Factors affecting cup wear and migration in total hip arthroplasty

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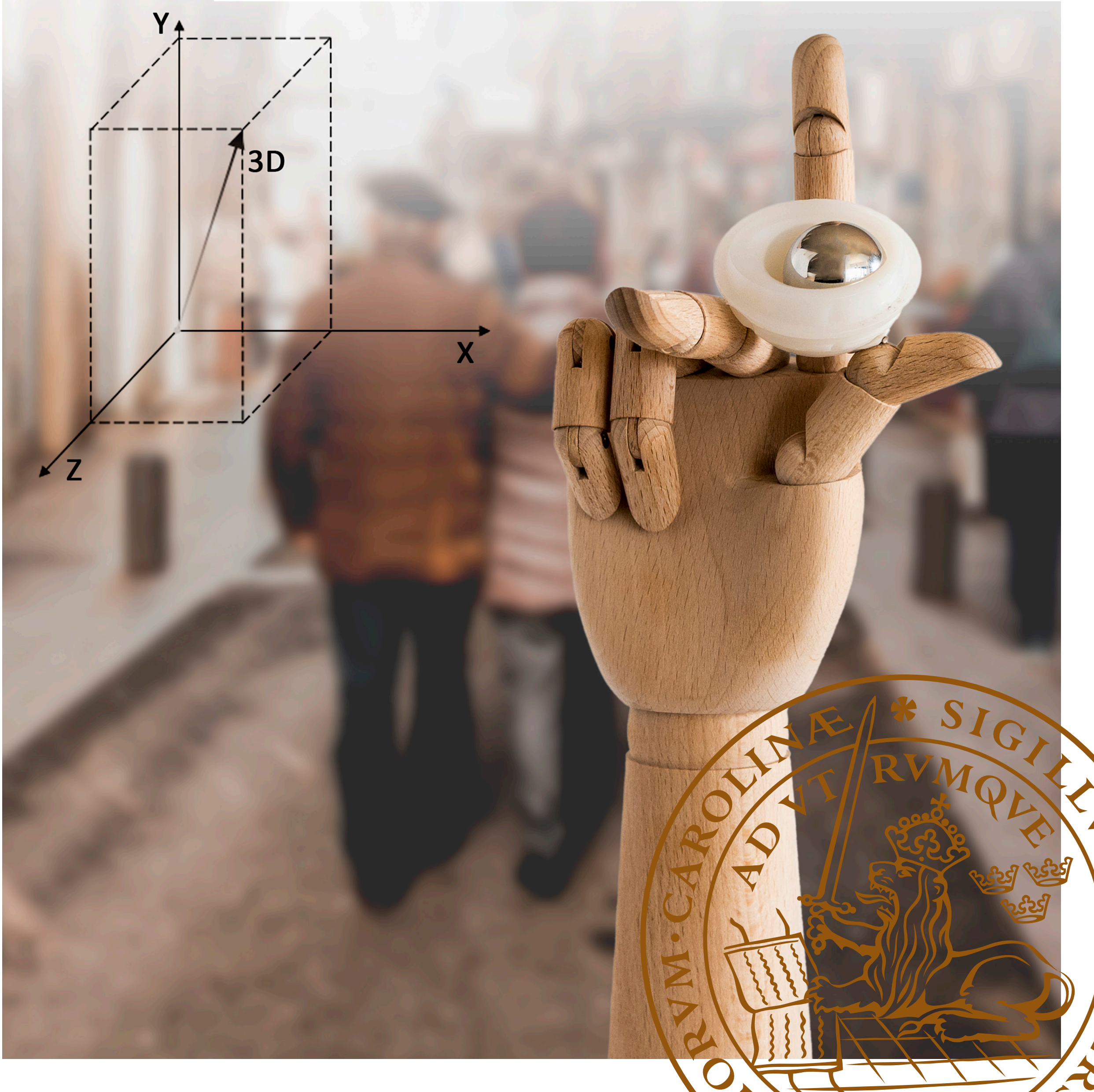

Factors affecting wear and migration in total hip arthroplasty

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Halldór R Bergvinsson

DOCTORAL DISSERTATION

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Abstract

Total hip arthroplasty (THA) is a well-established and successful surgical treatment. Wear of the polyethylene (PE) in the acetabular component has, however, been a limiting factor contributing to osteolysis, aseptic loosening, and increased risk for revision. The main aim of this thesis has been to study how PE wear is affected by different PE variants as well as different materials and sizes of the femoral head. Furthermore, as secondary outcomes, we have studied how these factors, as well as cup backshell surface design, affect cup migration. In all studies, we have used Radiostereometric Analysis (RSA) as the primary measuring method, the gold standard for wear and migration analysis. The patients have also been followed with patient-reported outcome measures (PROMs).

This thesis is based on 4 prospective studies, of which 2 are randomized controlled trials (RCT). The patients all had primary osteoarthritis, were aged 34-80, and operated in a specialized surgical center.

It has been proposed that ceramic femoral heads are superior to metal heads regarding wear, due to their tribological properties, with better resistance to third-body damage, better wettability, and decreased surface roughness. In an RCT (Study I) we could show that, up to 5 years, there is no difference in wear between ceramic and metal femoral heads, if they articulate against modern highly cross-linked polyethylene (HXLPE) in an uncemented cup. Furthermore, the choice of head material does not affect the cup migration.

In a study with a 10-year follow-up (Study II) we could show that modern HXLPE in uncemented cups, exhibits an annual wear rate of 0.01 mm/year compared to conventional ultra-high molecular weight polyethylene (UHMWPE) showing an annual wear rate of 0.1 mm/year, the latter earlier defined as a risk-threshold for osteolysis due to polyethylene wear. The HXLPE showed no signs of accelerated wear rate throughout the study. This confirms the superiority of the HXLPE compared with UHMWPE.

However, a disadvantage with HXLPE is that it can be vulnerable to oxidation when annealed during thermal treatment, which can result in increased wear. To shield the HXLPE from oxidative stress, vitamin E has been infused into certain types of polyethylene (VEPE). In a 5-year follow-up RCT study (Study III), we found that a cemented VEPE cup showed an annual wear rate of 0.01 mm/year compared with a cemented UHMWPE cup showing 0.08 mm/year. Both cups stabilized satisfactorily.

Another factor that has been shown to affect cup wear is femoral head size, indicating that larger heads generate more wear. We found (Study IV) that smaller heads deform the PE more than larger heads during the initial months after surgery, However, we found no difference in annual wear rate between head sizes of 32 and 36 mm, when articulating against HXLPE. Similar wear results were found for 28 mm heads in study II. Furthermore, no accelerated wear was observed for 36-mm heads up to 10 years.

In summary, in this thesis, we found that modern HXLPE is a durable and safe option for THA. We believe that it is unlikely that further development will result in a clinically relevant decrease in revision rates due to wear. We found that VEPE is a good alternative to HXLPE, although the long-term effects of vitamin E on wear performance are still somewhat unclear. With a modern HXLPE, the wear rate does not seem to be affected by the size of the femoral head or whether the head is made of ceramic or metal.

Key words: THA, THR, arthroplasty, osteoarthritis, Hip surgery, RSA, Radiostereometry, wear, cup wear, Polyethylene, HXLPE, VEPE, cup migration, HOOS.

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MADE IN SWEDEN

To my wife, Kristín
and my children Júlíana,
Vilberg, and Alexander

Table of Contents

Abstract

Total hip arthroplasty (THA) is a well-established and successful surgical treatment. Wear of the polyethylene (PE) in the acetabular component has, however, been a limiting factor contributing to osteolysis, aseptic loosening, and increased risk for revision. The main aim of this thesis has been to study how PE wear is affected by different PE variants as well as different materials and sizes of the femoral head. Furthermore, as secondary outcomes, we have studied how these factors, as well as cup backshell surface design, affect cup migration. In all studies, we have used Radiostereometric Analysis (RSA) as the primary measuring method, the gold standard for wear and migration analysis. The patients have also been followed with patient-reported outcome measures (PROMs).

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List of papers

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

Paper I

Polyethylene wear with ceramic and metal femoral heads at 5 years: A randomized controlled trial with radiostereometric analysis.

Bergvinsson H, Sundberg M, Flivik G.

J Arthroplasty. 2020 Dec; 35(12): 3769-3776.

Paper II

Highly cross-linked polyethylene still outperforms conventional polyethylene in THA: 10-year RSA results.

Bergvinsson H, Zampelis V, Sundberg M, Flivik G.

Acta Orthop. 2021 Oct; 92(5): 568-574.

Paper III

Vitamin E infused highly cross-linked cemented cups in total hip arthroplasty show good wear pattern and stabilize satisfactorily: a randomized, controlled RSA trial with 5-year follow-up.

Bergvinsson H, Zampelis V, Sundberg M, Tjörnstrand J, Flivik G.

Acta Orthop. 2022 Jan 20; 93: 249-255.

Paper IV

No difference in wear between 32- and 36-mm metal femoral heads in uncemented cups with highly cross-linked polyethylene. An RSA study with 5- and 10-years follow-up.

Bergvinsson H, Zampelis V, Sundberg M, Kiernan S, Flivik G.

In manuscript.

Abbreviations

3D – Three-dimensional
95% CI – 95% confidence interval
BMI – Body mass index
CAD – Computer-aided design
CI – Confidence interval
CN – Condition number
CoC – Ceramic-on-ceramic
CoCr – Cobalt-Chromium
CoP – Ceramic-on-polyethylene
EQ-5D – European Quality of Life (EuroQol) 5-Dimensions
HAC – Hydroxyapatite coating
HOOS – Hip Disability and Osteoarthritis Outcome Score
HXLPE – Highly cross-linked polyethylene
KOOS – The Knee Injury and Osteoarthritis Outcome Score
ME – Mean error of rigid body fitting
MTPM – Maximum total point motion
OA – Osteoarthritis
PE – Polyethylene
PGE_2 – Prostaglandin E_2
PROMs – Patient-reported outcome measures
PTFE – Polytetrafluoroethylene
RCT – Randomized control trial
RSA – Radiostereometric analysis
SD – Standard deviation
THA – Total hip arthroplasty
TNF-α – Tumor necrosis factor α
UHMWPE – Ultra-high molecular weight polyethylene
VEPE – Vitamin E infused polyethylene

Thesis at a glance

	Paper I	**Paper II**	**Paper III**	**Paper IV**
Type of study	Analytic Experimental Randomized controlled trial	Analytic Observational A prospective intervention Cohort study	Analytic Experimental Randomized controlled trial	Analytic Observational A prospective intervention Cohort study
Question	Do ceramic femoral heads generate less wear than metal heads when articulating against modern HXLPE?	What is the long-term wear performance of HXLPE vs UHMWPE?	To evaluate the migration pattern and wear properties of cemented VEPE cups in the mid-term.	Do 36 mm femoral heads generate more wear than 32 mm heads?
Population / years of follow up	50 patients 2012 – 2018	50 patients 2007 – 2018	48 patients 2014 – 2020	106 patients 2009 – 2021 2015 – 2021
Results	There is no difference in annual wear between ceramic and metal femoral heads for up to 5 years.	HXLPE shows almost 10% of the wear generated by UHMWPE up to 10 years and shows no signs of accelerated wear rate in later years.	VEPE cups express good wear performance in the mid-term. The VEPE cup shan ows increased migration pattern up to 2 years before stabilizing satisfactorily.	There is no difference in wear generated by 32- and 36-mm femoral heads up to 5 years. The 36 mm heads continued to show good wear rates up to 10 years without any signs of acceleration in later years.
Clinical perspective	From a wear perspective, ceramic femoral heads show no superiority compared with metal heds.	HXLPE performs well in long term, however, UHMWPE may be in the “risk zone”.	VEPE cups show promising wear performance and migration pattern up to 5 years.	There seems to be no difference in cup wear with 32 and 36 mm femoral heads if articulating in an HXLPE cup.

Description of contributions

Paper I

Study design: Gunnar Flivik, Martin Sundberg

Data collection: Halldor Bergvinsson

Data analysis: Halldor Bergvinsson

Manuscript writing: Halldor Bergvinsson

Manuscript revision: Halldor Bergvinsson, Gunnar Flivik, Martin Sundberg.

Paper II

Study design: Gunnar Flivik, Martin Sundberg

Data collection: Halldor Bergvinsson

Data analysis: Halldor Bergvinsson

Manuscript writing: Halldor Bergvinsson

Manuscript revision: Halldor Bergvinsson, Gunnar Flivik, Martin Sundberg, Vasilis Zampelis

Paper III

Study design: Gunnar Flivik, Martin Sundberg, Jon Tjörnstrand

Data collection: Halldor Bergvinsson

Data analysis: Halldor Bergvinsson

Manuscript writing: Halldor Bergvinsson

Manuscript revision: Halldor Bergvinsson, Gunnar Flivik, Martin Sundberg, Vasilis Zampelis, Jon Tjörnstrand.

Paper IV

Study design: Halldor Bergvinsson, Gunnar Flivik, Martin Sundberg

Data collection: Halldor Bergvinsson

Data analysis: Halldor Bergvinsson

Manuscript writing: Halldor Bergvinsson

Manuscript revision: Halldor Bergvinsson, Gunnar Flivik, Martin Sundberg, Vasilis Zampelis, Sverrir Kiernan.

Introduction

This thesis deals with the problem of polyethylene wear in the articulation of total hip arthroplasty (THA). Aseptic loosening of the hip implants, partly because of cup wear-related issues, has been one of the most prominent factors leading to revision surgery for patients with THA.

Osteoarthritis

Osteoarthritis (OA) is a degenerative joint disease that affects the cartilage and underlying bone. The cause of OA includes inherited factors but may even be caused by abnormal joint or limb development or previous injury to the joint. OA of the hip is a disease that may be symptomatic in 1 in 4 by the age of 85 years (1). The primary focus of treatment for OA is exercise, lifestyle changes, and analgesics. However, for about 10% of the population, the symptoms progress despite treatment, leading to severe pain, instability, decreased quality of life (QoL), and even decreased mental health (2). A THA surgery is a well-established treatment for these patients.

Total hip arthroplasty

Since Sir John Charnley revolutionized the total hip arthroplasty procedure in the 1960s with the low friction arthroplasty concept, these operative principles proposed have been implicated widely around the world (3). This has resulted in great improvement of QoL for patients with severe hip OA that have not responded to non-surgical treatment. In general, the results for patients undergoing THA have been very-good and this intervention has therefore been called “the operation of the century” (4).

However, with the expanding global population, improvements in general health, and increased life expectancy the demand for surgical treatment for OA is increasing and is likely to increase further (5-7). This has also led to the fact that younger patients are being operated on, which demands a longtime survival for the THA.

The most common cause of revision for THA, along with infections, has been aseptic loosening (8). Implant loosening, including osteolysis and bearing wear, accounted for almost 35% of THA revisions in the USA in 2014 (7) and 42.8% of all first-time revisions in Sweden in the period between 2010-2020 (9). Therefore, it is important to identify the factors responsible for wear and future failure of the THA to make this surgical treatment an even better and long-lasting option for the patient.

Polyethylene

Since its discovery, polyethylene (PE) has been used in many forms both for medical and non-medical indications. Ultrahigh molecular weight polyethylene (UHMWPE) has been the most popular PE used for medical purposes since its introduction by Charnley in 1961, after the early failure of polytetrafluoroethylene (PTFE, Teflon). UHMWPE resin is produced by polymerization of ethylene gas in the presence of hydrogen and a catalyst. The powder is then made into sheets or bars using compression or ram extrusion. When the UHMWPE has been machined, the components are sterilized and packaged.

This type of polyethylene became popular because of its tribological and mechanical properties and has been used for many years both for hips and knees. However, this material has its limitations, with wear being the most prominent factor leading to aseptic implant loosening, a process that will be described later in this thesis.

To increase the wear resistance of the PE, highly cross-linked polyethylene (HXLPE) was introduced in 1998 (10). By treating the PE with gamma-irradiation (50-100 kGy) the PE forms cross-linking between the polymers yielding longer polymer chains. This results in dramatic increases in wear resistance, as tested in simulators, compared to conventional polyethylene (11). However, the irradiation process produced residual free radicals that leave the PE prone to oxidation, degrading the abrasive wear resistance of the PE (12,13). This may jeopardize the positive effects of cross-linking and result in increased wear.

By heat-treating the irradiated PE, residual radicals could be substantially decreased or even eliminated. Heat treatment causes the crystalline regions of the PE to unfold, allowing for additional cross-linking of remaining residuals. Annealing is a method where the gamma-irradiated PE is heated just below the melting point (around 135°C). Although this method causes some residuals to remain in the PE, it allows for it to retain its mechanical properties. When the PE is remelted (above the melting point) it eliminates reactive residuals from the material. However, this causes decreased fracture resistance of the PE making it vulnerable for example chipping (14).

In an attempt to minimize the oxidation effect on the annealed HXLPE, an antioxidant compound, vitamin E, is incorporated into the PE, producing vitamin E infused PE (VEPE). This can be done in 2 ways. One is to blend the vitamin E into the PE powder before consolidation and irradiation. However, this can affect the efficiency of the cross-linking during the irradiation process. The other, and more widely used, alternative is to diffuse the vitamin E into the HXLPE after irradiation. This is done by doping the PE into a bath prepared with vitamin E and allowing for it to diffuse into the PE (15). This was first described around the millennium shift (16).

The wear of UHMWPE is discussed in papers II and III. The wear for HXLPE is discussed in papers I, II, and IV, and the wear of VEPE in paper III.

Femoral heads

The femoral head used by Charnley was small (22 mm) and made of metal (3). Since then, cobalt-chromium (CoCr) heads have remained the most used material for the femoral heads in THA. However, there has been a trend in increasing the size of the femoral head to increase the stability of the THA and lower the risk for revision due to early dislocations (17). Ceramic heads were later introduced to the market, both as ceramic-on-polyethylene (CoP) articulations and even ceramic-on-ceramic (CoC) articulation (18). Compared to metal heads, ceramic heads are believed to be superior due to their resistance to third-body damage, better wettability, and decreased surface roughness. All these factors are believed to contribute to more resistance against PE liner wear (19).

The effect of metal and ceramic heads on polyethylene wear is discussed in paper I.

Acetabular implants

There are 2 main concepts for how to fixate the acetabular implants to the bone, cemented or uncemented.

The cemented concept utilizes a PE cup that, when the acetabulum has been prepared, is fixated into the acetabulum with bone cement. In this manner, the cement has 2 interfaces, one to the PE cup and the other to the acetabular bone. Cement has been used since Charnley introduced his THA concept and is still today the main fixation concept for THA in many countries, for example, Sweden with 50% of inserted THAs in 2020 being cemented (9). However, there is a trend towards using more uncemented THAs, primarily for younger populations and for those with good bone quality. A combination of fixation methods so-called hybrid prosthesis, where the cup is uncemented and the stem is cemented accounted for 1.5% of all THA in Sweden between 2007-2010 and reversed hybrid prosthesis (cemented cups and uncemented stems) have increased to 7.1% in 2020.

Most modern uncemented cup shells are made of titanium or titanium-aluminum alloy. To obtain a stable uncemented acetabular cup a good initial fixation is needed with later bone osseointegration into the coating of the component. Initial fixation can be achieved by using press-fit or threaded cups with or without additional fixation as screws or pegs. For stable osseointegration, the cups need to have a rough surface, allowing for bony ingrowth of the acetabular bone. How this is achieved varies but can be done with titanium-plasma spraying, application of titanium balls, nets, or other grids. The modern surgeon has a variety of acetabular components to choose from with different roughened and porous surfaces. The roughness of the coating can vary between cups and manufacturers. Novel technology has allowed for the coating on the cups to be highly porous, trabecular metal, resembling cancellous bone, which is thought to contribute to complex bony ingrowth into the coating with the intention of more stable osseointegration.

The migration pattern of different roughness of cup coatings is discussed in paper II and the highly porous coating is mentioned in paper IV.

Radiostereometric analysis

Radiostereometric analysis (RSA) is a roentgen stereophotogrammetry system introduced by the Swedish mathematician and anatomist Göran Selvik in 1972 in Lund, Sweden (20). RSA is a highly accurate, three-dimensional method of evaluating and quantifying relative skeletal motion as well as implant motion relative to the host bone as well as wear analysis. This can have clear advantages in the clinical setting as this method can detect small continuous migration of implants before it is detected on conventional radiographic images or symptoms appear.

RSA has high accuracy and precision of the measurement technique and therefore a small number of patients can be used in these studies. To date, RSA is the gold standard method used to measure implant migration and cup wear and is, therefore, an important tool in evaluating new implants introduced to the market, as it can detect unwanted early migration or excessive wear in these implants.

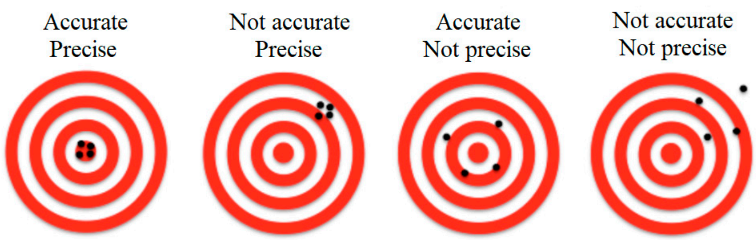

Figure 1: Schematic illustration of precision and accuracy. Accuracy is the closeness of agreement between the test result and the accepted reference (i.e. the true value). Precision is synonymous with repeatability; the closeness of agreement between independent test results obtained under stipulated conditions.

The principles of RSA are based on markers placed in the bone around the implant of interest. Tantalum markers, 0.5, 0.8, or 1.0 mm in diameter, are inserted into the bone or on/in the implant itself. To form a segment during the radiographic analysis, at least 3 non-colinear markers are needed but more markers make a better configuration of the segment and often 6-9 well-scattered markers are inserted to compensate for loose or invisible markers. This is important as the stability and distribution of markers will influence the accuracy of the motion calculations. Regarding RSA on THAs, markers are placed in the periacetabular bone and the proximal femur (figure 1). Furthermore, markers can be placed into or on the implants themselves or even in the bone cement if needed. However, production of implants with markers is an expensive alternative that may require new CE labeling. Therefore, the model-based RSA method was developed (21). This method uses computer-aided design (CAD) models or reversed engineered models of the implant instead of markers on the prosthesis. These three-dimensional (3D) surface models of the true implants are then fitted to the actual projection of the implant in the software during RSA analysis (22). Another alternative to determine the position of the cup without using markers is to measure the outlines, as well as the opening of the cup and model the cup as a hemisphere (23).

Figure 2: RSA image with tantalum markers in the periacetabular bone and polyethylene liner as well as trochanteric area. Markers have also been placed on the rim of the acetabular cup and on the stem. Markers in the cage can be seen on the edges of the image.

The radiographic imaging can be performed in numerous ways. However, they are based on dual simultaneous radiographic exposure and a calibration cage below the patient equipped with tantalum markers in fixed positions. These markers are either defined as control markers or fiducial markers and are used to create a three-dimensional reference coordinate system to calculate the positional placement of the 2 roentgen foci. The patient is placed so that the implant of interest is in the crossing of the X-rays in either a uniplanar or biplanar cage. When using a uniplanar technique, as we do in hip examinations, the recording media (film cassette or digital detector) are placed side-by-side (figure 2), as opposed to perpendicular to each other when using the biplanar technique, which is more often used in knee examinations. Examinations are normally performed with the patient supine but can also be done with the patient in a standing position. In wear studies, there seems to be no difference in outcome if the patient is examined in a standing or supine position (24).

Modern RSA examinations are analyzed using digital software. The software calculates the stability of the markers within a segment yielding the mean error of rigid body fitting (ME). This is the mean difference between the relative distances of the markers in a rigid body from one examination to another. Marker distribution is then assessed by evaluating how well the markers are scattered resulting in a value called condition number. Both values should be low and a value below 0.35 for ME and 150 for the condition number have been proposed as acceptable for using the examination for analysis (21).

Figure 3: Patient in position for RSA examination with the 2 X-ray tubes above the patient and the calibration cage beneath.

Using the markers in the cage, the software creates a coordinate system in which the implant is defined in position and orientation. This coordinate system is defined by 3 axes in an orthogonal system. When applying this coordinate system to the body, the X-axis corresponds to medial and lateral translation, Y-axis to cranial and caudal translation, and Z-axis to anterior and posterior translation. It has been proposed that for the anatomical situation the right-hand side of the body is used. In this manner, the positive translations are medial (X), cranial (Y), and anterior (Z). For this to be applicable to the left-hand side of the body, the X-axis should be reversed and the Y-axis and Z-axis for rotation (21).

Maximum total point motion (MTPM) is the length of the translation vector of a point in a rigid body that has the greatest motion. Therefore, this vector can only have positive values.

RSA allows for measurement of rotation of implants using the same 3 axes. As for the translations, X-axis rotation is flexion-extension, Y-axis represents internal-external rotation, and Z-axis adduction-abduction. As this thesis describes rotation of acetabular inserts, the positive rotation values around the 3 axes will be described as anterior tilt (X), anteversion (Y), and decreased inclination (Z).

Precision value is calculated using data obtained from “double examinations”. This means that the patient is radiographed twice in a standard position after repositioning. It is recommended that the patient is to leave the table between examinations and be repositioned in a similar position as expected in between study intervals. As it is assumed that the implant has not moved between examinations and precision represents the closeness evaluated in repeated measurements. This is crucial as precision is the basis of power calculations and can be an indicator of how many patients need to be included in a study for significant results to be obtained.

Polyethylene deformation, wear, and potential consequences

Wear in THA can be defined as surface damage with the loss of material due to motion between parts. These material losses can have catastrophic consequences for THA survival. Wear in THA is a complex phenomenon involving mechanical properties as well as lubrication and friction between the moving parts. Several wear mechanisms have been identified. However, in THA, the main focus is on adhesive, abrasive, and fatigue wear.

Initial deformation (creep)

When measuring linear penetration of the femoral head into PE, the initial translation of the femoral head is usually referred to as creep. Creep can be described as plastic deformation under the pressure of the femoral head over time. It has been hypothesized that this may cause an increase in the contact area and a decrease in contact pressure (25). The effect of PE creep seems to have a major role in early penetration measurements. This effect gradually diminishes over time and it has been proposed that after 6-12 months the PE creep effects are negligible (26). Furthermore, the effect of creep on long-term wear is probably non-significant (27). In wear studies, it varies how this initial deformation period is presented and many authors prefer to exclude the first 12 months from their analyses to minimize the effect of creep on the wear results (28).

In the papers in this thesis, we propose a narrower timeline for this phase.

Wear types

As previously mentioned, PE wear and subsequential material loss can play a major role in the survival of the THA. Adhesive and abrasive wear are the major sources of debris leading to osteolysis.

During the sliding motion of the moving parts in THA, adherence can occur between the PE and the femoral head. This results in a part of the PE being ripped off the surface, as the PE is the weaker part of the articulating materials. This is called adhesive wear (29).

Abrasive wear occurs when a rough, hard surface slides across an opposite, softer surface. The softer surface gets damaged by hard protuberances of the opposing side (two-body wear) or by hard, loose particles (third body wear) such as bone cement particles (30). The amount of wear generated depends on the size, shape, and hardness of the third body particle.

Fatigue wear occurs when the load applied to a material is higher than the fatigue strength of that material. This is caused by a repeated cycling loading during friction and results in cracking, pitting, and delamination of the PE (29).

Osteolysis and cup loosening

It is believed that the PE particles generated by wear are phagocytosed by macrophages that, as a response, release various proteolytic enzymes and osteolytic mediators such as interleukin-1β and interleukin-6, tumor necrosis factor-α (TNF-α) and prostaglandin E_2 (PGE_2). This triggers the immune system and inflammatory process that leads to osteoclastic bone resorption. The size of the PE debris particles seems to play a role in the adverse cellular reaction and particles of 0.3-10 µm in size seem to be the most biologically active (31). Furthermore, the amount of inflammation and osteolysis is related to the amount and shape of the particles (32).

Osteolysis following the adverse reaction to PE particles can present as radiolucent lines or cystic lesions on plain radiographs. These are generally without symptoms. The radiolucent lines indicate a fibrous tissue present between the cup and the surrounding bone which can gradually expand and is a risk factor for later clinical loosening of the implant.

Detecting early migration of a cup on conventional radiography is difficult. It has been proposed that this is only detectable as soon as the migration exceeds 3-4 mm (33). However, with the development of RSA, early-stage cup loosening is easier to detect at an earlier stage than was possible with conventional radiography. Due to the high accuracy of RSA, implant migration could be detected with a 99% significance interval between 0.15 and 0.6 mm and rotations between 0.3 and 2 degrees (34). With further advancements in measurement technique and software development accuracy has increased and migration values of 0.05 in translation can now be achieved in 2D measurements (35,36). However, 3D measurement is less accurate and precise and difficult to present since the precision is different for each direction (37).

Clinical outcome measures

Numerous scores have been introduced to evaluate the clinical results after THA (38). These standardized, validated questionnaires are generally called patient-reported outcome measures (PROMs). In the last decades, there has been an increased focus on generic and disease-specific outcome measurements, focusing on the patient's perspective.

Hip disability and osteoarthritis outcome score (HOOS) is a disease-specific outcome measure score that is an adaptation of the Knee injury and osteoarthritis outcome score (KOOS) (39). Its intention is to evaluate symptoms and functional limitations of the hip before and after THA. The questionnaire assesses 5 separate patient-relevant dimensions: pain, symptoms, activity limitations of daily life, Sport and recreation function, and Hip related quality of life. The HOOS 2.0 questionnaire has been validated and is proposed to be useful in evaluating the patient-reported results after surgery with high responsiveness (40).

EuroQol (EQ-5D) questionnaire is a generic measure of health status and quality of life. This score covers 5 categories (mobility, self-care, usual activity, pain/discomfort, and anxiety/depression) on 3 possible response levels (no problems, some/moderate problems, and extreme problems) in the patients current situation, which means "today" (41). A single weighted score is then calculated, the EQ-5D index, which can range from -0.594 to 1.0, worst to best.

HOOS outcomes are reported and evaluated in all papers in this thesis and EQ-5D is reported in paper III.

Aims

General aim

The general aim of this thesis was to study how polyethylene wear is affected by different polyethylene types and different femoral head materials and sizes in total hip arthroplasty using RSA. Furthermore, as secondary outcomes, to study cup design factors affecting migration.

Specific aims

The specific aims of each study were:

I. To investigate and compare if there are any differences in generated wear between 32 mm metal (CoCr) or ceramic femoral heads when articulating with modern highly cross-linked polyethylene (HXLPE) up to 5 years using RSA. Furthermore, to investigate if there are differences in cup migration and patient-reported outcomes between the groups.

II. To investigate the wear behavior of HXLPE compared with UHMWPE up to 10 years using RSA. Furthermore, to analyze the migration pattern of 2 similar uncemented cups with different surface coating, as well as patient-reported outcomes during the same study period.

III. To investigate wear behavior of vitamin-E infused polyethylene (VEPE) in cemented cups compared with UHMWPE up to 5 years using RSA. Furthermore, to investigate potential differences in migration pattern between the cups, as well as patient-reported outcomes.

IV. To analyze the wear of 32 mm and 36 mm femoral heads on modern HXLPE in uncemented cups with RSA up to 5 years. Furthermore, to investigate the wear pattern of the 36 mm femoral heads up to 10 years using RSA, as well as patient-reported outcomes.

Hypothesis of the studies in the Thesis

I. Ceramic heads generate less wear than metal (CoCr) heads when articulating against modern HXLPE.

II. HXLPE results in less wear compared to UHMWPE up to 10 years. Better cup stability is acquired when using a cup with a rougher surface.

III. Uncemented VEPE cups show less wear and similar stability compared with UHMWPE up to 5 years.

IV. Less wear is observed when using 32 mm femoral heads compared with 36 mm femoral heads when articulating with a modern HXLPE.

Patients and methods

Patient cohorts and Inclusion process

All 4 studies were prospective, single-center studies. All patients in the studies were osteoarthritis patients, graded Charnley class A or B. For studies I, II and IV the inclusions criteria were the same, patients with OA that had bone quality and morphology suitable for uncemented THA. For study III we used a cemented THA concept and therefore patients more suitable for an uncemented THA were excluded. Other exclusion criteria for the studies were previous surgery on the hip, contralateral THA, active infection, dementia, marked bone loss, perioperative fracture, immunosuppressive disease, malignant disease, rheumatoid arthritis, or alcohol or drug abuse. All patients were recruited from the THA waiting list at the Department of Orthopedics, Skåne University Hospital, Lund, Sweden. All patients enrolled in the studies have provided their written and verbal informed consent for participation by the Helsinki Declaration. All studies were approved by the ethics committee.

Table 1. Demographic data

Characteristics	Study I	Study II	Study III	Study IV
Date of operation	Sept 2012 – June 2013	Apr 2007 – June 2008	Jan 2014 – June 2015	Oct 2009 – Sept 2011 Mar 2015 – Feb 2016
Total number (n)	50	50	48	106
Number analyzed (n)	49	45	47	101
Male/female	34/16	27/23	11/37	68/38
Mean age at operation (yrs. (range))	60 (37−76)	63 (50−75)	71 (58−83)	59 (34−80)
Mean BMI at operation (kg/m^2) (SD))	27 (3.2)	28 (5.1)	26 (4.2)	27 (3.6)
BMI, body mass index; SD, standard deviation				

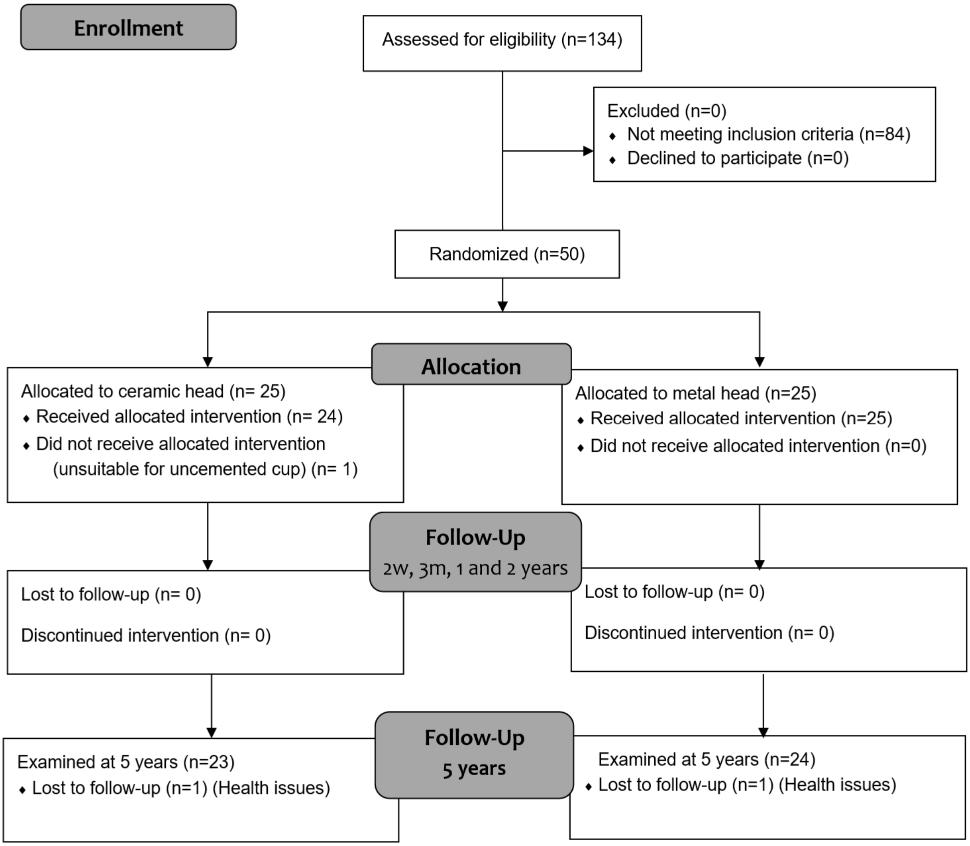

Figure 4. Layout of paper I

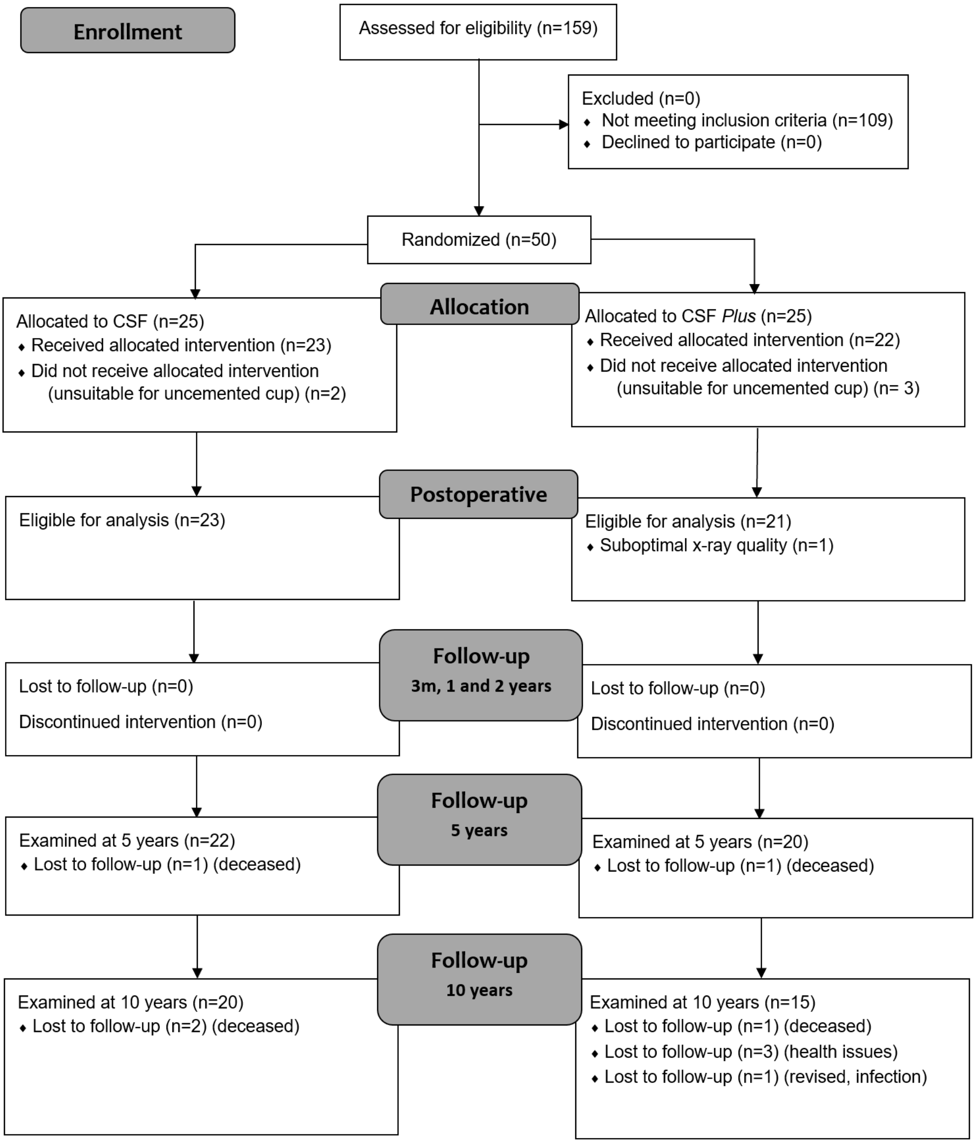

Figure 5. Layout of paper II

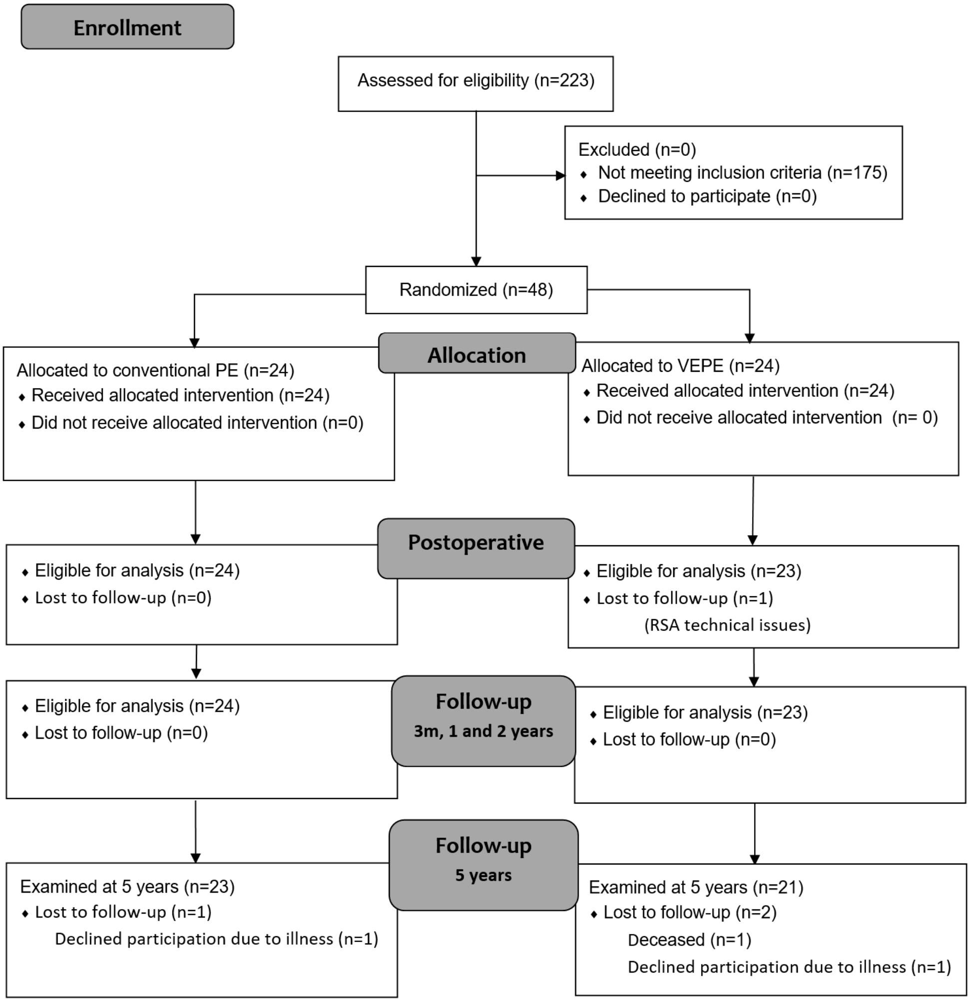

Figure 6. Layout of paper III

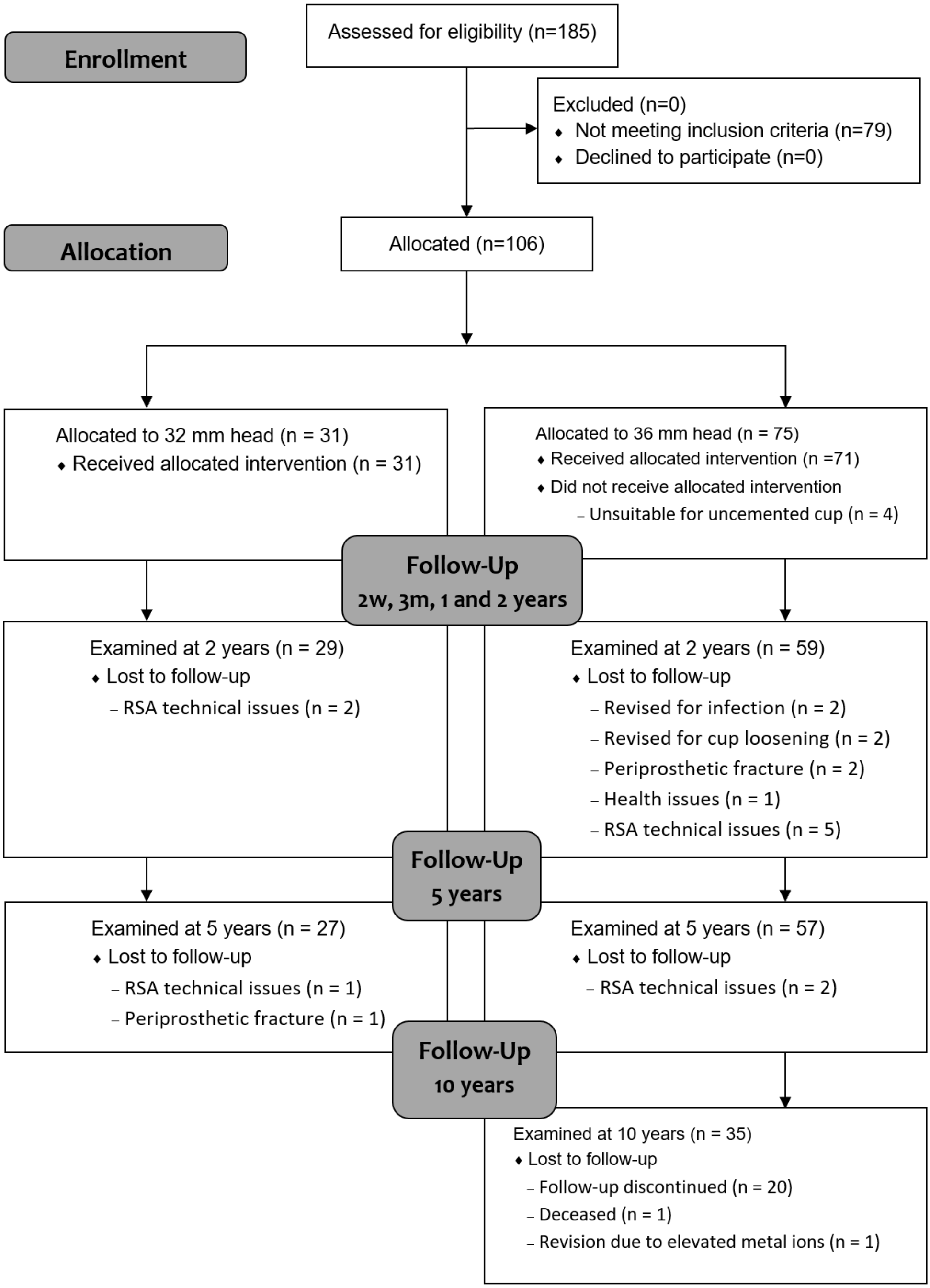

Figure 7. Layout of paper IV

Trial design

Paper I: Polyethylene wear with ceramic and metal femoral heads at 5 years: A randomized controlled trial with radiostereometric analysis.

In this randomized controlled trial, we recruited 50 patients with OA suitable with our inclusion and exclusion criteria. The patients were operated on between September 2012 and June 2013. The patients were randomized using blocked randomization and closed envelopes were opened during surgery to decide which implant the patient should receive.

Paper II: Highly cross-linked polyethylene still outperforms conventional polyethylene in THA: 10-year RSA results.

This study is a single-center prospective cohort study. 50 patients with OA were recruited and allocated to receive different sets of uncemented implants. The patients had been included in a randomized controlled trial comparing 2 different versions of the same stem concept (42). When this study started, only one type of acetabular cup and liner were available to us. Therefore, the patients could not be randomized to cup type and were instead operated consecutively, the first 25 patients receiving UHMWPE liner and cup and the second 25 patients receiving HXLPE liner and the same cup but with an improved cup coating. Surgery was performed between April 2007 and June 2008.

Paper III: Vitamin E infused highly cross-linked cemented cups in total hip arthroplasty show good wear pattern and stabilize satisfactorily: a randomized, controlled RSA trial with 5-year follow-up.

This is a randomized control trial where 48 patients with OA were recruited and randomly assigned to receive a cemented UHMWPE cup or a cemented VEPE cup. Apart from the type of PE, the cups had the same design. Blocked randomization was used and closed numbered envelopes were opened during surgery to decide which implant the patient was to receive. Surgery was performed between January 2014 and June 2015.

Paper IV: No difference in wear between 32- and 36-mm metal femoral heads in uncemented cups with highly cross-linked polyethylene. An RSA study with 5- and 10-years follow-up.

This study is based on 2 RSA trials. In the first trial 75 patients with OA were recruited and randomly assigned to receive an uncemented cup with either standard or highly porous coating, but with the same HXLPE liner and all with a 36 mm femoral head. Surgery in this trial was performed between October 2009 and September 2011. In the second study, 31 patients with OA were recruited and all were operated with the same standard coated cup as in the first study and the same HXLPE liner, but in this study with a 32 mm femoral head. These operations were performed between March 2015 and February 2016.

All patients in all studies were operated in lateral positioning with posterolateral incision using standard instrumentation as recommended by the manufacturers.

Implants

In paper I all patients were operated with a CSF *Plus* uncemented cup with a HXLPE liner (JRI Orthopedics Ltd, Sheffield, UK). No screws were used for cup fixation. The HXLPE was made from Ticona grade GUR 1050. The PE was treated with 80 kGy of gamma irradiation to produce the cross-linking and then remelted and finally sterilized in 25-40 kGy in a vacuum. The patients were randomized to receive either a metal femoral head (CoCr) or a ceramic head (BIOLOX delta; CeramTec, Plochingen, Germany). All femoral heads were 32 mm in diameter and all patients received an uncemented Furlong Evolution stem.

In paper II we used 2 types of cups and liners. The patients received either a CSF *Plus* cup (same as in paper I) or its precursor, the CSF cup. The CSF cup (JRI Orthopedics Ltd, Sheffield, UK) is a metal shell cup with a titanium coating of 50 microns and a Supravit® hydroxyapatite coating (HAC) of 150 microns yielding about 200 microns in total coating thickness and roughness of about 30-50 Rz. The CSF *Plus* cup (JRI Orthopedics Ltd, Sheffield, UK) has the same Supravit® and titanium coating. However, it has an additional layer of rougher titanium between the other 2, yielding a thicker coating and roughness of 60-100 Rz. No screws were used for cup fixation. The patients with the CSF cup received a UHMWPE liner that was Ticona grade GUR 1050, ram extruded, machined, and finally sterilized in 25 kGy. The patients with the CSF *Plus* cup received a HXLPE liner that is made from the same material as described in study I. All patients had a 28 mm metal (CoCr) femoral head.

In paper III all patients received an Exceed cemented cup (Biomet Orthopedics, Warsaw, IN, USA). However, they were randomized to receive either a UHMWPE version of the cup (ArCom) or a VEPE version (E1 Antioxidant Infused technology). The UHMWPE is made of GUR 1050 resin, compression-molded, machined, and sterilized. The VEPE is made from the same barstock as the UHMWPE and is gamma irradiated with 100 kGy in the cross-linking process. After irradiation, the parts are then infused with vitamin E. The VEPE is then machined, and gamma sterilized. All patients received a 32 mm metal (CoCr) femoral head and a Sirius cemented stem (Biomet Orthopedics, Warsaw, IN, USA).

In paper IV, as previously mentioned, the patients were recruited from 2 different trials. In one trial, the patients were randomized to receive either a Trident cup or a Trident Tritanium cup. The Tritanium cup has a thicker, 3-dimensional porous coating and a higher friction coefficient than the Trident cup. Apart from that, the cups have the same design. All these patients received a 36 mm metal (CoCr) femoral head and either an ABG II standard or ABG II modular stem (Stryker Orthopaedics, Mahwah, New Jersey, USA). In the other trial, all patients received a Trident cup, a 32 mm metal (CoCr) femoral head, and an ANATO stem (Stryker Orthopaedics, Mahwah, New Jersey, USA). All patients received the same type of liner, X3 highly cross-linked polyethylene that was gamma-irradiated with 30 kGy 3 times and annealed in between each irradiation (Stryker Orthopaedics, Mahwah, New Jersey, USA). The HXLPE was finally sterilized by non-radiating methods and packaged.

All patients in all studies received 8-9 tantalum markers (diameter 0.8 mm) that were placed in the periacetabular bone and additional 5-6 tantalum markers in the peripheral surface of the liner or cemented cup using a Tilly Medical instrument.

Follow up and Clinical assessment

Before surgery, all patients in all papers answered a clinical outcome questionnaire. Furthermore, all patients in all papers had their first examination, both conventional and RSA examination, on the first postoperative day. All patients had an RSA examination at 3 months. However, the patients from papers I and IV had their first RSA examination at 2 weeks. RSA examinations were performed at 1, 2 and 5 years for all papers as well as clinical outcome questionnaires that were answered by the patients. In 2 papers the patients were followed up to 10 years, papers II and IV. In paper IV an RSA examination was performed at 8 years and in both papers II and IV, RSA examinations, as well as clinical outcome scores, were performed at the 10-year follow-up.

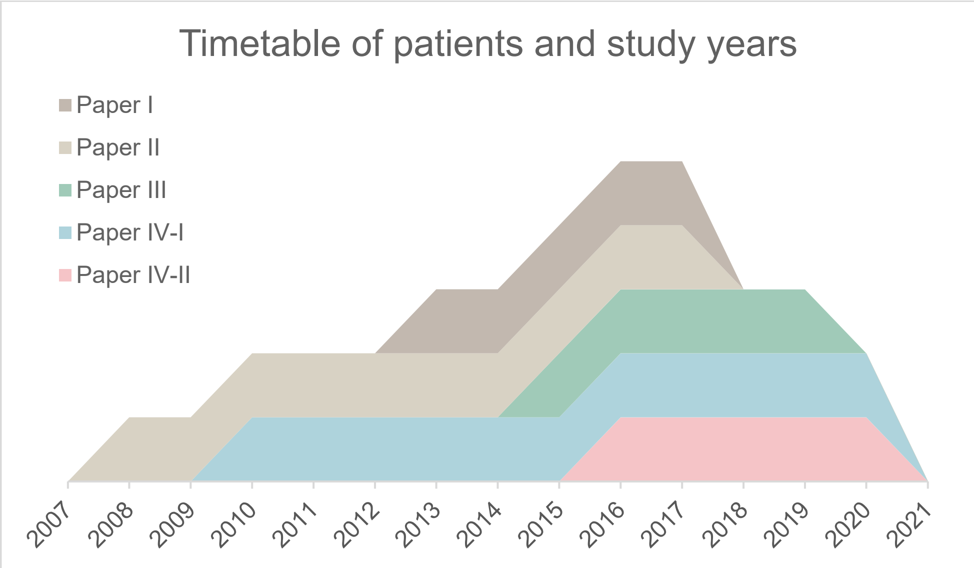

Figure 8: Timetable of study years from the time of surgery until last follow up

Radiostereometry (RSA)

In this thesis, as well as all included papers, the RSA values presented are expressed as translation or rotation about or along the 3 axes in an orthogonal coordinate system, as previously mentioned and described, named the X-, Y-, and Z-axis. The primary outcome in our papers is wear and is presented as the point motion of the center of the femoral head in relation to the cup segment compared with the reference examination. A positive Y-translation of the femoral head compared with the reference examination, therefore, is considered a proximal movement of the femoral head, i.e., proximal translation. The RSA examinations were done using a uniplanar RSA technique with the patient supine and the 2 X-ray tubes in a fixed, mounted position in the ceiling (21). All patients had at one time, usually postoperatively, a double examination to calculate the precision value of the examinations. All RSA examinations were performed according to the guidelines for standardization for radiostereometry (21). In all studies, the primary effect variables were proximal penetration of the femoral head (Y-translation) and 3D-penetration. Secondary effect variables were proximal (Y-translation) and medial (X-translation) migration of the cup segment as well as change in cup inclination (Z-rotation). All patients had their reference examination done on the first postoperative day, and thus our reported values represent the true and full magnitude of creep/wear/migration.

Table 2. A timetable of RSA examinations for respective papers

RSA follow-up timetable								
	Postop	2 weeks	3 months	1 year	2 years	5 years	8 years	10 years
Paper I	x	x	x	x	x	x		
Paper II	x		x	x	x	x		x
Paper III	x		x	x	x	x		
Paper VI	x	x	x	x	x	x	x*	x*
**Paper IV-II had follow-up at 8 and 10 years*								

Paper I

The RSA examinations were done using a type 43 calibration cage (Tilly Medical AB, Lund, Sweden), and the images were analyzed using UmRSA software (version 6.0; RSA Biomedical, Umeå, Sweden). Follow-up RSA examinations were performed at 2 weeks, 3 months, 1, 2, and 5 years with a time tolerance of ±5% for each examination. Reference examination was performed on the first postoperative day. The upper limit for ME was set at 0.30 and an upper limit for the CN was set at 125. The cup segment was made of tantalum markers in the liner periphery and the cup opening and backshell (23).

For the wear analysis, we analyzed the point motion of the femoral head in relation to the cup segment, with the cup opening and backshell as definitive points of the cup combined with the markers from the marked liner periphery.

Paper II

We used the same UmRSA software (version 6.0; RSA Biomedical, Umeå, Sweden) for the analysis in this study. However, we used another cage, a type 41 calibration cage (Tilly Medical AB, Lund, Sweden). The follow-up RSA examinations were carried out at 3 months, 1, 2, 5, and 10 years with a time tolerance of ±5% for each follow-up examination. An upper limit for the CN was set at 125 and the upper limit for ME was set at 0.30. Cup segment was defined as cup opening and backshell and markers in the liner periphery.

Paper III

For this study, we used a type 41 calibration cage (Tilly Medical AB, Lund, Sweden,) and the images were analyzed using Model based RSA 4.2 (RSAcore, Department of Orthopaedics, Leiden, The Netherlands). RSA examinations were performed at 3 months, 1, 2, and 5 years with a time tolerance of ±5%. Here, as we used cemented cups in this study, the tantalum markers placed in the periphery as well as in a line over the dome of the cup were used for the wear analysis. The upper limit for the CN was set at 150 and ME at 0.35.

Paper IV

As the patients were recruited from 2 trials, performed at 2 time intervals, 2 separate cages were used. In the first trial, a type 41 calibrations cage (Tilly Medical AB, Lund, Sweden) was used, and in the second, a type 43 calibrations cage (Tilly Medical AB, Lund, Sweden). However, all patients were analyzed using Model based RSA 4.2 (RSAcore, Department of Orthopaedics, Leiden, The Netherlands). RSA examinations were done at 2 weeks, 3 months, 1, 2, and 5 years with a time tolerance of ±5% at each examination. The patients operated with the ABG II modular stems had further follow-up at 8 and 10 years postoperatively with time tolerance ±5%. The CN was set for 150 and ME at 0.35. The cup segment, which is made up of the tantalum markers in the liner periphery as well as the cup opening and backshell was used for the cup segment.

Statistics

In all the papers in the thesis, we used mainly the same statistical tests. The IBM SPSS statistics software program in several versions (SPSS Inc., Chicago, IL, USA, and IBM Corporation, Armonk, NY, USA) was used for statistical analysis. Statistical significance was assumed at p-values of less than 0.05. However, confidence interval (CI) is often preferred over p-values as the CI not only tells us the significance of a difference but gives an estimation of the magnitude of that difference. Therefore, a 95% confidence interval is mostly used in the papers in this thesis. Continuous variables are presented using mean and SD or range, and categorical variables are presented using counts and percentages. The 3D-penetration was calculated using the Pythagoras theorem ($\sqrt{x^2 + y^2 + z^2}$). Precision values were based on 2 standard deviations (SD) of the error obtained between repeated examinations from the same visit. The Mann-Whitney U-test was used for the comparison of clinical outcome scores (HOOS and EQ-5D) between the groups. Power analysis for the studies were performed based on previously published RSA data. The assumption was made that the true difference in head penetration at 2 years was 0.1 mm with a common SD of 0.1. This way a power of 90% would be obtained using 21 patients in each group in order to find a statistically significant difference between the groups. To analyze wear over time a piecewise linear mixed-effect model with a knot (breaking point) at 3 months after surgery was used. The models included 3 fixed effects: group, time starting from surgery, and time starting from 3 months after surgery, and 2 interaction terms between group and the time variables. Subject was included as a random effect.

Results

Paper I

Initial deformation

During the first 3 months, the observed initial mean proximal deformation of the cup liner for ceramic and metal femoral heads was 0.12 mm and 0.08 respectively. Half of this initial migration had already taken place after 2 weeks (table 3). After 3 months, we observed a sharp change in the curves which we interpreted as a shift from the initial deformation phase to the wear phase. A mixed models analysis done on the Y-translation showed a statistically significant difference between the 2 groups (p = 0.03). However, this was not detected in a similar analysis done for the 3D-translation (p = 0.09).

Table 3: Wear measured as translation of femoral head in (mm). Numbers are: mean (95% CI). [a] Mixed models analysis between 0 and 3 months and 3 months to 5 years respectively.

		Mean values and (95% CI)		Ceramic - metal
Translation axis	**Months**	**Ceramic**	**Metal**	**p-value [a]**
Y-axis (mm)	0.5	0.06 (0.02 ; 0.10)	0.05 (0.02 ; 0.08)	0.030
	3	0.12 (0.05 ; 0.19)	0.08 (0.03 ; 0.11)	
	12	0.13 (0.06 ; 0.21)	0.10 (0.05 ; 0.13)	0.410
	24	0.13 (0.07 ; 0.19)	0.10 (0.05 ; 0.14)	
	60	0.14 (0.07 ; 0.20)	0.11 (0.07 ; 0.15)	
3D (mm)	0.5	0.20 (0.13 ; 0.26)	0.17 (0.12 ; 0.21)	0.091
	3	0.25 (0.15 ; 0.36)	0.22 (0.16 ; 0.26)	
	12	0.28 (019 ; 0.38)	0.21 (0.15 ; 0.26)	0.392
	24	0.28 (0.19 ; 0.36)	0.23 (0.18 ; 0.29)	
	60	0.26 (0.16 ; 0.35)	0.23 (0.17 ; 0.29)	

Cup wear

Proximal head penetration from 3 months and onwards was marginal for both groups or 0.14 mm for the ceramic heads and 0.11 mm for the metal heads at 5 years. This yields an annual wear rate of 0.003 mm/year for the ceramic group and 0.007 mm/year for the metal group. The measured 3D penetration showed a similar pattern for the ceramic and metal heads with 0.26 mm and 0.23 mm penetration at

5 years (Table 3). Mixed models analysis for both proximal penetration and 3D penetration showed no statistically significant difference between the groups.

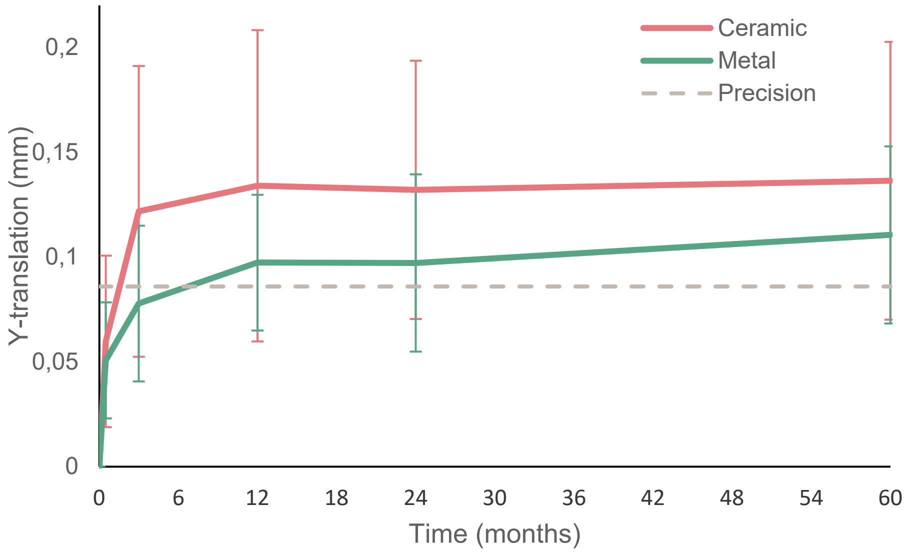

Figure 9. Graph showing proximal (Y-axis) penetration of the femoral head into the cup for ceramic and metal with 95% CI bars.

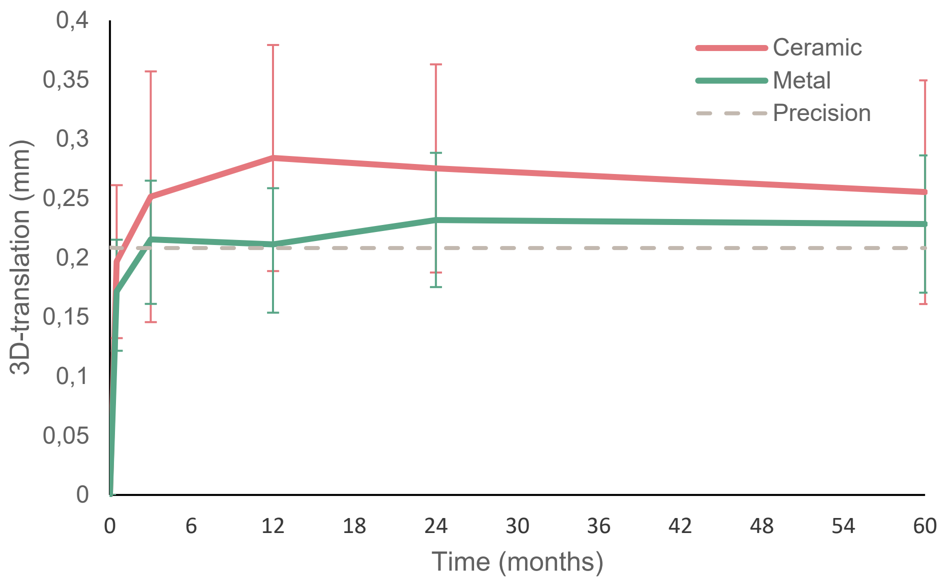

Figure 10. Graph showing 3D penetration of the femoral head into the cup for ceramic and metal with 95% CI bars.

Cup migration

Both groups showed a small bedding-in phase during the first 3 months with proximal migration of 0.03 mm for the cups with ceramic heads and 0.10 for the cups with metal heads. Both groups showed a stable migration pattern from 3 months to 5 years with no statistically significant difference between the 2 groups. The proximal migration at 5 years for the cups with ceramic heads was 0.08 mm and 0.12 mm for the cups with metal heads. None of the mixed-models analyses showed any statistically significant difference in the wear curves between the 2 groups.

Clinical outcome scores

Preoperatively, both groups reported similar HOOS scores. There was a significant improvement in patient-reported outcome postoperatively at 1 year for both groups, as expected, and these results were stable throughout the study period. There was no statistically significant difference between the groups at any time point.

Table 4. Cup migration for ceramic and metal femoral head groups in mm. Numbers are mean (95% CI). [a] Mixed models analysis between 0 and 3 months and 3 months to 5 years respectively.

Cup		**Mean values and (95% CI)**		**Ceramic - metal**
Translation axis	**Months**	**Ceramic**	**Metal**	**p-value [a]**
X-axis (mm)	0.5	0.04 (-0.03 ; 0.12)	0.08 (-0.02 ; 0.17)	0.741
	3	0.08 (0.00 ; 0.16)	0.10 (-0.04 ; 0.24)	
	12	0.06 (-0.10 ; 0.21)	0.07 (-0.07 ; 0.21)	0.565
	24	0.09 (-0.07 ; 0.26)	0.09 (-0.07 ; 0.25)	
	60	0.06 (-0.13 ; 0.25)	0.06 (-0.07 ; 0.19)	
Y-axis (mm)	0.5	0.02 (-0.03 ; 0.06)	0.04 (-0.01 ; 0.10)	0.124
	3	0.03 (-0.01 ; 0.06)	0.10 (0.02 ; 0.18)	
	12	0.06 (0.00 ; 0.12)	0.10 (0.02 ; 0.18)	0.696
	24	0.05 (-0.01 ; 0.10)	0.10 (0.02 ; 0.18)	
	60	0.08 (0.02 ; 0.15)	0.12 (0.03 ; 0.21)	
Z-axis (mm)	0.5	0.00 (-0.11 ; 0.11)	0.03 (-0.08 ; 0.14)	0.376
	3	0.02 (-0.08 ; 0.13)	0.13 (-0.04 ; 0.30)	
	12	0.08 (-0.10 ; 0.26)	0.14 (-0.06 ; 0.33)	0.324
	24	0.08 (-1.11 ; 0.27)	0.08 (-0.09 ; 0.25)	
	60	0.00 (-1.18 ; 0.18)	0.21 (-0.01 ; 0.43)	

Table 5: Cup rotations for ceramic and metal femoral head groups in degrees. Numbers are mean (95% CI). [a] Mixed models analysis between 0 and 3 months and 3 months to 5 years respectively.

Cup		**Mean values and (95% CI)**		**Ceramic - metal**
Rotation axis	**Months**	**Ceramic**	**Metal**	**p-value [a]**
X-axis (deg)	0.5	1.01 (0.19 ; 1.83)	0.83 (0.13 ; 1.52)	0.937
	3	1.54 (0.65 ; 2.44)	1.63 (0.70 ; 2.55)	
	12	1.84 (0.85 ; 2.83)	1.44 (0.72 ; 2.15)	0.193
	24	1.87 (1.03 ; 2.72)	1.57 (0.89 ; 2.25)	
	60	2.32 (1.55 ; 3.09)	1.50 (0.60 ; 2.40)	
Y-axis (deg)	0.5	1.53 (0.64 ; 2.43)	1.26 (0.28 ; 2.25)	0.567
	3	2.22 (1.30 ; 3.14)	2.46 (1.33 ; 3.59)	
	12	2.42 (1.55 ; 3.30)	2.05 (1.05 ; 3.05)	0.138
	24	2.34 (1.54 ; 3.13)	2.16 (1.22 ; 3.10)	
	60	3.10 (2.38 ; 3.82)	2.27 (1.23 ; 3.31)	
Z-axis (deg)	0.5	-0.61 (-1.23 ; 0.01)	-0.01 (-0.26 ; 0.24)	0.140
	3	-0.79 (-1.47 ; -0.12)	-0.29 (-0.64 ; 0.06)	
	12	-0.87 (-1.54 ; -0.19)	-0.23 (-0.58 ; 0.11)	0.875
	24	-0.62 (-1.28 ; 0.05)	-0.20 (-0.57 ; 0.17)	
	60	-0.86 (-1.52 ; -0.20)	-0.22 (-0.57 ; 0.13)	

Paper II

Initial deformation

From 0 to 3 months both groups showed an initial deformation in the proximal direction of 0.39 mm for the UHMWPE group and 0.21 mm for the HXLPE group, and for the 3D vector 0.62 mm and 0.40 mm respectively (table 6). After this there was a clear change in the translation pattern, indicating a change from the initial deformation phase to the beginning of the wear phase. A mixed-model analysis for both the proximal and 3D deformation showed no statistically significant difference between the groups (Table 6).

Cup wear

After the first 3 months, the wear curve for the proximal penetration of the UHMWPE group showed a continuous stable mean annual wear rate of 0.12 mm/year resulting in 1.56 mm at 10 years. However, the HXLPE group experienced minimal penetration after 3 months with a mean annual wear rate of 0.02 mm/year resulting in 0.40 mm at 10 years. The 3D penetration analysis showed a similar outcome for both groups with total penetration at 10 years of 1.69 mm for the UHMWPE and 0.56 mm for the HXLPE with annual wear rates of 0.11 mm/year and 0.02 mm/year, respectively. For both the proximal and 3D penetration, a mixed model analysis showed a statistically significant difference between the groups ($p < 0.001$) (Table 6).

Table 6: Wear measured with RSA as translation of femoral head in (mm). Numbers are presented as mean values (95% CI). [a] Mixed models analysis between 0 and 3 months and 3 months to 10 years, respectively.

		Mean values and (95% CI)		UHMWPE - HXLPE
Translation axis	**Months**	**Conventional PE**	**HXLPE**	**p-value [a]**
Y-axis (mm)	3	0.39 (0.22 ; 0.57)	0.21 (0.09 ; 0.32)	0.07
	12	0.51 (0.32 ; 0.70)	0.21 (0.04 ; 0.38)	< 0.01
	24	0.60 (0.42 ; 0.80)	0.24 (0.09 ; 0.38)	
	60	0.92 (0.68 ; 1.16)	0.27 (0.10 ; 0.45)	
	120	1.56 (1.21 ; 1.92)	0.40 (0.20 ; 0.60)	
3D (mm)	3	0.62 (0.38 ; 0.87)	0.40 (0.26 ; 0.55)	0.09
	12	0.71 (0.47 ; 0.96)	0.50 (0.32 ; 0.67)	< 0.01
	24	0.81 (019 ; 1.04)	0.50 (0.33 ; 0.67)	
	60	1.12 (0.86 ; 1.37)	0.54 (0.38 ; 0.70)	
	120	1.69 (1.30 ; 2.08)	0.56 (0.31 ; 0.81)	

Cup migration

The CSF cup showed a proximal migration of 0.28 mm at 3 months and had a stable migration pattern with 0.34 mm in total proximal migration at 10 years. The CSF *Plus* cup showed a similar migration pattern with 0.09 mm at 3 months and -0.04

mm at 10 years. Both groups showed generally low migration and rotation pattern along the other axis after the first 3 months up to 10 years (Table 7).

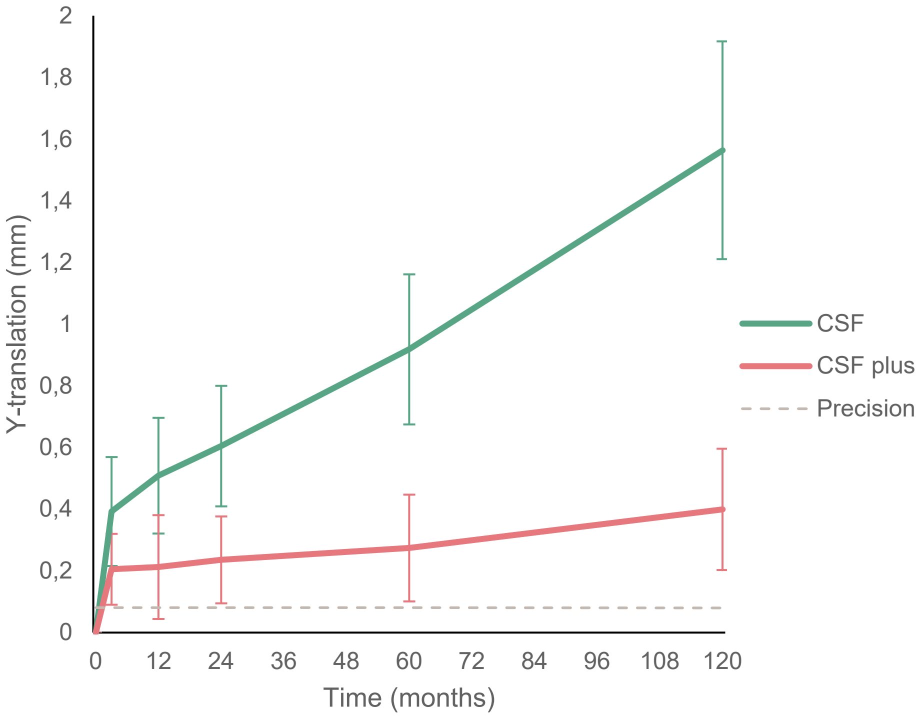

Figure 11: Proximal penetration of the femoral head for conventional PE and HXLPE with 95% CI bars.

Clinical outcome scores

The HOOS scores improved after surgery, compared with the preoperative scores, as expected. The HOOS scores remained similar and stable for up to 10 years for both groups.

Table 7: Cup migration. Numbers are presented as mean values (95% CI) as measured with RSA.

Cup		Mean Values and (95% CI)	
Translation/Rotation Axis	**Months**	**CSF**	**CSF Plus**
X-axis (mm)	3	0.37 (0.16 ; 0.59)	0.17 (-0.06 ; 0.40)
	12	0.35 (0.12 ; 0.57)	0.17 (-0.05 ; 0.40)
	24	0.37 (0.14 ; 0.59)	0.25 (-0.01 ; 0.50)
	60	0.31 (0.04 ; 0.58)	0.31 (0.03 ; 0.60)
	120	0.31 (0.02 ; 0.60)	0.30 (0.04 ; 0.56)
Y-axis (mm)	3	0.28 (0.13 ; 0.43)	0.09 (0.01 ; 0.16)
	12	0.34 (0.17 ; 0.50)	0.03 (-0.15 ; 0.20)
	24	032 (0.16 ; 0.49)	0.04 (-0.15 ; 0.22)
	60	0.33 (0.16 ; 0.49)	-0.01 (-0.23 ; 0.21)
	120	0.34 (0.13 ; 0.54)	-0.04 (-0.31 ; 0.22)
Z-axis (mm)	3	0.03 (-0.15 ; 0.21)	0.19 (-0.08 ; 0.46)
	12	-0.01 (-0.20 ; 0.17)	0.35 (-0.03 ; 0.74)
	24	0.10 (-0.09 ; 0.30)	0.38 (-0.04 ; 0.80)
	60	0.11 (-0.09 ; 0.32)	0.13 (-0.27 ; 0.53)
	120	0.04 (-0.21 ; 0.28)	0.23 (-0.27 ; 0.73)
X-axis (deg)	3	0.26 (-0.20 ; 0.71)	0.10 (-0.13 ; 0.33)
	12	0.40 (-0.01 ; 0.80)	0.21 (-0.24 ; 0.67)
	24	0.28 (-0.14 ; 0.71)	0.08 (-0.43 ; 0.58)
	60	0.25 (-0.26 ; 0.77)	0.17 (-0.37 ; 0.72)
	120	0.20 (-0.34 ; 0.74)	0.23 (-0.60 ; 1.06)
Y-axis (deg)	3	-0.15 (-0.60 ; 0.29)	0.05 (-0.33 ; 0.44)
	12	-0.11 (-0.49 ; 0.27)	0.00 (-0.42 ; 0.42)
	24	-0.16 (-0.57 ; 0.25)	-0.12 (-0.57 ; 0.33)
	60	-0.13 (-0.51 ; 0.25)	-0.29 (-0.77 ; 0.20)
	120	-0.03 (-0.56 ; 0.51)	-0.27 (-0.76 ; 0.22)
Z-axis (deg)	3	-0.02 (-0.49 ; 0.46)	-0.16 (-0.46 ; 0.14)
	12	0.00 (-0.52 ; 0.53)	-0.23 (-0.44 ; -0.02)
	24	0.07 (-0.44 ; 0.58)	-0.12 (-0.37 ; 0.12)
	60	0.06 (-0.46 ; 0.58)	-0.06 (-0.32 ; 0.19)
	120	0.01 (-0.61 ; 0.62)	0.06 (-0.21 ; 0.32)

Paper III

Initial deformation

Both cups showed an initial deformation of the cup during the first 3 months. The mean proximal head penetration for the UHMWPE was 0.07 mm and for the VEPE 0.06 mm. A similar pattern was observed in the mean 3D head penetration with 0.23 mm for the UHMWPE and 0.26 mm for the VEPE. A mixed-model analysis for both proximal penetration and 3D penetration showed no statistically significant difference between the 2 groups (Table 8).

Cup wear

After the first 3 months, the UHMWPE showed a continuous stable wear pattern with total proximal penetration of 0.46 mm corresponding to an annual wear rate of 0.08 mm/year. A similar wear pattern was observed in the 3D penetration with a total of 0.68 mm at 5 years. However, the VEPE cup showed a low, stable wear pattern with total proximal penetration of 0.09 mm at 5 years yielding an annual wear rate of 0.01 mm/year. When analyzing and comparing the wear curves between the groups, both proximal and 3D penetration, using a mixed-model analysis, a significant statistical difference was found (Table 8).

Table 8: Wear measured as translation of femoral head in (mm). Numbers are presented as mean values (95% CI). [a] Mixed models analysis between 0-3 months and 3 months to 5 years respectively.

		Mean values and (95% CI)		UHMWPE- VEPE
Translation axis	**Months**	**UHMWPE**	**VEPE**	**p-value [a]**
Y-axis (mm)	3	0.07 (0.03 ; 0.11)	0.06 (-0.01 ; 0.13)	0.62
	12	0.14 (0.09 ; 0.20)	0.07 (0.00 ; 0.13)	
	24	0.23 (0.17 ; 0.30)	0.07 (0.01 ; 0.14)	<0.01
	60	0.46 (0.36 ; 0.57)	0.09 (0.02 ; 0.16)	
3D (mm)	3	0.23 (0.15 ; 0.30)	0.26 (0.13 ; 0.39)	0.77
	12	0.42 (0.13 ; 0.71)	0.28 (0.14 ; 0.43)	
	24	0.50 (0.21 ; 0.79)	0.29 (0.15 ; 0.43)	<0.01
	60	0.68 (0.42 ; 0.95)	0.32 (0.17 ; 0.47)	

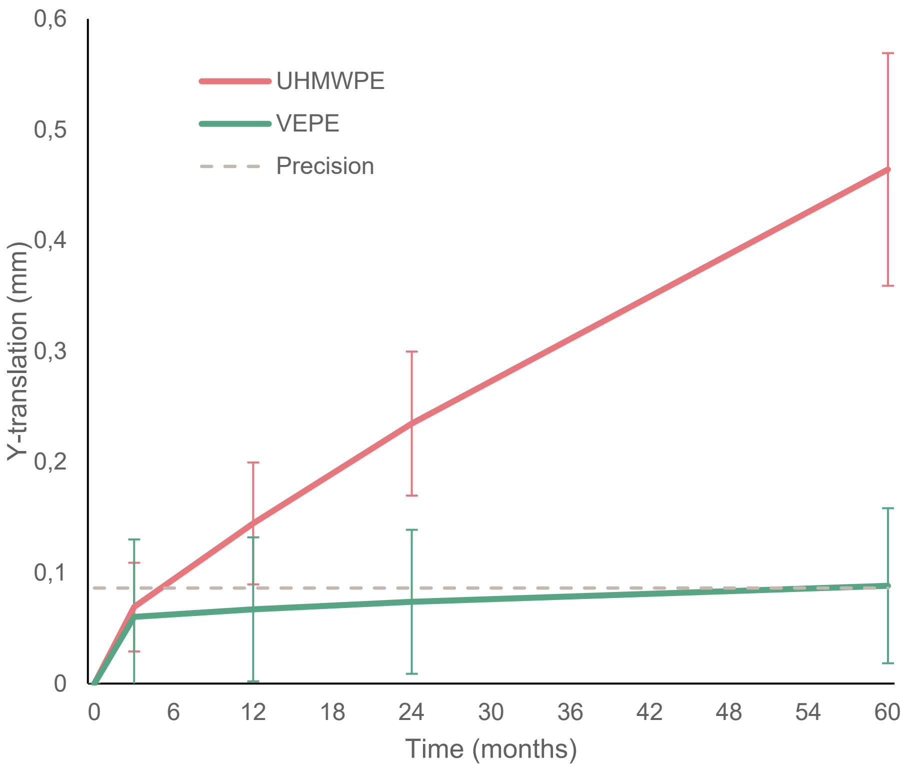

Figure 12: Proximal penetration of the femoral head for UHMWPE and VEPE cups with 95% CI bars.

Cup migration

During the initial bedding-in phase, up to 3 months, the VEPE cup showed greater initial proximal migration with 0.17 mm compared to 0.08 mm for the UHMWPE. Both cups showed a slight continuous proximal migration for up to 2 years. After that, the migration pattern stabilized for both cups with total proximal migration of 0.21 for the UHMWPE cup and 0.24 for the VEPE cup. Both cups showed generally low and stable migrations and rotation patterns along the other axis (Table 9).

Table 9: Cup migration. The numbers are presented as mean values (95 % CI).

Cup		Mean Values and (95% CI)		UHMWPE- VEPE
Translation Axis	**Months**	**UHMWPE**	**VEPE**	**p-value [a]**
X-axis (mm)	3	0.01 (-0.02 ; 0.04)	0.06 (-0.01 ; 0.14)	0.25
	12	-0.01 (-0.09 ; 0.07)	0.07 (-0.05 ; 0.18)	0.13
	24	0.01 (-0.06 ; 0.07)	0.09 (-0.04 ; 0.22)	
	60	0.02 (-0.09 ; 0.12)	0.16 (-0.02 ; 0.35)	
Y-axis (mm)	3	0.08 (0.03 ; 0.13)	0.17 (0.10 ; 0.24)	0.06
	12	0.14 (0.06 ; 0.22)	0.22 (0.13 ; 0.32)	0.28
	24	0.17 (0.08 ; 0.26)	0.24 (0.15 ; 0.33)	
	60	0.21 (0.04 ; 0.39)	0.24 (0.13 ; 0.36)	
Z-axis (mm)	3	0.06 (0.00 ; 0.13)	0.02 (-0.05 ; 0.09)	0.32
	12	0.04 (-0.22 ; 0.10)	-0.01 (-0.07 ; 0.05)	0.94
	24	0.02 (-0.04 ; 0.09)	-0.01 (-0.09 ; 0.06)	
	60	0.01 (-0.02 ; 0.22)	0.05 (-0.03 ; 0.13)	
Rotation Axis	**Months**	**UHMWPE**	**VEPE**	**p-value [a]**
X-axis (deg)	3	0.09 (-0.03 ; 0.22)	0.07 (-0.08 ; 0.23)	0.72
	12	0.10 (-0.13 ; 0.32)	0.13 (-0.03 ; 0.29)	0.01
	24	0.08 (-0.09 ; 0.26)	0.11 (-0.09 ; 0.30)	
	60	-0.02 (-0.35 ; 0.31)	0.29 (0.04 ; 0.55)	
Y-axis (deg)	3	-0.07 (-0.18 ; 0.04)	-0.11 (-0.26 ; 0.05)	0.93
	12	-0.11 (-0.37 ; 0.15)	-0.05 (-0.21 ; 0.10)	0.47
	24	-0.10 (-0.29 ; 0.08)	-0.13 (-0.29 ; 0.02)	
	60	-0.01 (-0.29 ; 0.26)	-0.11 (-0.35 ; 0.12)	
Z-axis (deg)	3	-0.07 (-0.16 ; 0.03)	-0.10 (-0.32 ; 0.12)	0.91
	12	-0.25 (-0.54 ; 0.04)	-0.17 (-0.48 ; 0.14)	0.21
	24	-0.20 (-0.40 ; 0.01)	-0.08 (-0.44 ; 0.27)	
	60	-0.24 (-0.55 ; 0.07)	-0.03 (-0.50 ; 0.44)	

Clinical outcome scores

The HOOS and EQ5D outcomes showed similar trends for both groups. As expected, the scores improved significantly compared to preoperative scores and remained good for up to 5 years for both groups.

Paper IV

Initial deformation

The 32 mm femoral heads had an initial proximal deformation of 0.09 mm and 3D deformation of 0.17 mm. The 36 mm femoral heads had, at 3 months, penetrated proximally 0.04 mm and 0.14 mm in 3D penetration. The differences were not statistically significant (Table 10).

Table 10: Wear measured as translation of femoral head in (mm). Numbers are presented as mean values (95% CI).

		Mean values and (95% CI)	
Translation axis	**Months**	**32 mm**	**36 mm**
Y-axis (mm)	0,5	0.08 (0.04-0.12)	0.03 (0.02-0.04)
	3	0.09 (0.05-0.14)	0.04 (0.03-0.06)
	12	0.10 (0.05-0.14)	0.07 (0.05-0.08)
	24	0.11 (0.06-0.15)	0.09 (0.07-0.10)
	60	0.11 (0.06-0.16)	0.10 (0.07-0.12)
	96	-	0.13 (0.10-0.16)
	120	-	0.13 (0.10-0.16)
3D (mm)	0,5	0.16 (0.11-0.21)	0.11 (0.09-0.13)
	3	0.17 (0.12-0.23)	0.14 (0.12-0.16)
	12	0.19 (0.13-0.24)	0.16 (0.14-0.19)
	24	0.20 (0.14-0.26)	0.17 (0.14-0.21)
	60	0.22 (0.16-0.28)	0.17 (0.15-0.19)
	96	-	0.19 (0.16-0.22)
	120	-	0.20 (0.17-0.23)

Cup wear

At 5 years the 32 mm heads showed a proximal penetration of 0.11 mm and a 3D penetration of 0.22 mm. The 36 mm heads had penetrated 0.10 mm in the proximal direction and 0.17 mm in the 3D direction. The 36 mm heads were further followed up to 10 years and showed 0.13 mm in proximal penetration and 0.20 mm in 3D penetration. The differences between 32 mm and 36 mm were not statistically significant up to 5 years (Table 10).

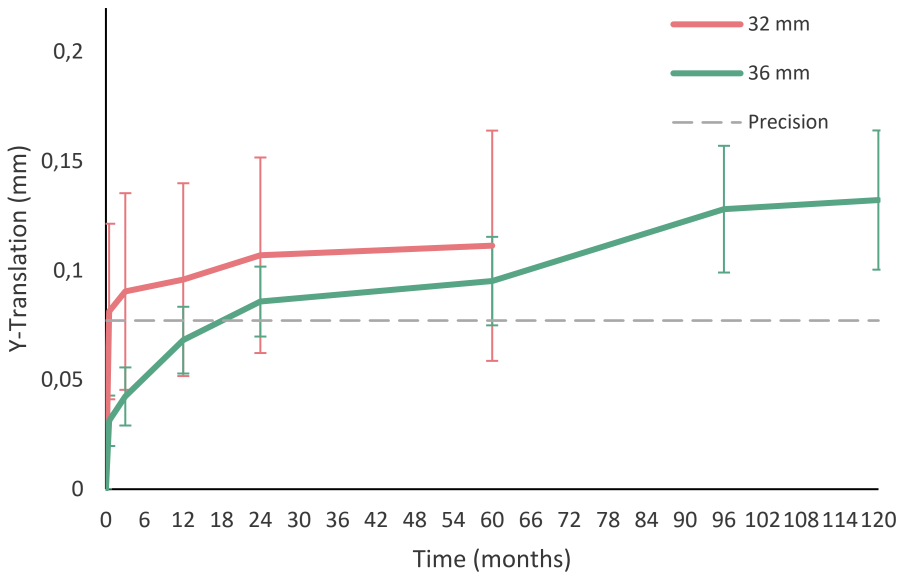

Figure 13: Proximal penetration of the 32 mm and 36 mm femoral heads with 95% CI bars.

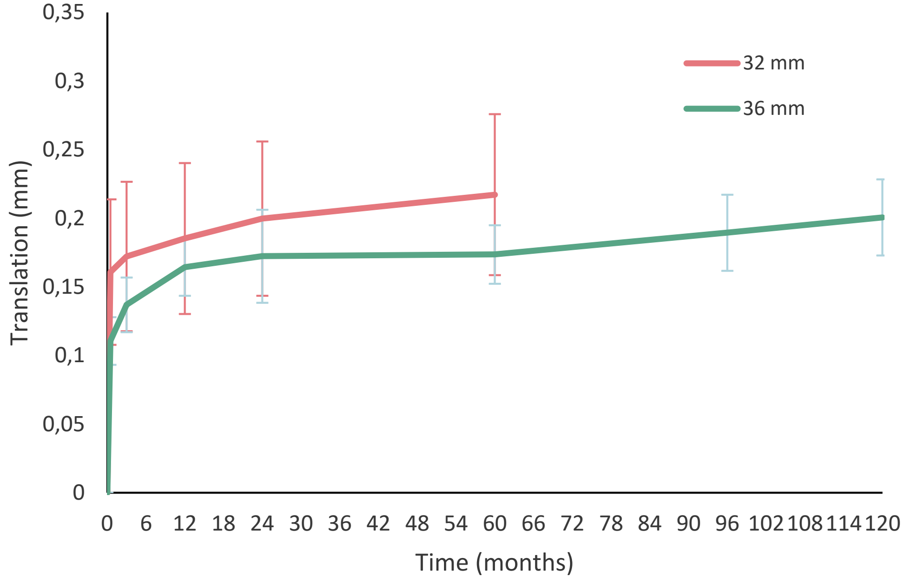

Figure 14: 3D penetration of the 32 mm and 36 mm FH with 95% CI bars.

Clinical outcome scores

The HOOS scores did, as expected, improve after surgery and remained consistent for both groups for up to 5 years. There was no statistically or clinically relevant difference between the groups. The same pattern was seen in the patient with further follow-up to 10 years.

Discussion

This thesis focuses on some of the most important factors that can affect the cup wear behavior of THA. We were able to measure and analyze the wear behavior of different types of PE as well as how different types and sizes of femoral heads affect cup wear. Furthermore, we were able to analyze if cup wear influences cup migration and how different cup coatings can affect the migration pattern of the cup in the acetabular bonebed. In general, we could confirm that the different implants used in this study were well functioning when it comes to cup wear and showed satisfactory results for the patients in the studies, at least throughout their follow-up period. Even though we observed different annual wear rates between the implants used, the patients reported good function and quality of life independent of the implants used.

If there is no difference between implant types, does it even matter which implant we use for our future patients? Moreover, is there any need for further improvement of the implants used today? We know that the patient population that needs surgical treatment for OA is growing as well as getting younger (6,7). It is, therefore, of utmost importance to be able to increase the longevity of the THA to minimize the risk for future revisions. In this thesis, we focused on the factors that, in our opinion, are potentially most important for the survival of the THA.

One of the most important techniques for evaluating implants and new designs or modifications of pre-existing implants is RSA. This method has been proved to detect early micromotion of implants in THA which has been linked to subsequent loosening of the implants (43,44). Cup wear is one of the most common factors leading to cup loosening and failure of the THA (8). It is therefore important to evaluate, with RSA, all new implants introduced to the market to detect eventual implant failure that might risk the survival of the THA. Furthermore, a long-term follow-up of implants is just as important to make sure that we can provide our patients with the safest choices of materials and implants available.

Initial deformation

In cup wear studies that follow patients postoperatively and onwards, the initial deformation phase of the cup or cup liner is inevitably a factor that needs to be taken into consideration. In the literature, early deformation, also known as creep, has been proposed to take place for the first 6-12 months (26,28) after surgery, and then gradually the wear phase takes over. There seems to be no consensus in the literature on how to report or account for this initial phase and many authors exclude the first year after surgery from the radiographic analysis to exclude the potential effect of this non-wear-related penetration of the femoral head in the wear analysis (45,46). In wear studies, it is important to understand that this phase probably starts from the first moment the patient is mobilized after surgery, and therefore, the timing of the first postoperative examination, i.e., the reference examination, can influence the interpretation of the following examinations. The timing of the reference examination can vary between studies and is often described as "taken within the first week" up to 6 weeks postoperatively or even not reported at all (47-49). This can make the interpretation of the sampled data more difficult for both the researcher as well as the reader. Moreover, if the patients in the cohort have their reference examination at different time points, the baseline for the wear curve will not be the same for all participants. In our studies, all patients had their reference examination performed on the first postoperative day, before full mobilization and standard rehabilitation was started. By doing this we believe that we can document the whole initial deformation phase, with all patients having the same baseline for the wear curve that is to be analyzed.

In all studies in this thesis, all patients have a follow-up examination at 3 months. When comparing the slope of the curves before and after 3 months there seems to be a distinct change in the slopes with a steeper slope before 3 months and a flatter curve after 3 months. This can be interpreted as that already at 3 months most of the deformation has already taken place and the wear phase begins. Furthermore, in papers I and IV all patients had their first follow-up examination at 2 weeks. What we can see is that at that time point, at least half of the deformation seen at 3 months, has already taken place at 2 weeks. This means that if the patients in a study have their reference examination somewhere in the first 1-2 weeks, this can influence the interpretation of the sampled data. However, we are aware that the deformation phase overlaps with the wear phase and as previously proposed it is most likely over within the first postoperative year, but we suggest that most of the initial deformation is over at 3 months.

We analyzed the deformation of 3 different femoral head sizes, 28-, 32- and 36-mm, on HXLPE cups or cup liners. We found that at 3 months, the 28 mm femoral head had the largest penetration and the 36 mm the smallest for both proximal penetration and 3D penetration. Although we did not do a direct comparison between these types of PE and femoral heads, this is still an interesting phenomenon to observe. This has previously been described in the literature. Lindalen et al. showed a similar phenomenon between 32 and 36 mm ceramic femoral heads and a VEPE cup liner (50) and Takahashi et al described in an in vitro study, the different deformation patterns of 28-, 32-, and 36-mm femoral heads (51). It showed the same phenomenon where 36 mm femoral heads showed less deformation than 32 mm, which in turn showed less deformation than 28 mm femoral heads. This correlates well with the mathematical definition of pressure. Pressure is equal to the magnitude of the force applied divided by the surface area on contact. Therefore, a smaller head generates more pressure than a larger head when the same force is applied, leading to more initial deformation.

Although the amount of initial deformation generated will probably have no significant effect on the long-term wear (27), we believe that it is important in wear studies to be aware of this phenomenon, report when the reference examination is taken, and account for this phase when reporting wear results.

Polyethylene types and effects on wear

As previously mentioned, cup wear, followed by osteolysis and later implant loosening is one of the leading causes of THA failure and revision surgery (8,9). In an effort to reduce the amount of wear generated, improvements have been made to the PE used in THA. In this thesis, we analyzed 3 main types of PE, UHMWPE, HXLPE, and VEPE.

Ultra-high molecular weight polyethylene

In papers II and III we analyzed the wear pattern of UHMWPE, made from the same material. They, however, articulate with 2 different sizes of femoral heads, 28 mm and 32 mm in size, and with 2 different fixation methods, cementless and cemented. What we observed, after the initial deformation phase, is that in both studies the UHMWPE showed a steady mean annual wear rate of about 0.1 mm/year up to 10 years. This is in consensus with what has previously been described in the literature (52-56) although both higher and lower wear rates have been described. This is important as the literature suggests that THA with annual wear rates > 0.1 mm/year show increased risk for osteolysis and aseptic loosening (57-59). Therefore, Dumbleton et al. proposed that an annual wear rate below the threshold of 0.1 mm/year would dramatically decrease the risk for osteolysis and a threshold of less than 0.05 mm/year would almost eliminate it (60). We observed, in these 2 papers, 45 patients out of a total of 49 with UHMWPE up to 5 years and 20 of those patients up to 10 years. None of these cups were revised during the study period. Overall, the UHMWPE in our studies, both cemented and uncemented, performed satisfactorily up to 5 and 10 years. However, with an annual wear rate of 0.1 mm/year, UHMWPE can be at risk and need to be monitored further.

Highly cross-linked polyethylene

In papers I, II, and IV we measured and analyzed the wear pattern of HXLPE from 2 different manufacturers with 3 different femoral head sizes, 28-, 32- and 36-mm, all with cementless technique and follow-up for 5 or 10 years. Furthermore, the liners were made using 2 different manufacturing processes. The HXLPE used in the first 2 papers was made by irradiating the PE with 80 kGy and remelting with irradiating sterilization method, while the HXLPE in paper IV was irradiated 3 times with 30 kGy with annealing in between the irradiation sessions, and finally sterilized using non-irradiation methods. What we could observe was that both types of HXLPE performed well, regardless of femoral head size or manufacturing processes. All cups showed a mean annual wear rate of 0.01 mm/year which is well within the proposed osteolytic thresholds of 0.1 or 0.05 mm/year (60). This is consistent with previously published studies indicating a good survival of HXLPE with a low annual wear rate (61-66). According to our results, there is good survival rate of the HXLPE available to the market today. Out of the 181 HXLPE liners that we followed in our studies, many up to 10 years, none were revised because of wear-related problems, or other problems related to the HXLPE itself. Although even longer follow-up is needed to declare the absolute safety of the modern HXLPE, it is safe to say, that with an annual wear rate of 0.01 mm/year, regardless of femoral head size, the future of the HXLPE we know today is promising. According to the knowledge we have now, further development of the HXLPE itself is not likely to further advance the longevity of the THA.

Vitamin-E infused polyethylene

In paper III we measured an analyzed the wear pattern of a cemented VEPE cup. One of the challenges with modern HXLPE has been oxidation resulting in decreased cross-linking density that can lead to increased wear (67). To address this problem and in order to provide enhanced oxidative stability vitamin-E (α-tocopherol) was added to the PE, either before or after cross-linking. This method has been studied in clinical trials and shown low wear at short- and mid-term follow-ups (50,68-73). However, these studies had been done on uncemented THAs. At the time when we initiated our study, there were no published articles on how cemented VEPE cups perform in vivo. We found that after the initial deformation phase, the VEPE cup showed a mean annual wear rate of 0.01 mm/year, similar to the HXLPE analyzed in our other papers, up to 5 years with no signs of accelerated wear and below the proposed wear thresholds of 0.1- or 0.05 mm/year. During the study period, there were 2 studies published on cemented VEPE cups that showed similar outcome for the wear analysis (74,75). Although our results show good wear performance of the VEPE up to 5 years, there is nothing that indicates that there is any superiority of the VEPE compared to the modern HXLPE during this early time period. There is, however, a possibility that the intended positive effects of the vitamin-E are latent and further long-term studies are needed to observe its full effect.

Femoral head sizes and types

In this thesis, as previously mentioned, we use 3 different head sizes for the wear analysis on 3 different PE concepts. It has been proposed in the literature that a larger femoral head size can increase the stability of the THA, decreasing the risk for dislocation. However, there have been concerns of larger head sizes generating more volumetric wear and therefore affecting the survival of the THA (76,77). Furthermore, there have been concerns regarding fretting of the head-neck junction with larger femoral heads (78). We found in our papers that, with modern generations of HXLPE or VEPE, femoral head size seems to have minimal effect on the linear wear rate of the PE. All cups tested had an annual wear rate of about 0.01 mm/year, regardless of head size, up to 5 or 10 years with no signs of accelerated wear in the later term. However, we did not analyze the volumetric wear of the heads. A larger head wears over a larger area in the PE and this could, in theory, result in more release of microparticles, inducing osteolysis and eventually aseptic loosening of the cup. It has been proposed that when using metal femoral heads on PE, the positive effects of a larger femoral head (> 32mm) do not decrease the overall revision risk for the THA, possibly due to PE wear and taper corrosion (79,80).

In paper I we analyzed and compared the effect of ceramic and metal femoral heads on the same HXLPE cup liner. Although metal femoral heads are still the most common head type to use in combination with PE, ceramic femoral heads have been growing in popularity during the last decade (9,46). The reason for this is that ceramic heads are thought to have better wettability, decreased surface roughness, and be more resistant to third-body damage compared to metal heads (19). We found in our study that after the initial deformation phase the ceramic heads showed a low, steady annual mean wear rate of 0.003 mm/year up to 5 years. Our results show that there is no significant difference in wear between metal or ceramic femoral heads up to 5 years. However, despite higher upfront implant costs, there might be good and beneficial reasons to use ceramic heads in younger patients due to the risk of taper corrosion (81), which in turn allows for larger head sizes to be used (80).

Cup migration

Although observing cup wear behavior is an important factor to monitor the safety and effectiveness of cups in THA, monitoring cup migrations is equally important. It can take years or even decades before cup loosening can be apparent on radiographic images. Therefore it is important to use RSA to monitor and evaluate implants, as this technique can detect motions as small as a fraction of a mm (34). Pijls et al. proposed that a proximal migration of up to 0.2 mm during the first 2 years is considered acceptable and migration of 1.0 mm or more is considered unacceptable (43). In papers I-III in this thesis, we analyzed the migration of the cups used, as a secondary outcome of the respective papers, all of which have a different basis of comparison.

In paper I we have the same type of cup, with the same type of liner but different types of femoral heads of the same size. In this paper, we analyze if the potential differences in wear, based on types of the femoral head, can affect the migration pattern of the cup. As previously described, there was no difference in wear between the 2 femoral head types. We did neither observe any difference in cup migration between the 2 study groups with a total proximal migration at 5 years below 0.2 mm. It is therefore logical to propose that different femoral head types do not influence the migratory pattern of the cup if the wear rate is the same.

In paper II we compared the migration pattern of the same cup type as was used in paper I, with its precursor. The differences between the cups are the coating, where the newer cup has a thicker and rougher coating, intended for earlier stabilization and better osseointegration. Studies published on the CSF cup showed stable migration pattern and good long-term survival (82-84) However, there are, to our knowledge, no studies published on the CSF *Plus* cup. We found in our study that the CSF *Plus* cup migrated less during the first 3 months, the so-called bedding-in period, however, from 3 months to 10 years both cups showed no signs of continuous migration or associated loosening. Apart from earlier stabilization, we could not find any superiority of the improved coating on the CSF *Plus* cup. Both cups are considered to have an acceptable migration pattern as proposed by Pijls.

In paper III we analyzed the migration pattern of the Exceed ABT cemented cup made from VEPE. There had been 2 papers published on this cup, thereof, one reporting small, continuous proximal migration of this cup up to 2 years, defining the cup as "at-risk", according to Pijls classification (74). The other study showed a similar migration pattern for this VEPE cup up to 2 years, however, a stable migration pattern was observed between 2 and 5 years. In our study, we also found that the VEPE cup showed higher migration values up to 2 years, however, after this, there was no further increase in proximal migration. The reason for this increased migration pattern in the first 2 years is unknown. For this cup, vitamin-E is infused into the cup after irradiation and one theory is that due to its lipophilic nature stability is delayed. Although the cemented VEPE cup showed good stability up to 5 years, a longer follow-up is needed to confirm the safety of this cup concept.

Patient outcome

It is expected after surgery that the patient experiences, not only the hip but general quality of life, to be improved. When doing research on hip implants it is therefore important to be able to document how the patient experiences the outcome after surgery as a means of pain, physical function, and general quality of life. These outcomes are documented using patient-answered questionnaires, such as HOOS and EQ-5D. This way, this most important outcome for the patient, can be documented in a scientific manner for use in research settings.

In this thesis, patient outcome was documented, in all papers, using the HOOS questionnaire. Furthermore, the EQ-5D questionnaire was used as well in paper III. In all 4 papers, the patient-reported outcomes improved significantly after surgery, as is to be expected. The scores remained good, and relatively stable, throughout the study periods, up to 5 or 10 years. However, one patient in paper III that received UHMWPE had a noticeable osteolytic zone in DeLee and Charnley Zone 1, already on the first postoperative (reference) examination. When followed with RSA examinations, this patient expressed higher migration values compared with the other participants in the study, however, the patient reported good outcomes on HOOS scores up to 2 years (100 pts) but markedly lower in the 5-year follow-up (65 pts) without signs of radiologic loosening when being analyzed by the clinician on plain radiographs. This, in our opinion, indicates that RSA examinations can detect a potential failure of implants before the onset of clinical symptoms and can be used to monitor these patient cases more closely.

Strengths

A common strength of the papers in this thesis is that they are all prospective studies, furthermore, papers I and III are randomized controlled trials (RCT). RCTs reduce bias and give a good examination of the cause-effect relationship between the intervention and the outcome, due to the randomization that balances patient characteristics between the groups. This way any differences are attributed to the outcome of the study intervention. Another strength of the papers is that all use RSA, which still is the gold standard when it comes to wear studies.

In all papers in this thesis, we were consistent with the first postoperative examination being done on the first postoperative day before full weight-bearing was allowed. By doing this, we can, in our opinion, document almost all deformation, wear, and migration of the components of interest. How this is done can vary in the literature, but we find it to be important strength in this thesis.

Limitations

A limitation for papers II and IV is that these papers are not randomized for the cup part of the studies. In paper II the stems used were randomized, however, the patients were operated consecutively for the cups. The reason for this was that when the trial started, the CSF *Plus* cup had not been released. This resulted in the first half being operated with the older version and the second half with the newer. In paper IV, we combined patients from 2 trials and analyzed the wear pattern between 2 femoral head sizes. This study design is not as strong as an RCT, but we believe, with the precise measurement techniques of RSA and statistical testing for homogeneity between the groups a reliable conclusion can be drawn from the results. Another limitation of these papers is that the patients were operated with 2 different types of stems. The migratory, or rotational pattern of the stems was not accounted for in our studies. The stems, used in each study, were very similar and came from the same manufacturer. We, therefore, do not consider that the differences in stems affected the outcome of the wear analysis.

In paper IV a part of the stems used had a modular head-neck junction. These stems were compared in a study conducted by our study group and found that the patient groups with modular stems had an increased whole-blood cobalt concentration compared with the patients with standard stems (85). It is uncertain if this can affect the wear performance of the THA, however, we find this unlikely.

Furthermore, in paper IV we followed the 36 mm femoral heads for 10 years and the 32 mm for only 5 years. The reason for this is that patients recruited and operated with 32 mm heads only had planned follow-up for 5 years. This resulted in us not being able to directly compare the 32- and 36-mm heads at 10 years. However, a subject of interest was how the 36 mm heads behaved up to 10 years, which we could analyze.

A potential limitation for paper II is that at 10 years we have had some dropouts which are mainly due to the age of the cohort. This leaves us with 20 and 15 patients respectively in the groups for the 10-year analysis which does not fully meet our criteria for the power in the study. However, as the differences between the groups are greater than what we used for the power calculations, we believe that our results do have sufficient power to be significant.

A limitation of paper I is that we are only comparing implants from one manufacturer and therefore it is difficult to generalize our results to other implants on the market.

In paper III, we compared VEPE with UHMWPE. By looking at the literature, there is strong evidence for the VEPE to be superior in wear. Therefore, from a purely scientific standpoint, it would have been more interesting to compare the VEPE to HXLPE cups to compare the pure effect of the vitamin E on wear. However, the outcome of this study was to analyze the wear pattern of the VEPE in cemented cups, which we could do. Our results can be used to compare the results from other studies analyzing the same VEPE cup.

Summary and conclusions

Background

The population that needs surgical treatment for osteoarthritis (OA) is getting younger and generally healthier than a few decades ago. This requires that the implants used survive for as long as possible. Cup wear has been one of the largest factors causing aseptic loosening that may lead to revision surgery. Therefore, it is important to understand the wear behavior of modern implants and continue monitoring new implants introduced to the market. Polyethylene (PE) has been used in total hip arthroplasty (THA) since the 1960s and since then, PE has evolved to provide our patients with the safest and most durable PE available. Furthermore, femoral head size has changed throughout the years as well as the materials used. These implants need to be methodically evaluated to confirm their safety and effects on wear behavior. This is best done with Radiostereometric analysis (RSA) which is the gold standard for wear studies today.

Patients and methods

The study patients in this thesis all fitted the inclusion criteria of having primary OA that needed surgical treatment. All patients were followed with RSA examinations and clinical outcome scores.

In paper I, we compared the wear behavior of 32 mm femoral heads made of 2 different materials, ceramic, and metal. Otherwise, the patients had the same implants with uncemented cups and highly cross-linked polyethylene (HXLPE). The patients were followed for 5 years.

In paper II we compared the wear pattern of 2 different PE in uncemented cups, ultra-high molecular weight polyethylene (UHMWPE) and HXLPE, articulating against a 28 mm metal femoral head. Furthermore, we compared the migration pattern of the same cup with 2 different surface coatings. The patients were followed for 10 years.

In paper III we compared the wear pattern of cemented UHMWPE and vitamin-E infused polyethylene (VEPE) cups articulating against a 32 mm metal femoral head up to 5 years. Furthermore, we compared the migration pattern of these cups in the acetabulum.

In paper IV 2 different head sizes, 32- and 36-mm were compared when articulating with a HXLPE in uncemented cups. The patients were compared up to 5 years and the 36 mm femoral heads were further evaluated up to 10 years.

Results

Paper I: Both groups showed very little wear of the HXLPE liner from 3 months to 5 years with no significant statistical or clinical difference between the groups. Both groups had an annual wear rate of < 0.01 mm/year.

Paper II: The HXLPE showed less annual wear rate than the UHMWPE or 0.02 mm/year and 0.12 mm/year respectively. Both cups showed a stable migration pattern up to 10 years. There was no difference in clinical outcome scores between the patient groups.

Paper III: The VEPE cup showed less annual wear rate (0.01 mm/year) compared with the UHMWPE (0.09 mm/year). The cemented VEPE cup migrated more than the UHMWPE during the first 2 years. However, both cups expressed a stable migration pattern between 2 and 5 years. Both patient groups reported good clinical outcome.

Paper IV: The 32 mm femoral heads had a greater initial deformation than the 36 mm heads. After the first 3 months, both groups showed a stable wear pattern with an annual wear rate of 0.004 mm/year for the 32 mm heads and 0.01 mm/year for the 36 mm heads. The 36 mm heads continued to have a stable wear pattern up to 10 years. Both patient groups showed good clinical outcome scores.

Conclusions

Paper I: Ceramic heads show no superiority in PE wear compared with metal heads.

Paper II: The HXLPE has a consistent low annual wear pattern up to 10 years in contrast to UHMWPE which shows a continuous wear of 0.1 mm/year. Both cups showed a stable migration pattern up to 10 years, regardless of coating type.

Paper III: Both cups show a stable migration pattern up to 5 years, however, the VEPE cup shows a statistically significant reduction in wear compared with the UHMWPE cup.

Paper IV: There is no statistically significant difference in wear between 32- and 36-mm femoral heads up to 5 years and the 36 mm heads continue to show a low, stable wear pattern up to 10 years.

Clinical implications

Paper I

It has been proposed that ceramic femoral heads are superior to metal femoral heads regarding wear, due to their tribological properties. This does not seem to be the case as we can, up to 5 years, show that both the ceramic and metal femoral heads generate the same wear and have almost the same annual wear rate. The ceramic femoral heads are substantially more expensive.

Paper II

Although the UHMWPE still shows good clinical results up to 10 years, it continues to show annual wear rates in the “risk zone”. HXLPE, however, shows a stable, low wear rate up to 10 years with no signs of acceleration of wear in the later years. A rougher cup surface results in an earlier cup stabilization, but once the cups have osseointegrated there is no difference in long-term migration.

Paper III

In order to counteract the oxidation effect on annealed HXLPE, a vitamin E infused PE was introduced. The cemented VEPE cup in our study showed promising results in wear up to 5 years. Prior concerns regarding cup stabilization could not be confirmed in our study as the cup showed low migrations values after stabilization, from 2-5 years.

Paper IV

Larger femoral head sizes have become more popular in recent years as these are to give increased stability to the THA. However, concerns have been made regarding increased wear with larger head sizes. We found no difference in wear between 32- or 36-mm femoral heads up to 5 years and the wear pattern for the 36 mm heads remained stable up to 10 years.

Summary in Swedish

Höftprotesoperationer har blivit en mycket vanlig operation med generellt goda resultat. Allt fler och allt yngre patienter opereras vilket ställer högre krav på att höftprotesen fungerar bättre och håller längre så att en omoperation kan undvikas. En av de vanligaste orsakerna till att höftproteser behöver omopereras är effekter av cupslitage, det vill säga slitage av plasten som utgör slitytan i den konstgjorda ledpannan (cupen). Detta slitage kan ha olika orsaker och vi har i denna avhandling undersökt några av de faktorer som man tror har störst betydelse för cupslitaget. Hur man tillverkar plasten kan påverka dess överlevnad men andra faktorer t.ex. höftkulans storlek eller vilket material kulan är gjord av tror man också har betydelse för i vilken takt plasten slits ner. Det har genom åren även skett en förbättring av protesdesignen och fixationsmetoderna vilket vi till viss del även undersökt,

För våra undersökningar har vi haft tillgång till den mest sofistikerade och känsliga mätmetod som finns för att mäta slitage och cuprörlighet, nämligen Röntgenstereometrisk analys (RSA).

Man har trott att ledhuvud av keramik har bättre slitageegenskaper än metall efter som den har slätare yta, är hårdare och glider lättare med hjälp av ledens vätska. Våra resultat (Studie I) visar att det inte finns någon skillnad i slitage mellan keramik och metallkula mätt upptill 5 år, förutsatt att man använder modern molekylärt högbunden plast. Dessutom visar våra resultat att val av material på ledkulan inte påverkar cupens fixation mot benet över tid.

I ett av våra delarbeten (Studie II) fann vi att modern molekylärt högbunden plast endast uppvisar en tiondel så mycket årligt slitage som konventionell plast (0.01 mm/år jämfört med 0.1 mm/år). Det är redan tidigare visat att molekylärt högbunden plast har mindre plastslitage än konventionell plast men vad vi kunnat påvisa är att den låga slitagehastigheten fortsatte vara låg ända upp till 10 år, utan tecken till ökad slitagehastighet, vilket man tidigare befarat. Vi fann även att cupar med grövre yta stabiliseras tidigare än de som har slätare yta men att det inte fanns någon skillnad i stabilitet över hela studietiden.

En nackdel med den moderna molekylärt högbundna plasten är att den kan utsättas för oxidering och därmed öka slitaget. För att motverka detta har man behandlat plast (polyethylen) med Vitamin-E för att neutralisera de fria radikaler som kan bidra till oxideringen. Vi undersökte (Studie III) en cementerad cup gjord av sådan vitamin-E behandlad polyethylen (VEPE) och jämförde med konventionell plastcup och analyserade slitaget upp till 5 år. Vi fann att VEPE-cupen har betydligt lägre slitagehastighet än konventionella plasten, något som liknar molekylärt högbunden plast. Stabiliteten av den cementerade VEPE cupen i bäckenet var bra fram till 5 år, något som hade ifrågasätts i tidigare publicerad studie.

En annan faktor som kan påverka slitaget är själva ledhuvudets storlek. Man har trott att större kula ökar slitaget, samtidigt som en större kula bidrar till bättre stabilitet och därmed mindre risk för protesluxation. Vi undersökte och jämförde slitage mellan 32- och 36-mm ledhuvud av metall (Studie IV) och fann ingen skillnad i slitage mätt med RSA. Vi följde 36 mm kulorna fram till 10 år och fann ingen ökad slitagehastighet upp till 10 år.

Sammanfattningsvis kan man säga att modernt molekylärt högbunden plast är ett mycket slitstarkt och säkert alternativ för höftprotesoperationer. Det är tveksamt om ytterligare vidareutveckling av plasten kommer leda till lägre revisionsrisk på grund av slitage. VEPE är ett bra alternativ till den molekylärt högbundna plasten men det är fortfarande oklart om Vitamin-E bidrar till längre hållbarhet av plasten. Med modernt molekylärt högbunden plast verkar det inte spela någon roll för slitaget vilken storlek av ledhuvud man använder, eller om det är gjort av keramik eller metall.

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About the Author

HALLDÓR R BERGVINSSON was born in Reykjavik, Iceland in 1986. He finished his medical degree from the University of Iceland in 2013 and became a resident in orthopedic surgery at Landspitali University Hospital in 2014. He moved to Lund, Sweden with his family in 2016 to continue his career as an orthopedic surgeon at Skånes University Hospital. Halldór has been a part of the Orthopedic department´s joint arthroplasty unit since 2020.

In this thesis, we focus on the most important factors that affect cup wear and migration in total hip arthroplasties, such as different types of polyethylene, femoral head size, and material. We used Radiostereometric analysis (RSA) which is the gold standard in wear studies as well as patient-reported outcomes.

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