Form and Finish of Implants in Uncemented Hip Arthroplasty

Effects of Different Shapes and Surface Treatments on Implant Stability

STERGIOΣ LAZARINIS
Dissertation presented at Uppsala University to be publicly examined in Grönwallsalen, Akademiska sjukhuset, Akademiska sjukhus, Uppsala, Friday, January 11, 2013 at 09:00 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

The design of an uncemented hip arthroplasty implant affects its long-term survival. Characteristics such as the form and the finish of the implant are crucial in order to achieve the best possible conditions for long-term implant survival. In this thesis we hypothesized that different shapes of stems and cups used in primary and revision total hip arthroplasty (THA), and their finish with hydroxyapatite (HA) coating affect implant stability and thus long-term survival.

In 2 prospective cohort studies the clinical outcome, the stability measured with radiostereometric analysis (RSA), and the periprosthetic changes in bone mineral density (BMD) measured with dual-energy x-ray absorptiometry (DXA) were investigated in 2 uncemented THA implants – the CFP stem and the TOP cup. In 3 register studies the effect of HA coating on uncemented THA implants used in primary and revision arthroplasty was investigated.

Both implants investigated in the prospective cohort studies showed an excellent short-term clinical outcome with good primary stability, but neither their novel form nor the finish with HA protected the implants from the proximal periprosthetic demineralization that usually occurs around other uncemented THA implants.

The register studies revealed that HA coating on cups used in primary and revision THA is a risk factor for subsequent revision of the implant. The use of HA coating on the stem in primary THA did not affect long-term survival. Additionally, the shape of an implant plays a crucial role for implant stability and survival.

In conclusion, this thesis highlights that the finish of implants with HA coating does not prevent periprosthetic proximal femoral bone loss and can even enhance the risk of revision of both primary and secondary cups. Importantly, the shape of uncemented THA implants affect their stability, showing that the implant form is a crucial factor for the long-term survival.

Keywords: Form, Finish, Total hip arthroplasty, Swedish Hip Arthroplasty Register, Hydroxyapatite, RSA, DXA, BMD, Stability.

Stergios Lazarinis, Uppsala University, Department of Surgical Sciences, Orthopaedics, Akademiska sjukhuset, SE-751 85 Uppsala, Sweden.

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The first step to success is to appreciate what you already have.

To Aliki and Hektor

Στην Αλίκη και τον Έκτορα
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I  **Lazarinis** S, Mattsson P, Milbrink J, Mallmin H, Hailer NP. A prospective cohort study on the short collum femoris preserving (CFP) stem using RSA and DXA. Primary stability but no prevention of proximal bone loss in 27 patients followed for 2 years. *Accepted for publication in Acta Orthopaedica*

II **Lazarinis** S, Mattsson P, Milbrink J, Mallmin H, Hailer NP. Demineralization around a stable uncemented modular cup: A prospective cohort study on a hemispherical, partly threaded and hydroxyapatite-coated cup using RSA and DXA. *Manuscript*


IV **Lazarinis** S, Kärrholm J, Hailer NP. Effects of hydroxyapatite on survival of an uncemented femoral stem. A Swedish Hip Arthroplasty Register study on 4,772 hips. *Acta Orthopaedica, 2011; 82(4):399-404*

V **Lazarinis** S, Kärrholm J, Hailer NP. Effects of hydroxyapatite coating of cups used in hip revision arthroplasty: A Swedish Hip Arthroplasty Register study on 1,780 revisions. *Acta Orthopaedica, 2012; 83(5):427-35*

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<td>ARA</td>
<td>American rheumatism association</td>
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<td>BMD</td>
<td>Bone mineral density</td>
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<td>BMI</td>
<td>Body mass index</td>
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<td>CCD</td>
<td>Caput-collum-diaphyseal</td>
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<td>CFP</td>
<td>Collum femoris preserving</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<tr>
<td>CN</td>
<td>Condition number</td>
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<td>CoCr</td>
<td>Cobalt chromium</td>
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<td>CV</td>
<td>Coefficient of variation</td>
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<td>DPA</td>
<td>Dual-photon absorptiometry</td>
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<td>DXA</td>
<td>Dual-energy x-ray absorptiometry</td>
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<tr>
<td>FN</td>
<td>Femoral neck</td>
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<td>HA</td>
<td>Hydroxyapatite</td>
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<td>HG</td>
<td>Harris-Galante</td>
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<td>HHS</td>
<td>Harris hip score</td>
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<td>HR</td>
<td>Hazard ratio</td>
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<td>ME</td>
<td>Mean error of rigid body fitting</td>
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<td>NARA</td>
<td>Nordic arthroplasty register association</td>
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<td>OA</td>
<td>Osteoarthritis</td>
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<td>RCT</td>
<td>Randomized controlled studies</td>
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<td>ROI</td>
<td>Regions of interest</td>
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<td>RSA</td>
<td>Radiostereometric analysis</td>
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<td>SHAR</td>
<td>Swedish hip arthroplasty register</td>
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<td>SOA</td>
<td>Swedish orthopedic association</td>
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<tr>
<td>SPA</td>
<td>Single-photon absorptiometry</td>
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<td>TCP</td>
<td>Tricalcium phosphate</td>
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<td>TH</td>
<td>Total hip</td>
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<td>THA</td>
<td>Total hip arthroplasty</td>
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<tr>
<td>Ti</td>
<td>Titanium</td>
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<tr>
<td>TM</td>
<td>Trabeculae metal</td>
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<td>TOP</td>
<td>Trabeculae oriented pattern</td>
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<tr>
<td>XLPE</td>
<td>Highly cross-linked polyethylene</td>
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Introduction

Uncemented total hip arthroplasty (THA) must achieve stability by other means than cemented THA. Force transmission and stability of the cemented THA are achieved by the cement mantle, whereas the uncemented THA must rely upon primary stability obtained by press-fit fixation. Secondary stability is then brought about by bone ingrowth.

**Form** – Press-fit → primary stability

**Finish** – Ingrowth → secondary stability

All manufacturers aim to develop implant designs that increase the implants’ durability. The terms “form” and “finish” of uncemented hip arthroplasty implants can include several variables in implant design: This thesis investigates the effects of form – meaning external shape – and finish – meaning surface treatment with hydroxyapatite (HA) – on the stability of uncemented hip arthroplasty implants.

Hip arthroplasty implants

Total hip arthroplasty

Osteoarthritis of the hip has been diagnosed since ancient years but the disease seems not to differ from today (Hogervorst 2012). Surgical treatment has been attempted only during the last 100 years. The first attempt began with the “interpositional arthroplasty”, using various tissues–including fascia lata, or skin, between the articulating surfaces of the hip. Resurfacing of the hip joint with a vitallium cup that covered the reshaped femoral head by Smith-Peterson in 1948 (1948) changed the concept by using artificial material to reconstruct the hip joint. All these early attempts of replacing the hip joint were marked by failures because of inferior materials and poor design. Introduction of low friction arthroplasty by Charnley (1961) revolutionized management of the osteoarthritic hip. Continuous efforts have been made in order to achieve longer survival of implants. Failure mechanisms are mainly aseptic loosening as a result of mechanical failure of
the fixation interface, infection, wear, and dislocation. This thesis describes developments of THA designed to provide a stable and durable implant in order to meet the high requirements of the patient suffering from osteoarthritis of the hip.

Uncemented total hip arthroplasty

John Charnley introduced the use of polymetacrylate bone cement to fix components to living bone and high-density polyethylene as a bearing material in THA. This concept of cemented THA shows very good results even today (Hailer et al. 2010, Swedish Hip Arthroplasty Register [SHAR] 2010). In the first generation of cemented hips early failure was reported mostly of the cemented stem. These failures were associated with localized areas of osteolysis mostly in the femur caused by a local inflammatory response believed to initiated by cement particles, a phenomenon called “cement disease”. Several investigators therefore proposed that the future of THA should be the development of prostheses that were implanted avoiding the use of cement. This triggered the development of uncemented implants which allow intimate bony apposition in order to enable biological stabilization. Characteristics such as the form and the finish of implants are crucial in order to achieve the best possible conditions for long-term implant survival.

Form of uncemented hip arthroplasty implants

Even small changes of the external shape of an implant may have a substantial positive or negative effect on long-term outcomes. Numerous theories on shapes of uncemented acetabular cups and stems have been proposed during the last decades.

Acetabular implants

Aseptic loosening of the acetabular component is the most common cause for revision after THA (SHAR 2010).

Uncemented acetabular cups were introduced in the belief that they would enable improved fixation compared to cemented cups. 2 types of uncemented cups are used: press-fit or threaded. Both achieve primary stability through form-fitting and frictional connection. They come in varying geometrical designs: hemispherical, parabolic, conical, or combinations of those. The hemispherical cup is the most commonly used in modern uncemented THA. With this design the subchondral bone can be preserved, the adaptation to bone is excellent, the medial acetabular wall is protected, and forces can be almost physiologically transmitted between the pelvis and the cup (Rodriquez 2006). In contrast, the conical shape

In order to achieve the desired stability of a hemispheric cup in a hemispheric cavity different fixation techniques can be applied. Initial stability and fixation are achieved by press-fit seating. Additional primary stability can be provided by pegs, spikes, or screws.

Modular hemispherical cups with the option of liner exchange are tending to become the standard cup design. However, a suboptimal locking mechanism of the liner has often been the cause of early cup failure through liner wear, subsequent extensive osteolysis and later cup loosening (Thanner et al. 1999, Hallan et al. 2006, Lachiewicz and Soileau 2006).

In this thesis the survival of some different shapes of cups were investigated: a) the hemispherical threaded Romanus cup (study III), b) the hemispherical press-fit cups Trilogy and Harris-Galante (HG) (studies III and V), and c) the hemispherical press-fit, partly threaded Trabeculae Oriented Pattern (TOP) cup (study II).

Stems

In an uncemented THA the mechanical properties of the stem provided by its shape are more crucial for stem stability than in a cemented primary THA due to the absence of a cement mantle.

Although a plethora of stem designs is currently on the market all fall into 3 broad categories: cylindrical, anatomical, or tapered. Cylindrical stems need distal cortical support to gain primary stability. To achieve distal fixation, the prosthesis must be canal-filling, generally requiring an implant of larger diameter. Increasing the stem diameter increases stem stiffness which may induce cortical atrophy, proximal stress shielding, and thigh pain, presumably due to elastic mismatch between the rigid stem and the biologically flexible femur (Bourne et al. 1994, Lavernia et al. 2004).

Anatomical stems are constructed with an anteroposterior curve to match the natural curvature of the femur (Grochola et al. 2008). The anatomic design supposedly imitates physiological loading of the femur, thus reducing stress shielding. However, several studies on anatomically shaped stems indicate a higher frequency of thigh pain than with other designs (Campbell et al. 1992, McAuley et al. 1998). Tapered stems use 3-point stem fixation to obtain immediate stability (Bourne et al. 2001, Reitman et al. 2003, Parvizi et al. 2004).

It is known that stem fixation with close cortical contact in the diaphysis is associated with distal loading, which predisposes to stress shielding and loss of proximal bone stock. Furthermore, cohorts of younger patients receiving uncemented stems are at greater risk for early revision surgery, and thus preservation of femoral bone “stock” is even more important in these patients. These factors provided an impetus for the development of short stems. Hip resurfacing theoretically provides the most marked preservation
of the proximal femur, but complications such as femoral neck fracture, early loosening due to osteonecrosis and development of “pseudotumors” have diminished the initial euphoria associated with this procedure (Lazarinis et al. 2008, Delaunay et al. 2010, Smith et al. 2010, Cuckler 2011). Short femoral stems provide the opportunity to avoid such resurfacing-specific complications while at the same time potentially preserving more femoral bone “stock” than conventional femoral stems. Short femoral stems could allow the preservation of proximal bone “stock” by i) subcapital resection of the femoral neck, and ii) putatively, by transmitting more proximal loading than distally anchored conventional stems. Although several different short implants are currently available only few clinical results have been published. One of the few short stem devices with a collar is the Collum Femoris Preserving (CFP) stem.

In this thesis the properties of different shapes of uncemented stems were investigated: a) the short neck-retaining CFP stem (study I) and b) the conventional tapered Bi-Metric stem (study IV).

Finish of uncemented hip arthroplasty implants

The finish or surface treatment of a hip implant is crucial in order to achieve ingrowth of bone tissue, providing secondary fixation to bone and improved long-term stability. Many different surface treatments have been proposed.

Hydroxyapatite

Bone consists of 2 major components: collagen and bone mineral. The mineral phase which makes up around 60-70% of bone mass consists of calcium phosphate with an apatitic structure and a composition close to HA.

HA is chemically described as $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ and is characterized by a Ca/P ratio of 1.67. Various HA phases can be formed, depending on the type of environment employed during synthesis. The most common is the hexagonal structure (Fig 1).

![Figure 1. The hexagonal structure of hydroxyapatite (HA).](image-url)
Apart from HA, several other types of calcium phosphates belonging to the family of biocompatible apatites or bioceramics are used in biological applications. Tricalcium phosphate (TCP), described as Ca$_3$(PO$_4$)$_2$, exists in small quantities (<5%) in most so-called HA coatings and in larger amounts (>40%) in mixed hydroxyapatite-tricalcium phosphate (HA-TPC) coatings.

HA is compatible with various tissue types and can adhere directly to human tissues such as osseous and muscular tissues without inducing an intermediate layer of fibrous tissue. It also displays high osteoconductivity, contributing to bone growth when applied to bone surfaces (Soballe et al. 1993). This property is extremely useful for an implant where rapid adhesion to bone is required.

The biological mechanism of bone formation with HA coating is believed to begin with surface dissolution of HA that releases calcium and phosphate ions into the space around the implant. After precipitation of apatite has occurred, HA binds serum proteins and cellular integrin receptors, allowing osteoblastic cells to adhere to the surface. Bone formation then follows.

HA is well tolerated by the organism without inducing foreign body reactions (Nery et al. 1975), HA coating enhances bone ingrowth (Jarcho et al. 1977), and implants coated with HA show improved fixation to surrounding bone tissue (Ducheyne et al. 1980). For this reason HA has been widely proposed as a suitable coating material to strengthen secondary fixation of uncemented prostheses.

The ideal HA coating for orthopedic implants should have low porosity, strong cohesive strength, good adhesion to the substrate, a moderate to high degree of crystallinity, and high chemical purity and phase stability (Yang et al. 1997). Manufacturers produce HA coatings that reach the above mentioned characteristics by varying their chemical composition. The degree of crystallinity in HA coating expresses the rate of the amount of the HA in its crystalline phase and in its amorphous phase. Crystallinity of HA coatings around 65-70% has been considered optimal for biomedical applications.

Several methods have been used in order to deposit HA coatings on titanium substrates such as dip coating-sintering, immersion coating, electrochemical deposition, hot isostatic pressing, solution deposition, ion-beam sputter coating, and thermal spraying techniques. The plasma-spray process, in which heated calcium phosphate particles are ejected at high velocity in a gas stream onto the prosthesis in order to build up the coating was developed in the 1980s and has gained prominence over the other techniques.

HA coating on uncemented THA was introduced in 1985 by Furlong and Osborn (Furlong and Osborn 1991) and in 1986 by Geesink (Geesink 1990, 1993).
**Acetabular implants**

By porous coating, roughening, or texturizing the cup can receive a surface that is similar to bone surface and at least theoretically enables improved implant fixation. On the other hand, a layer of material between the cup and the bone surface can also be an obstacle in the bone growth process between the implant and the bone.

HA has been used as a coating on cups to enhance bone ingrowth, stimulate bony gap closure and achieve improved secondary implant stability. The effect of HA coating on cups used in primary hip arthroplasty but also in revision surgery is extensively discussed in this thesis: a) in study II where the stability, the periprosthetic bone mineral density (BMD) and the short-term results of the HA-coated TOP cup were investigated, b) in study III where was investigated the risk of revision of HA-coated cups used in primary hip arthroplasty and c) in study V where the effect of HA coating on the survival of revision cups is analyzed.

**Stems**

The surface of most uncemented stems during the 1970s was smooth, for which strong adherence to bone could not be expected, and a macro lock implant was inserted into bone by press-fitting. The first generation of uncemented stems with a fully or extended porous coating surface introduced in 1980s. However, periprosthetic bone resorption in the metaphyseal region due to stress shielding and persistent thigh pain were reported. In order to provide proximal loading of the femur uncemented stems were designed with a porous surface located proximally. Bone ingrowth in this area was proposed to enhance physiological loading and avoid stress shielding and osteopenia of the proximal femur. However, until today none of these stems have been shown to protect the proximal femur from stress shielding (Kröger et al. 1998, Braun et al. 2003).

Many porous-coated tapered stems are made of cobalt chromium (CoCr). In contrast, titanium (Ti) is characterized by a higher elasticity than CoCr which possibly may result in decreased stress shielding and favorable femoral remodeling. On the other hand, Ti is more fragile, more susceptible to abrasion wear, and more sensitive to cracks if the stem is not well supported by bone.

Finish of uncemented stems with HA has been proposed to enhance bone ingrowth and result in better fixation and improved long-term results. The effect of HA coating on uncemented stems is discussed in this thesis: a) in study I where the clinical results, the implant migration and the periprosthetic BMD changes are investigated after insertion of the proximally HA-coated CFP stem and b) in study IV where the effect of HA coating on the uncemented Bi-Metric stem is analyzed.
Aims of the studies

The overall goal of this thesis is to investigate effects of form and finish on primary and long-term stability of uncemented hip arthroplasty implants. The term:

...“Form” denotes the shape of the implant.  
...“Finish” denotes the implant’s surface treatment.

The specific aims of the studies were:

I. To investigate the clinical outcome, primary stability and changes in periprosthetic BMD after use of a short, partially HA-coated uncemented stem.

II. To investigate the clinical results, primary stability and changes in periprosthetic BMD after use of a partly threaded, fully HA-coated uncemented cup.

III. To evaluate whether HA coating of cups influences the long-term risk of cup revision after primary hip arthroplasty.

IV. To evaluate whether HA coating of stems influences the long-term risk of stem revision after primary hip arthroplasty.

V. To evaluate whether HA coating of acetabular cups used in revision surgery influences the risk of re-revision of the acetabular component.
Patients, Materials and Methods

This thesis is composed of 2 types of studies:

a) Prospective cohort studies (studies I and II).

In these studies 2 implants (cup and stem) were investigated. Both implants are HA-coated and their form differs from convectional stems and cups: The CFP stem because it is a short, neck-preserving stem, while the TOP cup has a hemispherical shape with an additional row of threads around the equator. The hypothesis was that the CFP stem and the TOP cup by their novel form and by their HA surface treatment should provide good primary stability of the implants and prevent the periprosthetic bone loss.

b) Register studies (studies III, IV and V).

In these studies data were derived from the SHAR. The hypothesis was that coating of hip arthroplasty implants with HA could affect the long-term survival of these implants after primary and revision arthroplasty.

Prospective cohort studies

Study population

The studies were designed as prospective cohort studies where 30 patients with primary osteoarthritis (OA) of the hip and eligible for un cemented THA were consecutively included. Inclusion criteria were radiographically verified OA of the hip, age 20-65 years, and a body weight under 100 kg. Exclusion criteria were inflammatory diseases (rheumatoid arthritis and equivalent diseases) as diagnosed by ARA (American Rheumatism Association) criteria, long-term systemic glucocorticoid treatment, disabling diseases from the musculoskeletal system other than the hip, malignancy, alcohol or drug addiction and psychiatric disorders, chronic infectious diseases and osteoporosis (as determined by dual-energy X-ray absorptiometry [DXA]). Further exclusion criteria were severe joint deformities jeopardizing standard operating technique for the CFP stem. All 30 patients were planned to receive the un cemented implants CFP stem and TOP cup. Preoperative templating was performed in all cases.
Surgery was performed by 1 of 2 surgeons (JM or NPH). A transgluteal approach as described by Bauer (Bauer et al. 1979) with release of the anterior third of the gluteus medius muscle from the tip of the greater trochanter was used. A metal head with a diameter of 28 mm was used. None of the cups needed additional screw fixation. Postoperatively, patients were mobilized on crutches, immediate weight bearing was encouraged, and partial weight bearing was achieved by all patients upon discharge.

Study I
30 patients were included in the study, but 3 had to be excluded after the index procedure (2 received conventional straight femoral stems due to proximal femoral fissures that occurred during broaching for the CFP stem, 1 patient was revised due to an early deep infection), leaving 27 patients for analysis, and no further patients were lost at the 2 year follow-up.

Study II
The same cohort of patients as in the CFP study was included. The patient who underwent an early revision due to deep infection was excluded from the study. 8 more patients received an implant where an insufficient number of tantalum markers was visible during the radiostereometric analysis (RSA), leaving 21 patients evaluable for RSA. No further patients were lost at the 2 year follow-up.

Investigated implants

CFP stem
The CFP stem is an uncemented, short, neck-preserving stem that was designed and developed by Pipino (Pipino and Calderale 1987, Pipino and Molfetta 1993) and modified in 1996 to its current form. It is made of titanium alloy (Tilastan®) with a 70 μm microporous surface. The proximal 2 thirds of the stem are coated with a 15 μm thick HA layer applied by electrochemical deposition. There are left and right stem versions with a built-in anatomical anteversion of 14°. The stem is provided with 2 different curvatures in order to match variations of the proximal femoral anatomy. Caput-collum-diaphyseal (CCD) angles of 117° and 126° are available. It is one of the few short prostheses provided with a removable femoral neck plate.

TOP cup
The TOP cup is a press-fit hemispherical cup made of titanium alloy (Tilastan®). The shell has a 70 μm microporous surface and a 20 μm thick HA coating. To ensure stable anchorage in the acetabulum the shell has a segmental row of threads around the equator. The cup insertion handle
device is attached to the center of the implant through a threaded hole which is sealed with a titanium lid and allows observation of the acetabular floor during insertion. 3 additional holes in the shell allow additional screw placement if required. The shell is designed with a mediocaudal recess aiming at providing a wider range of motion in adduction and avoids impingement from the neck of the stem.

Clinical and radiographic outcome measures
The Harris hip score (HHS) (Harris 1969) was determined preoperatively and at follow-up visits 3, 12, and 24 months after surgery. Follow-up included also anteroposterior and lateral radiographs of the hip and a pelvic view, taken according to the recommended standardized technique for preoperative planning (Swedish Orthopedic Association [SOA] 2006), DXA scanning, and RSA of the hip in all patients.

Dual-energy X-ray Absorptiometry (DXA)
Judging BMD by visual observation and interpretation of a radiograph is imprecise because patient size and exposure influence apparent bone density. Bone densitometry, by contrast, measures BMD in numerical units and provides a more accurate representation of BMD (Adams 2009). In 1963, single-photon absorptiometry (SPA) was introduced. The energy level of this device was sufficient for BMD measurement of peripheral bones but not of central skeletal sites (lumbar spine and hip; Cameron and Sorenson 1963, Goodwin 1987). Dual-photon absorptiometry (DPA) was then developed (Wahner et al. 1988). Both SPA and DPA used radionuclide sources that decayed and required regular replacement. Both methods required considerable scanning time (15-30 min) because of low photon flux. With the slow scanning, undesirable incidents such as patient movements during scanning rendered poor quality of the images.

In the mid-1980s the radionuclide source used in SPA and DPA was replaced with a low X-ray source resulting to the development of DXA. Recent generations of DXA equipment take only 10-30 seconds to scan the investigated body area. Modern DXA devices offer improved spatial resolution, image quality and precision (Cullum et al. 1989, Mazess et al. 1989, Faulkner and McClung 1995, Fogelman and Blake 2000) and can be used to scan both central and peripheral bone sites. Assessing proximal femoral remodeling around hip implants can be also addressed by DXA scans of the operated hips.

In our study the proximal femur of the diseased side was preoperatively scanned by DXA (Prodigy®, GE-Lunar Co, Madison, WI, USA) in order to determine BMD (g/cm²) for 2 standard proximal femur regions of interest (ROI), the femoral neck (FN), and total hip (TH).
Calculation of Z-scores, i.e. standard deviations derived from a weight-adjusted, age- and gender-matched reference population of US-white Caucasians provided by the manufacturer was performed. The femur was scanned at the recommended standard position with the foot in 10-15° internal rotation, i.e. the femoral neck approximately perpendicular to the X-ray beams (Fig 2).

Figure 2. Preoperative DXA scanning of the hip in 0° rotation of the proximal femur.

The DXA analysis software “The hip implant software” was used for postoperative periprosthetic BMD measurements adjacent to the implant, i.e. the 7 Gruen zones (Gruen et al. 1979) for the CFP stem and the 5 ROIs around the cup according to Digas (Digas et al. 2003) for the TOP cup (Fig 3).

Figure 3. The 7 Gruen zones around the CFP implant and the 5 periacetabular ROIs according to Digas.
A baseline DXA measurement was performed during the first 2 postoperative days. Further DXA measurements were obtained at scheduled follow-up visits after 3, 12, and 24 months, and duplicate measurements with repositioning between scans were undertaken in order to calculate the precision error. Long-term precision error for the equipment, expressed as CV% for a lumbar spine phantom, was less than 0.3% during the study period. Precision errors for duplicate measurements for the different ROI zones were also calculated and expressed as CV%. In study II, BMD could not be measured in all ROI zones at all measured time points in all patients. Zones I and II were visible at all time points in 25 patients, zone III in 24 patients, zone IV in 19 patients and zone V in 26 patients.

**Radiostereometric analysis (RSA)**

Early postoperative implant micromotion is a predictor of long-term loosening (Freeman and Plante-Bordeneuve 1994, Kärrholm et al. 1994, Walker et al. 1995, Kobayashi et al. 1997). In order to measure and evaluate implant migration after THA several methods have been used and developed. Since the 1st generation equipment with uniradiographic 2-dimensional manual technique used by Charnley, techniques have been further developed to more sophisticated 3-dimensional computer-assisted methods.

The roentgen photogrammetry method originates from Hallert (Hallert 1960). Selvik modified and developed this method to the more sophisticated RSA (Selvik 1990). This method has been further improved and is applied to many fields in orthopedic surgery.

RSA of hip prostheses is obtained by exposing the patient simultaneously with 2 X-ray tubes placed at an angle to each other. The radiographs are obtained with the patient supine and the investigated hip above a calibration cage of Plexiglas which is equipped with tantalum markers with known positions (Fig 4).

![Figure 4. Patient exposure to the 2 X-ray tubes positioned at an angle of 40° in order to take the RSA radiographs.](image-url)

During surgery tantalum markers are inserted into the femur and around the acetabulum, and the implants themselves are also equipped with tantalum markers. Thus rigid bodies and their relative motions can be calculated. The movement of the implant relative to the skeleton can be assessed in all spatial dimensions with great precision (Selvik 1990; Fig 5).

![Diagram](image)

*Figure 5. RSA enables detection of implant motion along all 3 axes (rotation and translation).*

The high precision of this method enables measurements of both implant migration and polyethylene wear with a higher resolution than with conventional radiography (provided that at least 3 well-placed, stable tantalum markers are present in the surrounding bone and the implant).

In our studies the inserted CFP stems were preoperatively labelled with 5 tantalum markers by the manufacturer and the inserted cups were intraoperative labelled with 6-8 tantalum markers around the edge of the liner. An additional marker was welded onto the titanium locking screw prior to surgery. During surgery and before insertion of the cup, a minimum of 5 tantalum markers with a diameter of 1 mm was inserted into the skeleton around the acetabulum, spread into the superior pubis ramus, the ischial tuberosity, and in the acetabular roof. Moreover, at least 5 tantalum markers were inserted into the greater and lesser trochanter, followed by an extra marker that was inserted into the femoral diaphysis distal to the tip of the prosthesis.

The RSA analysis software UmRSA (RSA Biomedical, Umeå, Sweden) was used in order to determine the rotation and translation of the calculated rigid body of the implant relative to the rigid body derived from the tantalum markers in the femur and the acetabulum. The error of RSA measurements was determined on repeated examinations postoperatively according to
standard procedures and a 99% precision interval was calculated (Valstar et al. 2005).

The baseline RSA investigation was performed within 2 days post-operatively, and the follow-up investigations were performed after 3, 12 and 24 months. Mean errors of rigid body fitting (ME) and condition numbers (CN) were calculated in order to ensure marker stability and acceptable marker scatter over time. In study I, the ME and the CN were found below 0.3 and below 107, respectively, in all cases. In study II, in 5 of 21 patients the ME and/or the CN were found above the acceptable range, rendering further RSA measurements impossible, which left 16 patients eligible for RSA.

Register studies

The Swedish Hip Arthroplasty Register (SHAR)
The SHAR was initiated in 1979 (Herberts et al. 1989, Malcau et al. 1993, Herberts and Malchau 1997, 2000, Malchau et al. 2002, Malchau et al. 2005). All primary and revision hip arthroplasties performed in Sweden since 1979, both in public and private orthopedic units, are reported to the Register. Every Swedish citizen has a personal identification (ID) number that is linked to information on all changes relevant to the follow-up, such as change of address, date of emigration, or the date of death. Until 1991, data in the Register were aggregated at hospital level and were not linked to the personal ID number. From 1992 and onwards data were linked to the personal ID number of each patient, adding information on the type of implant, fixation, and technical details such as the use of HA coating on the implants. This enabled more detailed and reliable studies on individual implant designs and especially comparative analyses of components (Fig 6).
Figure 6. Annual report of the SHAR (available at: Annual reports SHAR).
Study populations

Study III
All primary THA registered in the SHAR 1992-2007 using an uncemented cup that was available with or without HA coating were identified (8,705 hips). There were 5 such cup designs: Trilogy (n = 5,536 hips), Romanus (n = 1,531), HG II (n = 976), Reflection (n = 437), and Biomex (n = 225). To reduce the risk of bias caused by patient selection, surgical preference and technique, and other factors not recorded in the Register, only cups with 500 or more registered hips per implant were included (Trilogy, Romanus, and HG). This left a study population of 6,646 patients with 8,043 THAs.

The group with HA-coated cups was larger (65%) than the group with uncoated cups (35%). The numbers of males and females were about equal. The largest number of patients was found in the age group between 50 and 75 years. Primary OA was the most common preoperative diagnosis. Different types of cemented and uncemented stems were combined with these cups, creating hybrid and totally uncemented systems. In paper III the number of cup revisions is stated wrong (page 56, left column, lines 7-9). The actual number of cups been revised by 2007 is 576 (7.2%) mostly due to aseptic loosening (5.4%).

Study IV
The only uncemented femoral stem used in primary THA registered in the SHAR during the time period 1992-2009 and that was available with or without HA coating was the Bi-Metric stem. We identified 4,772 THAs in 4,169 patients in whom the Bi-Metric femoral stem had been inserted.

The numbers of stems in the HA-coated and in the uncoated group were about equal. The gender distribution was similar. The largest number of patients was found in the age group between 50 and 59 years, and primary OA was the most common preoperative diagnosis. Different types of cemented and uncemented cups were combined with these stems, creating inverse hybrid and uncemented THAs.

Study V
In this study we used the reoperation database of the SHAR that includes personal ID numbers from the start of the Register in 1979. In this database reoperations are continuously recorded should the patient be subjected to multiple operations of the same hip. For the purpose of this study only primary revisions using uncemented cups available with or without HA coating and any subsequent revision of these cups (irrespective of the implant used at re-revision) were analysed. The term “cup revision” was defined as an intervention where 1 or more components of the cup (shell, liner or both) were removed. Thus, other types of reoperations where the
implant was left untouched – or where only the stem was exchanged – were disregarded in this study.

Uncemented cups that were available with or without HA coating registered in the SHAR reoperation database between 1979 and 2009 and used as components for the first acetabular revision performed after primary THA were identified (1,780 hips in 1,772 patients). There were 2 such cup designs: HG (I and II; n=340) and Trilogy (n=1,440). They had been used in revision procedures between 1986 and 2009.

The group with HA-coated cups was larger (71%) than the group with uncoated cups (29%). Primary OA was the most common pre-operative diagnosis for primary THA. There was no difference between the groups of HA-coated and uncoated cups with respect to gender distribution. The largest number of re-revisions was found in the age group between 50 and 75 years. The main cause for the index cup revision was aseptic loosening (87%). 45% of revisions were isolated cup revisions, and in 55% the stem was also revised. The use of bone grafts during the index cup revision was comparable in the 2 groups of cups.

Investigated implants

The described register studies include the Romanus, HG and Trilogy cups and the Bi-Metric stem.

**Romanus cup**

The Romanus cup (Biomet, Warsaw, IN) (Fig 7) was a hemispherical and threaded cup. It was introduced in the late 1980s and was made of titanium alloy supplied with a porous coating made of commercially pure titanium. The surface of the HA-coated version was covered with a mixture of HA (60%) and TCP (40%) with a thickness of 40-70 µm and 50-70% crystallinity. Until 1994, Hexloc type liners were used and then replaced by Ringloc liners with a new design. The insufficient hexagonal locking mechanism of the liner led to inferior results of the cup and was therefore withdrawn from the market (Lyback et al. 2004, SHAR 2010).

Figure 7. The Romanus cup.
Harris-Galante cup
The HG cup (Zimmer Inc., Warsaw, IN) (Fig 8) was a hemispherical press-fit shell. It was made of a titanium fiber mesh with a porous coating surface and a pore size of 400 µm. It was available with or without HA coating. The ceramic coating on the coated cups consisted of a mixture of HA (70%) and TCP (30%) with a thickness of 70 µm and 50% crystallinity. The HG I was introduced to the Swedish market in 1984. Four years later the HG II with a thicker acetabular shell and wider screw holes became available in order to achieve improved cup fixation. It was provided with conventional polyethylene liners. The main technical problem with the cup was the locking mechanism that secures the polyethylene liner, leading to liner wear and subsequent osteolysis (Thanner et al. 1999, Hallan et al. 2006). Despite this problem the HG cup has shown satisfactory results when used in revision cases (Tanzer et al. 1992, Templeton et al. 2001, Hallstrom et al. 2004).

Figure 8. The Harris-Galante II without HA coating.

Trilogy cup
The HG cup was gradually replaced by the Trilogy cup with an improved locking mechanism in 1993. The Trilogy (Zimmer Inc., Warsaw, IN) cup (Fig 9) is a hemispherical press-fit shell with a titanium porous coating surface. The implant is available with or without HA coating that consists of a mixture of 70% HA and 30% TCP, 50% crystallinity and thickness of 70 µm. The cup was provided with conventional polyethylene liners until 1999 when a liner consisting of highly cross-linked polyethylene (XLPE) was gradually introduced.
Figure 9. The Trilogy cup without HA coating.

Bi-Metric stem
The Bi-Metric stem (Biomet Inc., Warsaw, USA) (Fig 10) is an uncemented, tapered implant made of titanium alloy (Ti-6Al-4V) where the proximal third has a plasma-sprayed, titanium alloy porous coating with a mean pore size of 300 μm. The distal part has a textured surface with a roughness of 6.9 μm. In the HA-coated version, the proximal, porous coated part of the stem is covered with a plasma-sprayed HA layer. The HA coating has a thickness of 40-70 mm and a crystallinity of 50-70%, although the manufacturer has stated that changes in the composition of the HA coating have been made over time. It was introduced in 1986.

Figure 10. The Bi-Metric stem without HA coating.
Statistics

Prospective cohort studies
Prior to the study, a power analysis indicated that 20 patients would be sufficient to detect a change in periprosthetic BMD (1 of our primary endpoints) of 1 standard deviation (SD) with a power of 80%, given a 2-tailed $\alpha=0.05$. With the same sample size we were able to detect implant subsidence (the other primary endpoint) exceeding 2 mm with the same power. In order to compensate for drop-outs due to various reasons we included 30 patients in the study.

Standard descriptive statistics such as frequencies, means, medians, and standard deviations were used. BMD and RSA data were found to be normally distributed and within-subjects effects were analyzed by a general linear model with a repeated-measures design and planned contrasts; the assumption of sphericity was determined by Mauchly’s test. If sphericity was violated the Greenhouse-Geisser correction was applied. The Bonferroni adjustment was used for post-hoc pairwise comparisons. Parametric correlation analyses were performed using Pearson’s correlation coefficient. The level of statistical significance was set at $p<0.05$ in all analyses.

Register studies
Descriptive methods were used to describe frequencies and proportions. Analysis of implant survival was performed by using Kaplan-Meier survival analysis (Kaplan and Meier 1958). The log-rank test (Mantel-Cox) was used to investigate differences between groups. Cumulative survival probability was plotted against time. A Cox proportional hazards multiple regression model was used to analyse the hazard ratio (HR) for revision (studies III and IV) or re-revision (study V). Crude and adjusted HRs were calculated.

The Cox multiple regression model relies on hazards being proportional (Ranstam et al. 2011), meaning that the HR that is calculated when comparing several covariate levels is constant over time. The estimated HR is biased when this assumption is violated. In our analyses the assumption of proportional hazards was investigated by hazard function plots and log-log plots of all covariates. No sign of insufficient proportionality was detected in the hazard functions, and log-log plots ran strictly parallel for all investigated covariates.

95% confidence intervals (CI) were reported in order to illustrate estimation uncertainty. The level of statistical significance was set at $p<0.05$.

All statistical analyses were performed using the SPSS software (version 19.0) and the R software package (version 2.14.1).
Study III
Follow-up started on the day of primary THA and ended on the day of revision, death, emigration, or December 31st, 2007, whichever came first.

Kaplan-Meier survival analysis was performed on the entire study cohort with HA coating as the independent factor, and cup revision due to any reason, aseptic loosening or infection as the endpoints. A Cox multiple regression model was applied in order to analyze the relative risk of revision due to aseptic loosening, due to infection, or due to any reason, mutually adjusted for relevant covariates: absence or presence of HA coating, gender, age (< 50, 50-59, 60-75, > 75 years), primary diagnosis before arthroplasty (primary OA, inflammatory disease [e.g. rheumatoid arthritis, morbus Bechterew], femoral neck fracture, pediatric hip disease, idiopathic femoral head necrosis, secondary posttraumatic OA, tumor, and other diagnoses), cup design (HG, Romanus, Trilogy), and type of stem fixation (cemented or uncemented). The type of hospital at primary arthroplasty was inserted as a covariate in a separate exploratory analysis.

Further analysis after stratification for age groups (<50, 50-59, 60-75, >75 years) was performed. Analyses were also performed separately for the 3 investigated cup types HG, Romanus and Trilogy. Analyses excluding isolated liner revisions and excluding the second hip in bilaterally operated patients were also performed.

Study IV
Follow-up started on the day of primary THA and ended on the day of revision, death, emigration, or December 31st, 2009, whichever came first.

Kaplan-Meier survival analysis was performed on the entire study cohort with HA coating as the independent factor, and stem revision due to any reason or due to aseptic loosening as the endpoints. A Cox multiple regression model was applied in order to examine the influence of HA coating on the relative risk of stem revision, adjusting for the covariates age (<50, 50-59, 60-75, and >75 years), gender, primary diagnosis, and type of cup fixation (cemented or uncemented). The hospital type was entered in the statistical model as a covariate in a separate exploratory analysis. Adjusted HR were calculated of stem revision for any reason, or due to aseptic loosening, infection, dislocation, or fracture.

Study V
Follow-up started on the day of revision THA and ended on the day of re-revision, death, emigration, or December 31st, 2009, whichever came first.

Unadjusted survival with revision for any reason or due to aseptic loosening was calculated according to Kaplan-Meier. A Cox multiple
regression model was applied in order to analyse the relative risk of re-
revision of the cup component inserted at revision surgery, either due to any 
reason or due to aseptic loosening. The absence or presence of HA coating, 
gender, age at index cup revision (<50, 50-59, 60-75, >75 years), causes for 
the index cup revision (aseptic loosening, dislocation, infection, and other 
causes), cup design (HG or Trilogy), the use of bone graft at index cup 
revision and the type of cup fixation in primary THA (cemented or 
uncemented) were considered relevant covariates. Other putatively relevant 
covariates such as the type of hospital where the primary surgery or the 
revision surgery was performed, age at primary THA, diagnosis underlying 
primary THA or the type of stem fixation when the index revision was 
combined with a stem revision, were included as covariates in exploratory 
analyses. Further analyses were performed only on the younger cohort of 
patients (age<50 years) or only in procedures where the Trilogy cup was 
used. In another set of analyses, we separately investigated procedures where 
either only the liner or both the liner and the metal shell had been exchanged.
Results

Study I – the CFP stem

Clinical and radiographic outcome
We found excellent clinical outcome with an increase in HHS from 49 (24-79) to 99 (91-100) after 1 year and 99 (92-100) after 2 years. No signs of radiolucency around the stem or stem subsidence or rotation were visible in any patient after 2 years on plain radiography, as determined by 2 independent observers. Intramedullary pedestal formation adjacent to the distal tip of the stem was visible after 1 year in 10 cases and bone atrophy in the calcar region was observed in 23 of 27 patients 2 years after surgery.

Analysis of periprosthetic BMD
Preoperatively no patient suffered from low BMD, with Z-scores varying from -1.8 to 1.6 (mean -0.2). Substantial bone loss occurred in the proximal periprosthetic regions in all patients compared to the baseline obtained immediately after surgery, with the most marked decrease in BMD being observed in Gruen zones 6 and 7. In Gruen zone 7 the decrease was 31% (p<0.001), whereas a decrease of 19% was seen in Gruen zone 6 (p<0.001) 1 year after surgery. A smaller decrease was also seen in the other Gruen zones after both 3 and 12 months. The periprosthetic bone loss remained substantial after 2 years, in Gruen zones 7 (-28%) (p<0.001) and 6 (-19%) (p<0.001), without signs of recovery. In contrast, BMD did recover to baseline values in Gruen zones 1 and 3.

We found a moderate correlation of low preoperative total hip BMD with a higher amount of bone loss in Gruen zones with the most pronounced postoperative bone loss i.e. zones 2 (Pearson correlation coefficient r=0.6, p=0.001), 6 (r=0.5, p=0.005) and 7 (r=0.6, p=0.003).
## Analysis of implant stability

The absolute values describing micromotion around the 3 axes amounted to an implant migration mostly well below 2° or 2 mm (Table 1).

### Table 1. Mean values and range of stem migration along and around the 3 axes in space 2 years after implantation.

<table>
<thead>
<tr>
<th>Cup migration</th>
<th>mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) Medial / (-) Lateral translation (x-axis)</td>
<td>-0.01 (-0.3 – 0.4) mm</td>
</tr>
<tr>
<td>(+) Proximal migration / (-) Subsidence (y-axis)</td>
<td>-0.13 (-1.7 – 0.3) mm</td>
</tr>
<tr>
<td>(+) Anterior / (-) Posterior translation (z-axis)</td>
<td>0.08 (-0.3 – 0.6) mm</td>
</tr>
<tr>
<td>(+) Anterior / (-) Posterior tilt (x-axis)</td>
<td>0.13 (-0.8 – 1.0) °</td>
</tr>
<tr>
<td>(+) Ante- / (-) Retroversion (y-axis)</td>
<td>0.01 (-1.1 – 1.4) °</td>
</tr>
<tr>
<td>(+) Valgus / (-) Varus (z-axis)</td>
<td>-0.02 (-0.8 – 0.5) °</td>
</tr>
</tbody>
</table>

In the x- and z-axis no significant change in translation or rotation of the stem was detected when comparing the different time points with each other. The largest amplitudes were found in rotation around the y-axis, being equivalent to slight stem retroversion, and in translation along the y-axis, representing minimal stem subsidence. Stem subsidence at the measured time points was not significant (p=0.62 for 3 vs. 12 months; p=0.09 for 12 vs. 24 months), and maximal subsidence was 1.7 mm. Likewise, there was no significant rotation around the y-axis when comparing the different time points with each other (p=0.23 for 3 vs. 12 months; p=0.27 for 12 vs. 24 months), and maximal rotation was 1.8°. The general pattern was that the stems subsided and rotated slightly after 3 months, stabilized after 1 year, and remained stable 2 years after surgery.

Correlation analysis demonstrated that the BMD changes in any of the investigated zones did not correlate with the migration of the stem at any time point (data not shown).

## Study II – the TOP cup

### Clinical and radiographic outcome

The HHS increased from 49 (24-79) to 99 (91-100) 2 years after the operation. On plain radiography, the cups showed no signs of migration 2 years after the surgery in 28 patients as determined by 2 independent observers. In 1 patient an increased inclination of the cup was observed after 3 months but it had stabilized after 1 year. Unfortunately, we could not
verify this by RSA because this patient was excluded from the analysis due to insufficient number of identified tantalum markers. In 11 patients a gap of up to 2 mm between the pole of the cup and the medial acetabular wall was visible at the 3 months control. This gap seemed to be filled with bone in all patients after 2 years without any radiographic sign of cup loosening.

Analysis of periprosthetic BMD
Substantial bone loss occurred 1 year after the surgery in the proximal periprosthetic regions zone 1 (-18%, \( p<0.001 \)), zone 2 (-16%, \( p=0.001 \)), and zone 3 (-9%, \( p=0.027 \)), when compared with postoperative BMD measurements obtained immediately after surgery. A smaller, statistically non-significant decrease in periprosthetic BMD (-2%, \( p=0.25 \)) was also seen in zone 5 (the ischial tuberosity) 1 year after surgery. In contrast, zone 4 (ramus superior) showed a statistically insignificant increase of 7% (\( p=0.86 \)) after 1 year. The general pattern after 3 months and 1 year was that the most pronounced decrease in periprosthetic BMD occurred in the proximal regions (zones 1, 2 and 3), whereas the distal zone 5 displayed a more moderate loss in periprosthetic BMD.

A slight change of the periprosthetic bone loss 2 years after insertion of the cup was seen in zone 1 (from -18% to -13%, \( p=1 \) compared to 1 year), zone 3 (from -9% to -10%, \( p=1 \) compared to 1 year), and zone 5 (from -2% to -1%, \( p=1 \) compared to 1 year) but these changes were not statistically significant. BMD did not change in zone 2 (remained -16%, \( p=1 \) compared to 1 year). In zone 4 the BMD increase became more pronounced after 2 years but this was not statistically significant (from 7% to 13%, \( p=1 \) compared to 1 year).

Correlation analysis demonstrated that the preoperative total hip BMD did not correlate with the amount of bone remodelling in any of the investigated zones.

Analysis of implant stability
Migration of the cup along and around the 3 axes was very small at all measured time points with absolute values not exceeding 1 mm or 2.5° (Table 2).
Table 2. Mean values and range of cup migration along and around the 3 axes in space 2 years after implantation.

<table>
<thead>
<tr>
<th>Cup migration</th>
<th>mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+) Medial / (-) Lateral translation (x-axis)</td>
<td>0.01 (-0.3 – 0.4) mm</td>
</tr>
<tr>
<td>(+) Proximal migration / (-) Subsidence (y-axis)</td>
<td>0.3 (-0.1 – 0.8) mm</td>
</tr>
<tr>
<td>(+) Anterior / (-) Posterior translation (z-axis)</td>
<td>0.05 (-0.5 – 0.5) mm</td>
</tr>
<tr>
<td>(+) Anterior / (-) Posterior tilt (x-axis)</td>
<td>0.4 (-1.4 – 2.5) °</td>
</tr>
<tr>
<td>(+) Ante- / (-) Retroversion (y-axis)</td>
<td>0.01 (-1.6 – 2.2) °</td>
</tr>
<tr>
<td>(+) Increased / (-) Decreased inclination (z-axis)</td>
<td>-0.02 (-1.2 – 1.8) °</td>
</tr>
</tbody>
</table>

No significant cup translation along the 3 axes was observed when comparing the different time points with each other: medial/lateral translation (p=1 for 3 vs. 24 months), proximal migration/subsidence (p=0.17 for 3 vs. 24 months) and anterior/posterior translation (p=1 for 3 vs. 24 months). Likewise, there was no significant change in cup rotation around the y-axis equivalent to ante- or retroversion (p=1 for 3 vs. 24 months), and there was no significant change in cup inclination (p=0.29 for 3 vs. 24 months). A significant change in cup rotation around the x-axis (anterior/posterior tilt) was found after 12 months (p=0.02 for 3 vs. 12 months), representing a slight increase in anterior tilt, but no significant changes were found up to 24 months (p=0.19 for 3 vs. 24 months; p=0.89 for 12 vs. 24 months).

Study III – HA coating of cups in primary THA

In this study the effect of HA coating on the survival of acetabular cups used in primary hip arthroplasty was assessed. Data from the SHAR were analyzed and our primary end point was cup revision due to any reason. Secondary endpoints were cup revision due to aseptic loosening or due to infection.

Risk of cup revision due to any reason

Kaplan-Meier analysis showed a 15-year survival of 66% (CI: 59-73) for the HA-coated cups and 78% (CI: 76-80) for the uncoated cups with cup revision for any reason as the endpoint. There was no significant influence of the HA coating on unadjusted cup survival (p=0.26). This remained true even when the analysis was stratified by age groups (p>0.05). When separated for cup type, the Romanus cup showed significantly inferior
performance with HA coating than without HA coating using revision for any reason as the endpoint (p<0.001). No statistically significant differences between HA-coated and uncoated cups were found for the HG and the Trilogy cups (p>0.05). However, in all cup types the survival of the HA-coated versions was inferior to that of the uncoated cups.

The crude HR of HA coating for the risk of cup revision due to any reason without adjustment for covariates was 1.1 (CI: 0.9-1.3). After adjustment for relevant covariates HA coating was a risk factor of cup revision due to any reason, with an adjusted HR of 1.4 (CI: 1.2-1.8; Fig 11). Age at primary arthroplasty below 50 years and a diagnosis of previous pediatric hip disease also statistically significantly increased the risk of cup revision due to any reason. The use of Romanus or HG cups compared to the Trilogy cup was also found to be a risk factor of cup revision due to any reason.

![Cumulative survival for cups with HA coating (red line) and cups without HA coating (black line) when cup revision due to any reason was used as the end point.](image.png)

**Figure 11.** Cumulative survival for cups with HA coating (red line) and cups without HA coating (black line) when cup revision due to any reason was used as the end point.

**Risk of cup revision due to aseptic loosening or due to other reasons**

Kaplan-Meier analysis in the pooled study population containing all 3 cup types and ages indicated that there was no significant difference between
cups coated with HA and uncoated cups (p=0.08) with respect to revision due to aseptic loosening. The 15-year survival was 69% (CI: 62-76) for the HA-coated cups and 82% (CI: 79-84) for the uncoated cups. When stratified for age, the HA-coated cups showed significantly inferior survival in the age group <50 years when compared to uncoated cups (p=0.03). When separated for cup type, the HA-coated Romanus cup showed inferior survival compared to the identical cup without HA coating (p<0.001). The analysis of the 2 other cups indicated no obvious difference in unadjusted survival between implants with or without HA coating (p=0.83 for the HG cup and p=0.56 for the Trilogy cup).

The crude HR of HA coating for the risk of revision due to aseptic cup loosening was 1.1 (CI: 0.98-1.46) compared with uncoated cups and without adjusting for relevant covariates. In the next step, HRs for each covariate mutually adjusted for all other covariates were calculated. HA coating was a risk factor of cup revision due to aseptic loosening with an adjusted HR of 1.7 (CI: 1.3-2.1; Fig 12). In this analysis age at primary arthroplasty below 50 years, a diagnosis of previous pediatric hip disease (compared to OA as the primary diagnosis), and the use of Romanus or HG cups compared to the Trilogy cup, were also associated with a statistically significantly increased risk of cup revision due to aseptic loosening. It has to be mentioned that the mean observation time varied between the 3 cup types: 12 years for the HG cup, 11 years for the Romanus cup, and 4 years for the Trilogy cup.

![Figure 12. Cumulative survival for cups with HA coating (red line) and cups without HA coating (black line) when cup revision due to aseptic loosening was used as the end point.](image-url)

Figure 12.
In exploratory analyses, the type of hospital at primary arthroplasty was included in the Cox multiple regression model, but was found not to influence the parameter estimates mentioned above. The hospital at primary THA could theoretically influence our results due to heterogeneity of the population in different hospitals. In order to explore that issue, a Cox multiple regression analysis using the hospital performing the primary THA as a frailty term was fitted. We found that the individual hospital did not influence our risk estimates.

In an analysis including only the procedures where the Trilogy cup was used we found that HA coating did not statistically significantly affect the survival of the cup. The adjusted HR of HA coating was 1.1 (CI: 0.5-2.5) with the endpoint cup revision due to aseptic loosening (Fig 13).

![Figure 13. Cumulative survival for Trilogy cups with HA coating (red line) and Trilogy cups without HA coating (black line) when revision due to aseptic loosening was used as the end point.](image)

The risk of revision due to infection was not influenced by the presence of HA coating.

Further exploratory analyses separately investigating the procedures where either only the liner or both the liner and the metal shell had been revised were performed. HA coating continued to be risk factor of isolated liner revision and of combined liner and metal shell revision when adjusted
for relevant covariates. Additionally, when isolated liner revision was the end point HA coating was a significant risk factor of revision both without and with adjustment for the covariates mentioned above (Table 3).

Table 3. Crude and adjusted HRs of isolated liner revisions and of combined revisions of the liner and metal shell due to any reason and due to aseptic loosening

<table>
<thead>
<tr>
<th>Endpoint:</th>
<th>Crude HR (95%CI)</th>
<th>p-value</th>
<th>Adjusted HRb (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any reason</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolated liner revisions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- HA</td>
<td>1.0 (ref)a</td>
<td>1.0 (ref)</td>
<td></td>
<td></td>
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<tr>
<td>+HA</td>
<td>1.3 (1.0-1.7)</td>
<td>0.03</td>
<td>1.5 (1.1-2.0)</td>
<td>0.01</td>
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<td>Combined Liner and metal shell revisions</td>
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<tr>
<td>+HA</td>
<td>0.9 (0.7-1.2)</td>
<td>0.6</td>
<td>1.4 (1.1-1.9)</td>
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<td><strong>Aseptic loosening</strong></td>
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<td>Isolated liner revisions</td>
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<td>+HA</td>
<td>1.4 (1.1-1.9)</td>
<td>0.02</td>
<td>1.6 (1.1-2.3)</td>
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<tr>
<td>+HA</td>
<td>1.0 (0.8-1.4)</td>
<td>0.8</td>
<td>1.7 (1.3-2.3)</td>
<td>0.001</td>
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a ref: reference group

b A Cox multiple regression model was used to investigate the influence of HA coating on cup survival due to any reason and due to aseptic loosening. Crude and adjusted HRs were calculated. The covariates adjusted for were: HA coating, age, gender, primary diagnosis, cup design, and stem fixation.
Study IV– HA coating of an uncemented stem in primary THA

In this study the survival of an uncemented femoral stem that was available either with or without HA coating was analyzed. Our hypothesis was that HA coating influences the risk of stem revision due to any reason, which was our primary endpoint. Secondary endpoints were stem revision due to aseptic loosening, infection, fracture, or dislocation.

Risk of stem revision due to any reason

The use of HA coating did not influence the survival of the Bi-Metric stem: 15-year survival for the HA-coated stem was 97% (CI: 96-98) and 97% (CI: 95-99) for the uncoated stems.

A Cox multiple regression model showed that HA coating did not affect the risk of stem revision for any reason when adjusted for all relevant covariates (HA coating, gender, primary diagnosis, age, and type of cup fixation), with an adjusted HR of 1.0 (CI: 0.6-1.6). Patients operated due to other reasons than OA were found to have a higher risk of stem revision than those with primary diagnosis OA, displaying an adjusted HR of 2.8 (CI: 1.6-4.9).

Risk of stem revision due to aseptic loosening or due to other reasons

Kaplan-Meier analysis showed a 15-year survival of 99% (CI: 98-100) for the HA-coated stem and 99% (CI: 98-100) for the uncoated stem.

In a Cox multiple regression model the adjusted HR of HA coating for the risk of stem revision due to aseptic loosening adjusted for the covariates described above was 0.5 (CI: 0.2-1.5), indicating that there was no statistically significant effect of the coating on stem survival.

When stem revision due to infection, dislocation or fracture was used as the endpoint in the Cox multiple regression model it was found that the presence of HA coating did not have any statistically significant influence on the adjusted risk of stem revision.
Study V– HA coating of cups in revision THA

In this study we evaluated the effect of HA coating on acetabular cups used in revision hip arthroplasty. Data from the SHAR were analyzed and our primary endpoint was re-revision of the acetabular component due to any reason, and the secondary endpoint was cup re-revision due to aseptic loosening. Other endpoints were isolated re-revisions of the liner or combined re-revisions of both liner and metal shell due to any reason or due to aseptic loosening.

Risk of cup re-revision due to any reason

In Kaplan-Meier analysis 10-year survival was found to be 89% (CI: 86-92) for the HA-coated revision cups and 87% (CI: 84-91) for the uncoated cups revealing no difference in survival between the HA-coated and the uncoated cups (p=0.8).

After adjustment for all relevant covariates in a Cox multiple regression model HA coating did still not influence the risk of cup re-revision due to any reason, with an adjusted HR of 1.4 (CI: 0.9-2.0). Age below 60 years at the time of index cup revision, dislocation as the cause for the index cup revision, and use of the HG cup compared to the Trilogy cup significantly increased the risk of cup re-revision due to any reason.

Risk of cup re-revision due to aseptic loosening or due to other reasons

Kaplan-Meier analysis indicated that the use of HA coating did not influence the survival of the revision cups with aseptic loosening as the endpoint: 10-year survival of the HA-coated cups was 95% (CI: 92-98) and it was 92% (CI: 89-95) for the uncoated cups (p=0.1).

Using the Cox multiple regression model the crude HR of HA coating for the risk of cup re-revision due to aseptic loosening was 0.7 (CI: 0.4-1.1) without adjusting for covariates. After adjustment for the covariates mentioned previously it was found that HA coating did not influence the risk of cup re-revision due to aseptic loosening, with an adjusted HR of 1.1 (CI: 0.6-1.9). The covariates age below 60 years at the index cup revision, the use of a HG cup and the use of uncemented cups at primary arthroplasty were associated with an increased risk of cup re-revision due to aseptic loosening.

The endpoints isolated re-revision of the liner or combined re-revision of both liner and metal shell were separately analysed. We found that HA coating was a significant risk factor of isolated liner re-revision due to any reason with an adjusted HR of 1.8 (CI: 1.01-3.3; Fig 14).
Figure 14. Cumulative survival for revision cups with HA coating (red line) and revision cups without HA coating (black line) when isolated liner re-revision due to any reason was used as the end point.

However, HA coating did not influence the risk of cup re-revision due to any reason when isolated liner revisions were excluded (adjusted HR 1.0; CI: 0.6-1.7). When isolated liner revisions were excluded bone grafting was found to be a significant risk factor of re-revision of the metal shell due to aseptic loosening (adjusted HR 2.1; CI: 1.1-4.2).

Further analyses on patients younger than 60 years revealed that HA coating did not affect the survival of the investigated cups even in this specific subgroup of patients. We also found that the use of bone grafting during the index cup revision was associated with higher risk of cup re-revision due to aseptic loosening in these patients.
Discussion

Form and Finish: what matters?

Study I
A loss in proximal periprosthetic BMD has been described for both cemented and uncemented femoral stems, suggestive of diaphyseal load transfer. New types of implants aim at more proximal load transfer, potentially avoiding such proximal bone loss. Designs of short femoral implants such as the CFP stem that preserves the collum femoris by subcapital osteotomy should provide more proximal load transfer and thus reduce the proximal bone loss that occurs after insertion of conventional stems. The CFP stem is also partially HA-coated. The use of HA coating in the proximal region of the stem supposedly enhances bone ingrowth and protects the implant from proximal stress shielding and proximal femur bone loss. In contrast to the manufacturer’s expectations our findings indicate substantial bone loss around the stem in the proximal regions, especially in the calcar region (Gruen zone 7). This is in agreement with other studies regarding this type of stem using plain radiography or computer tomography-assisted bone densitometry (Briem et al. 2011, Schmidt et al. 2011). The most dramatic loss in BMD seems to occur during the first 3 to 6 months, whereafter a plateau with annual losses comparable with those that take place during ageing seems to be reached (Venesmaa et al. 2003). It seems that neither the novel form nor the finish with HA protect the CFP stem from proximal bone loss that occurs around other stems.

Although bone is lost around the CFP stem this does not affect its stability. We showed that the stem did not migrate significantly during the first 2 years although periprosthetic BMD decreased: Mean subsidence of 0.13 (-1.7-0.3) mm and mean 0.01° (-1.1-1.4) of retroversion were measured. This compares favorably with other uncemented stems that were previously investigated at our institution: the Wagner-Cone prosthesis showed a mean subsidence of 0.5 (-2.5-0.03) mm and 0.81° (-1.0-3.8) of retroversion after 2 years (Ström et al. 2006), and the CLS stem subsided 1.42 (range not reported) mm and showed 2.39° (range not reported) of retroversion after 2
years (Wolf et al. 2010). Kärrholm et al. (1994) stated that the early migration of uncemented stems should be less than 1-1.5 mm within the first 2 years in order to avoid early failure. Both the Wagner-Cone and the CLS stem have shown low long-term revision rates in the SHAR (SHAR 2010). Our study showed that few CFP stems subsided to a very small degree in the first months, and remained stable thereafter. These results are in agreement with the medium-term results of 98-99% survival at 6 years reported on this stem (Briem et al. 2011, Nowak et al. 2011).

Taken together, our study indicates that the CFP stem with its novel form provides excellent primary stability but proximal bone loss is not prevented, neither by its form nor by its finish.

Study II

The TOP cup with its novel design aims to achieve improved fixation by combining 3 stabilization mechanisms: the well-established fixation of uncemented hemispherical cups by press-fit, the vertical and rotational stability provided by the threads around the equator, and the HA coating of the implant aiming at additional secondary fixation. In our study we found that this cup has a good primary stability. Previous reports on the TOP cup also indicate good medium-term survival (Briem et al. 2011, Nowak et al. 2011), but to our knowledge there is no study investigating the stability and BMD changes around this cup with the accuracy achieved by RSA and DXA.

Literature on the subject of bone remodelling after implantation of uncemented cups is controversial. According to Wolff’s law one should expect an increase of the BMD in the proximal regions around the implant as a result of increased loading and bone remodelling in these areas. Field et al. (2006) found reduced stress in the non-weight-bearing zones but preservation of BMD in the proximal weight-bearing zones around the uncemented Cambridge cup. On the other hand, other authors agree with our results describing a persistent decrease in BMD in the dome of the acetabulum (Sabo et al. 1998, Wright et al. 2001, Mueller et al. 2006, 2009). A possible mechanism could be that rigid fixation of a press-fit cup transmits forces sideways to the periphery (Morscher et al. 1997, Wright et al. 2001). This theory has been supported by finite element analyses of press-fit cups showing a stress concentration around the rim of the implant, leading to a mechanical load transfer to the cortical bone and reduced stress within the trabecular bone proximal to the implant (Huiskes 1987, Morscher et al. 2002). The same pattern was also observed when quantitative computer tomography was used to evaluate periacetabular BMD changes after implantation of uncemented press-fit cups (Mueller et al. 2006).

Our findings indicate a different pattern of BMD changes in the distal periprosthetic zones compared to those in the proximal zones of the TOP
cup. Due to minimal loading in these areas one should expect a decrease of BMD. In contrast, we found that the most distal zone 5 (the ischial tuberosity) shows minimal BMD decrease that almost recovered to baseline after 2 years. Additionally, in the distal zone 4 (ramus superior) we observed an increase of BMD which became more pronounced over time. Although these BMD changes were not significant compared to baseline this indicates a different pattern of bone remodelling than that what should be expected according to Wolff’s law of bone transformation. Such findings have not been described previously and longer follow-up will reveal whether this phenomenon persists around this cup type.

HA coating of the TOP cup was thought to enhance bone ingrowth, stimulate bony gap filling and improve additional secondary implant stability. However, this type of coating seems not to prevent demineralization around the implant. The question of whether the bone loss proximal to the TOP cup is an early sign of osteolysis and subsequent cup loosening has to be further investigated by longer follow-up.

Although proximal periprosthetic BMD decreases around the TOP cup it seems that this phenomenon does not affect its primary stability. We found that migration of the TOP cup is minimal along and around all axes in space. The migration of the TOP cup is comparable with this found on other uncemented cups studied with RSA (Reflection, GOT, HGII, Trilogy; Carlsson et al. 2006, Zhou et al. 2006, Baad-Hansen et al. 2011). The Trilogy cup that is widely used in uncemented THA showed a mean cranial translation of 0.18 mm and a decreased inclination of 0.11° whereas the TOP cup migrated 0.32 mm and 0.02° respectively (Baad-Hansen et al. 2011). The TOP cup also compares favourable to the Allofit and Interop cups that were previously investigated at our institution (Wolf et al. 2012).

Taken together the study shows that the TOP cup with its novel design achieves good primary stability and excellent short-term results, but periacetabular demineralization cannot be prevented in the proximal zones around the implant.

Study III

Our register study on 3 different cups available with or without HA coating indicates that the cup design seems to be an important factor that determines long-term survival. The Trilogy cup had a better survival than the HG and the Romanus cups. The finding that the Romanus and the HG cups show inferior results was not unexpected and has been reported previously (Thanner et al. 1999, Lyback et al. 2004, Hallan et al. 2006, SHAR 2010). The main problem of the HG cup was excessive liner wear that was probably due to an insufficient locking mechanism, leading to “silent osteolyses” (Röhrle et al. 2006). The Romanus cup is a threaded hemispherical cup, and high failure rates of threaded cups have been previously reported (Capello et
al. 1993, Fox et al. 1994). On the other hand, it has also been described that threaded cups with HA coating perform better than some designs of hemispherical press-fit cups with the same coating (Reikeras and Gunderson 2006).

The use of different types of liners during the period investigated in our study could distort our results, for instance due to predominant use of XLPE liners in 1 of the investigated groups. Information on the type of polyethylene or on the sterilization of liners used in combination with the investigated cups was not available. However, general information about the use of XLPE liners in primary hip arthroplasty has been reported from the Register: 7,933 total hip arthroplasties using Trilogy or Allofit cups with either conventional or XLPE liners were included, and the results were adjusted for age, gender, primary diagnosis, type of cup and size of caput. According to that analysis, the use of XLPE liners does not affect the risk of revision due to any reason (SHAR 2010). Furthermore, the increased use of XPLE liners and the introduction of HA coated implants run in parallel. Thus, it is more likely that the cups that potentially benefit from the use of XPLE liners should be over-represented in the group of HA-coated cups.

HA coating as a finish on the investigated cups seems to be a risk factor of cup revision both due to aseptic loosening and due to any reason. These findings are in contrast with results of previous studies reporting improved survival (Moilanen et al. 1996, Roffman and Kligman 1999, Ali and Kumar 2003) or at least equal survival (Röhrl et al. 2004) when identical cups with and without HA coating were compared. Our finding is however in partial agreement with a large Danish register analysis of HA-coated hip implants that found no reduced risk of revision after the use of HA-coated cups (Paulsen et al. 2007). Howard et al. (2011) reported that patients operated with HA-coated cups had a 1.4-fold increased risk of cup revision compared to those patients operated with uncoated cups in a study on 9,584 THAs.

It could be speculated that resorption of the HA coating occurs before secure bone ingrowth onto the cup surface has been achieved. This would lead to inferior stability when compared to uncoated cups, where long-lasting bone ingrowth can take place immediately. Loss of periprosthetic BMD has in fact been described in the vicinity of HA-coated Trilogy cups (Digas et al. 2006). A retrieval analysis of HA-coated cups has shown degradation of HA on all retrieved cups (Rokkum et al. 2003). A retrospective study on Mallory-Head cups showed greater polyethylene wear in HA-coated cups compared to uncoated cups (Gottliebsen et al. 2012). This observation is also of interest since abrasion of HA particles from the coating can lead to increased wear of the polyethylene liner, thus leading to periprosthetic osteolysis and early loosening (Morscher et al. 1998). This explanatory model is supported by our results, since isolated liner revisions were more common in both primary and revision cups with HA coating (Table 3).
Taken together, both form and finish affect the stability of the investigated cups. The cup design, including liner locking mechanisms, determines both primary and long-term stability of the implants. HA coating seems not to provide additional stability of the investigated cups. In contrast to the commonly belief that HA coating improves long-term stability of implants, we found that HA coating can even enhance the risk of revision of primary cups, perhaps due to third-body wear.

Study IV

We found excellent long-term results of the investigated Bi-Metric stem. A low revision rate of the Bi-Metric stem was also found in a large Finnish registry analysis with a 10-year survival of 96% based on aseptic loosening as the endpoint (Eskelinen et al. 2006). The Bi-Metric stem is a tapered implant allowing for 3-point stem fixation in order to obtain primary stability. This type of straight stem with tight diaphyseal fit shows excellent stability, but bone ingrowth and remodeling around the distal part of the stem indicate load transfer in this region and stress shielding of the proximal metaphyseal femur. Periprosthetic proximal bone loss has been reported around this stem both after primary and revision THA (Sköldenberg et al. 2006, Adolphson et al. 2009). However, this phenomenon seems not to affect the stability of the Bi-Metric stem, and it seems that the design of this stem provides good primary stability.

The use of HA coating on uncemented stems was thought to provide a sealing effect, potentially reducing migration of wear debris to distal periprosthetic tissue. Additionally, HA coating should enhance bone ingrowth of the implant and protect the stem from proximal bone loss due to stress shielding. However, a review of the literature on HA-coated uncemented femoral components failed to show an improvement in long-term stability (Chambers et al. 2007). Meta-analyses on the subject of HA-coated femoral stems in primary THA also supported the notion that HA coating does not improve the survival of uncemented stems (Gandhi et al. 2009, Goosen et al. 2009). Even randomized studies on smaller cohorts including patients operated bilaterally with stems with or without HA coating indicate that HA coating neither influences radiological results nor clinical performance of these stems in the medium-term (Kim et al. 2003, Park et al. 2003). The Bi-Metric stem is more widely used with HA coating than without, and this probably reflects that HA coating is believed to improve stem fixation and long-term stability. Indeed, a retrieval study on this stem found that there was more bone ingrowth on stems with HA coating than on those without coating (Coathup et al. 2001). In contrast and in agreement with our results, a large Danish registry analysis including 3,158 Bi-Metric stems indicated that HA coating did not affect the survival of the implant (Paulsen et al. 2007).
Taken together, our analysis indicates that the HA finish of this well-functioning stem does not contribute to improved stem survival, indicating that the form but not the finish is the key for the excellent performance of this specific stem.

Study V

In contrary to our findings, some studies investigating the outcome of acetabular revision using uncemented HA-coated components showed promising results (Nivbrant and Kärrholm 1997, Dorairajan et al. 2005, Geerdink et al. 2007, Palm et al. 2007). However, the literature on revision hip arthroplasty is scarce and to our knowledge there is no study comparing identical cups with or without HA coating used in revision arthroplasty.

The use of the HG cup significantly enhanced the risk of cup re-revision due to aseptic loosening and due to any reason when compared with the Trilogy cup. Tanzer et al. (1992) reported only 1% component failure using the HG cup in acetabular revision after an average of 3.4 year follow-up. Long-term results for this cup used as a revision component were also reported to be good, reporting a 4% re-revision rate of the implant due to aseptic loosening at 12 year follow-up (Templeton et al. 2001, Hallstrom et al. 2004). However, these studies report on the results of the HG cup alone and do not compare with other cup designs. The Trilogy cup replaced the HG II cup in the market introducing changes in the liner fixation mechanism which was the “achilles heel” for the HG II cup. Additionally, the conventional liners that were used in the HG cups were gradually replaced by XLPE liners more commonly used with the Trilogy cups. Taken together, our observations confirm that differences in implant form influence the cup survival also after revision THA.

In summary, HA coating as a cup finish can enhance the risk for re-revision of revision cups, and the form of the cups inserted at revision surgery is important for long-term stability.

Characteristics of HA coating

Polyethylene wear particles contribute to bone loss around hip implants, creating osteolytic areas and subsequent implant failure. The reduction of the “effective joint space” (Schmalzried et al. 1992) by sealing off the bone-implant interface is therefore important to reduce migration of wear particles to the periprosthetic tissue. HA showed a sealing effect after 8 and up to 52 weeks in loaded stable implant models in animals (Rahbek et al. 2000, Rahbek et al. 2001). This potential effect of HA coating and its propensity to enhance bone ingrowth popularized this finish, and many hip prostheses are now produced only coated with HA.
Deposition of HA coating on the implant, coating thickness and crystallinity of the HA are basic characteristics of the HA and play an important role in its long-term survival. Many methods are used in order to apply HA coatings on implants but plasma-spraying is the most widely used technique. The thickness of the HA coating affects both its resorption and mechanical properties. Thicker coatings usually exhibit poorer mechanical properties. A thickness of 50-75 µm has been determined to be optimal by most manufacturers for commercially used orthopedic implants. Crystallinity is also an important characteristic of HA coating. It is an essential factor in the resorption of the HA coating (Maxian et al. 1993, 1994, de Bruijn et al. 1994, Klein et al. 1994, 1994, Dalton and Cook 1995). Resorption of the HA coating occurs around implants as a result of physiological bone remodeling. The initial resorption generally relies on the dissolution rate of the coating. Faster dissolution is preferred in order to initiate quicker and stronger fixation and resorbed HA coating is partly replaced by bone. Thus, if the resorption rate can be optimally controlled so that the new bone can replace the resorbed coating, the durability of the bone-implant fixation should not be negatively affected. Amorphous or less crystalline materials have been found to be more resorbable and there is evidence to suggest that they may be more beneficial for early bone ingrowth than coatings with high crystallinity (Maxian et al. 1993, de Bruijn et al. 1994). On the other hand, highly crystalline coatings generally have low dissolution rates under physiological conditions and can accelerate early mechanical fixation of the implant (Overgaard et al. 1999). It seems that there is a very delicate balance between dissolution/reprecipitation of the HA coating depending on its amorphous-crystalline phase ratio. The crystallinity of HA coatings for biomedical applications usually ranges from 65 to 70%. A combination of factors such as coating manufacture, implant material and design, bone bed preparation, bone quality and quantity, and surgical technique are of great importance for the final overall implant performance (Sun et al. 2001).

In studies III and V it could be assumed that the HA characteristics of the different implants could affect our results. The HA coating on the implants compared (Trilogy, Romanus and HG), had almost the same characteristics i.e. crystallinity 50-70%, thickness 50-70 µm and the HA coating was applied on the implant with the plasma-spraying technique indicating that this issue could not influence our results.
Other factors not related to form and finish of implants influence outcome

In our register studies on cups used in primary or revision THA we found that patients with an age below 60 years were at higher risk of cup revision or re-revision. The fact that younger patients have an inferior outcome after primary THA is well known (Wangen et al. 2008, SHAR 2010). Inferior survival of HA-coated cups in the group of younger patients has been previously reported (Manley et al. 1998, Puolakka et al. 1999, Wangen et al. 2008). THA in young, active patients is associated with a higher degree of polyethylene wear and osteolysis. Higher demands and a higher degree of physical activity in young patients may explain the higher revision risk in these patients. The HA coating in some designs may even facilitate these events due to an increased burden of released particles from the coating causing third-body wear.

We found that the outcome after primary THA in secondary OA after pediatric hip disease is inferior when compared with results of THA after primary OA. These findings are in agreement with reports from the SHAR and the Norwegian Arthroplasty Register: Patients operated with a total hip prosthesis due to secondary arthritis are at higher risk of loosening than those operated due to primary OA (SHAR 2010, Lehmann et al. 2011). In contrast, a large register study from the Nordic Arthroplasty Registry Association (NARA) including 14,403 THAs in patients with pediatric hip disease reported no difference in survival when compared with THAs previous inserted after primary OA, using a Cox multiple regression analysis and reporting a HR of 1.0 (CI: 1.0-1.1) when adjusting for age, gender, and type of prosthesis fixation (Engesaeter et al. 2012).

In our study on revision cups we found that cups that were originally revised due to dislocation were more likely to undergo re-revision. The fact that dislocation is a significant risk factor of re-revision is probably related to a high risk of recurrent dislocation after revision surgery. This may be due to patient-related factors but also due to soft tissue laxity (Patel et al. 2007). The problem of recurrent dislocation in revision surgery is well known and the use of conventional revision cups such as those investigated in our study does not sufficiently address this problem. Constrained acetabular components have been proposed to solve the problem of persistent instability but high failure rates of these devices have been reported (Noble et al. 2011). Recent register study on dual-mobility cups used in revision surgery reported good results with a low rate of re-revision at least in the short-term, and perhaps dual-mobility cups should be considered as to prevent recurrent dislocation after hip revision surgery (Bourne and Mehin 2004, Stroh et al. 2012, Hailer et al. 2012).
Study V indicated that the risk of cup re-revision is increased when in the primary THA used an uncemented cup. This phenomenon has not been previously described and the reasons for this finding are unknown but several explanations are possible: Loosening of cemented cups often leads to a wide sclerotic acetabular bed which can partly be used for fixation of an uncemented revision cup (Issack et al. 2009). In contrast, loosening of uncemented cups is commonly associated with focal osteolysis, large acetabular defects and decreased BMD due to stress shielding rendering fixation of the revision cup more difficult (Digas et al. 2006).

Statistical considerations

In all 3 register studies bilaterally operated patients were included. The Kaplan-Meier survival analysis and the Cox regression model are however based on the assumption of independent observations. Including both hips in bilaterally operated patients could therefore potentially create dependency problems. In order to investigate dependency issues separate analyses excluding the second hip in bilaterally operated patients were performed. The estimates did not differ from analyses including all joints. Moreover, previous authors have shown that inclusion of both sides in bilaterally operated patients in Cox regression models is feasible in register studies of this size (Lie et al. 2004, Thillemann et al. 2008).

HA coating of uncemented stems in primary THA did not statistically significantly influence the risk of revision. However, absence of significance does not necessarily imply significance of absence. In modern hip arthroplasty failure rates are low, resulting in small numbers of implant revisions compared to the total number of primary THAs. This is reflected in our results where the small number of events, i.e. revisions, reduces the precision and widens the CIs around the HR. In other words, the analysis is open to type II statistical error. On the other hand, the size of the investigated groups is relatively large and any potential differences between the groups would be so small that their clinical relevance can be questioned.

The unit where the index procedure was performed could exert an effect on outcome by selection bias of patients, varying degrees of surgical competence and other confounders. The individual hospital could not be included as a covariate in the Cox multiple regression analysis due to the fact that over 80 degrees of freedom would have resulted. Instead, the hospital performing the index procedure was introduced as a frailty term. This, however, did not change the previously determined risk estimates. We therefore believe that this covariate had a negligible impact on the endpoints of our analysis.
The register

3 studies in this thesis were based on data from the SHAR. A population-based observational study has its inherent limitations and uncertainties concerning completeness, reliability and validity of data. However, the SHAR has been repeatedly validated and was found to have a completeness of 98% for primary THAs and 94% for revision THAs (Söderman et al. 2000, 2001). An advantage of register studies is the large number of patients derived from the community that is being surveyed, be it a specific region, an entire country, or even a number of countries combined, such as in the NARA (Havelin et al. 2011). The fact that hospitals of various sizes, surgeons with different levels of expertise, and mixed groups of patients are included in register analyses renders such studies relevant to daily clinical praxis, whereas smaller cohort studies performed by dedicated experts tend to have a bias towards better than average results (Graves 2010). On the other hand, register studies can be distorted by various confounding factors that cannot always be controlled for in an observational study. This is a drawback when compared to prospectively randomized controlled trials (RCTs) where patients are comparable with respect to certain variables such as age, body mass index (BMI) or comorbidity. However, an RCT has to ensure that the trial is adequately powered to enable statistical difference for the relevant parameter(s) to be compared, something that is more easily obtained in register studies with a large number of patients included. The 5-year survival of an uncemented cup in modern THA with aseptic loosening as the endpoint is around 99.5% (SHAR 2010). Because of these successful results the number of patients needed in a RCT study with 5-year follow-up in order to detect a clinically significantly difference in survival is very large: i.e. to obtain a difference of 2% in 5-year cup survival due to aseptic loosening with a power of 80%, given a 2-tailed a =0.05, requires at least 40,000 patients included with a 5-year follow-up. That makes these studies impossible to perform.

Obviously, the most complete picture of an intricate issue such as the proposed value of HA coating of uncemented THA implants is obtained when combining different levels of evidence: RCTs, meta-analyses of RCTs, other prospective controlled studies, and register studies together provide important and valid information.

Limitations

Studies I and II were designed as prospective cohort studies. The absence of a control group forces us to compare our findings only with those from other cohorts investigating periprosthetic BMD or implant migration. The ideal study would be a randomized controlled trial comparing the implants with
other well-established conventional uncemented prostheses. On the other
hand, RSA results from different units and derived from different cohorts
have previously been compared with each other (Kärrholm 1989). RSA
provides precise and reproducible measurements and is considered a reliable
method for the evaluation of implant migration. In our institute other
uncemented implants such as the Wagner-Cone stem, the CLS stem and the
Allofit/Interop cups have previously been investigated using identical
methods, and this allows for cautious comparisons between groups to be
drawn. Furthermore, very few studies have investigated both the stability
and the change in periprosthetic BMD around uncemented stems and cups.

In study II the final number of patients (16 out of 29) eligible for RSA is
fairly low. In 8 of 29 patients an insufficient number of tantalum markers
was identified and they were thus excluded from the analysis. Loss of
patients due to the difficulty to identify the tantalum markers placed in
polyethylene liners of cups has been previously reported (Digas et al. 2007,
Wolf et al. 2012). Following the instructions for reliable and accurate RSA
measurements we were forced to additionally exclude 5 patients due to
unacceptably high values of CN and/or ME (Valstar et al. 2005). In contrast,
in study I where the CFP stem was analysed the CN and ME were
acceptable. An explanation for this difference is probably the positioning of
the tantalum markers on the implants. The CFP stems used were
preoperatively labelled with 5 tantalum markers but the TOP cups were
intraoperative labelled around the edge of the liner by the surgeons. This
could eventually lead to inferior stability of the markers reflecting to high
values of ME and/or poor distribution of the markers reflecting to high
values of CN in RSA.

Only few types of stems and cups are investigated in our register studies,
and that can be considered a limitation. However, the purpose of our register
studies was to investigate the effect of HA coating on hip implant survival
and only few implants were available with or without HA coating. In order
to reduce the risk of bias caused by patient selection, surgical preference and
technique, and other factors not recorded in the Register, only implants with
adequate numbers of registered hips per implant were included in our
studies. Furthermore, the implant designs with the largest numbers in our
studies (Trilogy cup, Bi-Metric stem) are still widely used with very good
results (Eskelinen et al. 2006, Isaac et al. 2007, Davies et al. 2010, SHAR
2010). Additionally, in study V on revision procedures, we present a
comparatively large number of revision operations and at least to our
knowledge there is no study on revision cups with comparable numbers of
patients.

Factors with a potential influence on our results were entered as
covariates in our multiple regression analysis, in some cases only in an
exploratory fashion. Some technical information such as the use of
additional screw fixation of the cups or the type of polyethylene liner is not

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registered in the database and was therefore not considered. Other possible confounding variables are patient-related factors that could have a direct or indirect influence on implant survival, e.g. osteoporosis, neurological, mental and endocrine disorders or overweight. These are not registered in the SHAR and cannot be analysed in our studies. The same applies to other possible confounding factors such as medication with steroids, non-steroidal anti-inflammatory drugs or bisphosphonates that are known to influence bone metabolism.

The severity of acetabular defects in cup revision surgery varies. Inferior outcome after revision arthroplasty has been reported in cases of severe acetabular defects such as Paprosky type III compared to such as defects Paprosky type I or II (Paprosky et al. 1994, Johansson et al. 2010). In study V, the lack of detailed information on the extent of the acetabular defects is as a further limitation. In order to address this potential weakness the use of bone grafting was introduced as a covariate. We found that the use of bone graft at the index cup revision was a risk factor of re-revision of the metal shell. This possibly reflects extended acetabular defects, difficulties in cup fixation and subsequently inferior long-term stability. The use of bone grafting was not unevenly distributed between the groups of HA-coated and uncoated revision cups, therefore we have no reason to believe that acetabular defects were unevenly distributed between HA-coated and uncoated cups. Taken together, we have no reasons to believe that the size of the bone defects at revision surgery skewed our results.
Conclusions

Study I
Use of the short curved, HA-coated CFP stem gave good clinical results in the short-term and the stem displayed excellent primary stability. However, substantial loss in proximal periprosthetic BMD occurred and loading forces seem to be transmitted distally. The HA finish and the novel shape of the stem can thus not prevent proximal periprosthetic bone loss.

Study II
Periprosthetic BMD in the proximal zones around the partly threaded, fully HA-coated TOP cup was found to decrease substantially and did not recover up to 2 years. This did not affect the stability of the cup when measured by RSA up to 2 years after implantation. The TOP cup with its novel form provides excellent primary stability but demineralization around the cup cannot be prevented, neither by its form nor by its finish.

Study III
Registry data on 8,043 hips indicated that HA coating was a risk factor of cup revision both due to aseptic loosening and due to any reason. The mechanism by which HA jeopardizes cup survival could be third-body wear, reflected by our finding that HA causes an increased risk of isolated liner revision. The form of the cup seems to be more important for the long-term stability than its finish.

Study IV
Registry data on 4,772 hips showed that there is no difference in stem survival between uncemented Bi-Metric stems with and without HA coating. Our findings do not support the belief that HA coating improves stem survival, although minimal effects cannot be excluded.
Study V

Register data on 1,780 acetabular hip revisions lend no support to the notion that HA coating improves the performance of revision cups. On the contrary, HA coating increased the risk of liner re-revisions, possibly due to third-body wear. The form of the cup inserted at the index cup revision also influenced the risk of subsequent re-revision of the cup.

In summary, the analysis of different types of stems and cups used in primary and revision THA revealed that the form of the implants is an important factor for primary stability and thus affects long-term survival of the THA. Furthermore, the finish of uncemented THA implants with HA can enhance the risk of revision of both primary and secondary cups, and does not prevent proximal periprosthetic bone loss.
Future research

- 5-year follow-up of the CFP stem and the TOP cup using the same clinical and radiography measures is planned. The findings at the 2-year follow-up showed proximal bone loss around both implants, but their primary stability was not affected. The 5-year follow-up will reveal whether the proximal periprosthetic BMD loss recovers after 5 years, and whether this affects implant stability and thus medium-term outcome.

- In study V we found that the use of uncemented cups in primary THA is a significant risk factor of cup re-revision after revision surgery when compared with revision of cemented cups. These findings have not been previously described and merit further investigation. We plan to investigate this phenomenon by an additional analysis of data from the SHAR.
Insättning av höftprotes är ett av de vanligaste kirurgiska ingreppen i utvecklade länder och har även kallats "seklets operation". I Sverige utfördes år 2011 över 16.000 primära höftprotesoperationer, och det framtida behovet av detta ingrepp förväntas stiga på grund av det ökande antalet äldre människor. Trots överlag positiva resultat kvarstår problemet att höftproteser lossnar, mestadels av mekaniska skäl. På patienter under 65 år är detta lossningsproblem mera omfattande, sannolikt på grund av en högre aktivitetsnivå och därmed följande ökad belastning.


Syftet med denna avhandling var att undersöka effekterna av form och ytbehandling på ocementerade höftprotesers primärstabilitet och långsiktig proteosöverlevnad. Denna avhandling bygger på 2 olika typer av studier:

- Prospektiva kliniska kohortstudier (studier I och II).

I dessa studier undersöks kliniska resultat, stabilitet av och bentäthet kring en ocementerad stem (I) och en ocementerad cup (II). Båda implantat har ytbehandlats med HA och deras form skiljer sig från konventionella cuppar och stammar: CFP-stammen är en kort, böjd stam där man till skillnad från sedvanliga stammar bevarar lårbenshalsen. TOP-cupen är en halvsfärisk cup med en rad gängor kring ekvatorn. Hypotesen var att dessa implantat tack vare form och ytbehandling både uppvisar god primärstabilitet och bevarar bensubstans i kringliggande ben. Proteskomponenternas primärstabilitet
undersöktes med radiostereometri (RSA) och förändringar i bentätheten kring implantaten mättes med "dual X-ray absorptiometry" (DXA).

- Registerstudier (studier III, IV och V).

I dessa studier har data erhållits från Svenska Höftprotesregistret. Hypotesen var att ytbeläggning av ocementerade höftproteser med HA påverkar överlevnaden av dessa implantat, både efter primär- och efter revisionsartroplastik.


I studie II undersöktes TOP-cupen. Dess primära stabilitet var god dock även kring detta implantat uppmättes en betydande minskning av bentätheten i proximala proteresnära områden i bäckenbenet. Således kunde varken den specifika utformningen av denna cup eller ytbehandlingen med HA förhindra periprostetisk demineralisering.


Η ολική αρθροπλαστική του ισχίου θεωρείται μια από τις πιο κοινές χειρουργικές επεμβάσεις στις αναπτυγμένες χώρες και μάλιστα έχει χαρακτηριστεί ως "Η χειρουργική επέμβαση του αιώνα". Στην Σουηδία πραγματοποιήθηκαν πάνω από 16.000 ολικές αρθροπλαστικές ισχίου το έτος 2011 και η ανάγκη για τέτοια χειρουργεία αναμένεται να πολλαπλασιαστεί καθώς ο αριθμός των ηλικιωμένων αυξάνεται συνεχώς. Παρά τα υψηλά ποσοστά επιτυχίας αυτής της επέμβασης, το πρόβλημα της απώτερης επιπλοκής με χαλάρωση των εμφυτευμάτων κυρίως εξαιτίας μηχανικών λόγους παραμένει. Ιδιαίτερα σε νέους ασθενείς κάτω των 65 ετών με υψηλότερες απαιτήσεις, η επιπλοκή αυτή είναι πιο συχνή λόγω της εντονότερης φάρτυγος του ισχίου.

Η ολική αρθροπλαστική του ισχίου σταθεροποιείται στο οστό με ή χωρίς την χρήση οστικού τσιμέντου. Η μετάδοση των δυνάμεων κατά την φόρτιση του ισχίου και η σταθερότητα της ολικής αρθροπλαστικής με οστικό τσιμέντο επιτυγχάνεται διαμέσου του μανδύα τσιμέντου ενώ στην ολική αρθροπλαστική χωρίς οστικό τσιμέντο βασιζόμαστε στην απόλυτη πρωτογενή σταθερότητα με την μέθοδο ενσφήνωσης "press-fit". Σε δεύτερο χρόνο, η ανάπτυξη νέου οστού και η διασύνδεση του με τα υλικά της αρθροπλαστικής παρέχει δευτερογενή σταθερότητα. Η χρήση της ολικής αρθροπλαστικής χωρίς οστικό τσιμέντο χρησιμοποιείται ευρέως ιδίως σε νέους και δραστήριους ασθενείς λόγω της γενικής πεποίθησης ότι προσφέρει καλύτερη σταθερότητα και τεχνικά ευκολότερη μελλοντική χειρουργική επέμβαση αναθέωρησης εάν αυτή κρίθηκε απαραίτητη.

Τα τελευταία χρόνια νέα μοντέλα ολικής αρθροπλαστικής χωρίς τσιμέντο έχουν προτάθει με διαφορές τόσο στο σχήμα όσο και στην επεξεργασία της επιφάνειας των υλικών, με απότερο σκοπό την βελτίωση της πρωτογενούς σταθερότητας και στοχεύοντας στην καλύτερη μακροχρόνια απόδοση της επέμβασης. Η επικάλυψη των υλικών με υδροζυκατερισμού καθιερώθηκε η μείωση της τελευταίας δεκαετίας πιστεύεται ότι προσθετεί την γρήγορη ανάπτυξη νέου οστού γύρω από την πρόθεση και επομένως καλύτερη δευτερογενή σταθερότητα.

Ο σκοπός της παρούσας διατριβής ήταν η διερεύνηση της επίδρασης του σχήματος αλλά και της επεξεργασίας των υλικών της αρθροπλαστικής χωρίς τσιμέντο στην σταθερότητα και επομένως στην μακροχρόνια απόδοση της χειρουργικής επέμβασης.
Η διατριβή στηρίζεται σε 2 διαφορετικές κατηγορίες μελετών:
- Προοπτικές κλινικές μελέτες (μελέτες I και II).
  Σε αυτές τις μελέτες εξετάστηκαν τα κλινικά αποτελέσματα, η σταθερότητα και οι αλλαγές στην οστική πυκνότητα γύρω από τα υλικά ενός τύπου ολικής αρθροπλαστικής ισχίου. Τα υλικά είχαν επικάλυψη με υδροξυαπατίτη και το σχήμα τους διαφέρει από τα ευρέως χρησιμοποιημένα συμβατικά υλικά μιας κοινής αρθροπλαστικής ισχίου: η κοτύλη TOP είναι μια ημισφαιρική κοτύλη με μια σειρά από σπερώματα στην περιφέρεια. Το μηριαίο στέλεχος CFP είναι ένα βραχυκάμπτο στέλεχος με το οποίο, σε αντίθεση με τα συμβατικά στελέχη, επιτυγχάνεται η διατήρηση του αυχένα του μηριαίου οστού κατά την εμφύτευση. Η υπόθεση εργασίας της έρευνας ήταν ότι αυτά τα υλικά λόγω του ιδιαίτερου σχήματος τους και της ιδιαίτερης επεξεργασίας της επιφάνειας τους με υδροξυαπατίτη παρέχουν καλύτερη σταθερότητα και διατηρούν την οστική πυκνότητα στην περιφέρεια τους. Η σταθερότητα μετρήθηκε με την χρήση της ραδιοστεροειδής ανάλυσης (RSA) και οι αλλαγές στην οστική πυκνότητα μετρήθηκαν με την χρήση της μεθόδου DXA.
- Μελέτες αρχειον επεμβάσεων αρθροπλαστικής (μελέτες III, IV και V).
  Σε αυτές τις μελέτες τα στοιχεία αντλήθηκαν από το Σουηδικό αρχείο επεμβάσεων αρθροπλαστικών ισχίου (SHAR). Η υπόθεση εργασίας των ερευνών ήταν ότι η επεξεργασία με υδροξυαπατίτη της επιφάνειας των υλικών της ολικής αρθροπλαστικής ισχίου χωρίς θυσία θεωρείται την απόδοση των υλικών τόσο στην χρήση τους στην πρωτογενή αρθροπλαστική όσο και στις επεμβάσεις αναθεώρησης της αρθροπλαστικής.

Στην μελέτη I εξετάσθηκε το μηριαίο στέλεχος CFP. Τα κλινικά αποτελέσματα ήταν εξαιρετικά και η πρωτογενής σταθερότητα εξεταζόμενη με την μέθοδο RSA βρέθηκε πολύ καλή. Η εξέταση της οστικής πυκνότητας με DXA έδειξε σημαντική απόλυτα οστικής μάζας στο εγγύς τμήμα του στελέχους ανάδεικνύοντας ότι η μετάδοση των δυνάμεων κατά την φόρτιση του ισχίου μεταφέρονται στο σημείο της οστικής της μηριαίου στελέχους. Αποδεικνύεται ότι τόσο η μοναδικό σχήμα όσο και η επεξεργασία της επιφάνειας με υδροξυαπατίτη δεν κατέστη δυνατή να εμποδίσει την απόλυτη οστικής μάζα του εγγύς τμήμα του μηριαίου στελέχους.

Στην μελέτη II εξετάσθηκε η κοτύλη TOP. Η πρωτογενής σταθερότητα βρέθηκε καλή αλλά σημαντική απόλυτα οστικής πυκνότητας μεταφέρθηκε στο εγγύς τμήμα του οστού γύρω από το εμφύτευμα. Συμπεραισματικά ώστε το ιδιαίτερο σχήμα αλλά ώστε και η επικάλυψη του εμφυτεύματος με υδροξυαπατίτη μπόρεσε να εμποδίσει την ελάττωση της οστικής πυκνότητας γύρω από το υλικό.

Στην μελέτη III αναλύθηκαν στοιχεία από 8.043 πρωτογενείς ολικές αρθροπλαστικές ισχίου. Τα αποτελέσματα έδειξαν ότι η χρήση υδροξυαπατίτη στην επιφάνεια των υλικών δεν αύξησε την απόδοσή τους. Αντιθέτως ο υδροξυαπατίτης αναγνωρίστηκε ως παράγοντας κινδύνου για
πρόκληση επέμβασης αναθεώρησης αλλά και κυρίως για την πρόκληση άσηπτης χαλάρωσης του υλικού. Επίσης παρατηρήθηκαν διαφορές στην διάρκεια διατήρησης των διαφόρων τύπων εμφυτευμάτων που εξετάσθηκαν αποδεικνύοντας επίσης ότι το σχήμα του υλικού της κοτύλης που χρησιμοποιείται στην αρθροπλαστική ισχίου επηρεάζει την μακροχρόνια απόδοσή της.

Στην μελέτη IV αναλύθηκαν στοιχεία από 4.772 πρωτογενείς ολικές αρθροπλαστικές ισχίου με την χρήση του μηριαίου στελέχους Bi-Metric. Δεν βρέθηκε διαφορά στην απόδοση του εμφυτεύματος όταν εξετάσθηκαν στελέχη με και χωρίς την επικάλυψη με υδροξυαπατίτη. Αυτά τα ευρήματα θέτουν σε αμφισβήτηση την γενικότερη πεποίθηση της καλύτερης απόδοσης των αρθροπλαστικών ισχίου με επικάλυψη υδροξυαπατίτη.

Στην μελέτη V αναλύθηκαν στοιχεία από 1.780 επεμβάσεις αναθεώρησης υλικών κοτύλης. Η μελέτη εδείξει ότι ο υδροξυαπατίτης στην επιφάνεια των υλικών που χρησιμοποιούνται σε αναθεωρήσεις ολικών αρθροπλαστικών δεν βελτιώνει την μακροχρόνια απόδοσή τους. Αντιθέτως η παρουσία υδροξυαπατίτη συνδέεται με αυξημένο κίνδυνο φθοράς του ένθετου πολυαιθυλενίου. Επίσης η μελέτη ανέδειξε ότι συγκεκριμένου τύπου υλικών κοτύλης αυξάνουν τον κίνδυνο για επαναλαμβανόμενες αναθεωρήσεις.

Ανακεφαλαιώνοντας, τα αποτελέσματα της διατριβής δείχνουν ότι η επικάλυψη με υδροξυαπατίτη των υλικών της αρθροπλαστικής ισχίου χωρίς τσιμέντο δεν εμποδίζει την απώλεια οστικής μάζας γύρω από αυτά. Αντιθέτως βρέθηκε ότι ο υδροξυαπατίτης αποτελεί παράγοντα κινδύνου για χαλάρωση των υλικών και επομένως αυξάνει τον κίνδυνο για επέμβαση αναθεωρήσης. Τελικώς επιβεβαιώνεται επίσης το γεγονός ότι το σχήμα των εμφυτευμάτων επηρεάζει την σταθερότητα της προθέσεως και επομένως την μακροχρόνια απόδοσή τους.
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Supporting me in every tough moment and sharing every agony!
Trusting me!
Being always there for me!
Loving me!
Giving me the greatest gift in my life: our boy Ηektor-Christos!
I will always be there for you!
I LOVE YOU BOTH!
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References


A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine.