Wear and migration in total hip arthroplasty measured with Radiostereometric Analysis

Methodological aspects and clinical studies

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Life Doesn´t Require That
We Be The Best,
Only That We Try Our Best

To my son Arian

ABSTRACT

Total hip arthroplasty (THA) aims to relieve pain, increase hip function and improve quality of life for patients with end-stage osteoarthritis of the hip who do not benefit from non-surgical treatment. Despite constant improvements in prosthetic component design and surgical techniques, prosthetic loosening, wear and dislocation remain the most common complications of a hip replacement procedure.

Roentgen Stereophotogrammetric Analysis (RSA) is a highly accurate technique that enables three-dimensional measurements of skeletal or implant micromovement with respect to the host bone in vivo. The method has been used in clinical research for the evaluation of penetration of the femoral head into the acetabular component of a total hip replacement as a result of polyethylene creep and wear. Wear has been identified as a common cause of aseptic implant loosening and late revision. The RSA method has the ability accurately to measure bone and implant movements, rendering it a very useful tool in the evaluation of new implants and surgical techniques.

Several studies have shown that RSA measurements of migration can be used to predict the risk of future revision based on a small group of patients and in a relatively short period of time. This thesis aims to study different aspects of RSA methodology with a potential influence on precision and accuracy. The opportunity to obtain clinically relevant information from studies of absolute motions of the pelvic segment over time and between supine and standing positions was explored. The RSA method was also applied in a randomised, clinical study of liner wear. Further, the method was used for a comparative analysis of two acetabular implants with differing properties relating to shell coating (RingLoc and Regenerex) for the development of radiolucent lines at the implant-bone interface and cup migration up to five years.

In Study I, femoral head penetration into cups with liners made of either vitamin E-infused highly cross-linked polyethylene (E1) or compression-annealed highly cross-linked polyethylene, ArComXL, was evaluated in 61 patients (70 hips) in a randomised, clinical study. At two years, the femoral head penetration did not differ between the groups.

Study II aimed to evaluate differences in the femoral head penetration rate between E1 and ArComXL with the emphasis on changes occurring between two and five years after THA. E1 demonstrated low proximal and total head penetration after the minimum five-year follow-up. The penetration rate was significantly lower for the E1 compared with the ArComXL liners. Both polyethylene types demonstrated increased liner penetration between two and five years.

In Study III, wear and migration in four uncemented cups with various geometries that are commonly used for THA in Sweden were evaluated. Further, the influence of cup design on the precision of model-based RSA (MBRSA), using marker-based RSA as a reference, was also evaluated. For three of the studied designs, the precision of MBRSA was as good as the reference method. Poorer precision

was observed for the fourth cup design (RingLoc), which indicated that the resolution of MBRSA may vary depending on the geometry of the implant or the surface coating.

In Study IV, the change in pelvic tilt angle (PTA) in a supine position and between supine and standing positions was evaluated in 106 patients up to seven years after THA using RSA. The pelvic tilt changed over time both when supine and when rising from supine to standing. At six months, the mean anterior tilt from supine to standing was 3.6° ± 3.8°, which increased to 6.4° ± 3.9° at seven years. In individual patients, this change reached about 11.0 degrees when supine and 18.0 degrees when standing.

In Study V, the migration of cups coated with a porous titanium layer (Regenerex) was recorded using a porous plasma-sprayed cup (RingLoc) as a reference in 92 patients (hips). We also evaluated any possible associations between the occurrence of progressive radiolucent lines and the migration of the acetabular component up to five years measured with RSA. Cups with a porous titanium coating demonstrated smaller absolute values of medial or lateral migration. The plasma-sprayed cups migrated more anteriorly than the porous titanium cups. Increasing relative length of radiolucent lines between the postoperative examination and five years follow-up of at least 20 percent of the interface was associated with increasing anterior or posterior cup migration.

Keywords
Total hip arthroplasty, radiostereometry, femoral head penetration, highly cross-linked polyethylene, polyethylene wear, radiolucent lines and pelvic tilt angle

SAMMANFATTNING PÅ SVENSKA

Den vanligaste orsaken till operation med höftprotes är artros i höftleden. I Sverige är medelåldern vid detta ingrepp strax under 70 år. Total höftledsplastik (THA) är en effektiv behandling av patienter som lider av höftartros i de fall då icke-kirurgisk behandling har misslyckats. Målet med THA att lindra smärta, förbättra rörlighet, funktion och livskvalitet uppnås i en stor majoritet av fallen. Antalet patienter som får behålla sin höftprotes livet ut utan allvarliga komplikationer är högt speciellt i åldersgrupperna 65 år och över. Antalet höftledsoperationer ökar i samhället vilket dock innebär att alltfler, framför allt yngre patienter kommer att bli aktuella för revision eller annan typ av reoperation. Resultaten efter omoperation är i allmänhet sämre än efter en primäroperation, framför allt beroende på att de mekanismer som orsakat omoperationen ofta medför skada av benvävnad och mjukdelar. De vanligaste orsakerna till omoperation är lossning/osteolys, luxation, infektion och periprotesfraktur.

Röntgen Stereofotogrammetrisk Analys (RSA) är en radiologisk mätmetod med mycket hög upplösning. Den används bland annat för att utvärdera tredimensionella rörelser efter operation av höftproteser. Styrkan i RSA kommer från dess förmåga att exakt mäta mikrorörelser av implantaten, vilket möjliggör att man kan erhålla viktig information baserat på en förhållandevis liten grupp av patienter. Med RSA kan man i ett tidigt skede avgöra om en ny protes är värd att studera vidare eller inte. Mätningar av implantats mikrorörelser redan under de första två åren efter operationen har visat sig vara av värde att förutsäga senare kliniska misslyckande på grund av aseptisk lossning och slitage. Noggrann bestämning av implantatens fixation har visat sig vara en viktig hörnsten när det gäller utvärdering av nya material som utvecklas i avsikt att förbättra en konstgjord leds slitage egenskaper. Denna typ av utvärdering har visat sig vara så informativ att metoden nu anses utgöra standard vid bedömning av nya proteskoncept.

Denna avhandling syftar till att studera olika aspekter av RSA-metoden med potentiellt inflytande på precision och noggrannhet. Möjlighet att erhålla kliniskt relevant information från studier av rörelser i bäckenet över tid samt mellan liggande och stående positioner. RSA-metoden appliceras även i en randomiserad klinisk studie av migration och slitage. Vidare används metoden för jämförelse av skillnader i utveckling av uppklarningszoner och migration av protesens ledskål vid användning av två implantat med olika ytbeläggning.

I Studie I och II, utvärderades skillnader i slitage av ledskålens plastdel vid användning av höggradigt korsbunden E-vitaminbehandlad polyetylen (E1) alternativt värmebehandlad höggradigt korsbunden polyetylen (ArComXL) hos 61 patienter (70 höfter) i en randomiserad klinisk studie. Separat analys gjordes efter två respektive fem års observation. Båda plasttyperna uppvisade ett ökat plastslitage mellan tre månader och två år. Det fanns ingen skillnad i plastslitage mellan E1 och kontrollgruppen (ArComXL) efter två år. I båda grupperna observerades ökad penetration mellan två och fem år. Slitagehastigheten två till fem år var högre för ArComXL gruppen.

I Studie III, utvärderades två olika sätt att mäta cupslitage respektive cupmigration. Fyra olika ocementerade cupmodeller (Trilogy, ABG, TMT och RingLoc) studerades både med konventionell RSA och med den nya metoden modell-baserad RSA (MBRSA). Vidare utvärderades påverkan av cupens geometriska egenskaper på precisionen av MBRSA genom att använda konventionell RSA som referens. Precisionen av MBRSA visade sig att vara likvärdig med referensmetoden för tre av de studerade cupmodellerna. För den fjärde cupmodellen (RingLoc) observerades en sämre precision med MBRSA, vilket indikerade att upplösningen av MBRSA kan variera beroende på implantatets geometri eller ytbeläggning.

I Studie IV studerades förändringar i bäckenpositionen i liggande läge och mellan liggande och stående med RSA upp till sju år efter operation. Bäckenets position förändrades över tid i ryggläge och från liggande till stående position. Från liggande till stående observerades en framåttippning av bäckenet hos samtliga patienter. Kvinnliga patienter visade större förändring av bäckenpositionen både i liggande och från liggande till stående position. I enskilda fall observerades en framåttippning på mellan 11.0 till 18.0 grader.

Studie V syftade till att utvärdera skillnader i förekomst av uppklarningszoner mellan två olika cupmodeller med olika egenskaper avseende ytbeläggning (Regenerex och RingLoc) samt undersöka eventuella samband mellan förekomst av zoner och migration av den acetabulära komponenten upp till fem år efter operation mätt med RSA. Vi observerade att cupar med porös titanbeläggning visade mindre medial eller lateral migration. Cupar ytbehandlade med plasma-spray (RingLoc) migrerade mer proximalt än de porösa cuparna. En ökad zonbildning vid cupens kontaktyta mot ben på 20% eller mer mellan den postoperativa kontrollen och röntgenundersökningen vid fem år var associerad med ökad migration av cupen i anterior-posterior riktning.

LIST OF PAPERS

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

I. Shareghi B, Johanson PE, Kärrholm J.
Femoral Head Penetration of Vitamin E-Infused Highly Cross-Linked Polyethylene Liners: A Randomized Radiostereometric Study of Seventy Hips Followed for Two Years.
J Bone Joint Surg Am. 2015 Aug 19;97(16):1366-71. doi: 10.2106/JBJS.N.00595.

II. Shareghi B, Johanson PE, Kärrholm J.
Wear of Vitamin E-Infused Highly Cross-Linked Polyethylene at Five Years.
J Bone Joint Surg Am. 2017 Sep 6;99(17):1447-1452. doi: 10.2106/JBJS.16.00691.

III. Shareghi B, Johanson PE, Kärrholm J
Clinical evaluation of model-based radiostereometric analysis to measure femoral head penetration and cup migration in four different cup designs.
J Orthop Res. 2017 Apr;35(4):760-767. doi: 10.1002/jor.23177.

IV. Shareghi B, Mohaddes M, Kärrholm J.
Pelvic tilt between supine and standing after total hip arthroplasty. 106 patients examined with RSA up to seven years after the operation.
In manuscript.

V. Shareghi B, Galea VP, Kärrhom J, Malchau H, Rolfson O.
Migration of uncemented cups and development of radiolucent lines. Radiostereometric evaluation of 92 cups with either porous titanium or plasma sprayed surface coating up to five years.
In manuscript.

CONTENTS

ABBREVIATIONS

3D	Three dimensional
AP	Anterior-posterior
CI	Confidence interval
CN	Condition number
CoCr	Cobalt-Chrome
HPS	Harris pain score
HSS	Harris hip score
MBRSA	Model-based radiostereometric analysis
ME	Mean error of rigid body fitting
OA	Osteoarthritis
PE	Polyethylene
PTA	Pelvic tilt angle
RSA	Radiosteremetric analysis, radiostereometry
SD	Standard deviation
SE	Standard error
THA	Total hip arthroplasty
UHMWPE	Ultra-high molecular weight polyethylene
XLPE	Highly cross-linked polyethylene

DEFINITIONS IN SHORT

Bone ingrowth:	Bone formation within an irregular surface of an implant
Bone remodelling:	Formation of new bone tissue in direct contact with the porous structured surface of an implant
Creep:	Plastic deformation of material without production of wear debris
Osseointegration:	The formation of a direct interface between bone and an implant
Oxidation:	The loss of electrons during a chemical reaction by a molecule, atom or ion
Porous coating:	Coating on an implant deliberately applied to contain void regions with the intent of enhancing the fixation of an implant
Press-fit:	Insertion of an implant into an undersized pre-made cavity
Radiolucent lines:	Linear radiolucencies lining the implant contour without densifications
Revision:	A procedure involving extraction or exchange of parts or the entire implant
Uncemented:	Implants designed for fixation by bone ingrowth
Wear:	Undesired removal of material from implants and other biomaterials
Radiostereometry:	A highly accurate radiographic technique enabling three-dimensional measurements of skeletal or implants micro-movement
Rigid body:	The number of markers forming a segment corresponding to either part of the body or the object of interest

01 INTRODUCTION

01

INTRODUCTION

1.1 Total hip arthroplasty

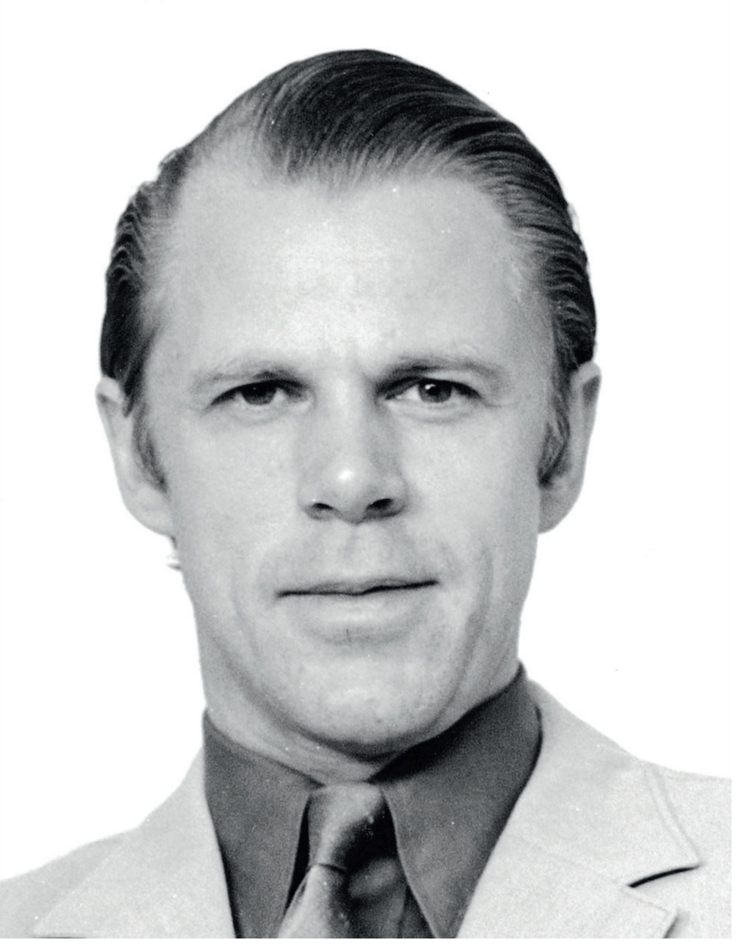
Total hip arthroplasty (THA) is one of the most successful, cost-effective surgical procedures in orthopaedic practice, with the primary goals of relieving pain, improving motion, restoring joint function and improving health-related quality of life. THA has been developing continuously in recent years in terms of prosthetic designs and materials, surgical techniques, treatment and the prevention of complications. Although major improvements have been recorded with regard to clinical outcomes and survival, the failure of the acetabular component continues to be the most frequent significant cause of revision. The majority of patients who undergo THA can expect a well-functioning prosthesis for a long period of time. In younger and more active patients, the risk of complications such as loosening and osteolysis is increased and may become high several years after the operation as a consequence of a more active lifestyle. In conventional radiography, early micromotions or wear of the socket are not usually detectable due to limited reproducibility and resolution for measuring these events and, after a number of years, this may result in detectable radiographic changes and clinical failure.

So far, the method of choice for measuring migration or wear is roentgen stereophotogrammetric analysis (RSA), which is a highly accurate technique that enables three-dimensional measurements of skeletal or implant micromovement at an early stage and already during the post-operative years. Due to its high resolution, important information on prognostic value can be obtained from a comparatively small patient population (Selvik, Alberius et al. 1983, Karrholm 1989).

1.2 Radiostereometric analysis, history

In Sweden, the method originates from Hallert, who presented the basic principles for roentgen photogrammetry (Hallert 1970). In 1974, Göran Selvik *(Figure 1)* modified and further developed the method and implemented mathematical principles of rigid body fitting to calculate three-dimensional motions. The method was initially called roentgen stereophotogrammetric analysis and was later named radiostereometric analysis (RSA) and became widely used. Many applications and mathematical algorithms have been developed and applied, including the semi-automated evaluation of digital X-rays and various types of measuring technique which do not require marking of the implant with tantalum markers (model-based RSA) (Valstar, Spoor et al. 1997, Borlin, Thien et al. 2002, Bragdon, Malchau et al. 2002).

Figure 1.
Göran Selvic
1938-1990.



The method has been used in clinical research to evaluate the penetration of the femoral head into the acetabular component of a THA as a result of polyethylene creep and wear (Bragdon, Malchau et al. 2002). This mechanism has been identified as a common cause of aseptic implant loosening and late revisions, especially when earlier generations of polyethylene were used (Clohisy, Calvert et al. 2004). The RSA method is able accurately to measure bone and implant movements, rendering it a very useful tool in the evaluation of new implants and surgical techniques. Several studies have shown that RSA measurements of migration can be used to predict the risk of future revision based on a small group of patients and in a relatively short period of time (Karrholm 2012, Pijls, Nieuwenhuijse et al. 2012, Klerken, Mohaddes et al. 2015).

The introduction of the RSA method in clinical research has facilitated the evaluation of new implant designs as a first clinical selection procedure to determine whether further studies with a longer follow-up can be regarded as justified. RSA has contributed to the improvement of outcomes in health care. Poorly performing implants can be identified at an early stage and long before the potentially negative effects have resulted in clinical symptoms. This valuable information has made it possible to phase out implants with substandard performance at an early stage and before a large group of patients have undergone surgery.

Marker-based RSA

The basic principles of marker-based RSA consist of four steps; the insertion of tantalum markers, radiographic examination, measurement on radiographs and analysis, i.e. calculations of three-dimensional movements *(Figure 2)*. The accuracy and precision of an RSA examination depend on several factors, the radiographic technique, analytical software and the positioning of tantalum markers.

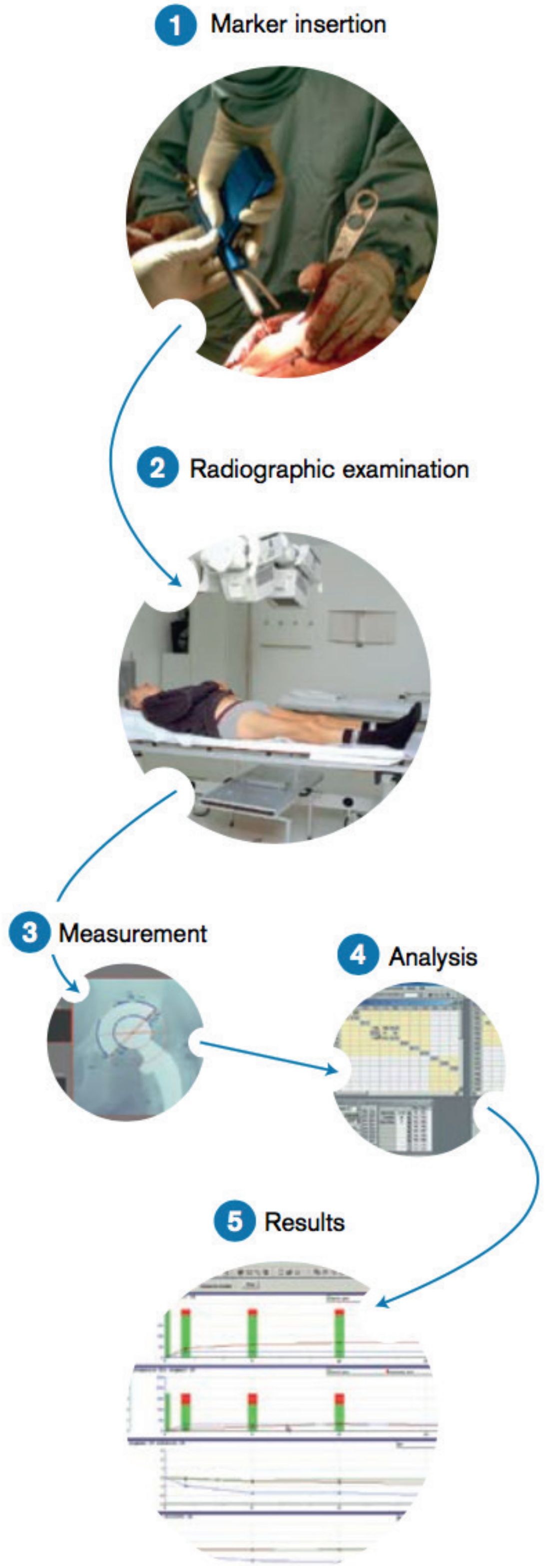


Figure 2.
Illustration of the basic steps in an RSA investigation. With permission from RSA Biomedical.

1.2.1 Marker insertion

Spherical tantalum markers with a diameter of 0.8 mm or 1.0 mm are inserted into the bone and the implant *(Figure 3)* during hip replacement surgery using a dedicated instrument equipped with a steel cannula *(Figure 4)*. Tantalum markers are easy to identify on radiographs because of their high atomic number. The scattering of the markers in the bone is important. Although only three visible, well-defined markers in each segment of interest are necessary for a complete radiostereometric evaluation, five to nine markers are usually inserted in each segment to optimise marker spread and compensate for loose or invisible markers.

Figure 3. Image of a hip with RSA marking in the pelvis bone, polyethylene liner and the femur bone.

Figure 4.
Illustration of the injector used for insertion of tantalum markers during a THA.

In order to increase the accuracy of RSA, tantalum markers need to be as scattered as possible to create large rigid bodies (Ryd, Yuan et al. 2000). Marking implants is time consuming and there is a potential risk that the tantalum markers will not be optimally localised, thereby reducing the measurement accuracy. Whole polyethylene acetabular cups and polyethylene liners in uncemented cups can be equipped with tantalum markers around the opening of the cup and, in certain circumstances, also in the dome. This should preferably be done by the manufacturer. Today, this is rarely (or never) performed, mainly because of concerns about the cost of a new CE-labelling procedure.

Markers can also be inserted into small titanium pegs attached to the outside of a metallic shell. The marking of metal implants has been performed by manufacturers, but this is currently rarely done due to the concerns presented above. The marking of cement, polyethylene or bone tissue is done at the time of surgery. During the last few years, some producers have raised concerns about the preoperative marking of polyethylene and claim that they do not allow it.

1.2.2 Radiographic examination

The RSA method uses dual simultaneous X-ray exposure associated with a calibration cage equipped with tantalum markers located in fixed positions in the cage). The cage markers that are located closest to the roentgen tubes identify the position of the tubes and are called control points. Markers that identify the laboratory co-ordinate system are called fiducial points and are located in the floor of the calibration cage *(Figure 5)*. In later versions of the analytical software, all the cage markers can be used for both purposes. Cage markers thus define the three-dimensional reference co-ordinate system and are used to calculate the positions of the two roentgen foci. Individual X-rays travelling between the two images of each patient marker and each focus are computed. The crossing of these X-rays defines the position of an individual marker in the laboratory co-ordinate system. At the examination, the region of interest can be placed above (uniplanar system) or inside (biplanar) the calibration cage *(Figure 6)*. RSA examinations can be performed in supine and standing positions *(Figure 7)*.

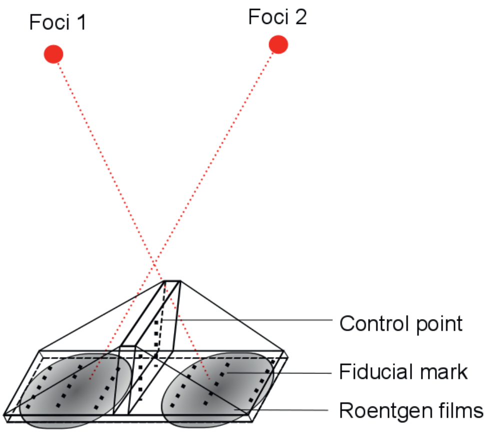


Figure 5. Schematic drawing of the uniplanar calibration cage showing the positions of the cage markers. With permission from Maziar Mohaddes.

Figure 6. a) Uniplanar RSA cage, b) Biplanar RSA cage.

Figures 7. Radiostereometric examination in supine and standing.

1.2.3 Measurement on radiographs

Until 1997 and in our laboratory, RSA analogue radiographs were measured manually using a high- precision measuring table (Karrholm, Herberts et al. 1997, Vrooman, Valstar et al. 1998). Between 1997 and 2004, analogue images were scanned into digital images. All the images were then directly digital, initially using film plates and then digital screens. These images are imported to the RSA using dedicated software (UmRSA DICOM Link). Measurements of cage and patient markers are performed with software (UmRSA Digital Measure) equipped with automated or semi-automated functions *(Figure 8)*. The UmRSA software computes the stability of markers (mean error of rigid body fitting) within one segment (e.g. the acetabulum) and a numerical parameter (condition number) that provides information about the magnitude of marker scatter.

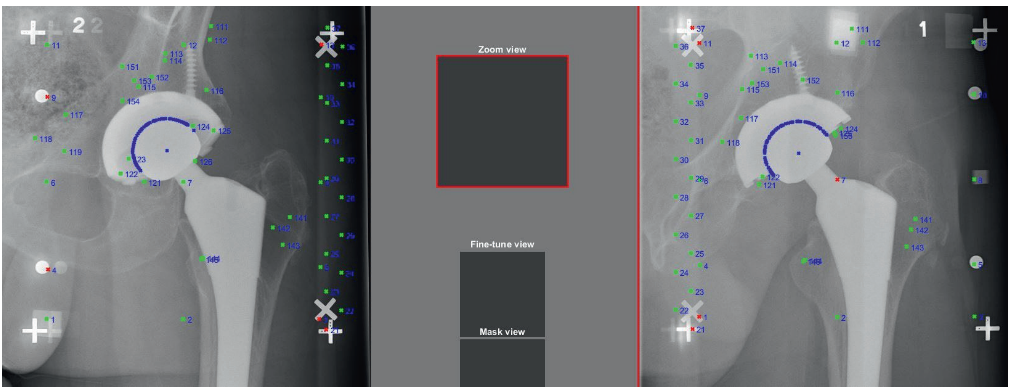


Figure 8. A pair of stereoradiographs illustrating identified tantalum markers in the calibration cage, the pelvis, the cup and the femur. The femoral head is defined by edge-detection (ellipse). Green represents marker identification within acceptable limits of error.

The absolute motions of each studied segment and the relative motions between two segments or a segment and a point are calculated. The absolute motions correspond to motions of a segment relative to the cage. This parameter thus describes in detail how the acetabulum, for example, has changed its position between two examinations. When relative motions are calculated, one of two segments is chosen to become fixed by "replacing" it in its original position at the reference examination by applying a mathematical algorithm. This algorithm describes the rotation and translation between the two examinations of interest and is reversed to find the original position of the segment at the reference examination. With a fixed reference segment, the relative motions of a second segment (e.g. the cup) or a point (e.g. a single cup marker or the cup centre) can be computed.

The mean error of the rigid body fitting (ME) and the condition number (CN) are crucial parameters as they determine the quality of the measurements. Both parameters should ideally be as small as possible. There is, however and to a certain extent, a trade-off between these parameters. If the mean error is very low, slightly higher condition numbers can be accepted and vice versa. Despite this and in the evaluation of the migration and wear of hip prostheses, mean errors above 0.350 mm and condition numbers above 130 are rarely used.

1.2.4 Analysis of motions

The UmRSA analysis software uses measurement data to compute the migration and wear of an implant. Translations of the femoral head component, the centre of the cup or the gravitational centre of the cup markers are commonly computed. These motions are described in relation to three body fixed axes; the transverse (medial/lateral, x-axis), the longitudinal (proximal/distal, y-axis) and the sagittal (anterior/posterior, z-axis) *(Figure 9)*. Migration can also be expressed as rotational movement, which is a mathematical expression of the three-dimensional rotation of a rigid body about the x-, y- and z-axes *(Figure 10)*. A complete migration analysis, including a description of translations and rotations, requires at least three visible, well-defined tantalum markers in each segment of interest. In cases with fewer than three visible markers, model-based RSA (MBRSA) can be used to determine the migration and wear of an implant. Motions of a rigid body can also be described as rotations and translation around and along one axis, the helical or screw axis (Karrholm, Jonsson et al. 1994). These analyses are supported by the software, but they were not performed in this thesis and will not be further discussed.

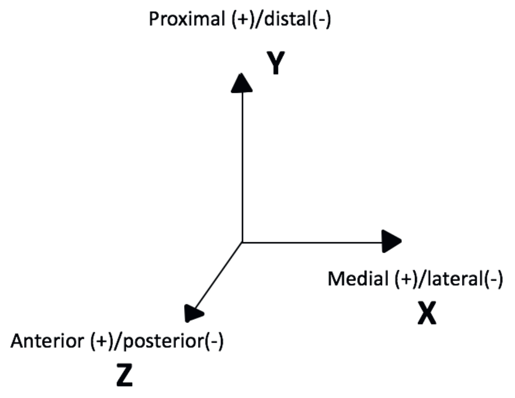


Figure 9. Illustration of the coordinate system defining translations of hip implant.

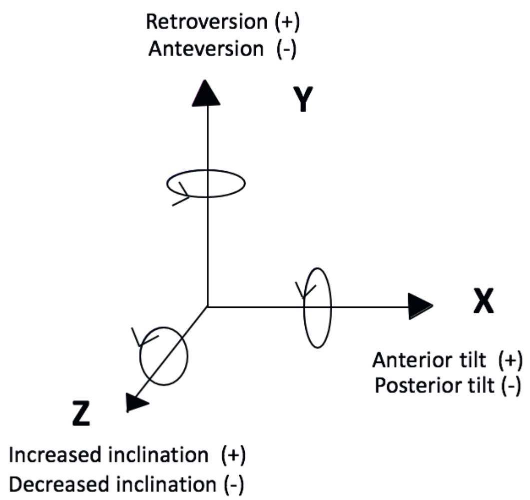


Figure 10. Illustration of the coordinate system defining rotations of the cup.

1.2.5 Model-based RSA

Model-based RSA (MBRSA) was developed for the purpose of evaluating the migration and wear of an implant without any attached markers (Valstar, de Jong et al. 2001, Seehaus, Emmerich et al. 2009). This technique uses three-dimensional surface models of implant components based on computer-aided design (CAD), reverse-engineered technologies or elementary geometrical shapes to compute the in-vivo migration or wear of an implant (Kaptein, Valstar et al. 2003). To determine implant motion, the scanned or reconstructed three-dimensional surface of the true implant models can be fitted to the contours of the implant projected on the RSA images and matched against the actual contours of the true implant. The three-dimensional surface model is translated and rotated by the pose-estimation algorithm until the best match between the actual and virtual contour is found (Kaptein, Valstar et al. 2004) *(Figure 11)*. This method requires information about the three-dimensional surface of each individual size used in the study. At present, it is uncertain whether it is necessary to scan each implant individually, due to small variations in cup size and surface structure between implants of the same size. The accuracy of the pose-estimation algorithm depends on both implant design and the accuracy of the surface model that is used (Seehaus, Emmerich et al. 2009).

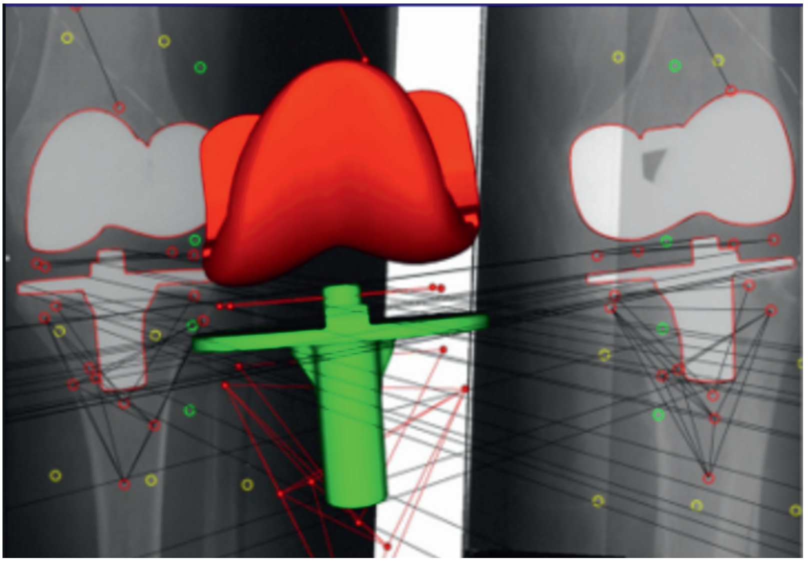


Figure 11. MBRSA based on scanned or CAD models.

Another way to determine the position of the cup is to measure its outlines and opening circle and model the cup as a hemisphere. This method has been described and has previously been used to study patients undergoing surgery with hemispherical porous coated cups with and without holes, pegs or screws (Valstar, Spoor et al. 1997, Valstar, de Jong et al. 2001, Borlin, Rohrl et al. 2006) *(Figure 12)*.

The accuracy and precision of the MBRSA method have been investigated in several studies and have been reported to be less accurate than conventional marker-based RSA but still an acceptable alternative for most clinical applications (Kaptein, Valstar et al. 2007, Hurschler, Seehaus et al. 2008).

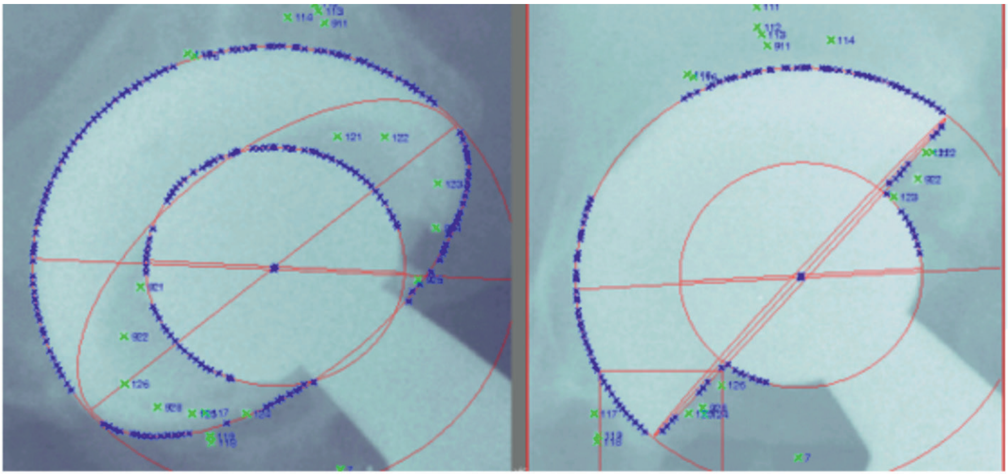


Figure 12. Marker-less RSA based on a hemispherical algorithm. The acetabular shell and femoral head are defined by edge detection (ellipses).

1.2.6 The accuracy and precision of RSA

The accuracy and precision of the calculations depend on several factors, such as the number of visible markers, marker scatter and marker stability. The accuracy is determined by comparing the closeness of agreement between measurements and an accepted reference value (Bragdon, Malchau et al. 2002). The precision of the method is the degree of closeness evaluated in repeated measurements (double examination), provided that the implant position is unchanged. For a double examination, the radiographic tubes, the calibration table and the examination table should be repositioned between the two examinations and the patient should leave the examination table and then be placed on the table in a similar position.

The precision is calculated as the difference between the double examinations under conditions of zero motion and is expressed as the 95% or 99% confidence interval of the standard deviation (SD) of the differences measured between the double examinations multiplied by the critical value (t) based on the T-table adjusted for the number of observations. In this thesis, we calculated the precision using the method proposed by Börlin et al. (Borlin, Rohrl et al. 2006) and Nebergall et al. (Nebergall, Rader et al. 2015). The accuracy and precision of RSA have been evaluated and reported in several in-vitro and clinical studies (Ryd, Yuan et al. 2000, Bragdon, Malchau et al. 2002, Valstar, Gill et al. 2005) . The reported precision measured with RSA varied between 0.05-0.50 mm for translations and 0.15° and 1.15° for rotations, partly depending on the direction analysed (Karrholm 1989).

1.3 Implant wear

Wear can be defined as damage to a solid surface, involving the progressive loss of material due to relative motion between surfaces in contact (McKellop, Hart et al. 2014). The wear process results in the generation of debris of various sizes, morphology, volume and number of debris particles. Ultrahigh molecular weight polyethylene (UHMWPE) debris particles of 0.3-10 μm in size have been identified as the most biologically active (Green, Fisher et al. 1998). The characteristics of wear particles may depend on the properties of the material, the loads and the sliding speed experienced at the contact surface (Billi, Benya et al. 2009). In joint replacement, the wear debris generated at the articulating surfaces can enter the tissues surrounding the prosthesis and cause adverse cellular reactions that may cause the aseptic implant loosening of the femoral or acetabular component in the long term (Fisher and Dowson 1991).

In THA, wear mainly occurs through three mechanisms; adhesion, fatigue and abrasion. The adhesive/abrasive wear of UHMWPE has been identified as the primary source of debris leading to periprosthetic osteolysis affecting the long-term performance of total joint implants. Radiation cross-linking of the material is one method to reduce this type of wear (Oral, Greenbaum et al. 2005).

Adhesive wear occurs when the atomic forces occurring between the materials in two surfaces during a sliding contact are stronger that the inherent material properties of either surface. During the articulation of the components, a varying amount of material is removed from the surface. In THA, the adhesive wear has been related to the plastic behaviour of polyethylene, which is the weaker of the two components and is therefore pulled off the surface. The removal of polyethylene results in the formation of fibrils and/or small pits. In acetabular components, when adhesive wear occurs on micron or submicron scale, the bearing surface can still appear highly polished to the eye.

Fatigue wear is cracking pitting and/or delamination caused by surface or subsurface cycling stress applied to the bearing surface. This process creates a subsurface plastic shear stress and deformation. Abrasive wear occurs when a hard material slides across a softer material, resulting in the removal of some parts of the material from the softer surface. This is called two-body abrasion. Another type of abrasion wear, so-called three-body abrasion, occurs when hard particles are trapped between two surfaces and scrape one or both surfaces or become embedded in the softer surface and scrape the opposite one. As the surfaces move relative to one another, the hard-foreign particles plough out material from the softer surface areas. Hard particles such as bone cement can cause damage to both the polyethylene surface and the metallic alloy femoral bearing counterface (Santavirta, Lappalainen et al. 1999).

In orthopaedic joint components, the UHMWPE is removed because the interactions of its chains are weak compared with those between the metal or ceramic atoms in femoral head components. It has been demonstrated that oxidative degradation results in the reduced abrasive wear resistance of the polyethylene and the formation of wear debris that may cause osteolysis (Besong, Tipper et al. 1998, Kurtz, Muratoglu et al. 1999).

Microscopic and macroscopic wear have been identified as two separate types of wear mechanism occurring during the sliding of UHMWPE on relatively smooth metallic and ceramic counterfaces. Microscopic wear is associated with the formation of small asperities of less than 0.2 μm in size on the smooth femoral counterface. The microscopic interaction is associated with producing larger polyethylene particles and related to the plastic deformation and strain accumulation of much larger surface asperities (Besong, Tipper et al. 1998). The macroscopic interaction is characterised by the material removal which supports large deformations due to surface and subsurface stress concentrations generated by the high asperity level of the polymer surface.

Wroblewski (Wroblewski, Siney et al. 1996) and Sychterz (Sychterz, Engh et al. 1997) described the wear pattern of polyethylene as a biphasic pattern consisting of a "bedding-in" phase, with high initial wear at the beginning, and a relatively slow "steady-state phase". This plastic deformation under load with time has been described as creep or the settling in of the liner. Polyethylene is a viscoelastic material with the ability to deform under the influence of load. The deformation is the result of complex molecular processes involving changes in the shape and relative position of the polymer chain. The creep is thought to play a role during the first six to twelve months after surgery and becomes negligible after that (Sychterz, Engh et al. 1999, Callary, Campbell et al. 2013). It has also been highlighted that the bedding-in phase is only caused to a small extent by abrasive wear and should be distinguished from true wear (removal of polyethylene particles) (Sychterz, Engh et al. 1999).

1.4 Surface coatings

Optimal material for bone in-growth was one of the most important issues in the development of uncemented fixation surfaces for total hips. The long-term survival of uncemented THA is dependent on early implant fixation securing early stability (Engh, Bobyn et al. 1987). The fundamental principle of metallic, uncemented designs is that a close, conforming and stable metal-bone interface is required to enable the successful osseointegration and longevity of the implant. The osseointegration and long-term success of a stable bone-implant or bone-cement interface are dependent on the mechanical stability of the implant relative to the host bone during the early healing period. The geometrical design of an implant surface may play an important role in affecting early implant stabilisation.

Surface modification is a method for improving bone response to an implant and increasing implant osseointegration. The in-growth of the components occurs when bone grows on a surface or into a porous surface. On-growth occurs when bone grows onto a roughened surface. The surface characteristics of an implant determine which occurs.

A variety of surface coatings are currently used to enhance the short- and long-term performance of implants by encouraging bone in-growth and providing enhanced fixation. These different surface treatments include fiber-mesh, sintered beads and plasma spray coatings (with or without hydroxyapatite) (Klika, Murray et al. 2007). Porous tantalum surfaces with increased porosity and optimal pore size compared with titanium fiber-mesh have recently been added to these.

Fiber-mesh coatings are metal pads attached to the titanium substrate using the diffusion bonding technique (Bourne, Rorabeck et al. 1994). The average pore size is 350 micrometres with a porosity of 35%. A sintered bead surface offers a porous coating of microspherical beads of various sizes made of either cobalt-chromium or titanium alloy. The beads are added to the surface at very high temperature (Pilliar 1983, Bourne, Rorabeck et al. 1994). The plasma spray technique involves mixing metal powders with an inert gas that is pressurised and ionised to form a high-energy flame. The molten material is sprayed onto the implant, creating a textured surface. The hot material impacts on the substrate surface and rapidly cools, forming a coating. In on-growth surfaces, 90% of the implant fatigue strength is retained, whereas only 50% is retained after diffusion bonding and sintering (Callaghan 1993, Bourne, Rorabeck et al. 1994). Calcium-phosphate compound, hydroxyapatite (HA), largely consists of calcium and phosphorus and is plasma sprayed directly onto the implant alone or over a porous coating. It is also often used to improve osteoconductivity and the growth of mineralised bone onto the implant surface (Cook, Thomas et al. 1988, Nakashima, Hayashi et al. 1997).

Acetabular components of porous tantalum (trabecular metal) have a porosity of approximately 75% to 85% and have been developed to provide a three-dimensional interlock of the bone and greater flexibility to minimize stress shielding in the acetabulum. This material is bone friendly with a high capacity for bone on- and in-growth, leading to excellent implant fixation to the bone. Trabecular metal has advantages over conventional porous metals such as titanium, including a high coefficient of friction against bone, a low modulus of elasticity, high volume porosity and excellent biological potential for fixation (Christie 2002, Bobyn, Poggie et al. 2004).

Coatings should improve the mechanical properties of the contact surface without changing the bulk materials (Lappalainen and Santavirta 2005). They should have high resistance to delamination and protect the substrate from corrosion. Coatings can act as an effective barrier to minimise the release of ions contributing to tribo-corrosion. They can also increase the hardness and reduce friction and wear rate, if supplied with excellent surface finishing.

1.5 Cup fixation

Periprosthetic bone resorption or osteolysis around a hip prosthesis is one of the most important factors for the maintenance of long-term durability after THA (Maloney, Jasty et al. 1990). The presence of wear particles primarily from the polyethylene bearing surfaces has been identified as the major source responsible for the eventual development of periprosthetic osteolysis (Harris 1994). It is thought that, by reducing polyethylene wear particles, the prevalence of osteolysis will be reduced and, subsequently, a better long-term outcome in THA can be expected (Cooper, McAllister et al. 1992, Stilling, Rahbek et al. 2009).

The initial implant fixation has a profound influence on the risk of late loosening (Kobayashi, Donnelly et al. 1997). Fixation has traditionally been achieved using bone cement (polymethylmethacrylate or PMMA). The late failure of the fixation of cemented acetabular components led to attempts to improve implant design, improvements in cementing techniques and the development of uncemented acetabular components with the goal of reducing aseptic loosening rates in THA.

The outcome for uncemented THA was poor in the 1960s, due to the smooth surface of implants for which strong adherence to the bone could not be expected. The pattern of osteolysis around the uncemented implants depends on their osseointegration to the bone, which relies on early stability, is influenced by the loads applied to it, the bone-implant interface that develops and the quality and quantity of the surrounding bone (Pilliar, Lee et al. 1986, Curtis, Jinnah et al. 1992, Widmer, Zurfluh et al. 2002). It has been argued that the design of uncemented acetabular cups, such as porous surface coatings, plays a major role in increasing implant stability, enhancing bone in-growth and reducing the risk of loosening (Stilling, Madsen et al. 2011). The primary fixation of uncemented acetabular cup designs is essential to provide stability and it is based on press-fitting the implant into the bone, sometimes with the addition of cancellous screws and the use of a threaded component which can be screwed into the bone (Snorrason and Karrholm 1990).

There are three types of surgical fit at the bone-implant interface; (1) interference, the diameter of the implant is larger than the defect, (2) line to line, the outer diameter of the implant and the diameter of the defect are equal and (3) gap fit, the diameter of the implant is smaller than the defect. The secondary fixation is achieved by bone growth to fill the gap between the bone and the implant surface. Failure of the primary and/or secondary fixation may result in the loosening of the uncemented implants within the first two years after surgery (Hansen and Stilling 2013).

The pattern of osteolysis around uncemented acetabular components depends on whether or not bone in-growth has occurred. If the component is not stable and in-grown, a slowly growing lesion with sclerotic margins at the implant-bone interface, probably as a result of micromotion, may cause loosening of the implant. A component is considered to be loose if it is surrounded by a complete radiolucent line at the bone-implant surface or if the component has migrated (Massin, Schmidt et al. 1989). Radiolucent lines are defined as areas in which the porous surface of the acetabular component is not in contact with the bone. On a radiograph, this displays as a periprosthetic zone of radiolucency around the bone-implant interface. The determination of whether an implant has bone in-growth is somewhat difficult on radiographs. An uncemented acetabular component that is radiographically stable is often assumed to be in-grown, although this may not be the case. Implants in which bone in-growth does not occur will most probably be subjected to late migration. The most reliable radiographic signs of loosening in uncemented cups are the migration or tilting of the component (Manaster 1996). Excessive micromotion at the bone-implant interface may promote fibrous tissue formation instead of the desired bone in-growth and may subsequently result in early implant loosening (Pilliar, Lee et al. 1986).

In a matched-pair study of fiber-mesh hemispherical press-fit cups with and without a tricalcium-phosphate (TCP) coating, Thanner et al. (Thanner, Karrholm et al. 1999) observed a higher frequency of postoperative gaps in zone II and a higher rate of gap disappearance but less rotational movement along the longitudinal axis for the cups coated with an HA/TCP coating as compared with uncoated cups. The gap disappearance was interpreted as the formation of new bone or remodelling due to an enhanced osseointegration process with the HA/TCP coating. In a study of porous-coated hemispheric cups fixed with screws, Udomkiat et al. (Udomkiat, Wan et al. 2001) found that progressive radiolucencies or new radiolucency greater than 1 mm in width were predictive of acetabular cup loosening. They also reported that there was no association between cup loosening and postoperative gaps. In 2002, Gruen et al. (Gruen, Poggie et al. 2005) evaluated serial radiographs of porous tantalum monoblock acetabular cups in terms of cup stability and osseointegration at a mean follow-up of 34 months. They found that 84% of the postoperative gaps had disappeared at the last follow-up. They also found no progression of any postoperative gaps, no evidence of radiolucencies and no revision due to loosening.

Unlike the overwhelming amount of survival data on cemented acetabular components, radiographic evaluations of the biological fixation of uncemented acetabular components have been relatively few in number and poorly studied and need to investigated in more detail in order to acquire more knowledge of implant survival and confirmation of the extent of bone in-growth. Evaluations of sequential radiographs are important for detecting progressive radiolucent lines and radiolucent lines greater than 1 mm in thickness two years postoperatively, which is an indication that the cup is likely to loosen.

1.6 Radiolucency

Conventional plain radiographic examination is widely used, because it is readily available at a low cost, simple and safe. The radiographic evaluation of the hip provides information on the type of prosthesis used, component positioning and implant fixation. Routine radiographs remain the most important diagnostic imaging modality in the evaluation of THA. The availability of follow-up examinations will be sufficient to assess whether or not the implant and its host bone have undergone any changes over time.

Standards radiographs include anterior-posterior (AP) and lateral views of the hip and an AP view of the pelvis. To improve diagnostic accuracy and comparisons between the examinations, the film focus distance and the exposure rate should be as standardised as possible.

The diagnosis of loosening of acetabular components has been defined as migration (Mjoberg, Brismar et al. 1985). Over time, this motion will result in secondary changes such as the development of radiolucent lines. A certain number of radiolucent lines can probably develop without the presence of any migration. Periprosthetic radiolucencies can occur adjacent to both acetabular and femoral components and are identified in both cemented and uncemented THA (Tigges, Stiles et al. 1994, Weissman 1997). Examinations of radiolucencies or osteolytic lesions at the bone-implant interface have been facilitated by a method using which the acetabular component is divided into defined zones. The most widely used radiographic classification method for the examination of radiolucencies around the acetabular component in THA was originally described by DeLee and Charnley (DeLee and Charnley 1976). To describe the location of various radiolucencies and osteolytic lesions, standard zones have been proposed. The acetabulum is divided into three equal zones labelled I (superior/lateral), II (central) and III (inferior/medial) on anteroposterior views *(Figure 13)*. Each region is normally inspected for the presence of radiolucency around the bone-cement or the bone-implant interface.

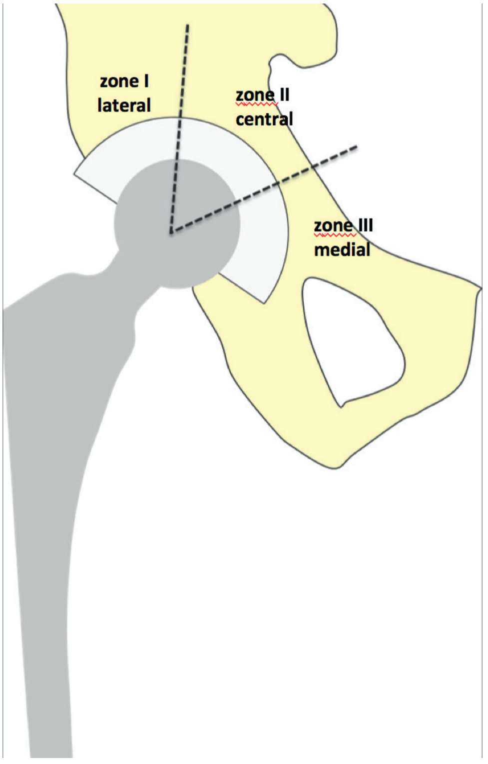


Figure 13. Zones modified after Delee-Charnley. With permission from Ola Rolfson.

The loosening of cemented acetabular components usually begins at the cement-bone interface. The problem of radiographic demarcation at the bone-cement interface of cemented Charnley cups was recognised in 1962 and it was described as a dark line between the cement and the bone of the acetabulum. In 1983, Dorr et al. (Dorr, Takei et al. 1983) defined the radiographic demarcation as a continuous radiolucent line at least 2 mm in width along all three zones at the bone-cement interface. In 1988, Hodgkinson et al.

(Hodgkinson, Shelley et al. 1988) further characterised the relationship between radiolucencies and loosening by demonstrating that gaps larger than 1 mm involving the lateral two thirds of the cup were predictive of failure. They also characterised the relationship between radiolucency and loosening by classifying the demarcation into five categories; no demarcation (0), demarcation of one third of zone I (1), demarcation of one third of zones I and II (2), complete demarcation in all three zones (3) and cup migration and cement fracture (4). Several studies have reported that the absence of postoperative demarcation at the acetabular cement-bone interface reduces the risk of aseptic loosening (Ranawat, Deshmukh et al. 1995, Garcia-Cimbrelo, Diez-Vazquez et al. 1997, Flivik, Sanfridsson et al. 2005).

In uncemented acetabular components, the same basic principles of radiographic assessment apply. The two predictors of clinical loosening are progressive radiolucency and migration. In uncemented cups, a gap is defined as the region in which the surface of the acetabular component is not in contact with the bone on the immediate postoperative radiographs. A radiolucent line is defined as space at the bone-implant interface that might develop on subsequent radiographs in areas where no such radiolucency previously existed. Since the bone-implant interface in uncemented components is a continuous biological interface, the development of partial radiolucencies in one or two zones is regarded as fairly common. Udomkiat et al. (Udomkiat, Wan et al. 2001) established five criteria for identifying the radiographic loosening of uncemented components; (1) radiolucent lines that initially appeared after two years, (2) the progression of radiolucent lines after two years, (3) radiolucent lines in all three zones, (4) radiolucent lines 2 mm or wider in any zone, or (5) migration. The same authors also reported that postoperative gaps were not associated with the subsequent presence of radiolucent lines, progressive radiolucencies or loosening of the acetabular cup. Prosthetic migration or/and progressive radiolucent zones are regarded as the most common radiographic signs of component loosening in both cemented and uncemented THA.

1.7 Polyethylene (PE)

In 1898, the German chemist, Hans von Pechmann, discovered polyethylene by accident while heating diazomethane. He created a new waxy substance that was recognised by long –CH2– chains and was termed polymethylene by Eugen Bamberger and Friedrich Tschirner. The first industrially practical polyethylene synthesis was discovered in 1933 and it was not until 1935 that a reproducible high-pressure synthesis for polyethylene was developed. It became the basis for the start of its industrial production in 1939.

Ultrahigh molecular weight polyethylene, UHMWPE, was introduced by Sir John Charnley in the early 1960s. Four decades after its introduction, this material is still the most frequently used bearing surface in total joint replacements. UHMWPE is a linear semi-crystalline polymer which can be described as a two-phase composite of crystalline domains embedded within an amorphous matrix (Oral, Malhi et al. 2006, Oral and Muratoglu 2007). The crystalline phase contains chains folded into highly oriented lamellae that are 10-50 nm thick and 10-50 μm long. The lamellae are randomly oriented within the amorphous phase with tie molecules linking the interconnected lamellae to one another, providing resistance to mechanical deformation (Sobieraj and Rimnac 2009). UHMWPE has many excellent mechanical properties including creep resistance, strength and wear resistance. Since its introduction, many attempts have been made to modify UHMWPE and improve its clinical performance. One unsuccessful attempt was the development of Poly II in the 1970s by blending UHMWPE with carbon fibres within the matrix of polyethylene. After implantation, many patients demonstrated osteolysis and the mechanical failure of their tibial bearing surface, probably due to the poor compatibility of carbon fibres with the UHMWPE matrix (Wright, Astion et al. 1988, Busanelli, Squarzoni et al. 1996).

In 1991, a modified UHMWPE named Hylamer was introduced by DePuy-DuPont Orthopaedics joint venture (Newark, DE, USA) as an alternative to conventional polyethylene. This modified UHMWPE was reheated under pressure, leading to the formation of extended regions of folded chains, and was expected to have less creep, better strength and less wear (Schmidt 1994). The clinical reports on Hylamer liners were mixed, from an equal to a greater incidence of excessive wear compared with conventional UHMWPE (Wright, Astion et al. 1988, Busanelli, Squarzoni et al. 1996, Chmell, Poss et al. 1996). Other studies reported high rates of wear and failure of Hylamer liners and it was decided to discontinue the use of Hylamer liners (Iwase, Warashina et al. 2003, Wroblewski, Siney et al. 2003). In 2002, Norton et al. reported the catastrophic early failure of a cemented THA using Hylamer and a zirconia ceramic head (Norton, Yarlagadda et al. 2002).

1.7.1 Highly cross-linked polyethylene (XLPE)

It has been demonstrated that the oxidative degradation of UHMWPE reduces its mechanical properties and leads to the formation of wear debris, which has been identified as the main factor responsible for osteolysis and implant loosening (Bloebaum, Zou et al. 1997, Kurtz, Muratoglu et al. 1999, Dumbleton, Manley et al. 2002, Brach Del Prever, Bistolfi et al. 2009). Many efforts have been made to develop improved orthopaedic materials with an extended service life. Investigations were made of the effect of radiation sterilisation and subsequent oxidative degradation on the structure and mechanical properties of the original UHMWPE, as well as the improvement of the material by cross-linking or the addition of antioxidants.

Conventional UHMWPE is a type of polyethylene for which no cross-linking process is performed. The molecular structure of UHMWPE changes due to oxidative degradation during gamma-irradiation sterilisation in the presence of air. The oxidation of UHMWPE is due to the interaction between free radicals produced by the irradiation of the polyethylene and leads to a reduction in mechanical properties, including wear resistance. Modified sterilisation including gamma sterilisation in a low-oxygen or inert-gas environment was developed to prevent oxidation and its effects on wear and the mechanical properties of UHMWPE. The potential for oxidation was reduced or eliminated due to the lack of oxygen during shelf storage. However, the free radicals created within the polymer still remained and in-vivo oxidation was still possible (Kurtz, Hozack et al. 2006, Medel, Kurtz et al. 2009).

Irradiating polyethylene to create cross-linking and reduce wear was established by Grobbelaar (Grobbelaar, du Plessis et al. 1978) and Oonishi (Oonishi, Kuno et al. 1997). Highly cross-linked polyethylene (XLPE) with the aim of reducing polyethylene wear and wear debris became available in 1998 (McKellop, Shen et al. 1999). Cross-linking occurs when free radicals on different polymer chains in the amorphous phase recombine, forming a chemical covalent bond between the chains (Oral and Muratoglu 2007). The last of the free radicals trapped inside crystalline regions are unable to recombine and are active for a long period of time and consequently increase the risk of long-term oxidative degeneration(Premnath, Harris et al. 1996, Cole, Lemons et al. 2002, Baker, Bellare et al. 2003).

One approach to remove residual radicals and improve resistance to the continuing oxidation of the polyethylene was thermal treatment, a method utilised in the so-called first generation of XLPEs. The thermal treatment could consist of re-melting the polymer below or above its melting point (150°). Above the melting temperature, all crystals are eliminated, the trapped free radicals recombine to form cross-linking and the polyethylene becomes oxidatively stable (Muratoglu, Bragdon et al. 2001). However, melting also decreases the crystallinity and lamellar thickness of the irradiated polymer, which causes a reduction in mechanical properties and fatigue strength (Oral, Wannomae et al. 2004, Pruitt 2005).

An alternative approach is to anneal the polymer below melting point after irradiation which reduces the concentration of residual free radicals but does not eliminate them all (Shen and McKellop 2002). Annealing does not adversely affect crystallinity. This approach is also associated with reduced oxidation resistance as compared to heating above the melting temperature (Oral and Muratoglu 2007). UHMWPE materials that have been exposed to large radiation doses and are then thermally stabilised are, as indicated above, known as first-generation highly cross-linked polyethylene.

Wear resistance is directly related to increased cross-link density. Cross-linking can be increased by exposing the material to larger radiation doses (Muratoglu, Bragdon et al. 1999). The gamma-sterilised UHMWPE used before the introduction of XLPE is exposed to radiation doses between 25 and 40 kGY, while highly cross-linked UHMWPE is exposed to doses ranging between 50 and 120 kGy (Gomez-Barrena, Medel et al. 2009).

Second-generation highly cross-linked polyethylene was developed with the aim of improving the efficiency of residual free radical elimination. New processing methods including sequential irradiation/annealing and the incorporation of vitamin E were developed in order effectively to reduce free radicals without affecting the mechanical properties of the material

(Kurtz, Mazzucco et al. 2006). Sequential irradiation and annealing has been introduced as a solution to the more effective reduction of free radicals without melting the material and without adverse changes in crystallinity. The material is irradiated and annealed in sequential steps; firstly, irradiated at a low dose of 30 kGy and then annealed for a given period of time. This process is repeated three times to achieve an irradiation dose of 90 kGy. It is believed that this process increases the amount of cross-linking and provides more chain mobility for additional cross-linking without changing the crystalline structure of the polyethylene (Dumbleton, D'Antonio et al. 2006).

Highly cross-linked polyethylene with the addition of antioxidants such as vitamin E was developed to achieve superior oxidation stability without affecting the mechanical properties of the UHMWPE. Vitamin E (α-tocopherol) is incorporated into UHMWPE either by diffusion or by blending followed by irradiation (Oral, Wannomae et al. 2007). Vitamin E serves as a free radical scavenger within the polyethylene structure. The free radicals generated by the irradiation process react with oxygen and start a chemical reaction. This antioxidant donates its own hydrogen atom from the OH group on its ring structure to react with the free radicals and interrupt this reaction (Oral, Ghali et al. 2012).

Hindered phenol antioxidant, pentaerythritol tetrakis [3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate], under the trade name of COVERNOX™ and developed by DePuy Synthes Joint Reconstruction, is an alternative antioxidant that is blended with UHMWPE resin powder prior to consolidation (Chen, Hallab et al. 2016). The antioxidant protects the polymer during consolidation, during radiation cross-linking, on the shelf before implantation and in vivo after implantation (Oral, Neils et al. 2014). It is claimed by the manufacturer that COVERNOX is extremely efficient at bonding with free radicals and preventing oxidation.

Third-generation highly cross-linked polyethylene involves a high degree of cross-linking by high-energy irradiation, followed by thermal stabilisation. AOX™ antioxidant polyethylene is a so-called fourth-generation polyethylene developed by DePuy which is available for total knee arthroplasty (TKA). In the manufacture of the AOX polyethylene, the annealing or re-melting process is eliminated. The hindered phenol antioxidant, COVERNOX, is added to the UHMWPE powder by diffusion. The compounded powder is then consolidated into either compression-moulded sheets or ram-extruded bars. The polyethylene is then machined, vacuum-foil packaged and irradiated.

1.8 Pelvic tilt

Acetabular component orientation (inclination and anteversion) during THA is essential to avoid complications such as dislocation, impingement and accelerated bearing wear, which can lead to osteolysis around the implant and cause loosening (Lewinnek, Lewis et al. 1978, Yoshimine 2006, Wan, Boutary et al. 2008). Dislocations are one of the most frequent complications after THA, leading to revision surgery (Woo and Morrey 1982, Hedlundh, Ahnfelt et al. 1996). Posterior dislocations are reported to occur more often than anterior dislocations, which may account for just about 20% of all dislocations (Dorr, Wolf et al. 1983, Di Schino, Baudart et al. 2009).

Despite the correct positioning of the acetabular component, the risk of dislocation may vary due to factors such as the characteristics of the patients, implant design and surgical technique (Amstutz, Lodwig et al. 1975, Matsushita, Nakashima et al. 2009). Pelvic tilt is defined as the angle between the anterior pelvic plane (APP) and a vertical line in the standing position. The rotation of the pelvis leads to anterior tilt (where the upper portion of the pelvis tips forward) and posterior tilt (upper portion of the pelvis tips backwards) (Lazennec, Charlot et al. 2004). Pelvic tilt can affect the functional orientation of the acetabular component in the sagittal plane of the body as compared with its anatomical position in the pelvic bone. There are variations in the position of the pelvis from supine to the standing position (Eddine, Migaud et al. 2001, Shon, Gupta et al. 2008), which changes the acetabular cup version dynamically.

The position of the acetabular components after surgery with THA is commonly evaluated on AP radiographs with the patients in a supine position. However, most daily living activities are performed in an upright position. There is also a difference in the orientation of the pelvis (pelvic tilt) between supine and standing positions and consequently that of the acetabulum. Standing radiographs may therefore represent a more natural functional pelvic position and may be more clinically relevant in the evaluation of changes in the position of the acetabular component over time. In addition to plain radiographs, computed tomography scans (CT) have also been used to measure the orientation of the acetabular components after THA. It has been reported that CT is more accurate for measuring anteversion (Olivecrona, Weidenhielm et al. 2004, Lin, Lim et al. 2008). However, in clinical practice, plain radiographs are the most important tool for evaluating cup position.

The position of the cup is determined during the operation, but the pelvic tilt might change when the patient is mobilised, partly because of the release of contractures during the operation and partly because of the subsequent stretching of the soft issue with time. These changes might influence the validity of determinations of cup position based on supine radiographs. In contrast to conventional radiography, RSA enables accurate evaluations of changes in the pelvis between different positions, such as supine and standing and over time. Detailed studies of pelvic tilt between supine and standing and over time may be of value in interpreting determinations of the acetabular component after THA using conventional radiography. Increased knowledge in this field may be of value in optimising the outcome of hip arthroplasty and may also facilitate our understanding of issues related to impingement and instability after THA. This information could be used to further refine the goal for optimal cup orientation on an individual patient basis.

02 AIMS

02

AIMS

I. To study the early-term femoral head penetration of vitamin E-incorporated highly cross-linked polyethylene (E1) compared with liners made of compression-annealed polyethylene (ArComXL) in a randomized, clinical study.

II. To study the liner penetration rate of E1 compared with ArComXL with the emphasis on changes occurring between two and five years after THA.

III. To evaluate the influence of cup design on the precision of model-based RSA (MBRSA) in four uncemented cups using conventional marker-based RSA as a reference.

IV. To evaluate the change in pelvic tilt angle (PTA) in the supine position over time and between supine and standing positions up to seven years after THA.

V. To investigate the fixation of cups coated with a porous titanium layer (Regenerex) using a porous plasma-sprayed cup (RingLoc) as a reference and also to evaluate any possible associations between the occurrence of progressive radiolucent lines and cup migration up to five years after THA.

03 PATIENTS

03

PATIENTS

Studies I-II

Between 2008 and 2010, sixty-one patients (seventy hips), aged 20-75 years, with non-inflammatory hip osteoarthritis, were recruited. All the participants received an uncemented RingLoc cup and an uncemented Echo Bi-Metric stem with a 32 mm Co-Cr head. The patients were randomised using closed envelopes to receive either a compression-annealed XLPE liner, ArComXL, or a vitamin E-diffused XLPE (E1). The flow of patients in study I and II are presented in *Figure 14*. There was no difference between the groups regarding the size and the thickness of the liner. The exclusion criteria were (1) inflammatory arthritis, (2) cortisone or chemotherapy treatment and (3) known osteoporosis or osteomalacia. Baseline patient demographics are presented in *Table 1*. Nine patients (18 hips) with bilateral hip disease were included. Bilateral cases underwent surgery on the same day (n=4) or within five to 18 months (n=5) and were randomised at the first operation. The contralateral side underwent surgery with the type of polyethylene that was not used on the first side. In Study I, the patients were followed up on four occasions (postoperatively, at three months, one and two years). At two years, three patients (three hips) were lost to follow-up (one left the study (not revised), one moved abroad and the third was revised due to stem subsidence). All three patients (three hips) were randomised to liners made of ArComXL. In Study II, the patients were followed up postoperatively, at three months, one, two and five years after the surgical procedure. The patients in Study II were recruited from the same cohort. At five years, an additional four patients were lost to follow-up (one left the study due to sickness and three left the study at their own request). Three of the lost patients were included in the control group, ArComXL, and one in the study group (E1). So, at five years, a total of seven patients were lost to follow-up (six patients in the ArComXL group and one in the E1 group).

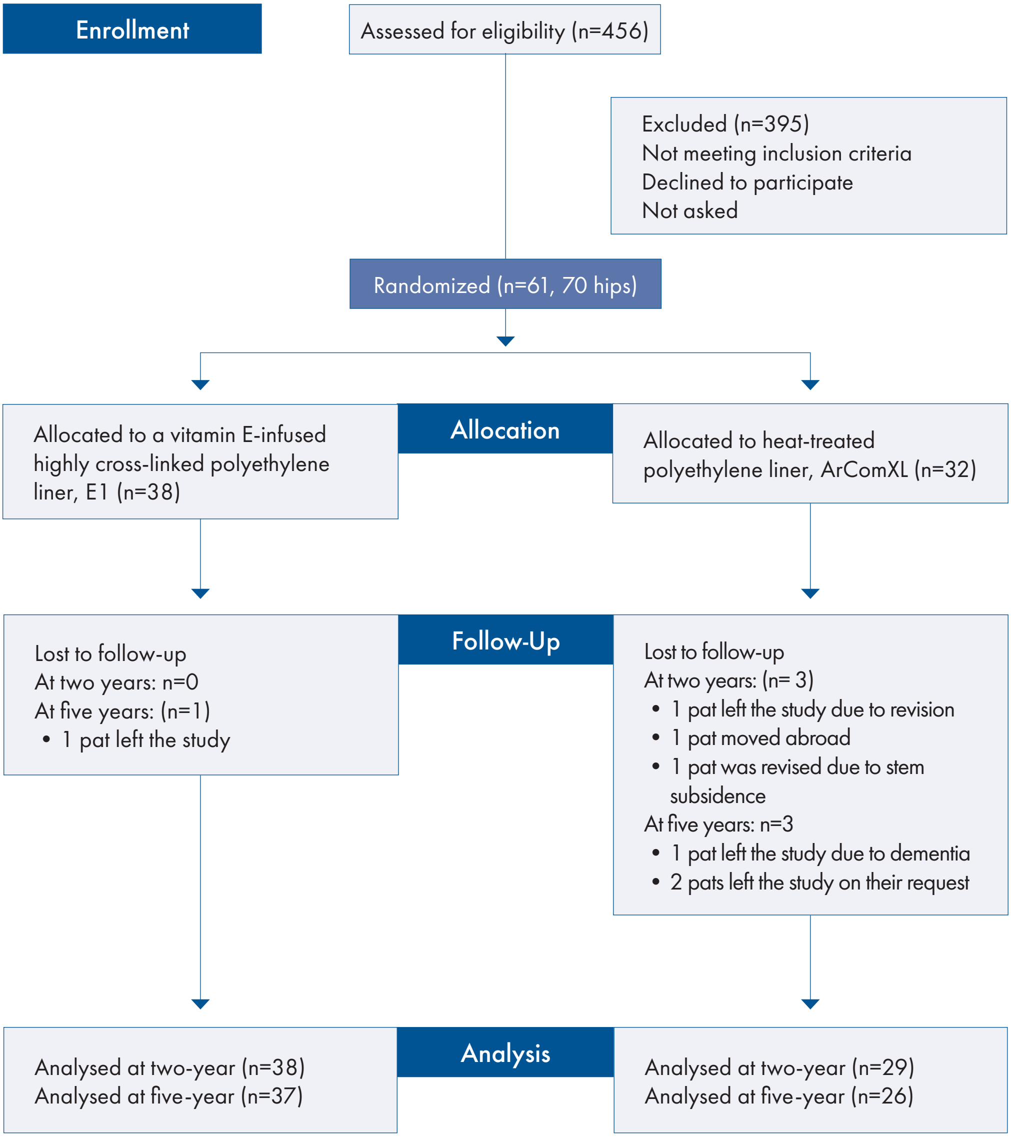


Figure 14. Flowchart of patients included in study I-II.

Table 1. Baseline demographic data in study I-II.

	E1 (n=38)	ArComXL (n=32)
Gender* Male Female	 22 16	 15 17
Age† (year)	58 (32 to 75)	58 (36 to 67)
Weight† (kg)	75 (55 to 114)	79 (54 to 120)
BMI† (kg/m^2)	25 (19 to 38)	27 (19 to 36)
Diagnosis of osteoarthritis* Primary Secondary	 30 8	 25 7

*Values are presented as the number of hips.
† Values are presented as median (range).

Polyethylene inserts

Study group (E1)

The polyethylene in the study group is produced in an isostatic compression-moulding process to manufacture bars from UHMWPE powder. The material is irradiated with a dose of 100 KGy and then infused with vitamin E below the melting temperature (120°). An inert gas oven is used to homogenise the vitamin E-coated blocks at 120°C, which allows the vitamin E to diffuse through the thickness of the polyethylene. Finally, the E1 liners are machined and sterilised by gamma radiation (25-40 KGy).

Control group (ArComXL)

ArComXL is a so-called second-generation XLPE developed in 2005 (Kurtz, Mazzucco et al. 2006). During manufacture, polyethylene bar blocks are irradiated with a dose of 50 KGy and then pre-heated below the melting temperature (130°). The next step is a low-heat process termed "solid state deformation", which extinguishes the residual free radicals without sacrificing the mechanical strength of the material. The polyethylene bar stock undergoes stress-relief processing by heating it to a temperature that is lower than annealing (130°). Acetabular components are then machined from the bar stock and finally gas plasma sterilised.

Study III

Eighty patients (80 hips) with a mean age of sixty (range 32-86) years with primary or revision cups were selected from four different prospective clinical studies and included in the current study. All the patients had undergone hip replacement surgery between 2003 and 2010. The inclusion criterion was radiostereometric examinations with at least three well-defined markers in each segment, corresponding to the acetabular bone and the cup with a scatter corresponding to a condition number (CN) less than 125 and a mean error of rigid body fitting (ME) corresponding to at most 0.35 mm. All the patients were studied on two occasions, postoperatively (double examinations) and at the two-year follow-up, in the supine position. Four types of uncemented cup with 20 patients (hips) in each group were analysed. In the first group (20 revision hips), all the patients had a cup fitted with a titanium fiber-mesh (Trilogy, Zimmer, Warsaw, USA). The second group (20 revision hips) had TMT cups with cemented liners (Trabecular Metal, Zimmer, Warsaw, USA). The third group (20 primary hips) had cups with a porous plasma spray coating (RingLoc, Biomet, Inc., Warsaw, USA) and the fourth group (20 primary hips) consisted of cups with a grit-blasted surface with a hydroxyapatite coating (ABG, Stryker).

Study IV

One hundred and six patients (106 hips) were selected from four different studies. All the patients underwent THA and were included in prospective clinical RSA trials evaluating cup migration and femoral head penetration at Sahlgrenska University Hospital between 1998 and 2005 *(Figure 15)*. The selection criteria were patients who underwent cemented or uncemented THA for primary or secondary osteoarthritis (OA) of the hip and who were scheduled for follow-up including supine and standing examination on least at two occasions (at six months and seven years after surgery), in addition to the supine postoperative RSA examination. The purpose of examining patients in supine and standing positions was initially to evaluate any potential differences in femoral head penetration between these two positions (Bragdon, Thanner et al. 2006). Patients demographic data are presented in *Table 2*.

Of 106 patients, 42 had a unilateral hip prosthesis, 16 patients underwent surgery with a hip prosthesis on the contralateral side during the follow-up period of seven years and 48 patients had bilateral hip prostheses when the study was initiated. In this latter group, the hip with the most optimum scatter and visibility on stereoradiographs of tantalum markers in the pelvis was selected.

To determine the condition of the contralateral hip in patients with a unilateral prosthesis at the last follow-up (n=42), conventional radiographs were reviewed. They revealed that 14 patients had a normal hip and 28 suffered from OA on the contralateral side. We also reviewed the medical records of all patients regarding the incidence of low-back pain. A history of low-back pain was considered to be or to have been present if the patients had visited our department because of this condition during the follow-up or had complained of low-back pain at any follow-up visit after the hip operation. These problems were documented in 28 of the 106 patients during the follow-up period. None of the patients had undergone spinal fusion surgery.

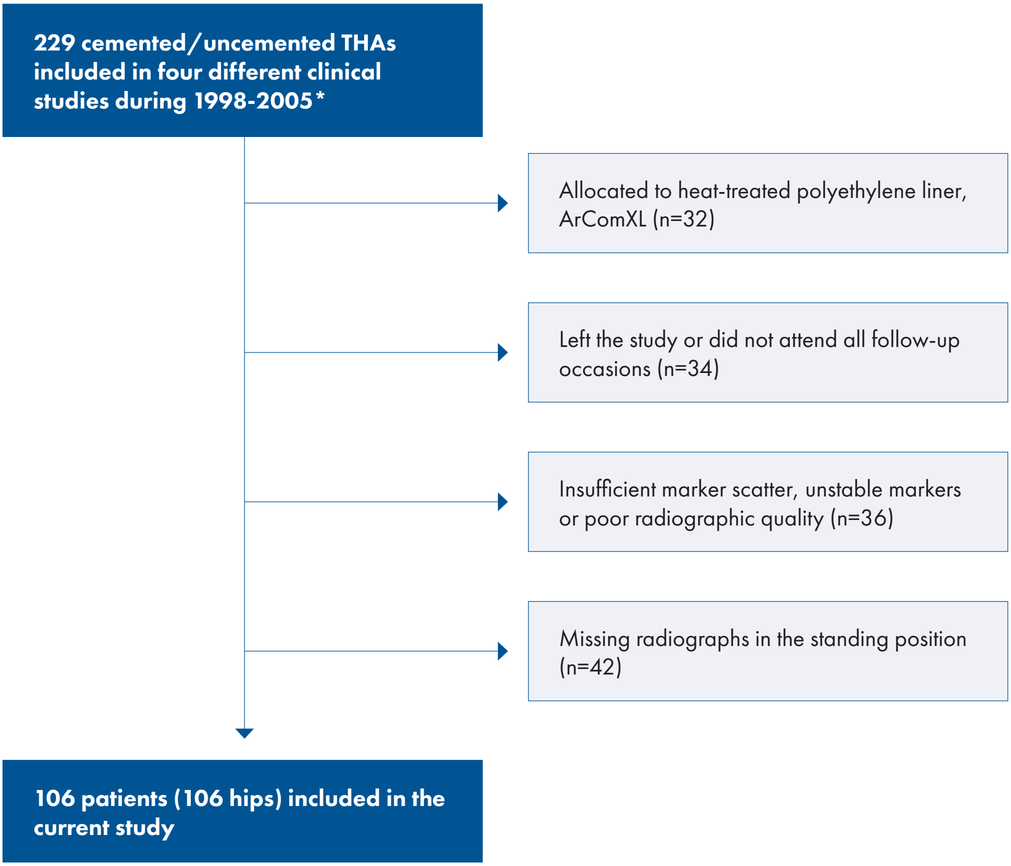


Figure 15. Flow chart of patients in study IV.

***The four studies included:**

(1) 61 cemented THAs in an evaluation of polyethylene quality (Digas et al.2003)

(2) 32 patients operated bilaterally with uncemented cups with different type of polyethylene quality on the two sides (Digas et al. 2004) The hip with most well-scattered pelvic markers include.

(3) 52 cemented THAs in an evaluation of two types of bone cement (not published previously).

(4) 84 cemented THAs in a study aimed to evaluate different types of stem design (Tien et al. 2010).

Table 2. Baseline demographic data of patients in study IV.

Gender Male Female	 39 67
Age (years)	59 (30-78)
Weight (kg)	75 (51-112)
Height (cm)	170 (155-195)
BMI (kg/m²)	26 (19-35)
Bilateral THA No Yes During the follow-up	 42 48 16
Low back pain No Yes	 78 28
Contralateral hip at 7 years Normal Osteoarthritis THA	 14 28 64

Values are presented as mean (range) or numbers.

Study V

Ninety-two patients (92 hips) with non-inflammatory osteoarthritis who received uncemented primary THA at two centres: Sahlgrenska University Hospital, Gothenburg, Sweden, and Massachusetts General Hospital, Boston, MA, USA, between 2008 and 2010, were selected and included in this cohort. The flow of patients in the study is presented in *Figure 16*. The patients were initially part of a multicentre follow-up study aiming to evaluate femoral head penetration of vitamin E-diffused XLPE (E1) in vivo using radiostereometry. The main inclusion comprised patients with complete RSA examinations on two occasions (postoperatively and at five years) after surgery. Thirty-nine patients (39 hips) underwent surgery at Massachusetts General Hospital in Boston, USA, with an uncemented porous titanium acetabular shell (Regenerex) and an uncemented femoral stem (Taperloc) with a 32 mm Co-Cr femoral head. In all 39 cases, a vitamin E-diffused XLPE (E1) liner was used. Fifty-three patients (53 hips) had undergone surgery at the Department of Orthopaedics, Sahlgrenska University Hospital in Gothenburg, Sweden. All these patients had received an uncemented RingLoc cup and an uncemented Echo Bi-Metric stem with a 32 mm Co-Cr head randomised to either a compression-annealed XLPE liner (ArComXL) or a vitamin E-diffused XLPE (E1) liner. All the components were manufactured by Zimmer Biomet

Holdings, Inc, Warsaw, IN, USA. In the total material, there were 57 males (62%) and 35 females (38%) with a median age of 60 years (range 31-82 years). Patients with a contralateral total hip (n=12) were only included with the first operated side. Additional screw fixation was used in 46 (50%) patients. Of these, 18 were RingLoc and 28 Regenerex *(Table 3)*.

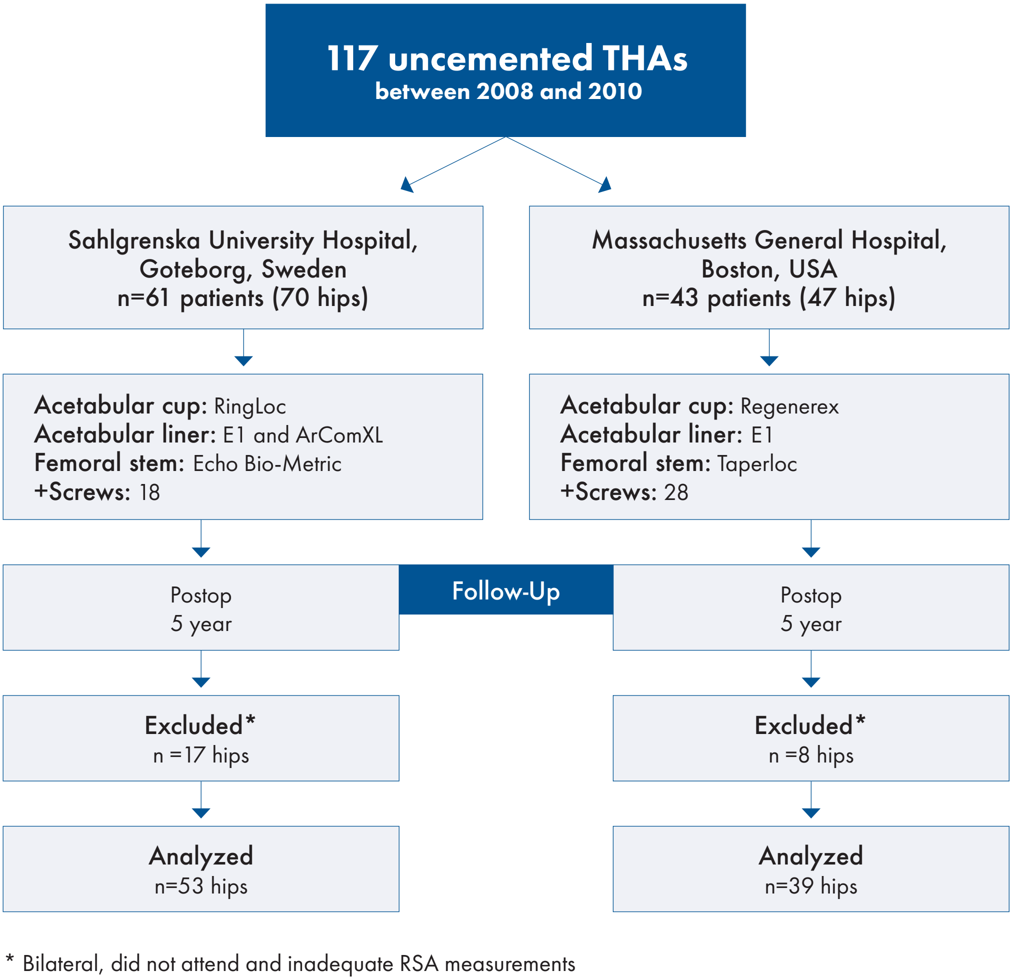


Figure 16. Flow chart of patients included in study V.

Table 3. Baseline demographic data in study V. Values are presented as median (range) or numbers.

	Median (range) or numbers
Center Massachusetts General Hospital, Boston, USA Sahlgrenska University hospital, Goteborg, Sweden	 39 53
Gender Male Female	 57 35
Age (years)	60 (31-82)
Weight (kg)	85 (54-120)
Height (cm)	175 (155-193)
BMI (kg/m^2)	27 (19-40)
Diagnosis Primary Osteoarthritis Secondary Osteoarthritis	 74 36
Acetabular cups Regenerex RingLoc	 39 53
Acetabular liners E1 ArComXL	 72 20
Femoral stems Taperloc Echo Bio-Metric	 39 53
Cup Size	56 (50-62)
Head Size (mm)	32
Regenerex + Screws - Screws	 28 11
RingLoc +Screws - Screws	 18 35

Implants

Two different types of acetabular shell were used in this study; Regenerex (Zimmer Biomet, Warsaw, IN) and RingLoc (Zimmer Biomet, Warsaw, IN). The porous titanium implant surface on Regenerex has an average porosity of 67%, with a pore size ranging between 100 and 600 μm (average 300 μm). The porous plasma-sprayed hemispherical coating on the RingLoc cups has an average porosity of 45%, with a pore size ranging between 100-1000 μm (average 250 μm) (Small, Berend et al. 2013). Both shells are made of a titanium alloy (Ti6Al4V).

04 METHODS

04

METHODS

Radiostereometry

Marker-based RSA was used in all the studies, I-V. A complete evaluation of all RSA radiographs was only performed if three or more markers in each of the segments could be identified with a scatter corresponding to a condition number (CN) less than 125 and a stability corresponding to a mean error of rigid body fitting (ME), at most 0.35 mm. In cases in which fewer than three well-defined markers were visualised, a hemispherical cup algorithm was used to define the position of the cup (model-based RSA). The postoperative examinations in all studies were performed within three to five days following surgery. In all the studies, examinations were performed with the patients in the supine position. In Study IV, examinations were also made with patients standing. All the patients were examined using a uniplanar technique (cage 43 and 77). Stereoradiographic measurements and analyses in all studies were performed with UmRSA Digital Measure and UmRSA analysis software 6.0 (RSA Biomedical, Umeå, Sweden).

Studies I-II

Early and mid-term proximal/distal femoral head penetration of both E1 and ArComXL was the primary outcome parameter in the studies. Penetration in the other directions (medial/lateral and anterior/posterior), three-dimensional head penetration, cup migration and femoral head migration were also calculated. Cup rotations were just evaluated in Study I. All the patients were examined postoperatively, at three months and one and two years. In study II, RSA examinations were also performed at five years. Acetabular cup migration was calculated using segment motion, comparing the pelvic segment relative to the cup segment. The femoral head migration was evaluated using point motion to measure movements of the centre of the femoral head relative to the femoral bone. Translations of the femoral head centre using the cup markers as a fixed reference segment represented the penetration of the femoral head into the polyethylene insert. Translation was defined as x-translation (medial [+]/lateral [-]), y-translation (proximal [+]/distal [-]) and z-translation (anterior [+]/posterior [-]). Stem rotations were not analysed. The total penetration (3D) at two and five years was computed.

In Study I, the precision of the technique was determined by documenting the differences between double examinations postoperatively. In Study II, the total penetration rate between two and five years was calculated as total point motion (TPM), which stands for the length of the translation vector of the centre of the femoral head (relative to the centre of the cup) during the interval of interest (Valstar, Gill et al. 2005). The total penetration between two and five years thus corresponds to a vector which might have a different direction from the one representing penetration postoperatively to five years. Penetration from years two to five was therefore computed using the examination at two years as a reference. The total penetration rate between two and five years was measured as TPM divided by three.

Clinical outcome measurements

Studies I-II

Clinical outcome was assessed prospectively using the Harris Hip Score (HHS), for which a score ranging from 90 to 100 is considered excellent, from 80 to 89 is good, 70 to 79 is fair and scores of less than 70 points are regarded as a poor result. The classical HHS is an examiner-derived score. In Studies I and II, patients answered the same questions on a self-reported questionnaire (Shervin, Dorrwachter et al. 2011). Harris Hip scores and pain scores were available for 66 hips preoperatively, for 69 hips at one year and for 63 hips at the five-year follow-up. In Study I, the activity level for patients was also evaluated preoperatively and at one year after surgery using the University of California Los Angeles (UCLA) activity score, which was available for 65 hips preoperatively and for 66 hips at the one-year follow-up.

Study III

Stereoradiographs of 80 patients (80 hips) were studied on two occasions, postoperatively (double examinations) and at two years. To determine the precision of both marker-based and MBRSA, each hip was examined twice postoperatively with an interval of 10-15 minutes. The precision was calculated using the method proposed by Börlin et al. (2006) and Nebergall et al. (2015). The precision was calculated from zero by assuming that there was no motion of the prosthesis between the two examinations. The double examinations were evaluated using markers inserted into the liner and with a hemispherical marker-less algorithm (MBRSA). A marker-less algorithm was also used to determine the position of the centre of the femoral head. The positions of tantalum markers inserted into the acetabular bone were computed using marker-based RSA. The medial/lateral, proximal/distal, anterior/posterior and the total (vectorial sum of medial/lateral, proximal/distal and anterior/posterior) cup migration and femoral head penetration up to two years were compared. Evaluations of cup migration and femoral head penetration required the presence of at least three stable, visible markers in each of the segments corresponding to the acetabular bone and the cup and visualisation of the femoral head on both radiographs. Four points were measured manually on the edge of the femoral head on both images to facilitate the identification of the projected ellipse using edge detection and a dual-projection head algorithm. In the evaluation based on hemispherical cup measurements, the outline of the femoral head, the cup shell and the opening circle of the cup were determined to locate the centre of the femoral head and the position, size and orientation of the cup. Because of the symmetrical shape of the hemispherical cup, rotations especially around the pole axis of the cup could not be determined.

Study IV

Stereoradiographs of 106 patients (106 hips) were analysed in supine and standing positions on three occasions (postoperatively, at six months and seven years). The pelvic rotations about the transverse axis (anterior or forward tilt [+] and posterior or backward [-] tilt) were calculated. To evaluate the reproducibility of patient positioning supine, two sets of RSA images (double examinations) of 20 patients in the supine position at the same visit were performed. The patients were repositioned between the examinations, without moving the calibration cage and X-ray tubes.

Study V

Stereoradiographs of 92 patients (92 hips) were evaluated at two occasions; postoperatively and at five years. The migration of the cup was measured as the translation of the cup in relation to the horizontal (x-axis), longitudinal (y-axis) and sagittal (z-axis) axes, where positive values are in the medial, proximal and anterior directions. The absolute migration values regardless of signs were also calculated. In the current study, seven patients (seven hips) with RingLoc cups were evaluated using MBRSA.

Radiographic evaluation

Study V

Standard clinical radiographs, including an AP and lateral radiographs, were obtained for all patients postoperatively, and at five years after surgery. In this study, only AP radiographs were studied, due to concerns about the quality of some of the lateral projections. The radiographs were visually evaluated for the absence of contact between bone and acetabular shell by trained orthopaedic surgeons. The assessment of any radiolucent appearance was performed using the Mdesk™ suite (RSA Biomedical). The acetabular components were divided on the AP radiographs into three equal regions of 60° (region 1: outer lateral, region 2: central and region 3: outer medial), modified after Charnley-DeLee (DeLee and Charnley 1976). The presence of radiolucent lines and the region in which they occurred was noted. Postoperative gaps or radiolucent lines on the follow-up examinations should have a minimum width of at least 0.5 mm. Gaps were interpreted as regions where the surface of the acetabular component was not in contact with the underlying sclerotic acetabulum at the postoperative radiograph. Radiolucency was defined as radiolucent lines developed at later follow-ups.

05 STATISTICS

05

STATISTICS

The statistical analyses in this thesis have been performed using statistical software IBM SPSS version 20.0.0. Statistical significance was assumed at p-values of less than 0.05. Descriptive statistics were used to describe the patient characteristics and outcome variables at the measurement points. Values were presented either as the mean (SD) with a 95% confidence interval (CI) for the mean or as the median and range or interquartile range (IQR). The total translations were computed using Pythagoras theorem ($\sqrt{x^2+y^2+z^2}$). The precision of the measurement was calculated in Studies I, III and IV by documenting the differences between repeated examinations of the patients on the same visit. The precision was calculated as the 95% confidence interval using the standard deviation (SD) of the difference measured between two examinations multiplied by the critical value (t) obtained from the T-table adjusted for the number of observations minus 1. The precision was calculated from zero by assuming that there was no motion of the prosthesis (Studies I and III) and the pelvic tilt (Study IV) between the two examinations.

Studies I-II

In Study I, a power analysis revealed that a total of 23 patients in each group would be required to detect a difference in proximal femoral head penetration of 0.1 mm with 90% power at the 5% type I error level. The corresponding group size to detect a 0.1 mm difference in proximal cup migration with 80% probability at the same significance level was 38 hips. The data are presented either as the median and range (minimum-maximum) or as the mean and standard deviation (SD) and/or 95% confidence interval. A non-parametric Mann-Whitney U-test was used for comparisons of femoral head penetration between the groups at two years in Study I and at five years in Study II. The Mann-Whitney test was also used to evaluate the clinical data (HHS and HHP) at one (Study I) and five years (Study II) after the operation. A paired non-parametric test (Wilcoxon's signed-rank test) was used to assess femoral head penetration over time.

Study III

Descriptive statistics were used to present the data as the mean, standard deviation of the mean (SD) and 95% confidence interval around the mean value for translations regarding all three axes (x, y and z) and the total translations at the two-year follow-up. Variances were compared using Levene's test of homogeneity. We used Wilcoxon's signed-ranked test to analyse the differences in penetration and migration between the two methods and for the different implant designs. In order to estimate reliability, we used Cronbach's α coefficient, which calculates the average correlation of variables in a test. A coefficient greater than 0.70 was regarded as having acceptable reliability. Bland-Altman scatter plots were used to assess the agreement between marker-based and MBRSA for each cup design at the two-year follow-up. The plots describe the average between each pair of RSA measurements on the x-axis in relation to the differences between them on the y-axis. We calculated and identified the limits of agreement (mean difference ± 2 standard deviations from the mean) on these plots. The smaller the range between these two limits, the better the agreement.

Study IV

A Shapiro-Wilk test for normality was performed to determine whether continuous data were normally distributed. All RSA data were normally or close to normally distributed (Shapiro-Wilk; $p > 0.05$). The data are presented as the mean with a 95% confidence interval (CI). A paired-samples t-test was used to evaluate any differences between two repeated observations in the same patients and an independent-samples t-test or one-way analysis of variance (ANOVA) was used for comparisons between different groups. Generalised linear models were constructed in which pelvic tilt in the supine position and from the supine to the standing position at six months and seven years were used as dependent variables, with gender, the status of the contralateral side (only at the seven-year follow-up) and low-back pain as predictors (only at the seven-year follow-up). Age was used as a covariate. The precision was calculated by analysing 20 double examinations.

Study V

The primary outcome of the study was acetabular cup migration in the medial/lateral (x-axis), proximal/distal (y-axis) and anterior/posterior (z-axis) directions. Absolute migration values regardless of signs were also calculated. The migration data were not normally distributed (Shapiro-Wilk test) and medians and interquartile ranges (IQRs) were calculated. We have also calculated mean values with corresponding 95% confidence intervals (CIs). The Pearson chi-square test was performed to compare the extent of radiolucent lines between the groups. Differences in the presences of radiolucent lines and proximal migration between the two groups at each follow-up were analysed with the Mann-Whitney U-test. Logistic regression analysis was conducted to evaluate any associations between cup migration and design and the development of radiolucent lines between the postoperative examination and the examination at five years. For this purpose, the dependent variable was categorised into a binary variable. If the extent of the radiolucent lines surrounding the cup had increased by 20 per cent or more (11 cases), we regarded this as a true increase. If less, it was regarded as no increase or uncertain. Absolute cup migration in all three directions, the type of cup and cases with postoperative gaps were used as predictive variables (covariates). Odds ratios (ORs) with 95% CIs and p-values were calculated.

Ethics approval

All patients included in studies I-V gave informed consent to participate. Ethics approval for the studies included in this thesis was obtained through the Regional Ethics Committee. Studies I-II (Dnr 279-08), Study III (Dnr 279-08, Dnr 539-06, Dnr R072-98, and Dnr 281-02), Study IV (S257-00, R312-98, Ö449-00, and Ö450-00), and Study V (Goteborg, Sweden Dnr 279-08, Massachusetts, Boston, USA 007P000337/PHS).

06 RESULTS

06

RESULTS

Study I

Precision

The precision of the measurements corresponding to the detection level for an individual observation varied depending on the type and direction of the motions measured *(Table 4)*. The 95 % detection limit in the individual case for proximal/distal femoral head penetration was 0.13 mm. Concerning translations, the highest resolution (95% confidence limits) was observed for proximal/distal cup displacements (0.07 mm) and the lowest for anterior/posterior femoral head translations (0.75 mm). The 95 % detection limit for cup rotations varied between 0.30 and 0.75 degrees (change of inclination and anterior/posterior tilt respectively).

Table 4. Precision measurements based on postoperative double examinations.

	n	SD	Precision (95% CI)
Wear (mm)			
Medial (+)/lateral (-)	65	0.07	0.15
Proximal (+)/distal (-)	65	0.07	0.13
Anterior (+)/posterior (-)	65	0.19	0.38
Cup migration (mm)			
Medial (+)/lateral (-)	64	0.08	0,16
Proximal (+)/distal (-)	64	0.03	0.07
Anterior (+)/posterior (-)	64	0.16	0.32
Cup rotation (degrees)			
Anterior (+)/posterior (-)	64	0.37	0.75
Anteversion (-)/retroversion (+)	64	0.35	0.69
Increase (+)/decrease (-)	64	0.15	0.30
Stem translation (mm)			
Medial (+) /lateral (-)	66	0.18	0.37
Proximal (+)/distal (-)	66	0.14	0.27
Anterior (+)/posterior	66	0.32	0.75

Femoral head penetration

The median proximal penetration in the E1 group was 0.04 mm at three months, which increased to 0.06 mm at two years. The corresponding figures for the ArComXL group were 0.03 mm and 0.10 mm (comparison at two years: p=0.30) *(Table 5)*. Both groups demonstrated a significantly increased penetration between three months and two years (E1, p=0.02; ArComXL, p<0.001), but between one and two years a significant increase was only observed in the ArComXL group (p= 0.002) *(Figure 17)*. The median medial/lateral, anterior/posterior and three-dimensional penetration recorded at two years did not differ between the groups (p=0.41 to 0.57). Eight patients with bilateral implants showed two-year median proximal penetration of 0.10 mm on the E1 side and 0.08 mm on the control side (ArComXL) (p=0.96).

Table 5. Femoral head penetration (mm). Median (range).

	E1*	ArComXL*	P value†
Wear (mm)			
Medial (+)/lateral (-)			
3 months	0.01(-0.22-0.16)	0.01(-0.13-0.21)	-
1 year	-0.01(-0.16-0.14)	- 0.01(-0.12-0.19)	-
2 years	0.01(-0.18-0.10)	- 0.02 (-0.12-0.19)	0.41
Proximal (+)/distal (-)			
3 months	0.04(-0.10-0.16)	0.03(-0.08-0.14)	-
1 year	0.05(-0.08-0.14)	0.04(-0.11-0.18)	-
2 years	0.06(-0.06-0.18)	0.10(-0.05-0.35)	0.30
Anterior (+)/posterior (-)			
3 months	-0.07(-0.41-0.38)	0.00 (-0.36-0.27)	-
1 year	0.04(-0.29-0.28)	0.06(-0.79-0.34)	-
2 years	0.02(-0.36-0.50)	0.03(-0.39-0.30)	0.50
Three-dimensional			
3 months	0.15(0.02-0.41)	0.15(0.04-0.45)	-
1 year	0.15(0.04-0.32)	0.18(0.03-0.82)	-
2 years	0.18(0.07-0.53)	0.19(0.04-0.46)	0.57

*N=38 in the E1 group at all time points; N=31 at three months and one year and N=29 at two years in the ArComXL group. † Mann-Whitney Test.

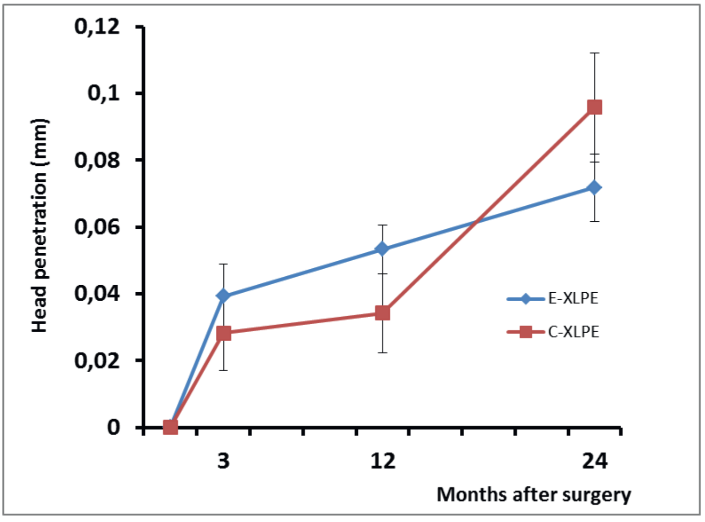


Figure 17.
Mean proximal femoral head penetration. E-XLPE= vitamin E-infused highly cross-linked polyethylene (E1), and C-XLPE= control highly cross-linked polyethylene (ArComXL). The I-bars represent the standard error of the mean.

Cup migration

The individual three-dimensional cup translations at two years varied between 0.1 and 1.0 mm without any difference between the two groups *(Table 6)*. There also was no difference apparent in translation along the any of the cardinal axes (p=0.16 to 0.71). At two years, the median cup rotations were small (-0.01° to 0.22°), again without any significant difference between the groups (p=0.11 to 0.26) *(Table 7)*.

Table 6. Cup translations (mm). Median (range).

	EI*	ArComXL*	P value†
Medial (+)/lateral (-)			
3 months	0.00 (-0.59-0.66)	-0.02(-0.24-0.32)	-
1 year	0.09(-0.49-0.56)	0.00(-0.39-0.62)	-
2 years	0.00 (-0.55-0.65)	-0.05(-0.48-0.49)	0.16
Proximal (+)/distal (-)			
3 months	0.02(-0.14-0.79)	0.07(-0.08-0.35)	-
1 year	0.02(-0.22-1.0)	0.09(-0.10-0.43)	-
2 years	0.03(-0.13-0.92)	0.08(-0.08-0.40)	0.14
Anterior (+)/posterior (-)			
3 months	0.09(-0.28-0.57)	0.13(-0.23-0.50)	-
1 year	0.11(-0.31-1,3)	0.06(-0.61-0.62)	-
2 years	0.09(-0.62-0.98)	0.15(-0.60-0.66)	0.71
Three-dimensional			
3 months	0.24(0.04-0.98)	0.29(0.07-0.54)	-
1 year	0.31(0.13-1.3)	0.30(0.09-0.80)	-
2 years	0.35(0.08-1.0)	0.26(0.09-0.69)	0.57

* N= 36 in the E1 group at all time points; N=29 at three months and one year and N=28 at two years in the ArComXL group. † Mann-Whitney Test.

Table 7. Cup rotations (degrees). Median (range).

	E1	ArComXL	P value†
Anterior (+)/posterior (-) tilt			
3 months	-0.07(-2.3-1.4)	0.08(-1.6-1.3)	-
1 year	-0.25(-2.9-3.6)	0.06(-1.5-2.9)	-
2 years	0.04(-1.7-1.5)	0.22(-0.74-2.3)	0.26
Ante- (-)/retroversion (+)			
3 months	-0.02(-1.3-2.9)	-0.05(-1.3-1.1)	-
1 year	-0.08(-1.9-3.5)	-0.03(-2.2-1.4)	-
2 years	-0.19(-2.9-0.68)	-0.01(-1.6-0.75)	0.25
Increase (+)/decrease (-) of inclination			
3 months	0.25(-0.79-1.3)	0.08(-0,56-2,0)	-
1 year	0.25(-0.72-1.5)	0.13(-0,64-2,1)	-
2 years	0.22(-1.3-1.6)	0.01(-0.94-2.2)	0.11

*N=35 at three months and two years and N=34 at one years in the E1 group; N=27 at three months and one year and N=26 at two years in the ArComXL group. † Mann-Whitney Test.

Femoral head migration

At two years follow-up, the femoral head centre had displaced from 4.3 mm laterally to 1.7 mm medially with median values close to zero in both groups (p=0.07) *(Table 8)*. The head centre on the stem revised before the follow-up at two years (which was in the control group) had migrated 5.2 mm medially at one year. Most stems subsided, with a maximum value at two years of -4.3 mm. The median subsidence was -0.16 mm in both groups (p=0.71), but at this time the stem with the most pronounced subsidence (-10.2 mm at one year, a stem in the control group) had been revised. Most stems translated posteriorly corresponding to retroversion. At two years, the median posterior translation values reached -0.49 mm in the E1 group and -0.34 mm in the ArComXL group (p=0.40).

Table 8. Femoral head translations (mm). Median (range).

	n (E1/ArComXL)	E1	ArComXL	P value†
Medial (+)/lateral (-)				
3 months	33/28	-0.01(-1.6-0.78)	0.09(-5.2-0.70)	-
1 year	33/28	0.01(-1.4-1.3)	-0.08(-5.2-0.64)	-
2 years	34/28	0.10(-1.5-1.7)	-0.08(-4.3-0.67)	0.07
Proximal (+)/distal (-)				
3 months	33/28	-0.16(-4.1-0.31)	-0.19(-10.3-0.17)	-
1 year	33/28	-0.19(-4.3-0.23)	-0.21(-10.2-0.22)	-
2 years	34/28	-0.16(-4.3-0.30)	-0.16(-3.6-0.26)	0.71
Anterior (+)/posterior (-)				
3 months	33/28	-0.37(-4.0-0.29)	-0.39(-3.0-0.49)	-
1 year	33/28	-0.61(-3.8-0.93)	-0.4 (-2.9-1.8)	-
2 years	34/28	-0.49(-4.0-1.7)	-0.34(-3.0-1.2)	0.40

† Mann-Whitney Test.

Clinical results

The median HHS score increased from 43(range, 21 to 86) preoperatively to 89 (range, 22 to 100) at one year in the E1 group and from 46 (range, 25 to 76) to 89 (range, 47 to 100) in the ArComXL group. The corresponding median pain scores increased from 10 (range, 0 to 40) to 40 (range, 10 to 44) and from 10 (range, 0 to 44) to 40 (range 20 to 44) without any significant difference between the two groups.

In patients with bilateral implants, the HHS increased from 54 (range, 27 to 72) preoperatively to 91 (range, 66 to 100) at one year on the E1 side and from 48 (range, 12 to 73) to 91(range, 38-96) on the ArComXL side. The median pain scores increased from 20 (range, 10 to 30) preoperatively to 44 (range, 11 to 44) at one year in the E1 group and from 10 (range, 10 to 30) to 44 (range, 20 to 44) in the ArComXL group. The median activity scores increased from 4 (range, 2 to 8) preoperatively to 6 (range, 2 to 190) at one year in the E1 group and from 3 (range, 2 to 10) to 5 (range, 2 to 9) in the ArComXL group, without any significant difference between the groups at two years (p=0.48). None of the clinical parameters studied preoperatively and after one year differed significantly between the groups.

Study II

Femoral head penetration at five years

At the five-year follow-up, the median proximal penetration in the E1 group (0.13 mm, range: -0.12 to 0.25) was lower than that in the ArComXL group (0.20 mm, range: 0.01 to 0.45) (p<0.001) *(Fig 18)*, *(Table 9)*. The corresponding median three-dimensional penetration was 0.21 mm (range: 0.08 to 0.80) and 0.28 mm (0.13 to 0.66) respectively (p= 0.004).

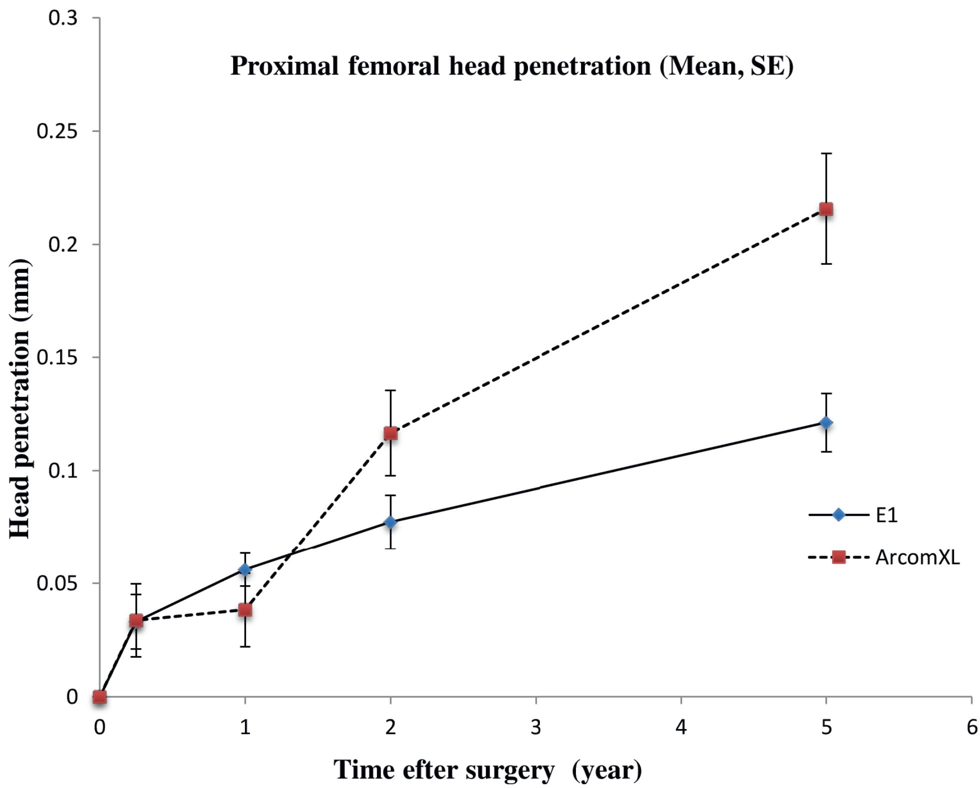


Figure 18. Line graph shows proximal femoral head penetration. The error bars indicate the standard error (SE).

Table 9. Femoral Head Penetration.

	n (E1/ArComXL)	E1* (mm)	ArComXL* (mm)	P value†
Medial (+)/lateral (-)				
2 years	38/29	0.01 (-0.22 to 0.16)	0.01 (-0.12 to 0.19)	0.41
5 years	37/26	0.03 (-0.20 to 0.18)	0.03 (-0.19 to 0.38)	0.11
Proximal (+)/distal (-)				
2 years	38/29	0.06 (-0.06 to 0.18)	0.10 (-0.05 to 0.35)	0.30
5 years	37/26	0.13 (-0.12 to 0.25)	0.20 (0.01 to 0.45)	<0.001
Anterior (+)/posterior (-)				
2 years	38/29	0.02 (-0.36 to 0.50)	0.03 (-0.39 to 0.30)	0.50
5 years	37/26	-0.01 (-0.32 to 0.33)	0.01 (-0.31 to 0.56)	0.77
Three-dimensional				
2 years	38/29	0.18 (0.07 to 0.53)	0.19 (0.04 to 0.46)	0.57
5 years	37/26	0.21 (0.08 to 0.80)	0.28 (0.13 to 0.66)	0.004

* Values are presented as the median with the range in parentheses. † Mann-Whitney test.

Femoral head penetration rate between two and five years

The median proximal penetration rate between two and five years was 0.02 mm/year (rang, -0.04 to 0.05 mm/year) in the E1 group and 0.04 mm/year (range, 0.03 to 0.09 mm/year) in the ArComXL group (p<0.001). The corresponding median three-dimensional rates were 0.04 mm/year (range, 0.01 to 0.15 mm/year) in the E1 group and 0.07 mm/year (range, 0.01 to 0.30 mm/year) in the ArComXL group (p<0.001). The observed maximum values of proximal penetration rates for both groups were below the osteolysis threshold of 0.1 mm/year (Dumbleton, Manley et al. 2002). In both groups, there was however a significant increase of the proximal and three-dimensional penetration between two and five years (in the E1 group, p=0.02 for the proximal penetration and p=0.01 for the three-dimensional penetration, and in the ArComXL group, p<0.001 for the proximal penetration and p=0.003 for the three-dimensional penetration).

The proximal cup migration was small in both groups, but tended to be somewhat higher in the ArComXL group (p=0.05) *(Table 10)*. The femoral head migration did not differ between the two group *(Table 11)*.

Table 10. Cup migration.

	n (E1/ArComXL)	E1* (mm)	ArComXL* (mm)	P value†
Medial (+)/lateral (-)				
2 years	36/28	0.0 (-0.55 to 0.65)	-0.05 (-0.48 to 0.49)	0.16
5 years	37/25	0.01 (-4.80 to 0.74)	-0.07 (-0.83 to 0.54)	0.15
Proximal (+)/distal (-)				
2 years	36/28	0.03 (-0.13 to 0.92)	0.08 (-0.08 to 0.40)	0.14
5 years	37/25	-0.02 (-0.58 to 0.93)	0.04 (-0.15 to 0.36)	0.052
Anterior (+)/posterior (-)				
2 years	36/28	0.09 (-0.62 to 0.98)	0.15 (-0.60 to 0.66)	0.71
5 years	37/25	0.09 (-2.40 to 1.33)	0.27 (-0.32 to 1.20)	0.050
Three-dimensional				
2 years	36/28	0.35 (0.08 to 1.0)	0.26 (0.09 to 0.69)	0.57
5 years	37/25	0.34 (0.07 to 5.40)	0.38 (0.10 to 1.17)	0.68

* Values are presented as the median with the range in parentheses. † Mann-Whitney test.

Table 11. Femoral head migration.

	n (E1/ArComXL)	E1* (mm)	ArComXL* (mm)	P value†
Medial (+)/lateral (-)				
2 years	34/28	0.10 (-1.5 to 1.7)	-0.08 (-4.3 to 0.67)	0.07
5 years	33/24	0.21 (-1.4 to 1.8)	0.13 (-3.9 to 0.90)	0.21
Proximal (+)/distal (-)				
2 years	34/28	-0.16 (-4.3 to 0.30)	-0.16 (-3.6 to 0.26)	0.71
5 years	33/24	-0.18 (-4.3 to 0.63)	-0.15 (-3.9 to 0.29)	0.90
Anterior (+)/posterior (-)				
2 years	34/28	-0.49 (-4.0 to 1.7)	-0.34 (-3.0 to 1.2)	0.40
5 years	33/24	-0.58 (-4.0 to 5.7)	-0.58 (-3.2 to 1.2)	0.82
Three-dimensional				
2 years	34/28	-0.49 (-4.0 to 1.7)	-0.34 (-3.0 to 1.2)	0.40
5 years	33/24	0.72 (0.22 to 6.5)	0.90 (0.28 to 5.7)	0.90

* Values are presented as the median with the range in parentheses. † Mann-Whitney test.

Clinical results

At five-year follow-up, the median Harris hip score was 95 (range, 35 to 100) in the E1 group and 94 (range, 36 to 100) in the ArComXL group (p=0.90). The corresponding median pain scores were 42 (range, 20 to 44) in the E1 group and 41 (range, 20 to 44) in the ArComXL group (p=0.80). In patients with bilateral hips, the HHS was 100 (range 35 to 100) on the E1 side and 100 (range, 36 to 100) on the ArComXL side. The corresponding pain scores were, 44 (range, 20 to 44) on the E1 side and 44 (range, 20 to 44) on the ArComXL side.

Study III

Precision (double examinations)

The precision of the proximal head penetration did not show any significant difference between the methods for Trilogy, TMT and ABG designs. For the RingLoc design a poorer precision along the y-axis was observed with the use of MBRSA *(Table 12)*. A similar result was observed for the precision calculated regarding the acetabular cup migration. We did not find any significant difference between the two methods for TMT, Trilogy or ABG, but a poorer precision was observed for the RingLoc cup with the use of MBRSA *(Table 13)*.

The precision of the three-dimensional penetration and migration did not differ between the methods for any implant design.

Table 12. Precision of marker-based RSA and model-based RSA in measuring femoral head penetration based on 80 double examinations, 20 observations in each group. The precision is defined by the standard deviation (SD) x critical value (t) obtained from the T-table adjusted for the number of observations minus 1.

	Marker-based		Model-based		
Head penetration	SD	Precision	SD	Precision	P value†
Medial (+)/lateral (-)					
RingLoc	±0.04	0.09	±0.09	0.19	0.06
TMT	±0.06	0.13	±0.09	0.18	0.08
Trilogy	±0.07	0.14	±0.06	0.13	0.89
ABG	±0.04	0.08	±0.05	0.09	0.14
Proximal (+)/distal (-)					
RingLoc	±0.05	0.09	±0.10	0.22	0.02
TMT	±0.06	0.13	±0.10	0.21	0.06
Trilogy	±0.06	0.11	±0.07	0.14	0.24
ABG	±0.07	0.14	±0.05	0.11	0.97
Anterior (+)/posterior (-)					
RingLoc	±0.12	0.26	±0.15	0.31	0.13
TMT	±0.16	0.34	±0.20	0.42	0.17
Trilogy	±0.16	0.33	±0.16	0.32	0.84
ABG	±0.18	0.37	±0.12	0.24	0.35
Three-dimensional					
RingLoc	±0.14	0.29	±0.20	0.43	0.14
TMT	±0.19	0.39	±0.23	0.48	0.67
Trilogy	±0.18	0.38	±0.18	0.38	0.59
ABG	±0.19	0.40	±0.14	0.28	0.18

† The P value was determined with use of Levene´s test.

Table 13. Precision of marker-based and model-based RSA in measureing acetabular cup migration based on 80 double examinations, 20 observations in each group. The precision is defined by the standard deviation (SD) x critical value (t) obtained from the T-table adjusted for the number of observations minus 1.

	Marker-based		Model-based		
Migration (mm)	SD	Precision	SD	Precision	P value†
Medial (+)/lateral (-)					
RingLoc	±0.05	0.11	±0.10	0.21	0.07
TMT	±0.10	0.22	±0.12	0.26	0.69
Trilogy	±0.07	0.15	±0.10	0.20	0.29
ABG	±0.06	0.13	±0.10	0.21	0.05
Proximal (+)/distal (-)					
RingLoc	±0.04	0.08	±0.09	0.18	0.01
TMT	±0.03	0.07	±0.05	0.11	0.21
Trilogy	±0.04	0.08	±0.06	0.13	0.07
ABG	±0.03	0.07	±0.06	0.13	0.08
Anterior (+)/posterior (-)					
RingLoc	±0.13	0.27	±0.15	0.31	0.43
TMT	±0.11	0.22	±0.12	0.26	0.32
Trilogy	±0.14	0.28	±0.12	0.24	0.02
ABG	±0.10	0.22	±0.10	0.20	0.85
Three-dimensional					
RingLoc	±0.15	0.31	±0.20	0.42	0.31
TMT	±0.15	0.31	±0.18	0.38	0.91
Trilogy	±0.11	0.23	±0.16	0.34	0.89
ABG	±0.12	0.26	±0.15	0.32	0.85

† The P value was determined with use of Levene´s test.

Proximal penetration and migration at two years

The mean proximal penetration at two years did not differ between the two methods for Trilogy, TMT and ABG. For the RingLoc design a significantly lower mean proximal penetration was observed with the use of MBRSA (p=0.01). This method underestimated the medial/lateral penetration for both RingLoc and TMT cups. The three-dimensional penetration was on the contrary higher when measured with MBRSA for 3 of the cup designs including RingLoc, but not for the ABG (p= 0.12) *(Table 14)*.

Table 14. Femoral head penetration based on 80 observations (20 observations in each group) at 2 years follow-up. Data are presented as Mean (Standard deviation) at a confidence level at 95%.

	Marker-based		Model-based		
Penetration (mm)	Mean	95% CI	Mean	95% CI	P * value
Medial (+)/lateral (-)					
RingLoc	-0.02 (0.06)	-0.03- -0.02	-0.08 (0.10)	-0.09- -0.07	0.01
TMT	0.00 (0.11)	-0.01-0.06	-0.07 (0.13)	-0.08- -0.06	0.00
Trilogy	0.05 (0.07)	0.04-0.05	0.00 (0.13)	0.01-0.01	0.11
ABG	-0.05 (0.08)	-0.05- -0.04	-0.05 (0.07)	-0.06- -0.04	0.77
Proximal (+)/distal (-)					
RingLoc	0.07 (0.08)	0.06-0.08	0.00 (0.09)	-0.01-0.01	0.01
TMT	0.07 (0.08)	0.06-0.08	0.03 (0.14)	0.02-0.04	0.12
Trilogy	0.03 (0.11)	0.02-0.04	0.02 (0.16)	0.00-0.04	0.67
ABG	0.23 (0.12)	0.22-0.24	0.22 (0.14)	0.21-0.23	0.30
Anterior (+)/posterior (-)					
RingLoc	-0.01 (0.11)	-0.02-0.00	-0.04 (0.19)	-0.06- -0.02	0.25
TMT	0.10 (0.20)	0.08-0.12	0.14 (0.27)	0.11-0.17	0.34
Trilogy	-0.03 (0.15)	-0.05- -0.01	-0.11 (0.27)	-0.14- -0.08	0.10
ABG	0.02 (0.14)	0.01- 0.03	-0.02 (0.11)	-0.03- -0.01	0.41
Three-dimensional					
RingLoc	0.15 (0.08)	0.14-0.16	0.22 (0.11)	0.21-0.23	0.00
TMT	0.22 (0.14)	0.21-0.23	0.31 (0.17)	0.29-0.33	0.02
Trilogy	0.18 (0.09)	0.17-0.19	0.27 (0.14)	0.26-0.28	0.00
ABG	0.28 (0.13)	0.27-0.29	0.26 (0.14)	0.25-0.27	0.12

* The p value was determined with use of Wilcoxon test.

The proximal and three-dimensional migration at two years did not differ between the methods for the Trilogy, TMT and ABG designs, whereas the RingLoc design showed higher mean values with the use of MBRSA (proximal migration, p=0.01 and three-dimensional migration, p=0.03). Model-based RSA showed significantly lower mean medial/lateral migration for the TMT design (p=0.01) and a higher medial/lateral mean migration for the RingLoc design (p=0.01) when compared conventional RSA. *(Table 15).*

Table 15. Acetabular cup migration based on 80 observations (20 observations in each group) at two years follow-up. Data presented as Mean (Standard deviation) at a confidence level at 95%.

	Marker-based		Model-based		
Migration (mm)	Mean	95% CI	Mean	95% CI	P* value
Medial (+)/lateral (-)					
RingLoc	0.02 (0.33)	-0.01-0.05	0.09 (0.29)	0.06-0.12	0.01
TMT	0.06 (0.74)	-0.02-0.14	-0.03 (0.29)	-0.06-0.00	0.01
Trilogy	0.07 (0.65)	0.00-0.14	0.05 (0.55)	-0.01-0.11	0.88
ABG	-0.01(0.27)	-0.04-0.02	0.07 (0.35)	0.03-0.11	0.19
Proximal (+)/distal (-)					
RingLoc	0.11(0.24)	0.08-0.14	0.19 (0.25)	0.16-0.22	0.01
TMT	0.20 (0.28)	0.17-0.23	0.18 (0.20)	0.16-0.20	0.75
Trilogy	0.29 (0.51)	0.24-0.34	0.29 (0.47)	0.24-0.34	0.91
ABG	0.17 (0.18)	0.15-0.19	0.18 (0.20)	0.16-0.20	0.27
Anterior (+)/posterior (-)					
RingLoc	0.01 (0.26)	-0.02-0.04	0.07 (0.22)	0.05-0.09	0.39
TMT	-0.11 (0.71)	-0.18- -0.04	-0.14 (0.62)	-0.20- -0.08	0.68
Trilogy	-0.27 (0.80)	-0.35- -0.19	-0.21 (0.76)	-0.29- -0.13	0.05
ABG	0.12 (0.20)	0.10-0.14	0.11(0.25)	0.08-0.14	0.59
Three-dimensional					
RingLoc	0.37 (0.32)	0.34-0.40	0.41 (0.26)	0.38-0.44	0.03
TMT	0.76 (0.76)	0.68-0.84	0.58 (0.46)	0.53-0.63	0.77
Trilogy	0.79 (0.82)	0.70-0.88	0.74 (0.81)	0.66-0.82	0.41
ABG	0.34 (0.26)	0.31-0.37	0.39 (0.35)	0.35-0.43	0.10

* The p value was determined with use of Wilcoxon test.

Reliability test

The alpha coefficient (Cronbach's α) for measurements of proximal head penetration ranged from 0.15 to 0.95. The corresponding values for proximal cup migration were 0.89 to 0.98. This analysis indicated high reliability for all four designs in measuring cup migration but not for all measurements of the penetration. The alpha coefficients for penetration were ≥ 0.70 for TMT and ABG and ≤0.5 for RingLoc and Trilogy. The poorest value was found for the RingLoc cup (0.15) *(Table 16).*

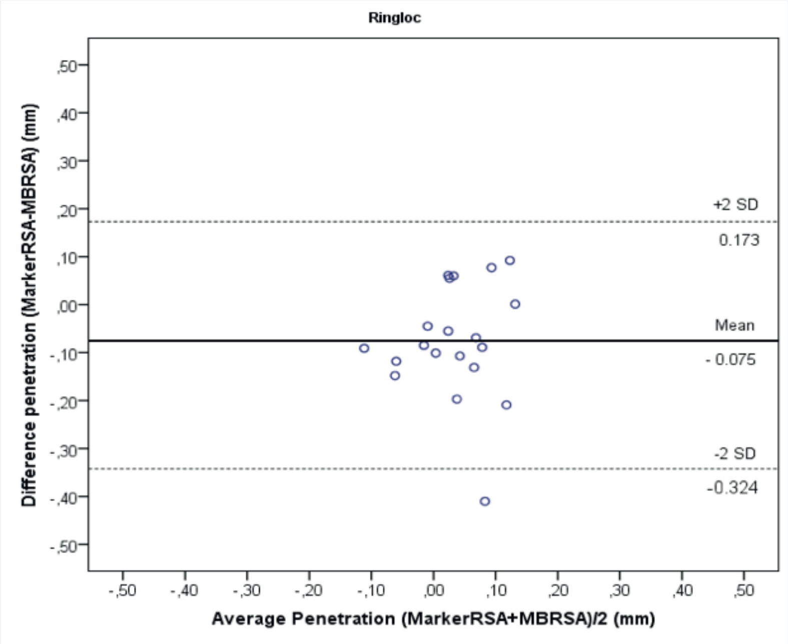
Table 16. Internal consistency reliability test, Cronbach´s alpha for femoral head penetration and acetabular cup migration at 2 years follow up.

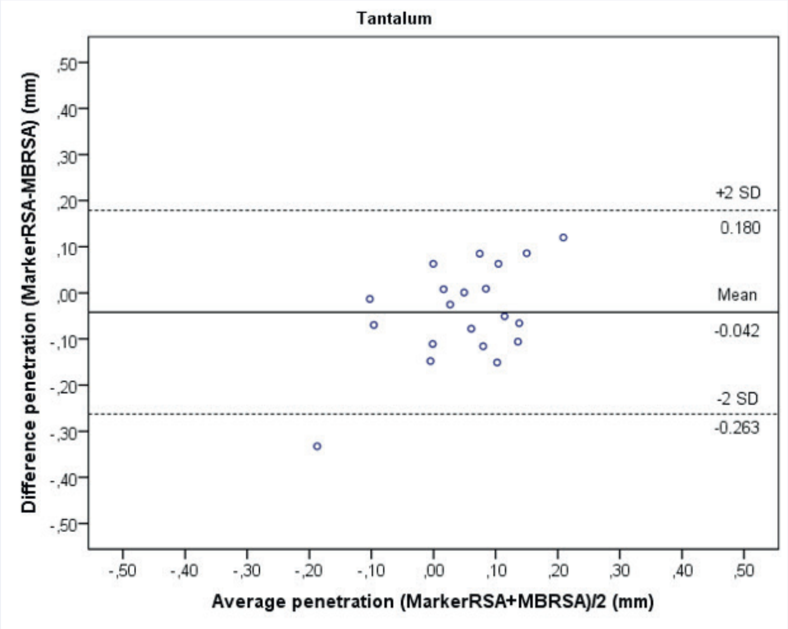
	Head penetration	Cup migration
	Cronbach´s α	Cronbach´s α
Medial (+)/lateral (-)		
RingLoc	0.73	0.96
TMT	0.78	0.98
Trilogy	0.41	0.98
ABG	0.72	0.69
Proximal (+)/distal (-)		
RingLoc	0.15	0.95
TMT	0.70	0.89
Trilogy	0.47	0.94
ABG	0.95	0.98
Anterior (+)/posterior (-)		
RingLoc	0.64	0.68
TMT	0.82	0.95
Trilogy	0.73	0.99
ABG	0.76	0.94
Three-dimensional		
RingLoc	0.71	0.89
TMT	0.65	0.94
Trilogy	0.77	0.99
ABG	0.96	0.96

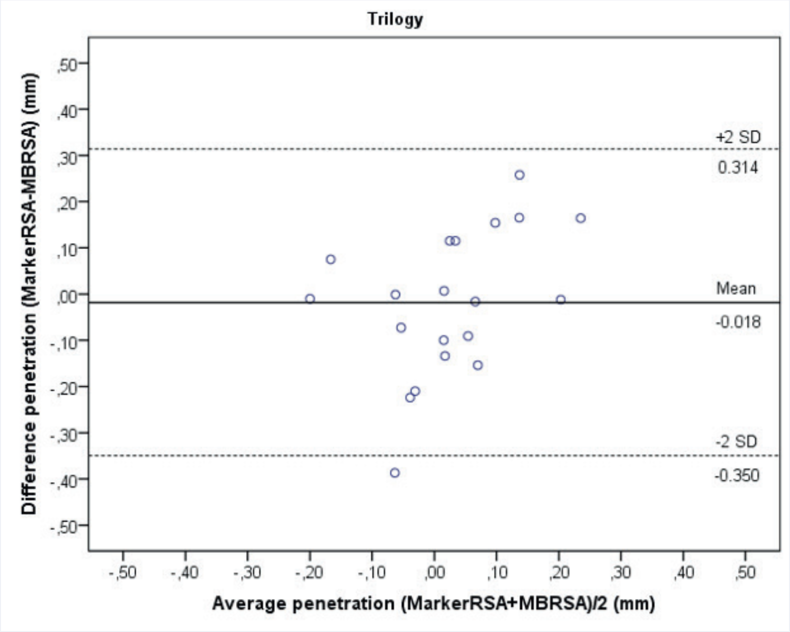
Agreement tests

The Bland and Altman plots of data at two years follow-up showed a tendency for MBRSA to underestimate the proximal penetration and overestimate the proximal migration in RingLoc cups. The best agreement was observed for the ABG design regarding both proximal penetration and proximal migration *(Figures 19 and 20)*.

Figure 19. Bland-Altman plots illustrating agreement between marker-based and model-based RSA at two years follow-up. The difference between the proximal penetration is shown against the average of the penetrations.






Trilogy
Difference penetration (MarkerRSA-MBRSA) (mm)
Average penetration (MarkerRSA+MBRSA)/2 (mm)
+2 SD
0.314
Mean
-0.018
-2 SD
-0.350
,50
,40
,30
,20
,10
,00
-,10
-,20
-,30
-,40
-,50

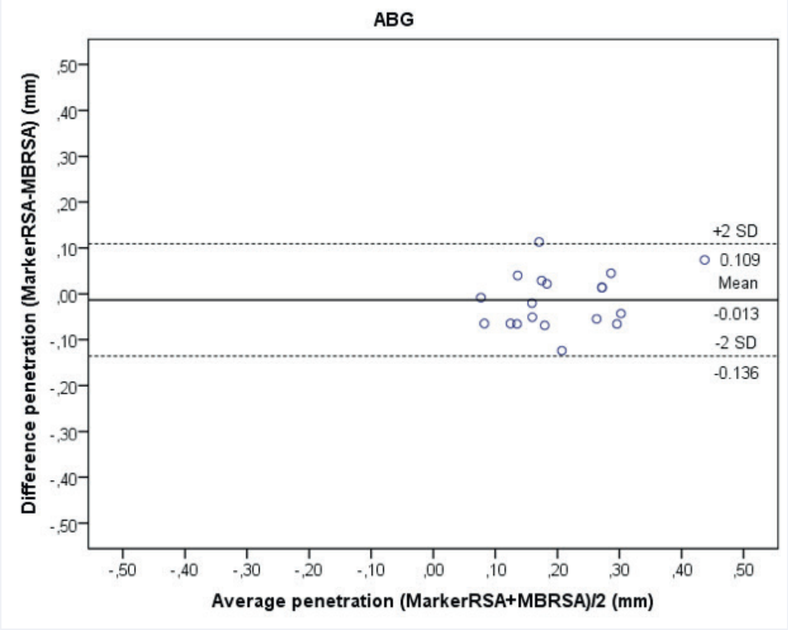
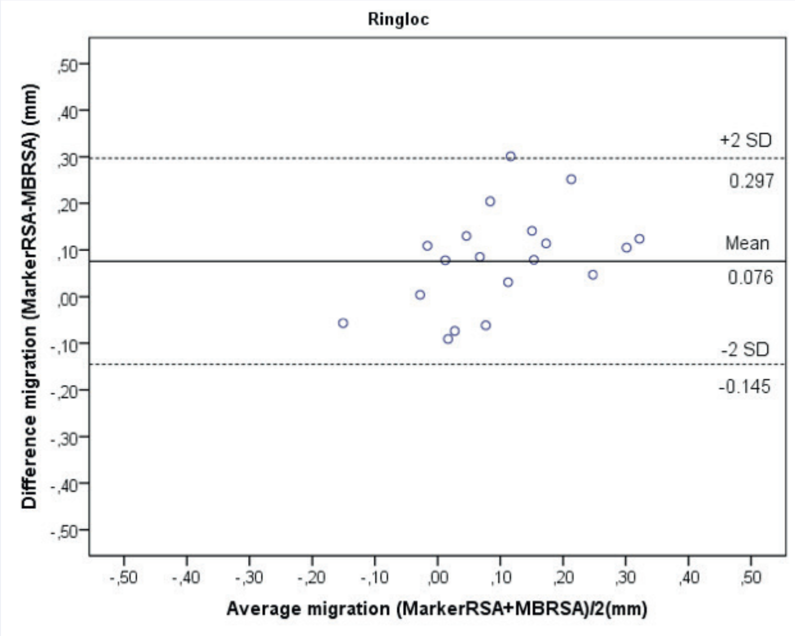
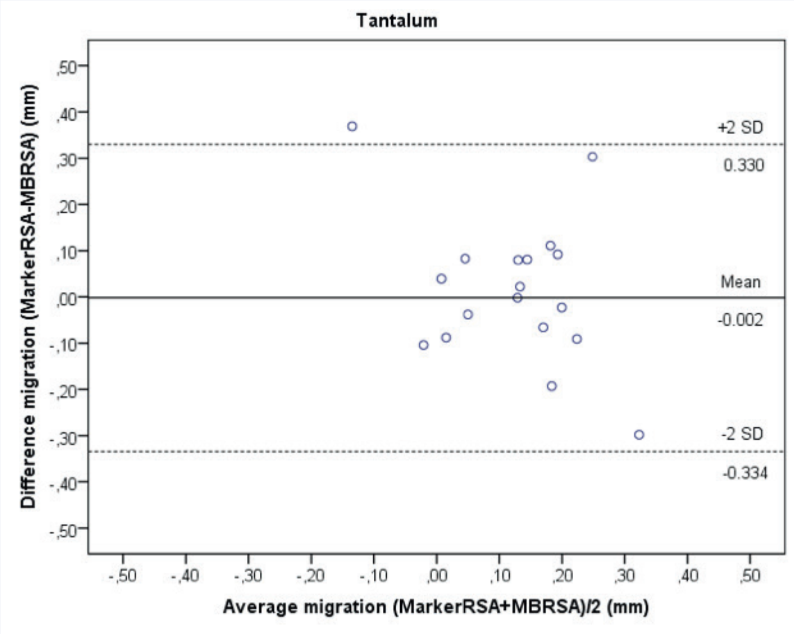
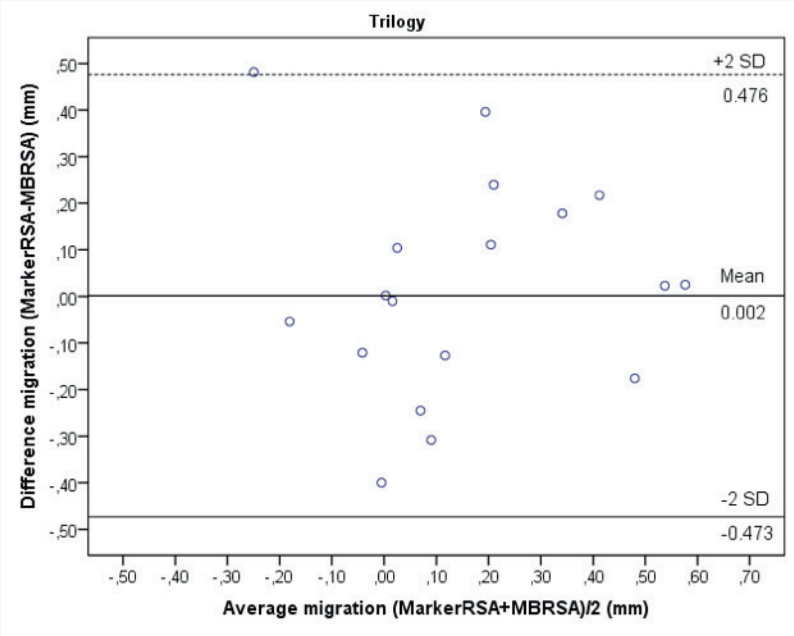
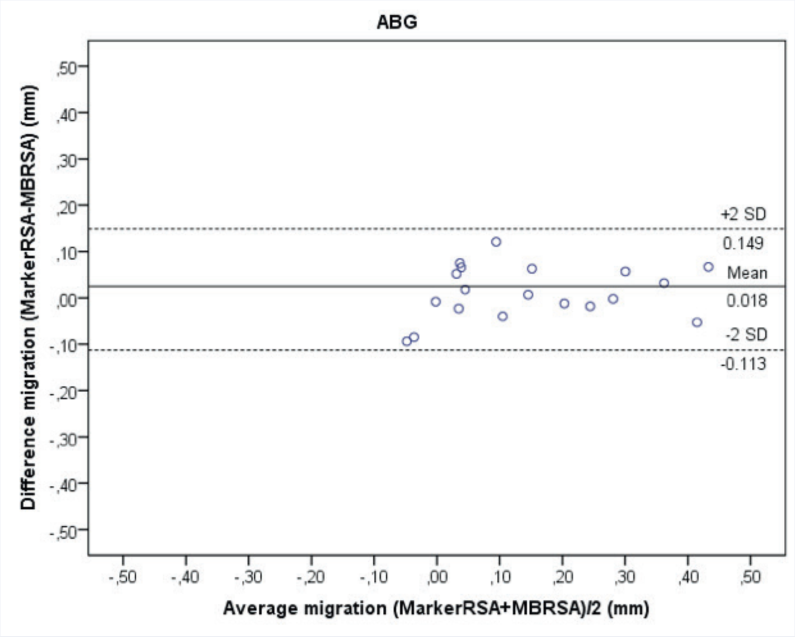

ABG
Difference penetration (MarkerRSA-MBRSA) (mm)
Average penetration (MarkerRSA+MBRSA)/2 (mm)
+2 SD
0.109
Mean
-0.013
-2 SD
-0.136
,50
,40
,30
,20
,10
,00
-,10
-,20
-,30
-,40
-,50

Figure 20. Bland-Altman plots illustrating agreement between marker-based and model-based RSA at two years follow-up. The difference between the proximal migration is shown against the average of the migrations.






Trilogy
+2 SD
0.476
Mean
0.002
-2 SD
-0.473
Difference migration (MarkerRSA-MBRSA) (mm)
,50
,40
,30
,20
,10
,00
-,10
-,20
-,30
-,40
-,50
-,50 -,40 -,30 -,20 -,10 ,00 ,10 ,20 ,30 ,40 ,50 ,60 ,70
Average migration (MarkerRSA+MBRSA)/2 (mm)


ABG
+2 SD
0.149
Mean
0.018
-2 SD
-0.113
Difference migration (MarkerRSA-MBRSA) (mm)
,50
,40
,30
,20
,10
,00
-,10
-,20
-,30
-,40
-,50
-,50 -,40 -,30 -,20 -,10 ,00 ,10 ,20 ,30 ,40 ,50
Average migration (MarkerRSA+MBRSA)/2 (mm)

Study IV

Precision

Measurements of 20 double examinations regarding the precision of pelvic positioning (rotations about the transverse axis) was ±3.3° (95% CI for studies of individual patients).

Changes in PTA in supine position and between supine and standing

In supine, the pelvis tended to show an increased posterior tilt with increasing follow up. Between the postoperative and the follow up examination at six months the posterior tilt reached a mean of -2.0°±3.0° (CI: -2.6° to -1.4°), which increased to -2.7°±2.9° (CI: -3.3° to -2.2°) at seven years ($p=0.01$) *(Table 17)*. From supine to standing, the mean change was 3.6°±3.8° (CI: 2.8° to 4.3°) at six months which increased to 6.4°±3.9° (CI: 5.7° to 7.2°) at 7 years ($p<0.001$). At six months, five patients demonstrated anterior tilt above 10 degrees reaching a maximum of 18 degrees *(Figure 21)*. Nineteen patients demonstrated anterior tilt above 10 degrees at the seven years follow-up *(Figure 22)*.

Table 17. Anterior (+)/posterior tilt (-) in the supine and standing positions in 106 patients up to 7 years after THA.

	n	Mean (SD)	95% CI	P value*
Supine				
Postop-6 months	106	-2.0° (3.0°)	-2.6° to -1.4°	
Postop- 7 years	106	-2.7° (2.9°)	-3.3° to -2.2°	0.01
Supine to standing				
6 months	106	3.6° (3.8°)	2.8° to 4.3°	
7 years	106	6.4° (3.9°)	5.7° to 7.2°	<0.001

*Student's t-test.

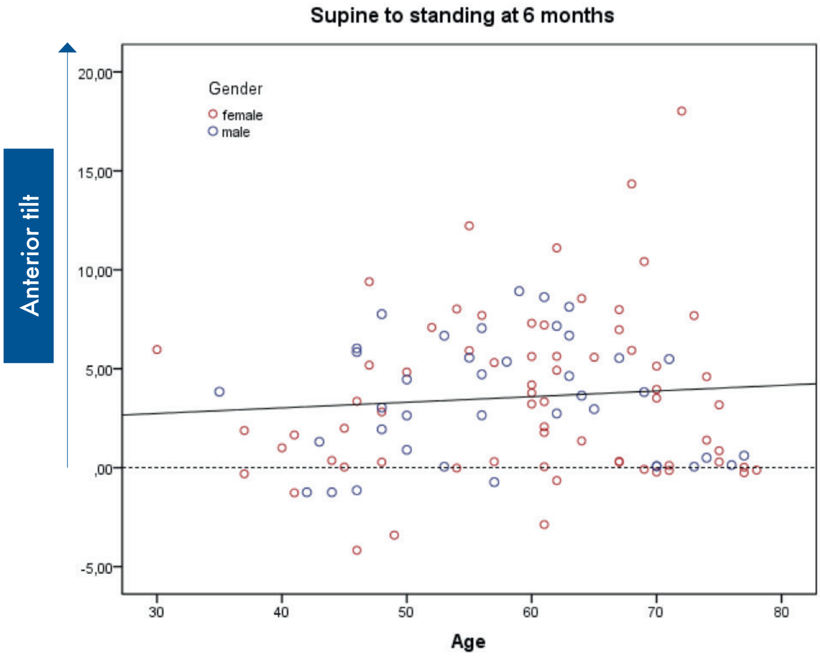


Figure 21. Scatterplot showing changes in pelvic tilt angle (PTA) between supine and standing position at six months.

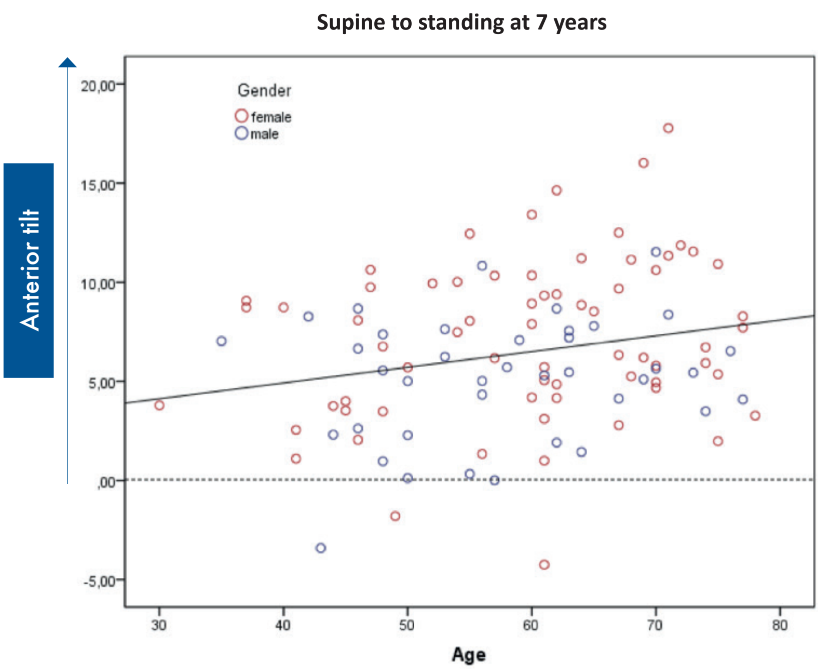


Figure 22. Scatterplot showing changes in pelvic tilt angle (PTA) between supine and standing positions at seven years.

Influence of different factors on PTA (gender, status of the opposite hip and low back pain)

In supine, the pelvis tilted more posteriorly in females (mean -2.5°±3.0°) than in males (-1.1°±2.6°) during the first period (p=0.02) *(Table 18)*. At seven years this posterior tilt had increased in both females and males to -3.1° ±3.0º and -2.1°±2.8°, respectively (females vs. males: p=0.08). Between supine and standing, there was no difference between the genders at six months. Compared to the male participants, females showed a significant larger anterior tilt from supine to standing at seven years (7.2°±4.1° vs 5.1°±3.2°; p= 0.01).

Any influence of the status of the opposite hip was only studied for supine to standing at seven years, because the exact time frame for the development of OA on the non-operated side could not be established. Studies of supine to standing at seven years did not reveal any significant differences between the three groups (normal, OA or THA on the opposite side, p=0.52). In supine, no significant differences in PTA were observed between the patients with or without low-back pain at any of the two follow-up occasions (p>0.05). From supine to standing, a weak and insignificant tendency towards larger anterior tilt was observed in patients with no low-back pain at both occasions (six months; p=0.07 and seven years, p=0.08).

Table 18. Anterior (+)/posterior tilt (-) in the supine and standing positions in males and females.

		Female		Male		
	n	Mean (SD)	95% CI	Mean (SD)	95% CI	P* value
Supine						
Postop-6 months	67/39	-2.5° (3.0°)	-3.2° to -1.7°	-1.1° (2.6°)	-2.0° to -0.29°	0.02
Postop-7 years	67/39	-3.1° (3.0°)	-3.8° to 2.4°	-2.1° (2.8°)	-3.0° to -1.2°	0.08
Supine to standing						
6 months	67/39	3.6° (4.2°)	2.6° to 4.6°	3.5° (3.0°)	2.5° to 4.5°	0.84
7 years	67/39	7.2° (4.1°)	6.2° to 8.2°	5.1° (3.2°)	4.1° to 6.2°	0.01

*Student´s t-test.

Linear Regression Analysis

Regression analysis of the supine position postoperatively to supine at six months showed an increased posterior tilt in females (p=0.01) and a tendency towards increasing posterior tilt with age (p= 0.06) *(Table 19)*.

Low-back pain was added to the model when evaluating supine postoperatively to supine at seven years. This model demonstrated a tendency towards posterior tilt with gender (p=0.06) but no association with age (p=0.56) or back pain (p=0.35).

From supine to standing at six months, neither gender nor age was significantly correlated with pelvic tilt.

In the model constructed for supine to standing at seven years, the status of the opposite hip as well as back pain were also added to the list of predictors. This model reveled a significantly increased anterior tilt in females (p=0.004), an increased tilt with age (p= 0.02). Though a tendency, no significant effect of back pain on pelvic tilt (p=0.06) was observed. The conditions of the opposite hip had no certain influence on the recorded PTA.

Table 19. Linear regression analysis: gender, age, opposite hip and low back pain with pelvic tilt.

	Supine-supine						Supine-standing					
	Postoperative - 6 months			Postoperative - 7 years			6 months			7 years		
	β	95 % CI	P value	β	95 % CI	P value	β	95 % CI	P value	β	95 % CI	P value
Gender												
Female	-1.4	-2.6 to -0.32	0.01	-1.1	-2.2 to 0.06	0.06	0.09	-1.4 to 1.6	0.90	2.1	0.69 to 3.6	0.004
Male[a]	0[a]											
Age	0.05	-0.00 to 0.10	0.06	0.02	-0.04 to 0.06	0.56	0.03	-0.04 to 0.09	0.40	0.07	0.01 to 0.13	0.02
Opposite hip												
Normal[a]										-0.01	-2.1 to 2.1	0.99
OA										1.3	-0.36 to 2.9	0.13
THA												
Low-back pain												
Yes				-0.58	0.63 to -1.8	0.35				-1.5	-3.1 to 0.05	0.06
No[a]				0[a]	-	-						

a Reference

Study V

Implant migration

At five-year follow-up, The Regenerex cups displayed a tendency to more proximal migration compared to the RingLoc cups (median 0.06 mm, interquartile range: 0.10 mm and median 0.01mm, interquartile range: 0.24 mm respectively) (p=0.05). The medial/lateral translation was low in both groups. At five years, the center of the cup had migrated 0.04 mm (interquartile range: 0.13 mm) medially in the Regenerex group and -0.02 mm (interquartile range: 0.35 mm) laterally in the RingLoc group.

The RingLoc cups demonstrated a more pronounced anterior/posterior translation (p=0.03). At five years, the RingLoc cup had migrated 0.12 mm anteriorly while the Regenerex migrated in the opposite direction (-0.01 mm posteriorly). Analysis of absolute values at five years demonstrated increased medial or lateral migration in the group with plasma-sprayed coating (p<0.001), whereas the proximal or distal and anterior or posterior migration did not differ *(Table 20)*.

Table 20. Cup migration. Migration as absolute values are presented as x-translation (medial/lateral), y-translation (proximal/distal) and z-translation (anterior/posterior).

	Regenerex (n=39)			RingLoc (n=53)			
Direction of cup migrations signed (mm)	**Median**	**IQR**	**Mean (95% CI)**	**Median**	**IQR**	**Mean (95% CI)**	**P value***
Medial (+)/lateral (-)							
5 years	0.04	0.13	0.04 (0.01 to 0.07)	-0.02	0.35	-0.04 (-0.13 to 0.04)	0.09
Proximal (+)/distal (-)							
5 years	0.06	0.10	0.06 (0.03 to 0.08)	0.01	0.24	0.05 (-0.01 to 0.10)	0.05
Anterior (+)/posterior (-)							
5 years	-0.01	0.32	0.02 (-0.05 to 0.10)	0.12	0.41	0.16 (0.06 to 0.26)	0.03
Absolute values (mm)							
x-translation							
5 years	0.06	0.09	0.08 (0.06 to 0.10)	0.18	0.24	0.23 (0.17 to 0.28)	<0.001
y-translation							
5 years	0.07	0.06	0.08 (0.06 to 0.10)	0.10	0.15	0.15 (0.10 to 0.19)	0.08
z-translation							
5 years	0.18	0.14	0.19 (0.14 to 0.24)	0.22	0.41	0.28 (0.20 to 0.35)	0.15

*Mann-Whitney U test.

Radiographic evaluation

Of the 92 hips followed in this study, 48 cases demonstrated gaps on the postoperative radiographs. Gaps were observed around 16 (41.0%) of the Regenerex cups and 32 (60.3%) of the RingLoc cups. In 8 of the Regenerex cases, postoperative gaps appeared in region I, in 16 in region II and in 7 in region III. The corresponding figures for the RingLoc cups were 25 in region I, 30 in region II and 20 in region III. In both group, most of the gaps were located in region II *(Table 21)*. At five years, out of 44 cases without postoperative gaps, new radiolucent lines were detected in 5 (21.7% of 23) cases with Regenerex cup and 6 (28% of 21) cases with RingLoc cup (p=0.61). Between the postoperative and five-year examinations, 4 cases with Regenerx cup and 7 cases with RingLoc developed radiolucent lines occupying at least 20% of the interface(p=0.67).

Table 21. Number of cases with postoperative gaps or radiolucent lines in the three regions studied. Total percent of postoperative gaps/zone development at each follow-up are presented as median and range.

	Regenerex (n=39)		RingLoc (n=53)	
	region 1-3	**median (range)**	**region 1-3**	**median (range)**
Postoperative	8-16-7	40 (0 to 86)	25-30-20	50 (0 to 93)
5 years	5-11-6	18 (0 to 100)	4-10-7	43 (0 to 90)

After adjusting for type of cup and presence of postoperative gaps, z-translation was the only independent risk factor for development of radiolucent lines (p=0.02). According to this analysis, for every mm of increased translation in anterior or posterior direction, the risk of developing radiolucent lines increased 19 times. This analysis also revealed that the incidence of postoperative gaps tends to have a preventive effect against the development of radiolucent lines (OR=0.15, p=0.05) *(Table 22)*.

Table 22. Odds ratios (ORs) for development of more than 20% radiolucent lines between postoperative and five- year follow-up.

Independent variable	OR	CI 95% of OR	Sig
Acetabular cup design	0.94	0.18 to 5.3	0.99
x-translation	2.56	0.04 to 161.0	0.66
y-translation	7.39	0.03 to 1834.4	0.48
z-translation	19.07	1.6 to 224.6	0.02
Postoperative gap	0.15	0.02 to 0.98	0.05

Results of logistic analysis with cup design, absolute migration values and postoperative gaps as predictors.

07 DISCUSSION

07

DISCUSSION

Failure of the acetabular components is the most common reason for revision surgery. Micromotion or wear of the socket are generally not detectable by conventional radiography in the early postoperative period and clinical symptoms usually occur much later. After a number of years, these events may result in detectable radiographic changes which may finally result in obvious clinical failure.

RSA plays an important role in the development and evaluation of new prostheses and has been used to document equivalent or even better performance with a new implant design (Nelissen, Pijls et al. 2011). As the early micromotion of implants in primary hip arthroplasty has been highlighted as a predictor of subsequent loosening (Pijls, Nieuwenhuijse et al. 2012, Klerken, Mohaddes et al. 2015, Johanson, Antonsson et al. 2016), RSA provides an insight into the stability and long-term survival of each device. It has been reported that migration exceeding the detection level of RSA is predictive of clinical implant loosening (Karrholm 2012). In clinical research, RSA has been used to evaluate the penetration of the femoral head into the acetabular component of a THA as a result of polyethylene creep and wear.

Wear in the polyethylene liner is often a limiting factor for the longevity of the implant and it has been identified as the most common cause of implant loosening and a major limitation in terms of the long-term survival of THA, at least when used with earlier generations of polyethylene (Maloney, Galante et al. 1999, Dumbleton, Manley et al. 2002).

7.1 Femoral head penetration of vitamin E-infused highly cross-linked polyethylene at two years

During the past few decades, major improvements in manufacturing technology have been made with the emphasis on the development of polyethylene materials with lower wear rates, reduced amounts of free radicals and subsequent osteolysis. A number of XLPE formulations have become available during the past decade and have shown reduced wear at short- and medium-term follow-ups (Bragdon, Greene et al. 2007, Digas, Karrholm et al. 2007, D'Antonio, Capello et al. 2012, Bragdon, Doerner et al. 2013). Cross-linking has been used to improve the wear characteristics of UHMWPE, resulting in increased oxidation and the reduced fatigue strength of the polyethylene material due to irradiation, re-melting and the annealing process used in this technique. In an attempt to prevent oxidation and improve mechanical strength, a new generation of XLPE materials has been developed by incorporating vitamin E into the polyethylene material. The potential benefits of vitamin E-infused cross-linked polyethylene should include a reduced risk of fracture and probably also greater oxidative resistance in the long term. In the shorter perspective, the resistance to deformation and penetration could be expected to be of the same magnitude as previously observed in studies of first-generation cross-linked polyethylene.

At the time this study was conducted, no clinical reports were available. A number of in-vitro studies of vitamin E-incorporated polyethylene liners have reported similar wear, higher resistance to oxidation and improved mechanical and fatigue properties compared with several first-generation XLPEs (Oral, Wannomae et al. 2004, Bracco and Oral 2011).

In Study I, we evaluated femoral head penetration, implant migration and clinical outcome two years after THA. The primary outcome parameter was to study the early-term proximal femoral head penetration of E1 in order to evaluate whether the expected low in-vivo penetration rate of this type of polyethylene could be confirmed in a clinical study. A comparison of our results with previous RSA studies of first-generation XLPEs indicated that the penetration of E1 observed by us at two years was of about same magnitude as that previously reported for first-generation XLPE (Digas, Karrholm et al. 2004, Kadar, Hallan et al. 2011, Thomas, Simpson et al. 2011). In 2012, Röhrl et al. (Rohrl, Nivbrant et al. 2012) reported a very low penetration rate for the femoral head in first-generation XLPE liners up to 10 years (<6μm/year). The main penetration pattern of XLPE involves an initially steep increase in penetration up to one year, regarded as creep or bedding-in (Estok, Bragdon et al. 2005, Glyn-Jones, McLardy-Smith et al. 2008). After one year, a steady-state phase begins with very low penetration rates (Thomas, Simpson et al. 2011, Johanson, Digas et al. 2012, Rohrl, Nivbrant et al. 2012).

E1 demonstrated an early penetration pattern similar to that of heat-treated XLPE. Most of the early penetration in the E1 liners occurred before three months and was about the same amount as heat-treated XLPE, except for sequentially annealed XLPE (Callary, Field et al. 2013) which has shown unusually low initial penetration. A longer follow-up will be needed to discover whether the penetration pattern of E1 continues to be similar to the pattern of heat-treated XLPE.

The creep and penetration pattern of the ArcomXL liners differed from both E1 and heat-treated XLPE. In both E1 and ArComXL liners, the creep mainly occurred up to three months. However, the proximal penetration in the ArComXL liners continued to increase over the entire period of two years and seemingly even appeared to accelerate after the one-year follow-up. This finding indicates that this material has a more complex phase of bedding-in or might be subjected to wear to some degree. ArComXL is manufactured with a compression-annealing process, which induces the linear orientation of the polyethylene crystalline regions. Even if the subsequent stress-relief step reduces the amount of anisotropy (Kurtz, Mazzucco et al. 2006), this unique property might explain its unusual creep behaviour. On the other hand, the cross-linking radiation dose of ArComXL is 50 kGy, which is the lowest dosage limit used for XLPE. This low dose may result in an insufficient cross-linking density and a higher steady-state penetration rate. However, it has to be mentioned that Marathon (DePuy, Warzaw IN, US), a re-melted XLPE manufactured with the same dose, also has a steady, low penetration rate up to six years (Callary, Campbell et al. 2013). On the other hand, in studies using RSA (Flatoy, Rydinge et al. 2015) and Hip Suite Analysis (Engh, Hopper et al. 2012), Marathon has displayed linear steady-state wear similar to our result for ArcomXL.

Since the mechanical properties of the liner and the wear particles that are produced are also able to influence fixation from a theoretical point of view, we also measured component migration. There were no significant differences between the groups regarding cup migration, cup rotation and femoral head migration.

We were unable to find any RSA studies reporting the migration of either the cup or the stem used in our study. The RingLoc cup displayed a proximal migration of about the same magnitude as that found for similar press-fit cups with a porous coating (Thanner, Karrholm et al. 2000). At two years and excluding the revised case, the Echo Bi-Metric stem subsided slightly more on average than has previously been found for some porous coated stems (Karrholm, Anderberg et al. 2002). The subsidence of the Echo Bi-Metric stem mainly occurred within the first three months after surgery, after which it stabilised without any difference between the groups. We found no significant difference in terms of the HHS and hip pain scores between the two polyethylene types, indicating similar clinical results in the short term.

7.2 Wear of vitamin E-infused highly cross-linked polyethylene at five years

In Study II, we evaluated the femoral head penetration rate of E1 compared with ArComXL, with the emphasis on changes occurring between two and five years after THA in the same randomised, clinical trial as discussed above. We also evaluated implant migration and clinical outcome.

Vitamin E-infused XLPE has been in clinical use since 2008 (Oral and Muratoglu 2011) and, since its introduction and at the time we reported our five-year results, a few short-term clinical studies had been conducted and published, presenting promising outcomes for E1, with very low penetration similar to previous types of XLPE (Lindalen, Nordsletten et al. 2015, Salemyr, Muren et al. 2015, Shareghi, Johanson et al. 2015).

The mid-term results revealed that the median proximal penetration of E1 was significantly lower than that of ArComXL five years after THA. Between two and five years, E1 liners displayed an almost 50% lower penetration rate compared with ArComXL. The reason for the difference in penetration rate between these two types of polyethylene is not known. One possible explanation could be that liners incorporated with vitamin E are subjected to more than double the radiation dose, which could increase their wear resistance. It could also be that E1 liners are subjected to less oxidation from the environment due to their content of vitamin E. There might be other differences between these materials associated with their manufacturing process that could have an influence. However, this difference in penetration does not appear to be of any clinical significance in the five-year perspective.

At the time when we reported our five-year results, only one published report on the mid-term penetration of E1 was available (Nebergall, Troelsen et al. 2016). In contrast to our study, the authors had no control group and the reported mean femoral head penetration at five years was less than half that observed by us. Contrary to the results observed by us, the earlier study did not report any differences in penetration between two and five years. In both studies, cobalt-chromium heads with a diameter of 32 mm were used, but the cup and stem designs were different, albeit from the same manufacturer.

The increased proximal and three-dimensional penetration for both E1 and ArComXL between two and five years that was observed by us most probably reflects a true wear process, as most of the deformation or creep in the material could be expected to have decelerated to a very low level after two years.

Previous studies of other types of XLPE liner with a minimum of five years of follow-up have reported lower penetration rates for the studied liners compared with the control liners of conventional types (Dorr, Wan et al. 2005, Digas, Karrholm et al. 2007, Callary, Field et al. 2013). These studies have used different approaches to report wear parameters. Callary et al. (2013) used radiostereometry to evaluate the penetration of X3 liners five years after THA. They reported a median penetration rate between one and five years that was 20% lower compared with the penetration rate between two and five years observed by us.

The proximal cup migration was small in both groups, but it tended to be slightly higher in the ArComXL group. We found no significant difference regarding femoral head migration and clinical outcome between these two polyethylene types at five years. Contrary to our observations at two years, we found significantly lower proximal and total penetration of E1 liners compared with liners made of ArComXL when studied at five years. So far, the clinical performance in these two groups has been about the same.

Hitherto, the wear pattern for XLPE beyond 15 years is not known and the available data do not include all the types of material available on the market. The use of an additive such as vitamin E could be an advantage. The long-term biological effects of the wear particles from these materials are still unknown, although laboratory studies have shown the absence of any adverse effect (Oral and Muratoglu 2011).

It should be noted that vitamin E-infused liners displayed a penetration rate of about the same magnitude as that observed for some previous types of highly cross-linked polyethylene, without any addition of substances to increase resistance to oxidation. Compared with ArComXL, vitamin E-infused XLPE showed less penetration after five years, which might suggest a clinical advantage in the long term. So far, no complications related to polyethylene wear have been observed in any of the hips included in the study. It is not known whether the difference in femoral head penetration that is actually observed will result in increased implant longevity and a reduced number of future cup revisions due to wear-related problems in the study group. Further follow-up is necessary before any clinical advantage from using vitamin E-infused XLPE can be established. It is also important to ensure that this new material is not associated with any other unexpected adverse events.

7.3 Precision of model-based RSA (MBRSA) in measuring femoral head penetration and cup migration

Radiostereometric analysis is regarded as the most accurate radiographic method in orthopaedic research for assessing the early migration and wear of a prosthetic implant. The accuracy and precision of RSA have been validated with phantom studies (Valstar, Vrooman et al. 2000, Onsten, Berzins et al. 2001, Bragdon, Malchau et al. 2002, Allen, Hartmann et al. 2004, Makinen, Koort et al. 2004), mathematical analysis (Yuan and Ryd 2000) and test-retest investigations (Ryd, Yuan et al. 2000). Conventional marker-based RSA requires the attachment of tantalum markers on the implant, which may be difficult to visualise. Model-based RSA (MBRSA) was developed for the evaluation of implant migration without needing to bead-mark the implants. However, it is uncertain whether this method has the same precision as marker-based RSA.

In Study III, we evaluated the precision of MBRSA in measuring wear and migration in four uncemented cups using the conventional marker-based RSA as a reference. Further, we evaluated whether cup design has any influence on the precision of MBRSA. Four different implants with slightly different geometric shapes were evaluated postoperatively (double examinations) and two years after a THA using both methods.

The evaluation of the postoperative double examinations confirmed that the precision of MBRSA in measuring proximal head penetration and cup migration was comparable to that of conventional RSA for TMT, Trilogy and ABG designs. The fourth design, RingLoc, displayed less precision in both migration and penetration measurements with the use of MBRSA. Furthermore, RingLoc showed significant differences in the mean value of the measurements postoperatively to two years between the two compared methods. The total penetration was higher with MBRSA for RingLoc, TMT and Trilogy. MBRSA showed a significantly lower mean medial/lateral migration for TMT and a higher mean medial/lateral migration for RingLoc compared with conventional RSA. These findings indicate that the precision of MBRSA in measuring penetration and migration was good and acceptable for Trilogy, TMT and ABG but slightly inferior for the RingLoc design.

The reliability test (Cronbach's alpha), as well as the agreement measurements (Bland-Altman plots) between the two methods regarding proximal penetration and cup migration at two years showed the best outcome for the ABG cup, which we believe is related to the shape and geometry of this implant. An evaluation of the Bland-Altman plots revealed a tendency for MBRSA to underestimate the proximal penetration and overestimate the proximal migration in RingLoc cups. Better consistency for cup migration than for penetration at two years was observed when evaluating the Cronbach alpha values and this could be due to greater variability from the migration measurements.

In clinical research, lower precision means that a larger number of cases is required to reveal a significant difference. To avoid any misinterpretation of the results, the presence of a systematic error corresponding to an over- or underestimation of mean values that can be related to a specific cup design and especially in any comparison with an alternative design should be known before the data are interpreted. Despite the poorer outcome for the RingLoc cup using MBRSA, the observed magnitude of the precision relating to proximal penetration, for example, was still reasonably low (about 0.2 mm), as was the systematic error, which means that RSA studies of this design based on MBRSA will still imply much better resolution compared with studies based on conventional radiographs.

Despite its high porosity and rough surface, the TMT cup in our study showed minor differences when studied with conventional RSA and MBRSA. One possible explanation of this could be that this cup is made of a more radiodense material than the RingLoc cup. These findings can be interpreted as meaning that, the rougher and more irregular the surface of an implant is, the poorer the precision of MBRSA when using a hemispherical cup algorithm, provided that the manufacturing material has the same radiographic density.

Several studies have evaluated the precision of MBRSA in measurements of femoral head penetration and cup migration in hemispherical acetabular cups and have reported that this marker-less algorithm is an accurate alternative and is comparable to the conventional RSA (Valstar, Spoor et al. 1997, Borlin, Rohrl et al. 2006). In a laboratory environment, Baad-Hansen et al. (Baad-Hansen, Kold et al. 2007) evaluated the precision of three different RSA techniques, including a marker-free hemispherical algorithm, in migration measurements of a hemispherical (Trilogy) and non-hemispherical component (Trabecular Metal Monoblock component). They reported poorer precision for their marker-free hemispherical algorithm compared with the other two methods that were studied; the conventional RSA, which was only used for Trilogy cups, and the MbRSA 3.0 based on CAD models. Contrary to our results, poorer precision was found in studies of the Trilogy cup when algorithm-based RSA was compared with marker-based RSA.

It has to be pointed out that these findings observed by us are only valid for the implants investigated in the present study. Most probably, the resolution of the measurements is similar for marker-based and different types of model-based RSA when hemispherical cups are studied. Our findings indicate that this need not always be the case and we therefore believe that this presumption has to be verified for new designs and those previously not studied with RSA. Implants with completely different geometries must be investigated to determine whether sufficient precision can be attained using MBRSA by using the marker-based method as a reference. The reason why MBRSA was associated with a poorer resolution when applied to a porous plasma-sprayed cup is unknown, but it could have been caused by its geometry or surface coating. More cup types therefore need to be studied to evaluate whether the RingLoc design is exceptional with regard to its geometry. It appears very probable that this is not the case. This would therefore mean that each new cup design studied with the mathematical algorithm used by us has to be validated against conventional RSA. Most probably, this also applies to shape-based algorithms, at least in those where the implant shape differs from the standard pattern.

7.4 Changes in PTA in supine and standing positions

The position of the prosthetic components after surgery with THA is commonly evaluated on conventional radiographs which are routinely performed in the supine position. A steep cup position increases the risk of dislocation and is also regarded as an important reason for increased polyethylene wear.

Routinely, the inclination of the cup is determined postoperatively on radiographs exposed in the supine position. The patient will, however, perform numerous activities when upright and, between supine and standing, the rotation of the pelvis about the transverse axis might change. The positioning of the pelvis might also change over time. These changes in pelvic positioning have not previously been mapped out with a high-resolution method such as RSA.

Anterior dislocation may occur, due to the large anteversion of the cup caused by excessive posterior pelvic tilt (Biedermann, Tonin et al. 2005, Di Schino, Baudart et al. 2009, Sato, Nakashima et al. 2013). Concern has been raised about the inaccurate measurement of cup position after THA due to pelvic tilt (Lembeck, Mueller et al. 2005, Haenle, Heitner et al. 2007, Babisch, Layher et al. 2008). Consequently, it is important to improve the evaluation of the PTA after THA.

In Study IV, we evaluated the change in PTA in the supine position over time and between supine and standing positions up to seven years after THA. We also studied whether factors such as gender, the condition of the contralateral hip or any low-back disability have any influence on PTA after THA. There are several reports evaluating PTA before and after THA (Nishihara, Sugano et al. 2003, Blondel, Parratte et al. 2009, Taki, Mitsugi et al. 2012). However, there appears to be some disagreement in the literature about the impact of preoperative pelvic tilt on the extent of postoperative tilting of the pelvis in the standing position.

Nishihara et al. (2003) combined 3D CT-scan reconstruction and standard AP radiographs of the pelvis to compare the PTA in the standing position before and one year after THA and found a change greater than 10° in 13% of patients. Blondel et al. (2009) evaluated pelvic tilt in the standing position preoperatively and three years after THA on standing lateral radiographs in 50 patients and reported no significant change between these two occasions. They reported that no patient showed a difference of more than 10° in PTA in the standing position. Taki et al. (2012) calculated the PTA on anteroposterior radiographs in 86 patients in the supine and standing positions two to four years after surgery. At three years, they reported a significant change exceeding 10° when standing in 25% of the patients. Four years after surgery, a change of more than 10° was only observed in 16% of the patients.

In a gait analysis study of 21 patients, Parratte et al. (Parratte, Pagnano et al. 2009) found a change greater than 5° in pelvic tilt following THA in 31% of the included patients. In 2011, Ishida et al. (Ishida, Inaba et al. 2011) reported that patients with large preoperative anterior tilt demonstrated greater changes in pelvic tilt after surgery. In 2015, a report presented by Maratt et al. (Maratt, Esposito et al. 2015) measuring pelvic tilt in 138 patients in the standing position preoperatively and six weeks after surgery reported no significant difference. These variations in results may be explained by differences in sample size, inclusion criteria and the methodology used. Blondel et al. excluded patients with a spinal deformity and bilateral arthritis. Taki et al. included all the patients that had undergone THA. Parratte et al. only included 21 patients with unilateral hips. The author excluded patients with any type of disease that could have an effect on normal gait.

In our study, we found that, after THA, the pelvic position with the patient in the supine position changes over a period of seven years. This change in terms of increasing posterior tilt was comparatively small and more pronounced in females than in males. After surgery, soft-tissue contractures caused by the hip disease can be expected to decrease and even disappear. Our observation of increasing posterior tilt over time could reflect the fact that the soft-tissue distraction continues up to at least six months after the operation and even longer in some patients. From supine to standing, the pelvis tilted in the opposite direction, namely anteriorly. This anterior tilt increased with time and was significant at the seven-year follow-up, especially in females. The increased pelvic tilt in women may be associated with age-related changes of the spine due to osteoporosis, which increases with age and especially in females (Fon, Pitt et al. 1980, Ensrud, Black et al. 1997, Boyle, Milne et al. 2002). Female gender and increasing age have previously been found to be consistent with larger variations in PTA (Taki, Mitsugi et al. 2012), which is consistent with our findings.

We also observed that any change in PTA is not affected by the status of the contralateral hip. It is possible to speculate that untreated osteoarthritis on the opposite side in these patients would result in more anterior pelvic tilt than in those with a normal hip on the opposite side, due to soft-tissue contracture. According to our findings, this was not the case, with findings of close to equal positioning of the pelvis, regardless of the status of the opposite hip. However, it should be pointed out that we only recorded changes between different predefined positions. We were therefore unable to account for any differences between the groups at the starting or reference supine position for each comparison. If present, small variations of this kind are probably difficult to detect based on skeletal landmarks determined on conventional radiographs.

Patients with low-back pain could be expected to have reduced mobility of the spine and the pelvis. The evaluation of low-back pain in our study was retrospective and could therefore be regarded as suboptimal. We found no differences in

PTA in the supine position between these patients and those without low-back pain. From supine to standing, the pelvic tilt was smaller in patients with low-back pain on both follow-up occasions. However, the differences between patients with or without low-back pain were small and amounted to only one to two degrees on average. These findings were consistent with a meta-analysis (Laird, Gilbert et al. 2014) comparing pelvic kinematics in patients with and without low-back pain, which reported no difference in PTA in the standing position between these patient groups. It may be that, as long as no spinal fusion has been performed, low-back problems do not affect hip stability significantly.

In our study, we observed that the pelvic tilt changes by varying degrees after THA. The pelvis tilted posteriorly in the supine position. In individual patients, this tilt reached about 11.0° in the supine position and 18.0° when standing. A large change in PTA may cause hip instability and influence the wear of articular surfaces, depending on the position of the components. An improved understanding of postoperative changes in pelvic tilt may contribute to our understanding of adverse outcomes after THA and ways of reducing the risk of their occurrence.

7.5 Migration of uncemented cups with different types of coating and development of radiolucent lines

Implant loosening and polyethylene wear are two critical factors limiting the longevity of uncemented cups. Several orthopaedic manufacturers have introduced numerous uncemented acetabular implant designs and materials over the past few decades to improve bone-implant in-growth and the long-term survival of prostheses. Porous surfaces were introduced to increase implant stability, to enhance osseointegration and to reduce cup loosening. Several studies have reported high rates of stable fixation for porous-coated designs in primary THA (Clohisy and Harris 1999, Garcia-Rey, Garcia-Cimbrelo et al. 2009, Hailer, Garellick et al. 2010).

Despite major improvements relating to clinical outcomes and survival, acetabular component loosening remains one of the most common causes of failure and revision. The continuing evolution of hip arthroplasty entails a continuing need to evaluate the clinical performance of any new material reaching the market, in order to identify the beneficial properties and to determine whether this new material is associated with any adverse characteristics.

The Regenerex acetabular shell is a press-fit hemispherical acetabular implant made of highly porous titanium alloy metal which was developed to increase volumetric porosity and friction against bone and reduce the modulus of elasticity with the aim of improving fixation and bone remodelling compared with older designs of porous press-fit cups. With an average porosity of 67%, Regenerex has a trabecular-like titanium coating. The manufacturer claims that this design increases the initial stability and enhances bone in-growth into the titanium construct. Currently, however, there are few clinical data and trials relating to the performance of this porous titanium metal.

In Study V, we therefore aimed to compare the fixation of this novel cup with the use of a clinically well-established porous plasma-sprayed cup with a similar basic design from the same manufacturer as a reference (RingLoc). We also evaluated whether the development of progressive radiolucent lines was associated with increased acetabular cup migration.

The radiostereometric evaluation at the five-year follow-up showed that the pattern of migration was not the same for these two designs. The Regenerex cup tended to migrate more proximally ($p=0.05$). The absolute medial/lateral migration values were increased in the RingLoc group ($p<0.001$) and the Regenerex cups tended to migrate medially, while the RingLoc cups tended to migrate laterally. The RingLoc cups displayed more pronounced anterior/posterior translation compared with the Regenerex cups ($p=0.03$). We are unable to exclude the possibility that the higher micromotions observed for the RingLoc cups were an effect of bias, because, in seven of the RingLoc hips, model-based methodology was used because there were too few visible markers. We have previously reported that this design using MBRSA displayed higher migration values compared with evaluations based on liner markers (Shareghi, Johanson et al. 2015). The variability in the direction of migration between the two cup designs could also be due to the different geometry and degree of porosity and/or presence of screws, which may change the lever arm for forces transmitted to the cup from the femoral head.

The postoperative radiographs showed gaps around 16 (41.0%) Regenerex cups and 32 RingLoc cups (60.3%). These gaps were observed in all three zones. In both groups, most of the gaps were located in zone II. The regression analysis showed that there was no association between the presence of a postoperative gap and the development of radiolucent lines five years after operation. On the contrary, the presence of postoperative gaps had a preventive effect on the development of progressive radiolucent lines. The reason for this finding is unknown. It could be that cups with central gaps had more osseous fixation at their periphery. If sufficiently extensive, this kind of fixation could be expected to protect the cup from tilting more effectively.

Radiographic findings of new or progressive radiolucent lines and cup migration are often indicative of unsatisfactory clinical results and may result in revision surgery (Fisher, Mallory et al. 1990). In Study V, we used a limit of newly developed radiolucent lines of 20% or more to be considered as a "true" increase. This limit was chosen arbitrarily with the aim, with a fairly wide margin, of accounting for errors caused by variations in patient positioning and the radiographic projection, in addition to errors related to the measurements themselves. Further studies based on repeated radiographic examinations on the same day are needed in order more firmly to establish the "true" detection limit for the progression of these lines. At the five-year follow-up, four cases with Regenerex and seven cases with RingLoc had developed radiolucent lines occupying at least 20% of the interface. According to the regression analysis, the presence of this extent of newly developed radiolucent lines was associated with increased anterior or posterior migration. These motions thus appeared to have an influence on the quality of the fixation.

It has been shown that even small amounts of migration are incompatible with in-growth (Pilliar, Lee et al. 1986). In a radiosterometric study of fiber-mesh hemispherical press-fit cups with and without a tricalcium-phosphate coating (TCP), Thanner et al. (1999) observed a higher frequency of postoperative gaps in zone II in cups with a TCP coating. They also found a higher rate of postoperative gap disappearance for TCP cups. The gap filling was interpreted as the development of new bone or could represent remodelling due to enhanced osseointegration with the TCP coating. In a biomechanical study, Small et al. (Small, Berend et al. 2013) evaluated the stability of porous titanium cups compared with plasma-sprayed cups. The authors reported an improvement of 23% to 65% in initial stability for porous titanium cups compared with plasma-sprayed cups. Reina et al. (Reina, Rodriguez et al. 2007) studied 145 hips with hemispherical plasma-sprayed cups (RingLoc) for an average of 8.5 years and reported no case of progressive radiolucent lines, migration or cup loosening.

The type of surface coating available for uncemented acetabular cups most probably plays an important role in the establishment of initial stability to allow successful osseointegration and increase the longevity of the implant. Our radiostereometric and radiographic observations between the two cup designs with different coatings revealed small differences five years after surgery. The porous titanium cups showed smaller medial/lateral migration. However, the clinical significance of this finding remains to be studied. Currently, there are lack of data on the performance of this design. The next step would be to initiate a prospective randomized study comparing Regenerex against a well-established design.

08 CONCLUSION

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CONCLUSION

- At two years, the proximal and total penetration, implant stability or clinical outcome did not differ between THAs with cups fitted with liners made of vitamin E-infused XLPE and ArComXL. The femoral head penetration pattern of E1 was similar to that of previous types of XLPE, with an initial bedding-in phase and an apparent subsequent phase of low steady-state wear.

- At five years, cups with liners made of E1 showed less penetration than in the control group, which suggests a clinical advantage in the long term. The penetration rate in the group with vitamin E-infused liners was of about same magnitude as that observed for some early versions of XLPE without the addition of antioxidants.

- The precision of MBRSA in measuring wear and migration at two years was poorer for one of four cup designs studied. This finding indicates that the resolution of MBRSA may vary, depending on the surface coating and implant geometry. The resolution of MBRSA therefore needs to be studied for each type of basic design.

- We observed that pelvic tilt changed with time after THA, both in the supine position and when rising from supine to standing. In individual patients, this change reached about 11.0 degrees in the supine position and 18.0 degrees when standing. Female patients in particular displayed larger changes in pelvic tilt in both supine and standing positions.

- The migration pattern between Regenerex and RingLoc differed, but the median values were all less than 0.2 mm. We observed an association between progressive radiolucent lines and the magnitude of anterior/posterior migration, suggesting that even a small amount of migration in uncemented cups will influence the quality of fixation. There appear to be no or only small beneficial effects from using porous titanium when it comes to the quality of fixation.

09 FUTURE PERSPECTIVES

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FUTURE PERSPECTIVES

Polyethylene material in THA has undergone significant improvements over time, with the development of highly cross-linked polyethylene. The introduction of new XLPE materials using antioxidants such as vitamin E and COVERNOX, which increase the oxidative stability and wear resistance of the material, has the potential to improve the results for both cemented and uncemented THAs in terms of wear-related issues. The initial results when it comes to reducing wear in second-generation XLPE are promising, but long-term results are not yet available. New materials introduced into clinical use need to be closely monitored and long-term studies are required to determine whether the low wear of XLPE in the short term continues in the long-term perspective. Close monitoring of all types of new XLPE in clinical studies is the key to increasing our knowledge of the wear pattern of these materials developed with different manufacturing procedures.

The use of RSA as the gold standard for evaluating the wear and migration of orthopaedic joint implants should be continued. Given the increasing number of new implant designs reaching the market, every new design should be monitored by RSA in a small group of patients. Implants with less favorable characteristics could be identified at an early stage and this would lead to better patient care, a reduced number of revision surgeries and a reduction in the costs associated with these procedures. In order to save time and costs, the marker-less alternative (MBRSA) to the conventional marker-based RSA could be used more frequently in clinical studies. However, we have previously reported that the precision of this marker-less methodology could be affected by the shape and geometry of implants. For this reason, we recommend that the precision of MBRSA in wear and migration measurements of new implants with different shapes and geometries should be validated by using the conventional marker-based RSA as a reference. Although MBRSA does not require the attachment of markers to the implant, the need to insert markers into the surrounding bone still remains and could be regarded as a limitation. A completely marker-less RSA could be the solution to this limitation. Efforts have been made to establish a method of this kind based on bone surface models instead of marker insertion (Seehaus, Olender et al. 2012). The examined joint needs to be CT scanned before and after the implantation of the prosthesis. However, the accuracy and the precision of this marker-less approach are currently lower compared with marker-based RSA, making it less suitable for migration measurements. Further research and development in relation to this method might make it possible to achieve satisfactory migration measurements with an accuracy and precision closer to those of conventional RSA.

Another area in which the use of conventional RSA could be beneficial is in the evaluation of the position of the pelvis after THA. A steep cup position has been regarded as an important reason for increased wear. Comparatively little is known about how the pelvic position changes over time and between different positions and the studies presented so far have not been totally unanimous. Further, the relationship between pelvic tilt and polyethylene wear needs to be further investigated. One limitation when using the RSA method in these evaluations is the lack of stereoradiographs prior to surgery. The need for marker insertion that only takes place during the operation makes it impossible to obtain images prior to surgery and, moreover, does not enable any comparison of the pelvic position before and after surgery. The EOS imaging system could be used as an alternative to RSA, conventional radiographs and CT scans in studies of pelvic and acetabular parameters. EOS has been proven to be an accurate, reliable method compared with standard radiographs and CT scans, without any significant inconvenience caused by the metallic artifacts of implants. The EOS system is a high-resolution radiological imaging system providing 3D images with a low radiation dose. This method provides simultaneous capture in orthogonal planes in standing and sitting positions. The ability of EOS to obtain precise data on implant orientation according to the patient's posture opens new perspectives for the analysis of the pelvic frontal and sagittal balance and its potential impact on implant function and failures.

The continuous evaluation of uncemented cups with different surface properties and different kinds of treatment or coating is essential. New implants will continue to reach the market and there is still scope for improvements, not least in terms of both the reproducibility of positioning and fixation, especially in revision surgery. The development and evaluation of preoperative planning based on three-dimensional images and navigation systems is part of this development and requires accurate instruments to study their potential beneficial and less desirable effects. The use of high-resolution techniques that make it possible to identify potential early problems and predict long-term performance after a relatively short period of time will be mandatory in this process.

The RSA method should be further developed to facilitate its use and make this method even more accessible. To achieve this goal, the software used to measure digital radiographs and the computations and controls necessary to obtain the final data should be even more automated. A development of this kind has already been initiated. This development should also include RSA measurements based on CT images, which would open the door to a simpler way of implementing model-based RSA (Otten, Maguire et al. 2017). In the longer perspective, new ways of obtaining information on skeletal and implant positions that not are based on radiographic techniques will most probably emerge (Hoffmann, Schroder et al. 2012).

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