarbakke AS, Bryne, Norway) from a metal cone made of titanium alloy (Ti6Al4V, grade 5) (Table 2). All implants were tapered and had a collar to provide good initial stability. The alloy was selected because it is extensively used in orthopaedic applications and possesses a balance between strength and biocompatibility (61). The biocompatibility of TiAl6V4 is comparable to that of commercially pure titanium, in favour of commercially pure titanium (62, 63).

7.1.1 Acetabular cup and caput components

The taper of the stem was manufactured on both stems to the specifications of the caput (HDP, Biometrix, Boonton NJ, USA). The acetabular component (made from UHMWPE) and caput (cobalt chromium) were supplied from the same manufacturer. The acetabular diameters ranged from 23-25 mm with a caput diameter of 17 mm and an offset of +0, +3, and +6 mm.

7.1.2 Implant used in Study 1

In Study 1, the design was based on preoperatively radiographing the 12 goats planned for use in the experiment. Study 1 aimed to provide a coating that would allow ingrowth into the grooves on each side and towards the stem. The

tricalciumphosphate (CP = Bonit®) coating used in Study 1 had the advantage of being applied at room temperature and electrochemically, which also allows the coating of geometrically difficult structures, such as the porous titan, used in the groove. The ordered pore size was 40-300 µm but was delivered at an average of 40 µm (Figure 7, CP).

7.1.3 Implant used in Study 2

In Study 2, the distal end of the stem was curved to avoid a possible hypomochlion, and hydroxyapatite was added as the coat. The stem was coated outside the groove in the proximal part to provide a circumferential seal against particles from the joint reaching the bone/implant interface. Distally, the aim was to only have fixation in the groove. Roughness of the stem was decided by the manufacturer of the HA to ensure adequate bonding of the coat. The stem was polished outside the coated area to avoid bondage to bone. The stem size was based on the preoperative radiographs from 10 of the 35 goats, and two different sizes were made: the medium size had the same outer shape as in Study 1 (apart from the distal tip), and the small size was 1 mm less in width in both planes, proximally and distally. The porous, commercially pure titanium was replaced with 69 canals, each of 1 mm in length, connecting the grooves on each side. The selection of 1 mm was to allow both bone and connective tissue to form a bond between the grooves. In addition, 1 mm was a practical lower limit when the stems were produced (Figure 7, HA).

7.2 Animals

The animals in Study 1 were nine years old with a range of 8-10 years and were obtained from a farm in Voss, Hordaland, Norway. They were radiographed to estimate the size of the femoral canal and then returned to the farmer until the production of the implants was completed. Three weeks before the operation, the

animals were transported from the farm to the experimental animal facility, Vivariet, in Bergen, Norway. The mean pre-operative weight was 48 kg (range, 40-54), and the animals were acclimatised before the operation.

The animals in Study 2 had a mean age of five years (range, 2-7 years) and were obtained from a farm in Bjerkreim, Rogaland, Norway. They were moved to the animal research facility at Høyland, Sandnes, Norway, three months before surgery. Ten animals were radiographed to confirm the size of the femoral canal, and the decision was made to manufacture two different sizes to accommodate the femurs. The average pre-operative weight was 50 kg (range, 40 – 65).

In both groups, the animals underwent screening blood work (including haemoglobin (Hb), leukocytes, and minerals) and were treated for parasites. All animals were healthy, and in Study II specifically, none had signs of Caprine arthritis encephalitis (CAE), which has a low prevalence in Bjerkreim, Norway. All had been vaccinated against paratuberculosis (*Mycobacterium avium* subspecies paratuberculosis) as kids. Food was withdrawn for 24 hours, and water was withheld for 6-8 hours prior to surgery.

The euthanising method used in Study 1 was a bolt gun, and in Study 2, an overdose of pentobarbital was administered. In both instances, the method was followed by exsanguination. Both methods enabled a predictable outcome, and the animals experienced no unnecessary pain.

7.2.1 Animal ethics

The 3 Rs (64) – *Replacement, Reduction and Refinement*–form the foundation for all animal research, as proposed by Russell & Burch in 1959 (65), and were later developed into legal requirements in most European countries in Article 7 of Directive 86/609/EEC. Later, the fourth dimension of *Rehabilitation* was also introduced (66). The Rs are discussed according to the animal model used in the current project as follows:

Replacement: There was no adequate in vivo model that could replace the present animal model in the current studies. These two studies aimed to test the in- and ongrowth of bone upon a large implant, as well as the pull-out strength.

Reduction: Prior to the first study, in vitro experiments were performed in which a prototype stem was embedded in different cements and pulled out with and without the “unlocking” of the stem (Figure 17). The force reduction observed here led to selection of the initial group of 12 goats. In the second study, the sample size increased due to the results from the first study. Important factors included the rate of fracture occurrence, cachexia and a smaller difference in pull-out strength than was expected from the in vivo experiments.

Refinement: The stem in Study 2 was refined into two separate sizes to better accommodate the femurs of the goats. Each goat that was newly operated upon was reintroduced to the main herd at night to prevent butting. The custom-made sails were reinforced with chains in front to prevent the goats from chewing the ropes and escaping, and possibly damaging the hip.

Rehabilitation: In both studies, the animals were euthanised if they luxated a hip, fractured a limb, or developed an infection that did not respond to antibiotics within 14 days. The studies aimed for the goats to have as natural a rehabilitation as possible following the immediate postoperative period.

Both studies were approved by the Norwegian Animal Research Authority (reference numbers: 2006350 and 07/82783).

7.3 Clinical evaluation

The gait of the goats was scored using a modified de Waal score (67) (Table 3). This score has been used previously in other comparable studies (68). The expected natural improvement in the score during the postoperative period was observed. The score was also a valuable tool to identify goats with poor performance of the hip replacement, and thus allowed for intervention. All scoring of the goats was

videotaped for documentation purposes. The score was discussed with the caretakers who saw the goats on a daily basis, but no inter-rater or intra-rater values were calculated.

Table 3. Gait score modified after de Waal

Walking score	Explanation (with reference to operated leg)
0	Not used at all
1	Used occasionally while standing still
2	Used when standing still, occasionally when walking
3	Used when standing still and walking, some limping
4	Hardly visible limping during walking and running
5	No limping

The goats were monitored for weight loss and gain as a measurement of how well they were thriving. One goat was euthanised in each study due to cachexia, which is a known risk when operating on goats (69).

7.4 Evaluation of the bone/implant complex

7.4.1 Retrieval of implants

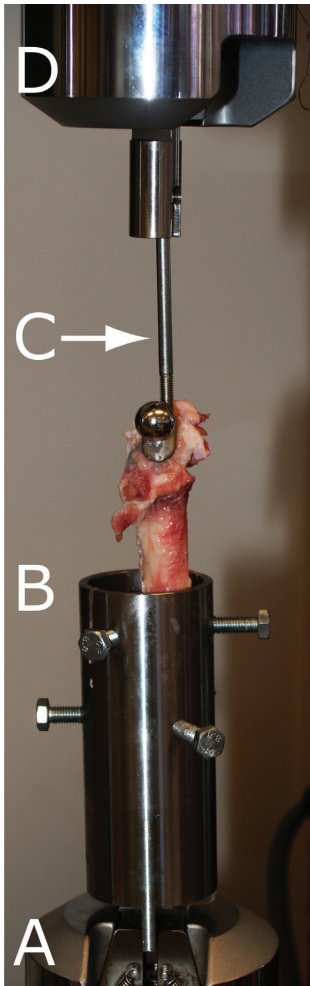
The pelvis was divided into two parts, and the soft tissue was removed from the pelvis and femur. The femur and pelvis were separated. The samples were kept on ice until biomechanical testing could be performed, except during the short period of radiographic imaging.

7.4.2 Radiography

Each femur and hemipelvis was radiographed and CT-scanned the same day as the implants were retrieved. To evaluate the anteversion of the implants, scanning both

femurs in the same scan is important due to the great variability of anteversion in goats.

7.4.3 Biomechanical testing



The femurs were all tested the day after retrieval in a servohydraulic biomechanical testing machine (MTS 810, Minneapolis, Minnesota, USA). The femur was adjusted to vertical alignment and embedded in dental cement (Meliodent, Heraeus-Kulzer GmbH, Hanau, Germany). The head of the top screw had been ground to fit into a custom screw head retainer (Figure 8).

Before the final testing, the top of the stem was cleared of any overhanging soft tissue. Pull-out measurements were recorded in the machine's software and also continuously plotted on a printer.

The presence of gross instability was evaluated clinically once the testing had begun.

Figure 8. Experimental setup for measuring pull-out force. Lower grip of servohydraulic testing machine (A); Retaining cylinder with embedded specimen (B); Pull-out screw inserted in a proximal threaded hole of the experimental stem (C). Upper grip of testing machine (D).

In both studies, all stems were randomised by a coin toss into two subgroups: drilled (D) and nondrilled (ND). All tissue in the grooves was removed by a 4.5 mm drill-bit

in the drilled subgroup. The test was performed with a cross-head speed of 0.25 mm/s.

To test the effect of the bonding of the coatings to bone, the subgroups from both studies that had the longitudinal grooves drilled on each side were compared. In this manner, the difference of the anchoring of the groove to the surrounding bone was minimised (Figure 9). The testing took place at room temperature, keeping the specimens moist throughout the procedure, according to the recommendations of An (70).

7.4.4 Histology

After the biomechanical testing, the proximal part of each femur was immersed in 4% neutral buffered formalin. The femurs were kept on formalin for a period of 4

months, and then, each femur was cut with a bone saw into a proximal and distal part. The proximal cut was performed slightly below the level of the medial part of the collar of the stem. The distal cut was located at the distal 1 cm of the stem (Figure 9). Both cuts were approximately 3 mm thick.

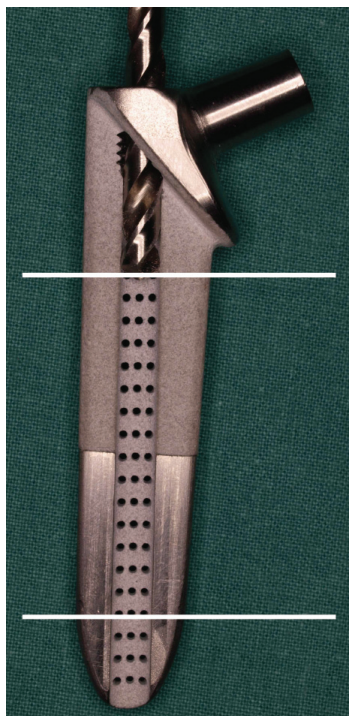


Figure 9. Hydroxyapatite-coated area (HA). Drill bit (D). Groove (G). White lines represent levels of sectioning. Transverse canals are one millimetre in diameter.

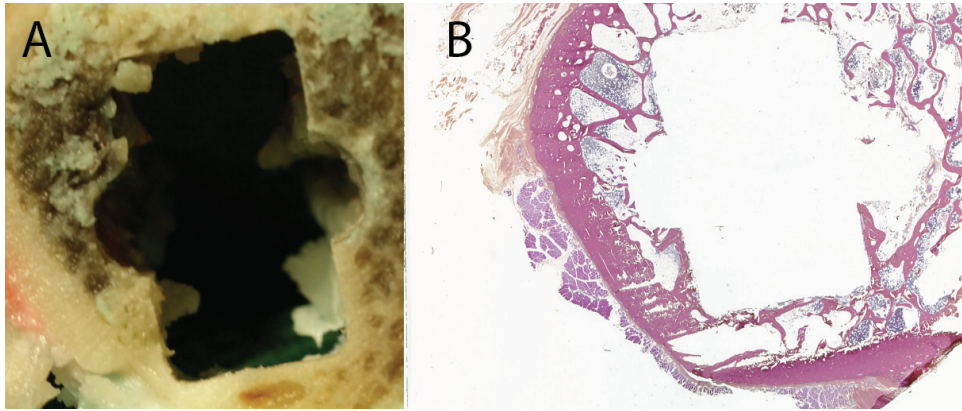


Figure 10. Drilled specimen after stem removal with drilling of longitudinal grooves. A: Macroscopic appearance. B: Histological appearance.

The slices (Figure 10) were then decalcinated with EDTA demineralising solution (1000 ml of 4% unbuffered formalin, 75 g EDTA, and 14 g NaOH) for a period of approximately 3 months. The EDTA solution was changed every week. The canisters with the bone and EDTA were kept on a rotating platform for the duration of the period. The bone samples were tested with a needle at every exchange of EDTA to ensure an appropriate level of decalcination. The slices were then embedded in paraffin, cut into 2-3 μm slices with microtome and stained with standard HES (haematoxylin, erythrosine, saffron).

7.4.5 Histological evaluation

In both studies, bone ingrowth into the gutter and surrounding the extracted stem was evaluated. The presence of immunological cells, which could indicate an adverse reaction to the coating, was noted (Figure 14).

In Study 2, the evaluation was extended to quantify the bone apposition and tissue in accordance with a new scoring system. All samples were evaluated independently by two investigators, and a semi-quantitative score was assigned for each parameter. In the event of any discrepancies, a joint examination was performed to reach

consensus. The stems were only evaluated outside the groove to compare the drilled and non-drilled specimens.

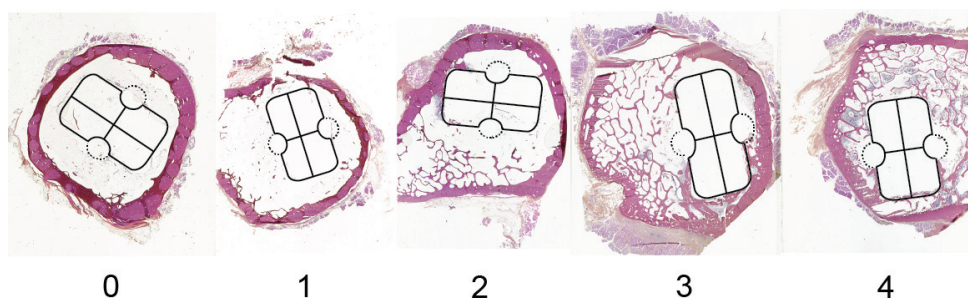


Figure 11. Example of evaluation of score. The score corresponds to the number of quadrants with a visible reaction to the implant with ongrowth. Some distortion of scale of the stem outline due to artefacts of the production of histological slices.

Bone apposition towards the stem in 4 quadrants was evaluated according to the example in Figure 11, and the sum of the 2 levels of slices was calculated, resulting in a score ranging from 0-8. All stems were photographed, and no significant residual bone was documented on the stems.

7.5 Statistics

Pull-out values and histological bone apposition scores were compared using the Mann-Whitney two-sample test. Kappa values were calculated for the inter-rater's correlation of the bone score. The Spearman rank correlation was used to compare bone scores. Linear Pearson correlation was used to investigate correlations between the bone score and pull-out strength. The Wilcoxon signed rank test was used to compare the bone growth outside the grooves. The significance level was set at $p < 0.05$ for all tests.

8 Methodological considerations

8.1.1 Implants

The implants and differences between them are described in the general discussion.

8.1.2 Animal model

Choice of the animal model

Goats were selected due to their large femoral cavity, which is able to accommodate a large implant. Experience in the use of goats in orthopaedic research is not widespread, but the loading pattern of goats has been shown to adequately simulate that of the human hip (71-73). Other more commonly used animals include canines, rabbits, rats, sheep, and the Göttingen minipig. Canine animal models are not common in Norway and would pose practical difficulties in their postoperative storage as the facilities available was not made for canines. Rabbits and rats are too small for the current implants. Sheep are readily available and have large femoral cavities. However, the present model was previously established using goats. The Göttingen minipig would be an excellent alternative because they are relatively small, easy to carry and very homogenic. However, they are docile and would not properly load an operated leg.

Challenges to the animal model

Five goats (of 35 in Study 2) were lost due to acetabular loosening, which must be considered in any new studies that evaluate total hip arthroplasty in goats. Sheep have been used as a model for sclerotic bone (74), and particular care was taken to place cancellous bone in contact with the cement. However, the bone quality of the acetabulum could explain the loosening. One other option would be to use hemiarthroplasty, in which the acetabular component is not studied.

The challenge of anaesthetising the goats is the narrow therapeutic range of some of the drugs used (75). No problems with the anaesthesia protocol were noted, apart from a need to conduct reversion of the anaesthesia in some cases, which must be performed carefully because the goats are easily excited and there is a risk of injury. During the operation, monitoring the core temperature of the animal is also important. A warming pillow was used in Study 2 to assist in keeping the animals warm.

Postoperative fixation in the sling described by Peters (76) (Figure 12) enables a safe observation of the goats for the first 2-3 days after surgery. Securing the collar of the neck of the goat to the sling is important to prevent the goat escaping. Having chain attachment of the sling to the roof or walls in front of the animal is also recommended because the goat will chew likely through soft restraints. The goats must be weight-bearing in the sling, or they will not relax. The sling is primarily a support to avoid falling in the postoperative period. Despite all these constraints to the sling, one goat in Study 2 managed to escape and was later found to have a previously unnoticed dislocation of the hip with formation of a neo-acetabulum.



Figure 12. Sling of Peters. White arrow: Chain attachment in front. Black arrow: surgical wound.

The goats were all active animals, and lack of mobilisation was not an issue. The main problem with goats is the social system between females. The rank of the animals is decided by butting. In Study 1, one early fracture (likely due to butting) was found. To reduce the risk of this occurring in Study 2, the animals were joined with the rest of the herd at night on postoperative day 5 or 6, and no fractures due to butting were found. Allowing the goats to have access to hills and shelter stimulated the animals to move about as naturally as possible. An evaluation of their gait was performed every 14th day, and the animals were weighed every 4th week. These assessments were performed as an indirect measurement of the animals' health. Due to these examinations, one animal in Study 1 and two animals in Study 2 (one with an extra articular abscess around the stifle (knee) and two due to cachexia) were euthanised during the follow-up period. The animals' feed was continuously adjusted to avoid too much weight gain after the weight had resumed its preoperative level.

8.1.3 Clinical evaluation

In the current study, a modified gait score was used to evaluate the clinical progress of the goats. The advantage of this method is the possibility of observing the goats in their natural environment and monitoring their movement without interference. The score was adjusted slightly by introducing a new value between score levels 3 and 4 because the variability was too great to capture the clinical difference between full function and limping. As with all subjective scoring systems, there is room for discrepancy between observers. However, the goats were scored at 14-day intervals by two different observers, and no great variation over time was observed.

Some alternative means of clinical evaluation other than gait score deserve to be mentioned. The addition of pedometers may have provided more objective data with the use of the operated leg vs. unoperated leg. However, the behavioural nature of the goats prevented this measure from being a practical solution because they tend to chew on their restraints and other objects, including the restraints used on themselves and on other animals. The use of a pressure plate could be an alternative evaluation

method, but this approach is also difficult to implement because the goat must walk naturally on two plates at any given point.

8.1.4 Biomechanical testing

The main outcome was the pull-out force because it is the main parameter that limits the removal of a well-fixed femoral stem. The lower fixture used to hold the femur in place before dental cement was added enabled a vertical alignment (Figure 8). The alignment was measured with a line that had a weight at its end.

The clinical evaluation of gross instability was intended to non-destructively test the motion between the stem and femur. The femoral head and the greater trochanter were loaded at a right angle to the long axis with a low force (4 N) while recording the relative movement of the head (spring loaded force applicator and differential displacement recorder). Instability could be an indication of poor integration of the stem. When evaluating the micro-motion with strain gauge measurements and physiological loading in a hip simulator (77, 78), destruction of the bone/implant interface could be an outcome, which would interfere with the main endpoint.

8.1.5 Histology

The method of decalcination was selected because it allows a slow process to occur without the risk of reabsorbing the specimens, which occurs with more acidic solutions. Hard tissue slices were used to evaluate the excluded goats with loose acetabular components, but proved too costly. In addition, Hagen's method (79) was used in the second study to embed material from one goat in epoxy resin. The histological quality was inferior to the ordinary method; thus, Hagen's method was not continued, and this goat was excluded from the evaluation.

It was not possible to directly study the interface between the bone and the prosthesis because the prostheses were pulled out during the biomechanical testing.

8.1.6 Scoring system of the histological evaluation

The scoring system was a practical approach because the in situ specimen was not in position. The Kappa values indicated a fair correlation if the score was divided into a dichotomous score with poor or good ingrowth.

More common evaluations of the bone/implant interface are conducted with the specimen in situ (80). The measurements of the area of contact can then be used to compare differences between ingrowth and ongrowth, which was not possible in the present setting because the main outcome was pull-out force.

9 Summary of results

The results from the two studies are summarised below.

9.1 Paper I

The results of the Study 2 version of the stem were evaluated. The stem was used for drilled/non-drilled randomisation in 23 goats. A significant difference in pull-out force was observed between the drilled and non-drilled stems (mean, 1526 N vs. 2033 N, $p = 0.028$), as shown in Figure 13.

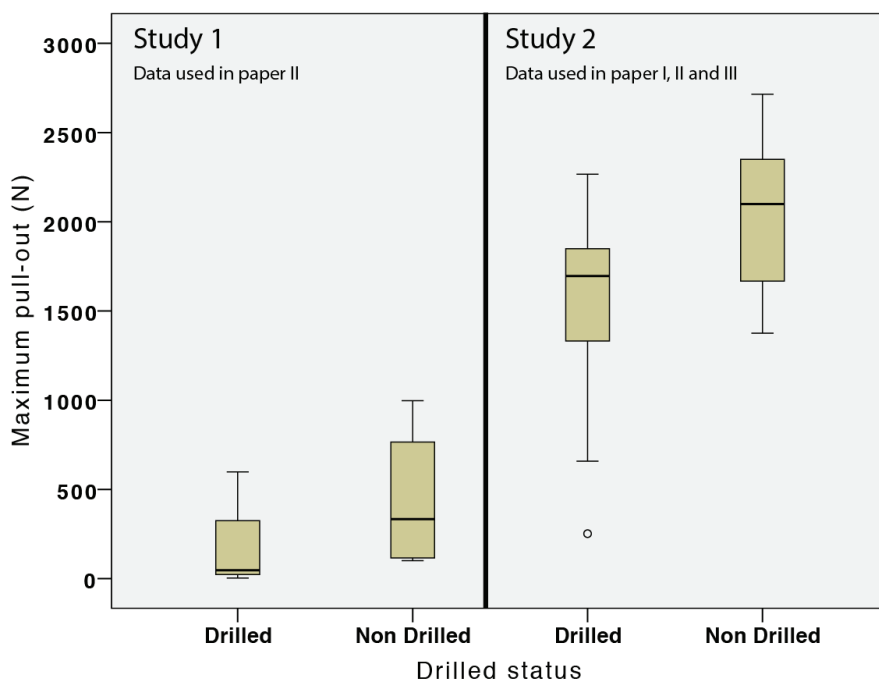


Figure 13. Box-plot of pull-out force in the two studies (one outlier is marked). The use of data in the papers is noted. Medians, quartiles, and the lowest and highest values are presented.

9.2 Paper II

This paper aimed to compare the retention force outside the longitudinal groove on the Study 1 and Study 2 stems. A lower pull-out force in Study 1 with the calcium phosphate coating vs. Study 2 with the hydroxyapatite coating (mean, 174 N vs. 1526 N, $p = 0.003$) was observed, as shown in Figure 13.

9.3 Paper III

This paper showed no correlation of the retention force with the amount of bone growth towards the stem outside the groove (Figure 14). Bone apposition towards the stem was classified into poor or good categories with fair agreement. There was little evidence of foreign bodies.

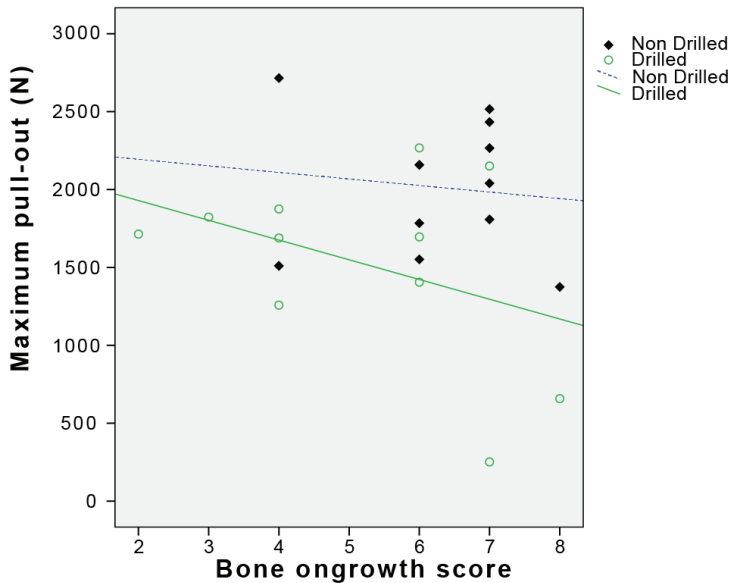


Figure 14. Correlation bone on growth score vs. maximum pull-out force.

10 General discussion

Reports on the incidence of total hip replacement indicate increases in this procedure throughout the world (1, 81-84), with the revision burden remaining steady at 14-15% (1). Although the ideal femoral stem/acetabular cup would never have to be replaced, the issue of revision cannot be ignored when designing a new total hip replacement. There are many reasons for revisions (Table 1). Occasionally, a well-fixed femoral stem must be revised, and some of the causes are discussed here briefly.

First, the increasing rate of infections among uncemented implants is concerning. Dale et al. showed a 5.3% increase risk of revision due to infection when comparing 1987-1992 to 2003-2007 (30). Second, there can be a failure of other parts of the total hip replacement, i.e., the caput or acetabular component (85, 86). When there is a fracture in a ceramic caput component, the taper of the femoral component is at a high risk of damage and therefore necessitates a replacement (Figure 15). Third, the revision of a damaged or loose acetabular component can require the removal of a fixed stem to access the acetabulum. Finally, a peri-prosthetic fracture not including the proximal femur may need a long replacement stem to bridge the fracture (37, 87).

As mentioned in the introduction, there are several challenges at the time of femoral revision, including but are not limited to bone loss, femoral fractures, healing of osteotomies, the availability of a bone transplant (if necessary), and a higher infection and dislocation rate of revision surgery.

Patients are subject to these challenges, and better primary implants, revision techniques and rehabilitation methods for these patients should be sought.

The implant industry is driven by innovation processes to improve these factors, and a short introduction to these innovation processes and how they affected the present project is discussed here.

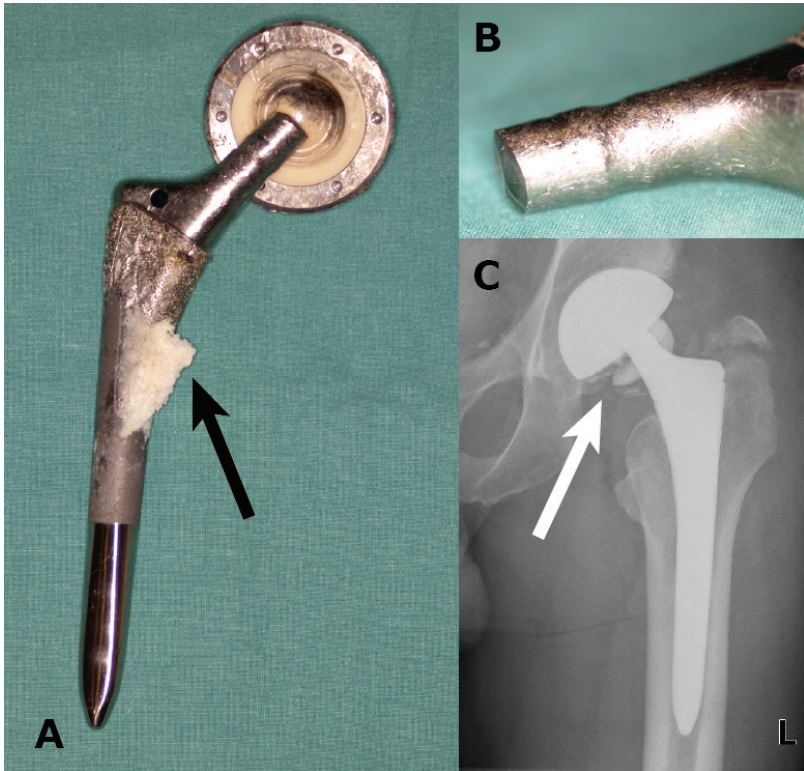


Figure 15. Example of a well-fixed femoral stem that had to be removed due to breakage of the ceramic head and destruction of the taper. A: Black arrow: residual bone after removal with extended trochanteric osteotomy. B: Damage to taper from articulating directly with uncemented cup with ceramic liner. C: Pre-operatively X-Ray. White arrow: fragments of fractured ceramic head.

10.1 General introduction to innovation processes regarding surgical implants

The term innovation, according to the Oxford English Dictionary, means “new method, idea, product, etc.” (88). It is derived from the Latin word “innovare,” which means “to renew or create something new.” In different fields, the strict definition of the term varies. The innovation process can be described as taking an invention into

the market in such a manner that the invention creates revenue or provides some practical benefit. The inventor can perform this process, or more commonly, someone who sees the potential in an invention can do so.

The approach of the present work was a combined scientific and experienced-based innovation process. It has been described as STI (Science, Technology and Innovation) and DUI (Doing, Using, Interaction). This mixture of the two processes can be very beneficial (89).

This process of innovation demands strong teamwork to be able to evolve from one iteration to the next. In our experience, the collaboration of clinicians, engineers, manufacturers and post-production are of the utmost importance. As much as possible, processes from the beginning of design changes through packaging must be in place before a new production can begin.

10.1.1 IDEAL initiative

In surgical sciences, the framework for innovation appears to be less established compared with the recognised phases of medical drug development (i.e., Phase 1, 2 and 3 trials, and later phase 4). To counter this challenge, the IDEAL (Idea, Development, Exploration, Assessment, Long-term study) initiative has been proposed (90-92). This framework is not directly applicable for the present studies on animals, but a simplified example for the future research is shown in Figure 16.

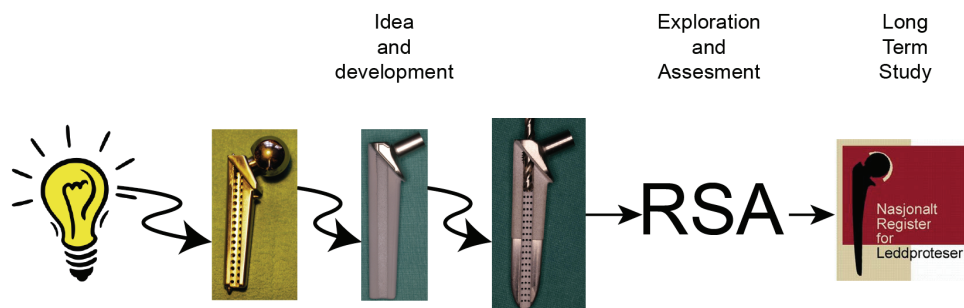


Figure 16. A simplified example of the stages of IDEAL. RSA = radiostereometric analysis. Far right, logo for the Norwegian Arthroplasty Registry

10.1.2 Stepwise introduction of orthopaedic implants

The term “stepwise introduction” was introduced by Malchau in 2000 (93). The first step is the preclinical testing, which comprises laboratory investigations (94). The two present animal studies would be included in this stage. The next step in the present setting would be a small patient series in which radiostereometric analysis (RSA) would be used to compare a stem with and without grooves or with a reference stem, which is referred to as clinical step I. In the IDEAL framework, this step would correlate to stage 2a. Here, the longevity of the implant can be predicted by the RSA method as a pseudo endpoint (95). RSA allows for detection of very small changes in vertical, horizontal and rotation position (0.05 to 0.2 mm), and thus the number of patients needed is small (15-25 patients in each group) with an observation time of two years. The study design should be randomised between the best standard of care and present innovation. The acetabular component should be the same, and the femoral component should be the only difference.

The next step in the stepwise introduction is multicentre trials, corresponding to stage 2b in the IDEAL framework. Several collaborating hospitals should be included to explore the difference in surgical experience and techniques while retaining a strict protocol with preferably a randomised selection of patients; the follow-up time in

such studies would be long. The value of the study will increase over time. In orthopaedic studies, following patients for more than 10 years is not uncommon.

The final step of the stepwise introduction is the post-marketing surveillance registry studies, which correlates to stage 4 in the IDEAL framework.

10.1.3 Economical frameworks for innovation

Frameworks for innovation are developed in most countries. In Norway, the institution responsible for the coordination of national innovation is Innovation Norway (96). Here, one can apply for the resources needed to take an invention to market. Different programs contribute to these resources. The first step is a validation study, and the second study was eligible for this program and received a contribution of approximately 800.000 NOK. A market analysis was performed, additional funding was sought, and the second study was funded.

10.1.4 Regulatory aspects

In order to place a new implant on the market, it is required that several regulatory aspects are considered. According to the EU Medical Device Directive (Council Directive 93/42/EEC of 14 June 1993) (97), hip implants are classified as “medical devices”, together with a wide range of other implants, appliances and materials. Generally, the different devices are classified into four “risk categories”; hip implants now being in the highest risk category (Class III) meaning that they are subject to stricter controls than devices in lower categories (98). Conformity with the directive’s essential requirements allows the use of the mandatory CE-mark, based on technical and other information describing the implants’ safety, but not data on efficacy.

In the United States there is a comparable regulatory procedure (Class II – With Special Controls) (99). In the US, the application for approval could be based on “substantial equivalence” (510k route). One important difference is the demand for documentation of efficacy in the US.

10.2 The present innovation process

10.2.1 The idea, initial laboratory testing and pilot study

The idea was to find a stem design that would allow for solid integration, longevity of the implant, and easy removal, if deemed necessary. The invention therefore is both an idea and prototype design, which is discussed in the next section.

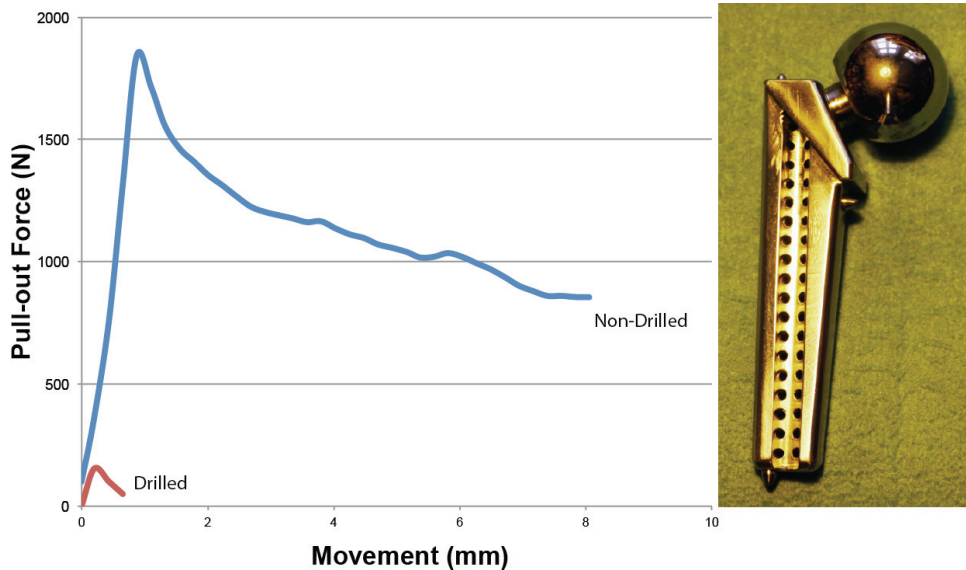


Figure 17. First push-out test of prototype stem embedded in plaster cement. Drilled and non-drilled specimens. Tested in servo-hydraulic testing machine.

This project has been part of an innovation process that started in 1999. The first stem was made of 316L stainless steel (Figure 17). The 35 canals were approximately 2 mm in diameter. The stem was tested in plaster cement, and the effect was promising. This first stem was also implanted in two goats in 1999, but the results of this experiment were not conclusive. The idea and experience from this small pilot study were considered in the present two studies discussed further below.

10.2.2 First design, Study 1, Paper II

In Study 1, the stems were produced from TiAl6V4 because it has been well documented, as mentioned in the description of the implants. There were further modifications from the pilot study. The proximal part of the longitudinal groove was made more than 180 degrees to prevent the drill bit from going astray. The surface treatment of the groove was selected to be commercially pure titanium, and the whole stem was coated with calcium phosphate because this can be applied electrochemically. The process is therefore does not rely on being dependent on the line of sight. With a porous surface, coating all the small openings is important. In addition, calcium phosphate forms a very thin coat with a short resorption period and thus also a reduced chance of third body wear. The area outside the groove was grit-blasted to the specifications of the manufacturer of the coating but not more to ensure that the effect of drilling the groove would be greater than the retention force outside the groove.

The first study indicated that the porous coat in the groove was not made with the requested scatter in pore size (near 40 μm instead of a range from 40-400 μm). The retention force was too low, and the bone apposition outside the groove was not convincing. The limit for capillary ingrowth necessary for new bone formation is approximately 140 μm (100, 101), which may also be a factor for the lower retention force of the nondrilled stems in this group.

10.2.3 Second design, Study 2, Papers I and III

In Study 2, canals from one side to the other were used, as previously tested in the first pilot study. In addition, a hydroxyapatite coating similar to the one used on the most commonly used stem in Norway was used (1). Because this coating requires a rougher surface (3-7 μm R_a) as a substrate for the plasma spray application, the coated area outside the grooves was reduced approximately 50 %. The stem was also made in two different sizes to fit different femoral canals in the goats. The end of the stem was curved to lessen the risk a hypomochlion at the angle of the stem distally. The diameter of the holes was selected to be 1 mm because 1 mm was the practical

lower limit of the manufacturing method and is well above the size required for bone ingrowth.

These design changes resulted in a considerably higher retention force (up to 3-4-fold that of the first Study). The retention force was higher for both the drilled and non-drilled groups (Figure 13).

The differences in stem design and surface treatment between the stems were discussed in Paper II, and the stems were comparable in geometric size and surface area outside the groove.

Hydroxyapatite provided stronger and more reliable retention than calcium phosphate.

10.2.4 Factors influencing retention force

Factors influencing the retention force (Figure 18) are discussed below.

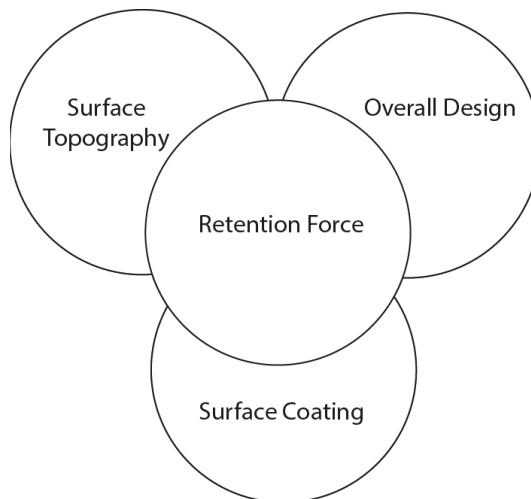


Figure 18. Factors influencing retention force.

10.2.4.1 Overall design considerations

The overall design involves the shape of the stem as it is from the machining unit before the surface is altered.

The longitudinal grooves are implemented to control the area of retention. The number of grooves and placement are important. In both studies, one groove was made on either side of the stem. Despite the large animal model, this limit was the practical machining limit. In a human application of the stem, the area controlled by the grooves must be as large as possible, in contrast to the area outside the grooves, to maximise the effects of drilling. A strength analysis of the human design (finite element analysis, FEA) should also be performed to ensure adequate strength of the final stem, and this process is also dictated by ASTM standards (102).

All implants require bone auto- or allografts to fill the longitudinal grooves. In the present studies, the morcellised femoral head was used for bone packing of the grooves. In a clinical setting, filling the grooves would add time to the primary operations theatre time. An exact and thorough preparation of the femoral canal is required to achieve primary stability. Adaptation of the collar can be achieved by the use of a calcar reamer.

Stress shielding from the collar of the stem is a known problem with collars (103). In the present setting, in which the primary stability of the implant was an important factor, such a collar was used. In addition, the observation period of six months is too limited to expect a significant remodelling of the calcar region according to Wolff's Law (104).

10.2.4.2 Surface topography considerations

The commercially available uncemented stems have a large variation of surface topography. To stimulate ongrowth of the bone, the outer material of the stem is of the utmost importance. Titanium has osteoinductive and osteoconductive properties and therefore is widely used in different alloys (105). The most common alloy is the

Ti6Al4V. The stems have a geometric surface to both obtain an initially stable fixation and then enhance osteointegration of the stem into the host bone. Indentations on the stem are used (Corail® and ABG-II®). Other different designs include a rough surface (Furlong® and Zweimüller®), trabecular metal (Trabecular Metal Hip®) and large holes (Mittelmeier®). The integration of bone onto the femoral stem depends on a stable fixation to enable vascular generation as the bone grows. Too much movement will not allow the bone to bind to the stem, as observed in the Mittelmeier® (106).

The stem was designed with as smooth a surface as possible outside the area of the stem that was controllable with drilling, i.e., the grooves. The Bonit® required less roughening before application and was a good alternative with the documentation available at the time. This choice was made later in the second study to return to the better-documented hydroxyapatite; however, using hydroxyapatite also demanded a greater degree of roughening, and hence, the area outside the groove with surface treatment was reduced. Even with turned and polished TiAl6V4 implants, bone ongrowth occurs (107).

10.2.4.3 Surface coating considerations

Chemical surface treatments that enhance the osteoinductivity/conductivity of the stem have been studied to bridge the period from the insertion of the implant until osteointegration has occurred. Currently, the most common treatment is hydroxyapatite (1). It has shown the ability to bridge the implant/bone distance, even in unstable conditions, as long as the micro-motion does not outrange approximately 50 µm (108). The early applications of hydroxyapatite used thick layers (>200 µm), and the risk of scaling and third body wear (109-111) led to the development of new manufacturing techniques that allow a thinner coat. Presently, Corail® uses a thickness of 80 µm to reduce this problem.

There has been controversy on the use of hydroxyapatite in femoral components, and a meta-study showed no difference in the functional result, regardless of whether

osteointegration or migration was used (112). This study included 6 randomised studies (113-118) that included evidence of earlier osteointegration of the hydroxyapatite-coated stems but not of long-term survival. The present study aimed to have immediate load-bearing for the goats, and therefore, calcium phosphate and later hydroxyapatite was used as the surface treatment. In this experimental (and later, clinical) setting, the use of hydroxyapatite is advocated because the ability to bone-bridge gaps with the use of hydroxyapatite is important to induce bone ingrowth into the longitudinal grooves on an implant.

One other option regarding surface treatment was to add a layer of commercially pure titanium (CPT) over the entire length of the implant. CPT is more osteoconductive than the most commonly used alloy, TiAl6V4 (119). The implant in Study 1 had CPT in the groove but not outside. Coating with calcium phosphate (Figure 19, A) and later hydroxyapatite was selected because the aim was earlier ongrowth than possible with CPT alone (120). Calcium phosphate also allows application with a plasma beam to areas unavailable in the line of sight application, on which the hydroxyapatite relies.

In the second study, hydroxyapatite was selected (Figure 19B) because the calcium phosphate performed inadequately. The treated surface outside the groove was reduced to decrease the retention force that was not controllable outside the grooves.

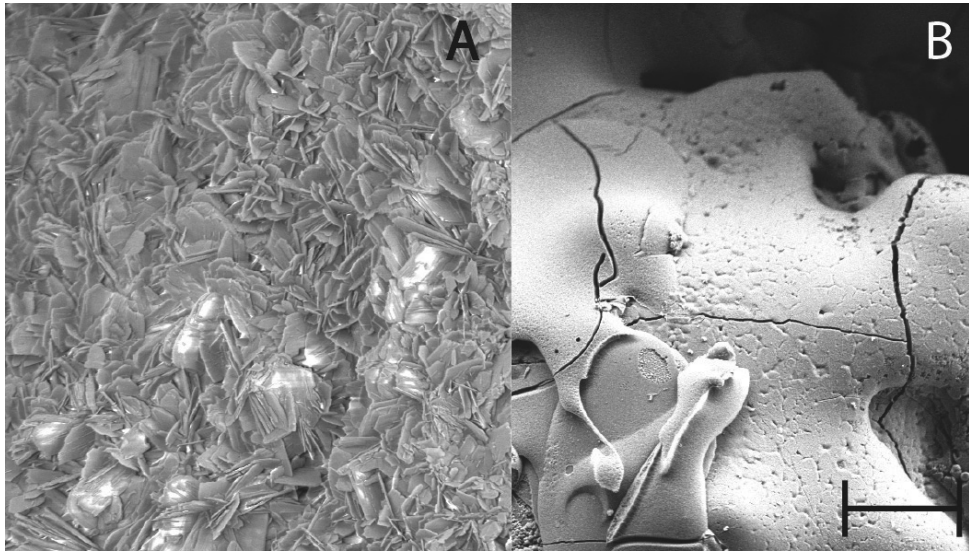


Figure 19. Scanning electron microscope pictures. A: Calcium phosphate. B: Hydroxyapatite. Scale bar = 10 μm .

10.2.5 Revision-related considerations

In a revision setting, surgeons depend on several factors that allow them to explant a retained femoral implant. First, regardless of the fixation of the implant, the adherence to the surrounding bone must be reduced to a level below the threshold of the force produced in the axial direction of the implant. Secondly, the assistant must retain the lower extremity of the patient. The weight, technique and power of the assistant will influence how much of the axial power produced by the surgeon is translated into breaking the bone/implant interface.

During a revision, the patient is positioned on the operating table with fixtures to ensure that they will not fall off the table when handled by the surgeon. However, the patient is not fastened rigidly, and some elasticity will always exist in the femur and surrounding soft tissue when trying to remove a stem.

In previous studies on the difficulties of removing the early edition of the long Exeter® revision stem (44), the redesign decreased the initial retention force from

3244 N to 1337 N, which was found to be acceptable. The stem in Study 2 showed a mean retention force of approximately 1526 N after drilling the longitudinally orientated grooves and is comparable to the Exeter® stem.

In the present study, the retaining force of the lower fixture was only limited by the strength of the femoral bone, and no flexibility in the hold of the femur was observed, which rarely occurs in clinical settings. In the pull-out end of the setup, the force was increased gradually with no slap hammer effect. In a clinical setting, a slap hammer of some sort would be used to induce transient peak forces to break the bone/implant interface. The peak force observed (above 2500 N) is not possible to withhold in a clinical setting. In Study 2, the reduction in force of approximately 25% has uncertain clinical significance because a retention force of 1500 N may still be too high in a clinical setting.

The bone loss at the time of revision with “unlocking” the stem with the present design is approximately half of the groove volume multiplied by the number of grooves. This bone may need to be replaced to accommodate a stable fixation of the revision stem; however, this step depends on the design of the revision stem and the type of fixation.

10.3 Other proposed solutions for bone sparing primary operations

Large diameter metal-on-metal bearings used in resurfacing total hip replacements performed well, with the intention of providing young, demanding patients more freedom of movement in the joint, and the procedure was very popular in some countries (especially Great Britain). The most common implant has been the Birmingham hip replacement®. At revision, bone loss would not be as significant, and the bone in the trochanter and femoral area would be almost virginal. After the initial success, there have been reports of pseudotumours and pain in some patient

groups (121), with females being more susceptible to these pseudotumours. Only carefully selected patient groups should be considered for this implant.

Modular stems with separate tapered necks that are inserted into the femoral stem were considered promising. They could both address the different problems noted during the primary operation with adjustment of the anteversion of the femoral neck, the offset, length and varus/valgus angles. In the event of damage to the cup, head or the neck of the femur at revision, all components could be replaced more easily by first removing the modular neck. However, the challenge of removing a well-fixed stem in the event of infection remains. Other concerns have arisen later, with the increased incidence of pseudotumours occurring when metal-on-metal bearings are used. The fretting issue is also present in the neck/femur junction of the implant, and several cases have been reported (122, 123). Implants have also been recalled due to this issue (124).

The use of midneck resection stems has emerged with the rationale that they bear more physiological loading, and bone-sparing surgery is performed in preparation for a future second procedure. Little documentation of the long-term survival of such implants is available, but there are on-going RSA studies (poster presentation (125)) investigating this issue. Short femoral stems are also in the same category. These stems are assumed to bear more physiological loading and are bone-sparing. Long-term results are also lacking (126, 127).

An exciting new development is the introduction of the additive production of prostheses. The advantage from a production standpoint is the ability to make complex 3D structures from the start. One layer is added at a time, and each layer is welded to the previous one, typically with a laser (128, 129). The long-term strength obtained with this production is not proven, however, as has the ability to make identical objects and the postproduction costs (i.e., machining of the surface of the taper and so forth). Different techniques exist, and achieving approval for these products with the FDA is an extensive process (130).

11 Conclusions

As part of an innovative process, this project demonstrated that:

A stem with longitudinal grooves coated with hydroxyapatite was well fixed, and “unlocking” the stem was possible in a revision setting by longitudinal drilling that reduced the retention force. Bone loss outside the area of longitudinal drilling was negligible.

A significant difference in retention force in favour of hydroxyapatite over calcium phosphate coatings was observed.

No correlation between the bone apposition towards the stem outside the longitudinal grooves and the retention force was observed. The drilling of the longitudinal grooves was the only significant factor controlling the retention force.

12 Future directions

The development process thus far still poses several questions. First, what is the threshold force necessary to predictively enable disimpaction of a stem? This threshold could be investigated using human donor femora with uncemented femoral stems from humans tested with simulated slap hammer motion.

Second, what is the correct proportion of surface area needed to be controlled by the grooves to being able to reduce the retention force below the above threshold with drilling the grooves?

Third, is a groove on the calcar side of the stem needed to ensure solid integration or are grooves in the AP plane sufficient?

Fourth, a first-in-human study involving a final human design implementing the longitudinal grooves would be RSA-based and compared with a reference stem. This study would not provide proof of concept regarding ease of removal at revision because follow-up would be too long. The RSA studies are intended to show early instability as a pseudo endpoint for the longevity of an implant.

Finally, the second study demanded the establishment of collaboration with the Norwegian School of Veterinary Science, Sandnes. This research facility may perform other orthopaedic studies using goats or pigs as models. This project is an exciting new direction for Stavanger University Hospital because the hospital has not had an animal laboratory in the last several years.

13 Source of data

Data collection was ended in June 2014.

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