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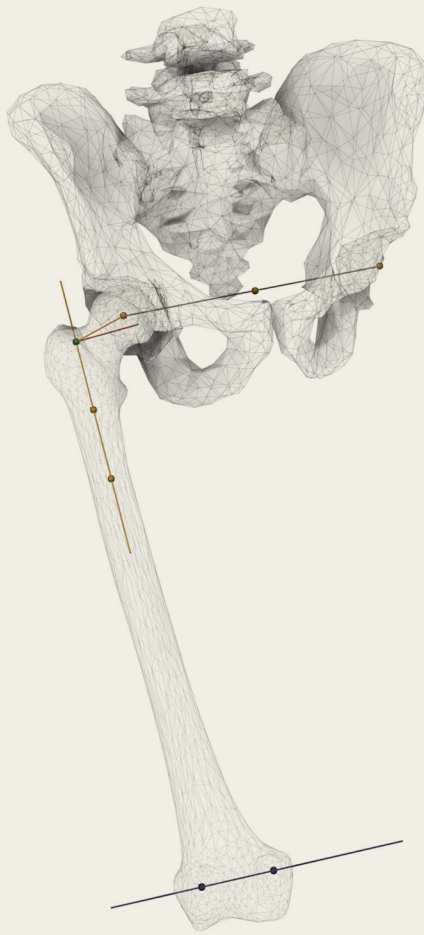
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The importance of biomechanical restoration for total hip arthroplasty

SVERRIR ÞÓR KIERNAN

CLINICAL SCIENCES, LUND, ORTHOPAEDICS | LUND UNIVERSITY



The importance of biomechanical restoration for total hip arthroplasty

The importance of biomechanical restoration for total hip arthroplasty

Sverrir Þór Kiernan



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DOCTORAL DISSERTATION

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Arkan Sayed-Noor, Professor. Umeå University

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Abstract Total hip arthroplasty (THA) has become a safe and very successful surgical intervention. A vast majority of patients get their expectations met. Improvement of materials, implant designs, and surgical techniques, have extended prosthetic survival. However, inferior placement and sizing of a hip prosthesis are known to increase the risk of mechanical failure, wear, and early loosening as well as patient dissatisfaction. The main objective of this thesis was to evaluate the importance of improved biomechanical restoration for the function and survival of THA, as well as finding ways of achieving this improvement. We used radiostereometry (RSA), low dose computer tomography (CT) for 3D measurements, 3D templating, prosthetic modularity, and 3D gait analysis, together with patient-reported outcomes. We found a strong correlation between initial postoperative femoral neck anteversion (FNA) and subsequent posterior rotation and loosening of cemented stems. Our 3D measurement techniques showed near-perfect inter- and intraobserver agreements regarding our femoral offset (FO), acetabular offset (AO), and global offset (GO) measurements. We did not see any differences in RSA migration between uncemented modular and standard stem types, both stabilised well with good migration pattern. Postoperative FNA and FO/AO quota had no impact on uncemented stem migration, maybe due to the study being underpowered. The standard stem tended to result in insufficient GO, whereas the modular stem did not. 3D templating was superior in the correct prediction of the final stem size and neck, but 2D templating overestimated stem-size and underestimated neck-length. There was no statistically significant difference regarding cup size predictions. We found an unexpected progressive varus deformation, with concomitant corrosion-related cobalt ion release, from the modular stem-neck junction. However, the ion-concentrations did not correlate with adverse local tissue reaction (ALTR) as measured with MRI up to 8 years. Biomechanical restoration during THA does positively impact the quality of postoperative overall gait pattern, with faster walking speed and with less trunk lean over the affected side. Increased FNA was associated with increased internal hip rotation during walking. An increase in external hip adduction moments was, on the other hand, not associated with a change in FO/AO quota but with a more upright walking position and increased walking speed. Biomechanical restoration is important for THA and our studies confirm the need for precise measuring- and evaluation-tools for this kind of research.		
Key words: THR, THA, Hip arthroplasty, Osteoarthritis, Hip surgery, RSA, Radiostereometry, Anatomical Restoration, 3D-CT, 3D-measurements, 3D-templating, Anteversion, Femoral Offset, Acetabular Offset, Global Offset, Gait analysis		
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The importance of biomechanical restoration for total hip arthroplasty

Sverrir Þór Kiernan



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MADE IN SWEDEN 

To Marisa my wife and my two sons, Victor & Tómas

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Abstract

Total hip arthroplasty (THA) has become a safe and very successful surgical intervention. A vast majority of patients get their expectations met. Improvement of materials, implant designs, and surgical techniques, have extended prosthetic survival. However, inferior placement and sizing of a hip prosthesis are known to increase the risk of mechanical failure, wear, and early loosening as well as patient dissatisfaction. The main objective of this thesis was to evaluate the importance of improved biomechanical restoration for the function and survival of THA, as well as finding ways of achieving this improvement. We used radiostereometry (RSA), low dose computer tomography (CT) for 3D measurements, 3D templating, prosthetic modularity, and 3D gait analysis, together with patient-reported outcomes.

We found a strong correlation between initial postoperative femoral neck anteversion (FNA) and subsequent posterior rotation and loosening of cemented stems. Our 3D measurement techniques showed near-perfect inter- and intraobserver agreements regarding our femoral offset (FO), acetabular offset (AO), and global offset (GO) measurements. We did not see any differences in RSA migration between uncemented modular and standard stem types, both stabilised well with good migration pattern. Postoperative FNA and FO/AO quota had no impact on uncemented stem migration, maybe due to the study being underpowered. The standard stem tended to result in insufficient GO, whereas the modular stem did not. 3D templating was superior in the correct prediction of the final stem size and neck, but 2D templating overestimated stem-size and underestimated neck-length. There was no statistically significant difference regarding cup size predictions. We found an unexpected progressive varus deformation, with concomitant corrosion-related cobalt ion release, from the modular stem-neck junction. However, the ion-concentrations did not correlate with adverse local tissue reaction (ALTR) as measured with MRI up to 8 years. Biomechanical restoration during THA does positively impact the quality of postoperative overall gait pattern, with faster walking speed and with less trunk lean over the affected side. Increased FNA was associated with increased internal hip rotation during walking. An increase in external hip adduction moments was, on the other hand, not associated with a change in FO/AO quota but with a more upright walking position and increased walking speed.

Biomechanical restoration is important for THA and our studies confirm the need for precise measuring- and evaluation-tools for this kind of research.

Sammanfattning på svenska

Höftprotesoperationer har blivit ett säkert och mycket framgångsrikt kirurgiskt ingrepp och lever upp till mycket av de förväntningar som patienterna har. Förbättring av material, protesdesign och kirurgiska tekniker har förlängt protesöverlevnaden påtagligt. Emellertid är icke optimal protesplacering och felaktigt val av komponentstorlekar känt för att öka risken för biomekaniska problem och ökat slitage vilket kan leda till tidig lossning såväl som missnöje hos patienterna. Huvudsyftet med denna avhandling var att utvärdera vikten av förbättrad biomekanisk kirurgisk rekonstruktion avseende funktion och protesöverlevnad, samt att hitta sätt att uppnå denna förbättring. Vi använde radiostereometri (RSA), lågdos datortomografi (CT) för 3D-mätningar, 3D-mallningssystem, modularitet av proteskomponenter samt 3D-gånganalys, tillsammans med patientrapporterade resultat.

Vi fann en stark korrelation mellan hur man initialt positionerade en cementerad protesstam i anteversion och hur den senare migrerade med bakre rotation. Våra 3D-mättekniker uppvisade nästan perfekt precision vad gäller våra mätningar av femoral offset (FO), acetabular offset (AO) och global offset (GO). Vi såg inga statistiska skillnader i RSA-migration mellan modulära och standardtyper av ocementerade stammar, båda stabiliserades och uppvisade bra migrationsmönster. Postoperativ anteversion och FO/AO-kvota hade ingen påverkan på stammigrationen, möjligen kan uteblivna skillnader bero på för få patienter i studien. Standardstammen tenderade att resultera i otillräcklig GO, medan modulära stammen inte gjorde det. 3D-mallning var överlägsen för korrekt förutsägelse av den slutliga stamstorleken och halslängden, men 2D-mallningen överskattade stamstorlek och underskattade halslängd. Det fanns ingen statistisk signifikant skillnad vad gäller förutsägelser om cupstorlek. Vi hittade en oväntad progredierande varusdeformation, med samtidig korrosionsrelaterad koboltjonfrisättning från den modulära stam-hals-kopplingen. Jonkoncentrationerna korrelerade emellertid inte med lokala vävnadsreaktioner (ALTR) mätt med magnetkamera upp till 8 år. Biomekanisk förbättrad rekonstruktion vid höftproteskirurgi påverkar positivt kvaliteten på det totala gångmönstret med snabbare gånghastighet och med mindre bållutning över på den drabbade sidan. Förändring i höftrotation under gång var associerad med förändring i stammens anteversion i samma riktning. En ökning av externa höftadduktionsmoment var däremot inte förknippad med förändring av FO/AO-kvoten utan med en mer upprätt gångposition och ökad gånghastighet.

Biomekanisk rekonstruktion är betydelsefull vid höftproteskirurgi och våra studier konfirmerar behovet av noggranna mät- och utvärderingsverktyg för denna typ av forskning.

List of papers

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

- I. The importance of adequate stem anteversion for rotational stability in cemented total hip replacement. A Radiostereometric study with ten-year follow-up**
Sverrir Kiernan, Kirstine Lintrup Hermann, Philippe Wagner, Leif Ryd and Gunnar Flivik
Bone Joint J. 2013 Jan;95-B(1):23-30. doi: 10.1302/0301-620X.95B1.30055.
- II. Effect of symmetrical restoration for the migration of uncemented total hip arthroplasty. A randomised RSA-study with 75 patients and 5-year follow-up**
Sverrir Kiernan, Mats Geijer, Martin Sundberg and Gunnar Flivik
J Orthop Surg Res. 2020 Jun 17;15(1):225. doi: 10.1186/s13018-020-01736-0.
- III. Unexpected varus deformity of modular neck hip stems and concomitant metal ion release and MRI findings. Data from a randomised RSA-study in 75 hips with 8-years follow-up**
Sverrir Kiernan, Bart Kaptein, Carl Flivik, Martin Sundberg and Gunnar Flivik
Acta Orthopaedica (conditionally accepted 2020-07-02)
- IV. Evaluation of 2D vs. 3D templating in uncemented total hip arthroplasty. An observational cross-sectional study**
Sverrir Kiernan, Martin Sundberg, and Gunnar Flivik
Manuscript ready for submission
- V. Pre- and postoperative offset and femoral neck version measurements and validation using 3D computed tomography in total hip arthroplasty**
Mats Geijer, Sverrir Kiernan, Martin Sundberg, and Gunnar Flivik
Submitted to *Acta Radiologica Open*
- VI. Anatomical restoration during total hip arthroplasty is related to change in gait pattern. A study based on computed tomography and three-dimensional gait analysis**
Anna-Clara Esbjörnsson, Sverrir Kiernan, Louise Mattsson, Gunnar Flivik
Submitted to *BMC Musculoskeletal disorders*

Abbreviations

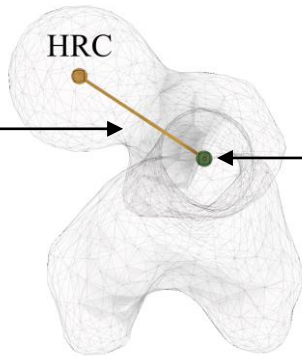
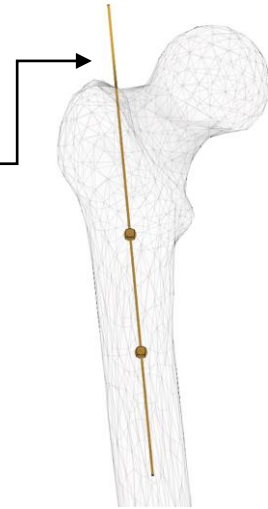
3D	Three-dimensional	LLD	Leg length discrepancy
3D-CT	Three-dimensional Computer Tomography	MACC	Mechanically assisted crevice corrosion
95%-CI	95%-Confidence Interval	MARS- MRI	Metal Artefact Reduction Series Magnetic Resonance Imaging
ABG	Anatomique Benoist Gerard	MBRSA	Model-based Radiostereometric analysis
ALTR	Adverse local tissue reaction	MoM	Metal on metal
AO	Acetabular Offset	MoP	Metal on polyethylene
AP	Anteroposterior	MPRs	Multiplanar reformations
BMI	Body mass index	MRI	Magnetic resonance imaging
CAS	Computer-assisted surgery	OA	Osteoarthritis
Co	Cobalt	PACS	Picture Archiving and Communications System
CoCr	Cobalt Chromium alloy	PHM	Posterior head migration
Cr	Chromium	PPFF	Periprosthetic femoral fracture
CTDIvol	Computer Tomography dose index by volume	RLL	Radiolucent lines
EGS	Elementary geometry shape	ROM	Range of motion
EQ-5D	EuroQol – Five Dimensions	RSA	Radiostereometric analysis
FFO	Functional Femoral Offset	SD	Standard deviation
FNA	Femoral neck anteversion	SF-36	Short-Form 36
FO	Femoral Offset	TFO	True Femoral Offset
FO/AO	Femoral Offset/ Acetabular Offset quota	THA	Total hip arthroplasty
GDI	Gait Deviation Index	THR	Total hip replacement
GO	Global Offset	Ti	Titanium
HOOS	Hip Osteoarthritis Outcome Score	TMZF[®]	Titanium, molybdenum, zirconium, and iron alloy (Ti-6Al-4V)
ICC	Intraclass correlation	VAS	Visual analog scale
IQR	Interquartile range		

Definitions

We used the following definition for our CT measurements:

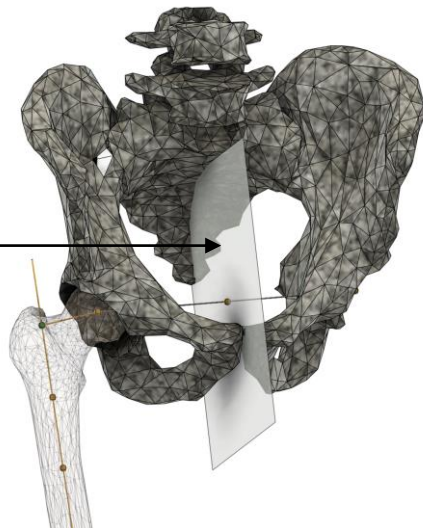
We defined the longitudinal axis of the proximal femur as the line between the center of two best-fit intramedullary spheres, one at the distal level of the trochanter minor and the other 6cm further down in the femoral shaft.

True femoral offset (FO) was defined as the perpendicular distance from the long axis of the proximal femur to the hip rotational center (HRC).

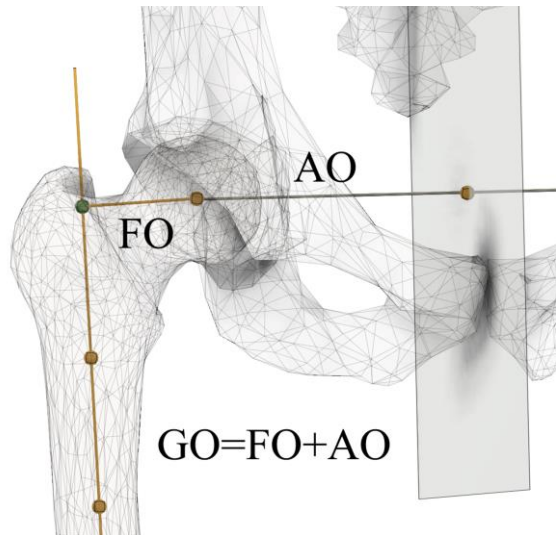


We will refer to the point where the FO line intersects with the longitudinal axis of the proximal femur as point A.

We defined the symphyseal plane as a plane in the middle of the symphysis and perpendicular to the bi-ischial line.

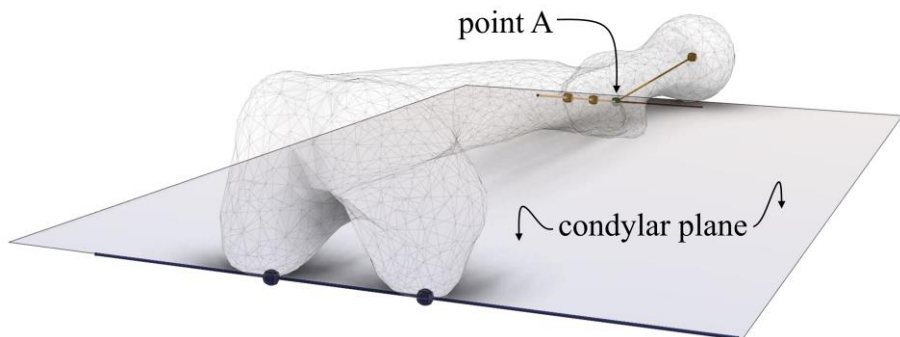


We defined the Acetabular Offset (AO) as the shortest distance from the symphyseal plane to HRC.

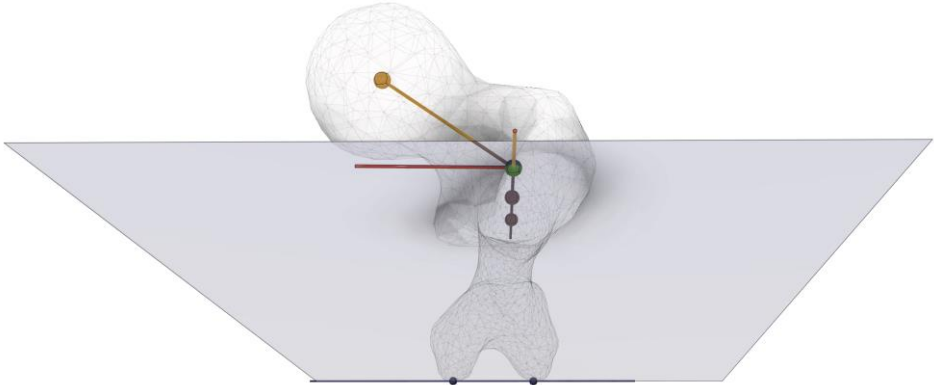
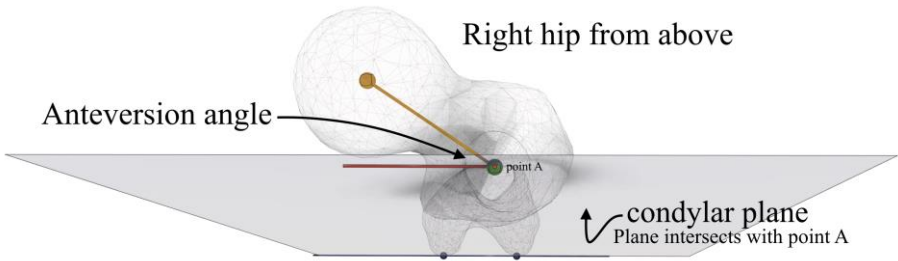


We defined the Global Offset (GO) as the sum of the FO and AO

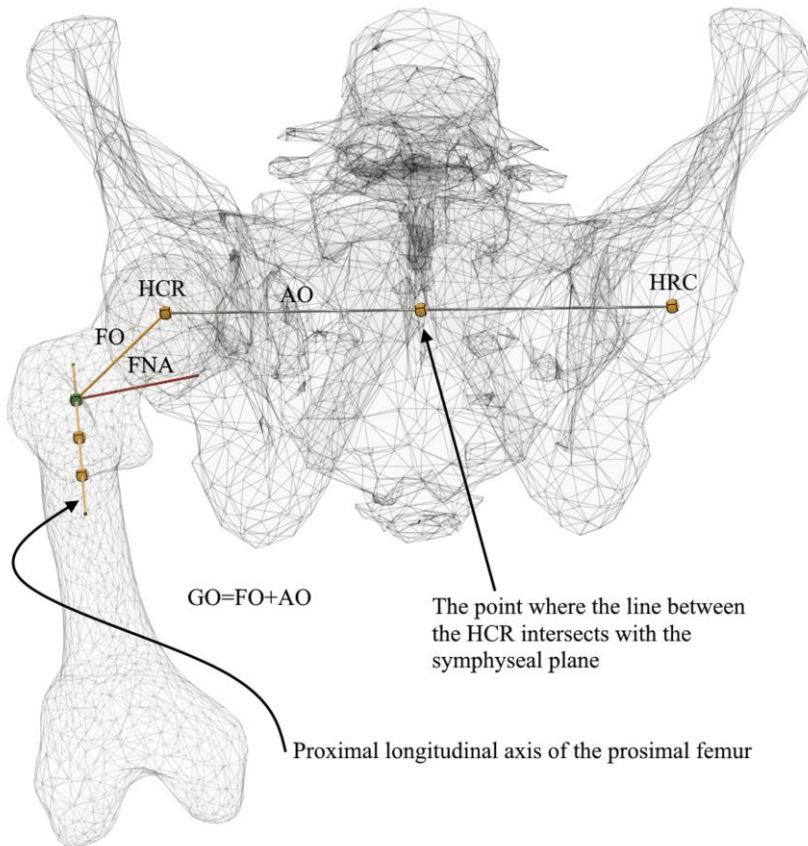
We defined the condylar plane as the posterior subchondral joint surface of the medial and lateral femoral condyles projected proximally through point A.



We defined the femoral neck anteversion (FNA) as the angle between the condylar plane and the line representing the FO. The lines for the anteversion angle measurement were perpendicular to the axis of the proximal femur.



Summary of definitions



Thesis at a glance

	Paper I	Paper II	Paper III	Paper IV	Paper V	Paper VI
Type of study	Analytical Observational A prospective intervention Cohort study	Analytic Experimental Randomised controlled trial	Analytic Observational Cohort study	Analytic Observational Cross-sectional study	Diagnostic study	Analytic Observational A prospective intervention Cohort study
Question	Is there a relationship between postop femoral neck anteversion (FNA) and prosthetic stability?	Does restoration of original hip anatomy benefit the survival of total hip replacement (THR), and is there a use for stem modularity?	Is there a loss of integrity in our implanted modular-neck hip stems?	Is 3D templating better than 2D templating	To evaluate the accuracy of new software in measuring proximal femoral anatomy on low-dose CT	Is there a relationship between change in hip anatomy and gait patterns
Population/year	60 patients 1995–1998	75 patients 2009–2011	75 patients 2009–2011	30 patients 2015–2016	75 patients 2009–2011	75 patients 2009–2011
Results	< 10° of FNA had significantly more aseptic loosening resulting in 40% revisions within 10 years	Postop FNA, GO, and FO/AO quota had no impact on stem migration. The modular stem was better in restoring GO	There is a corrosion-related release of especially cobalt ions with a correlated starting progressive varus deformation of the neck-stem	3D templating was better in correctly predicting stem-size and neck-length. 2D overestimated stem-size and underestimated neck-length	The 3D-analytic software produced reproducible results with near-perfect inter- and intraobserver agreements	An increase in hip adduction moment resulted in less trunk and pelvic obliquity and increased speed of walking. Our modification in the FO/AO quota did not impact the adduction moment during gait. However, increased anteversion was accompanied by reduced pelvic rotation and inward rotation of the hip during walking.
Clinical perspective	Avoid implanting stems in less than 10° of FNA	There are no clinical implications for using the modular type to counteract postop stem migration	Caution should be taken regarding the observed progressive varus deformation and Co ion release in the neck-stem junction. RSA can be used for measuring the integrity of an implant	3D is better than 2D templating	We now have an accurate tool available for measuring anatomical variables in 3D on low-dose CT	It is of clinical importance to understand to what extent a change in FO/AO quota and FNA affects postoperative gait patterns

Description of contributions

Paper I

Study design: Gunnar Flivik

Data collection: Sverrir Kiernan

Data analysis: Sverrir Kiernan

Manuscript writing: Sverrir Kiernan

Manuscript revision: Sverrir Kiernan, Gunnar Flivik, Kirstine Lintrup Hermann, Leif Ryd

Paper II

Study design: Sverrir Kiernan, Gunnar Flivik, Martin Sundberg

Data collection: Sverrir Kiernan, Mats Geijer

Data analysis: Sverrir Kiernan

Manuscript writing: Sverrir Kiernan

Manuscript revision: Sverrir Kiernan, Gunnar Flivik, Martin Sundberg, Mats Geijer

Paper III

Study design: Sverrir Kiernan, Gunnar Flivik, Bart Kaptein

Data collection: Sverrir Kiernan, Carl Flivik

Data analysis: Sverrir Kiernan, Bart Kaptein

Manuscript writing: Sverrir Kiernan

Manuscript revision: Sverrir Kiernan, Gunnar Flivik, Bart Kaptein, Martin Sundberg

Paper IV

Study design: Sverrir Kiernan, Gunnar Flivik, Martin Sundberg

Data collection: Sverrir Kiernan

Data analysis: Sverrir Kiernan

Manuscript writing: Sverrir Kiernan

Manuscript revision: Sverrir Kiernan, Gunnar Flivik, Martin Sundberg

Paper V

Study design: Sverrir Kiernan, Gunnar Flivik, Mats Geijer, Martin Sundberg

Data collection: Sverrir Kiernan, Mats Geijer

Data analysis: Mats Geijer, Sverrir Kiernan

Manuscript writing: Mats Geijer, Sverrir Kiernan

Manuscript revision: Mats Geijer, Sverrir Kiernan, Gunnar Flivik, Martin Sundberg

Paper VI

Study design: Sverrir Kiernan, Gunnar Flivik, Louise Mattsson

Data collection: Sverrir Kiernan, Louise Mattsson

Data analysis: Anna-Clara Esbjörnsson, Sverrir Kiernan

Manuscript writing: Anna-Clara Esbjörnsson, Sverrir Kiernan

Manuscript revision: Anna-Clara Esbjörnsson, Sverrir Kiernan, Louise Mattsson, Gunnar Flivik

Introduction

General background

Total hip arthroplasties (THA) are safe and effective surgical interventions for relieving pain and improving physical function caused by arthritis or other reasons for hip deformation and pain. Annually there are more than one million THAs performed worldwide. There is a wide variety of implantation rates, indications, and types of prosthesis used for THA procedures among different countries. Generally, the femoral head and parts of the femoral neck are typically removed and replaced with a metal stem fixed with or without bone cement into the femoral canal. A femoral head made of metal or ceramic is fixed to the stem. For uncemented fixation of the cup, we use an outer shell of metal and an inner surface of polyethylene or more rarely ceramic or metal. For cemented fixation, we use polyethylene cups. The operation is for patients suffering from severe pain and thus reduced quality of life. The most significant predictor for postoperative patient satisfaction concerning pain relief and physical function is, not unexpectedly, their preoperatively perceived pain and functional impairment. Although the majority of patients with the correct criteria for surgical intervention substantially improve, not all are satisfied after receiving THA. Furthermore, as outcomes after hip replacement surgery have improved over time, the contraindications against surgical intervention have been reduced. As a consequence, we now, to an increasing extent, receive patients with active lifestyles and higher expectations regarding surgical outcomes, which in turn calls for further improvements in surgical techniques.

Successful joint replacement surgery is not only associated with prosthetic design, but also a surgical technique aiming at restoring the hip anatomy for optimal function (1-4). The restoration of anatomy by accurate placement of stem and cup increases the likelihood of successful prosthetic operation as it will result in a correct biomechanics and hip function (1-4).

There is an ongoing discussion about the biomechanical aspects of aseptic loosening of stem and/or cup in relation to stem anteversion, prosthesis offset, stem size, and body mass index (BMI)(5-7). One aspect to take into consideration is that we normally deepen the acetabular socket to make room for the acetabular component (for anatomical definitions see page 16-19). We are thereby reducing the acetabular offset (AO). A concomitant increase in femoral offset (FO) is needed to restore global offset (GO) symmetry with the contralateral hip. GO as the sum of AO and

FO and femoral neck anteversion (FNA) are measurements that we use in our studies to evaluate postoperative outcomes regarding implant position and degree of restored anatomy in THA. There are several different ways and techniques for measuring these variables, some better than others, but traditionally the different offsets are measured on anteroposterior (AP) pelvic radiographs (8, 9). Nevertheless, for correct measurement of true FO and degrees of FNA, we have to rely on measurements using 3-dimensional computer tomography (3D-CT) scans. To know what implant to use and in what position to put it in, we commonly prepare ourselves for surgery by making a preoperative plan, a so-called templating. We use 2D templating software to facilitate anatomical restoration (10), and there is an increasing awareness for the need to advance from 2D projections to more accurate 3D measurements (11, 12). Preoperative templating gives the surgeon the means to measure and access individual anatomical landmarks and predict the type, size, offset, and orientation of the prosthetic components (13-15). This process is valuable as it gives the surgeon a means to individually anticipate specific problems with postoperative hip function due to malposition of implants (16, 17). If the affected side, planned for surgery, is too deformed, we can use the hopefully unaffected contralateral side. For templating, asymmetry of the different elements or measurements of the hip-joints may, however, render the contralateral hip unsuitable, and several articles have reported significant asymmetry of different measurements(18-20). A high degree of hip joint symmetry is, however, the norm (21, 22).

The use of modular necks has been suggested to facilitate anatomic restoration (23). Modular hip stems with different neck options can adapt to different femoral geometries by adjusting neck version, femoral neck angle, and neck length. These modifications are valuable for improving the range of motion (ROM) and soft tissue balance(24-27). However, not much is known about other effects of increased modularity (28). Further, we now have Computer Assisted Surgery (CAS) (29) to facilitate the placement of a prosthesis into its exact planned position.

Specific background

Reduced hip adduction moments, hip joint rotations, and sagittal plane motion are common gait deviations in individuals with hip osteoarthritis(30-32). To facilitate hip abductor strength, we need a firm soft-tissue balance around the joint. Asymmetrical GO may lead to limping, and reduced FO may increase acetabular polyethylene wear(33). In patients exhibiting recurrent dislocation following THA, the soft tissue tension is fourfold lower, compared to in patients with no dislocations(34). Soft tissue tension is determined by a combination of leg length and global offset (GO), which consists of true FO and acetabular offset (AO) (see under definitions). A change in the balance between AO and FO is often required,

and advocated (35). A decrease in AO is usually the result of reaming the acetabulum. We normally medialize the cup within a safe zone defined for patients individually (36). Cup malposition is a common cause of impingement, limitation of ROM, acceleration of cup wear, liner fracture, and instability(37-41). Cup position measurements can be unreliable due to pelvic tilt, but a safe zone for placement of the cup to minimize risk for instability is within $43^{\circ} \pm 12^{\circ}$ of operative inclination and $31^{\circ} \pm 8^{\circ}$ of tilt adjusted operative anteversion(42). However, medialization of the cup reduces the GO. To restore the GO towards symmetry, we need a stem with an FO greater than that of the native contralateral hip. We consider the compensatory increase of FO needed as this strategy appears to reduce polyethylene wear (33, 43) by improving lever arm biomechanics resulting in less load transferred to the cup (44). It also improves prosthetic stability, decreasing the risk for dislocation(45), and restores soft tissue tension (34). Moreover, restoring FO has a positive impact on isometric hip abductor strength (46, 47) and on walking speed and on knee flexion and extension during walking one year after THA (48). Restored FO also impacts knee joint moments but with no apparent impact on hip joint moments (49).

In vivo measurements demonstrate that stair climbing is the activity that applies the highest forces, including torsion to the shaft of a femoral stem(50). The anteroposterior load on the femoral head during stair climbing is well over 7 times body weight(51). This force transmitted to the stem acts on it with a torque around the femoral shaft that promotes retroversion of the stem. Such torque may endanger the implant's stability(50). This phenomenon led to stem designs with increased rotational resistance(52). However, factors such as the degree of anteversion in which the stem initially is implanted may still play an essential role in the loading equation. Previous studies have shown a substantial increase in the torsional moment with decreasing stem anteversion angles(53). Furthermore, there is a correlation between a low postoperative stem anteversion and later posterior head migration (PHM)(5). Early stem migration as a result of posterior rotation and subsidence is predictive of aseptic loosening(54).

Leg-length-discrepancy (LLD) can result in biomechanical changes in hip joint load both on the long and the short side, which may cause problems in the long term (55). The size of clinically significant LLD is, however, unclear (56). Excessive leg-lengthening after THA may be associated with complications such as nerve palsies(57), low back pain(58), and abnormal gait(59, 60). Moreover, LLD is a common cause for filing a law-suit against orthopedic surgeons(61).

Today preoperative hip templating is standard practice and traditionally done on 2D anteroposterior pelvic (AP) radiographs(10). Some measurements and templating of implant orientation like cup inclination and stem varus-valgus position can be done adequately on plain 2D radiographs. In contrast, other measurements like the cup and stem anteversion and true offset are more challenging to measure due to the rotational uncertainty in 2D. These disadvantages have caused an increasing interest

in advancing from the limitations of 2D projections to the more accurate 3D measurements(11, 12). Calculations in three dimensions (3D)(62) have provided more precise measurements. Measurements performed using 3D data sets have shown high consistency for both intra- and interobserver agreements(63). Moreover, 3D measurements using CT have provided measurements with high reproducibility(64) and can now be done with a substantial dose reduction compared with standard CT while maintaining sufficient image quality(99).

Mechanically assisted crevice corrosion (MACC) became clinically relevant with the emergence of large metal-on-metal (MoM) total hip arthroplasty (THA) early in the 21st-century (65). Recently, there have been reports on corrosion for metal-on-polyethylene (MoP) THA in a variety of stem designs caused by fretting in the head-neck junction (66-69). The increased number of interfaces introduced by modular prosthetic systems has the potential of increasing the risk for adverse local tissue reaction (ALTR) caused by the release of metal ions and inflammatory mediators (65, 70). Taper corrosion at the modular junctions of THA femoral stems are known to cause ALTR (71, 72). Furthermore, there have been cases of revisions as a consequence of ALTR associated with neck-stem taper(73, 74). They should be considered as a potential cause for new-onset progressive, disabling pain in the groin (75). There is an ongoing debate about the cause of corrosion in the neck-stem junction. Some say that the shape of the neck-stem tapers may deviate from ideal design dimensions, contributing to relative motions between the neck and stem (76). Others state that corrosion occurs regardless of design and state the primary cause to be mixed metal couples with an unequal modulus of elasticity (Young's modulus), allowing for increased metal transfer and surface damage (galvanic mode of corrosion) (77).

Measurements on AP pelvic radiographs (functional FO) underestimate the true FO(78, 79). How the patients orient their hips during the radiographic analysis can significantly impact this measurement(80) and flexion(81). FNA measurements are dependent on the positioning of the femur for radiographic analysis as well as for two-dimensional CT analysis(82). Therefore, there is a need for more exact measurement techniques for exact templating methods and navigational assistance(83) at surgery.

When deciding the anteversion of the stem, we must also reflect on the anteversion of the cup. The combined anteversion, regulates the risk of hip impingement and dislocation(84). According to previous studies, the FNA and cup anteversion safe zone is about 15–25° degrees, respectively. Although, the safe zone estimates vary significantly in literature since it depends on varying anatomical definitions of measurements(85). Nevertheless, to achieve the proposed safe zone, in some cases, the FNA needs to be changed substantially from its original orientation, possibly leading to a shift in the hip rotation range of motion for the individual. Earlier studies show no association between change in FNA and self-rated function or pain (28, 86). However, the association between changes in FNA and a person's gait pattern

is not clear in the current literature. Despite well-documented improvements following hip replacement surgery, long-term deviations in gait and function often persist possibly attributable to muscular weakness (87) and compensatory movements (88-90). Most studies have focused on FO concerning gait and function. However, both the FO and AO are essential to consider when restoring hip joint anatomy. In our study, we have examined the relationship between FO and AO, i.e., the FO/AO quota. Unlike FO by itself, the AO/FO quota is a relative measure and thus independent of the size of the pelvis.

In previous studies, we have seen a correlation between low postoperative stem anteversion and later posterior head migration (PHM)(5), and that in conjunction with subsidence is predictive of aseptic loosening(54). However, the literature is lacking long term follow-up of stems with low postoperative anteversion and the risk of increased revision rate.

There have been no studies reporting the effect of stem modularity on the migratory behavior of the stem.

To our knowledge, there are only two clinical studies published evaluating whether 3D templating is better than 2D templating in predicting the implant size for uncemented total hip arthroplasty(91, 92).

During the follow-up and data-processing of study II, we got some unexpected results regarding the modular design. At the 5-year follow-up, we noted that the complex consisting of the stem-neck-head as a rigid body used for RSA was no longer a fixed segment, and the prosthetic head seemed to have migrated with respect to the body of the stem. We are the first to report on this phenomenon.

Radiostereometric analysis (RSA)

RSA is the method used in our studies to measure the migration of prosthetic components and is the gold standard because of its high accuracy and precision. The measurements in RSA is done in an orthogonal coordinate system where the x-axis runs horizontally from right to left, y-axis runs vertically from caudal to cranial, and the z-axis horizontally from posterior to anterior. The measurements are translation and rotation along and around these axes. Accuracy is how spot on the measurement is to the correct result. Precision is how consistent the measurement is using the same method. Precision without accuracy is when the method gives the same wrong result each time measured. Accuracy without precision is when the method gives results clustered around the right result but without a bullseye. For RSA, we express precision as a 95 or 99% confidence interval distance from zero (bullseye).

RSA examinations are done with the patients in a supine position with two X-ray tubes above and a calibration cage underneath the patient (Fig. 1). The two X-ray

images are taken at an angle of about 40° from each other. The calibration cage is a radio-translucent box that contains radiodense tantalum markers at defined 3D positions. The software then calibrates itself about the position of these markers using the two images. In this way, the exact position of each implanted marker can be determined relative to the markers in the calibration cage.

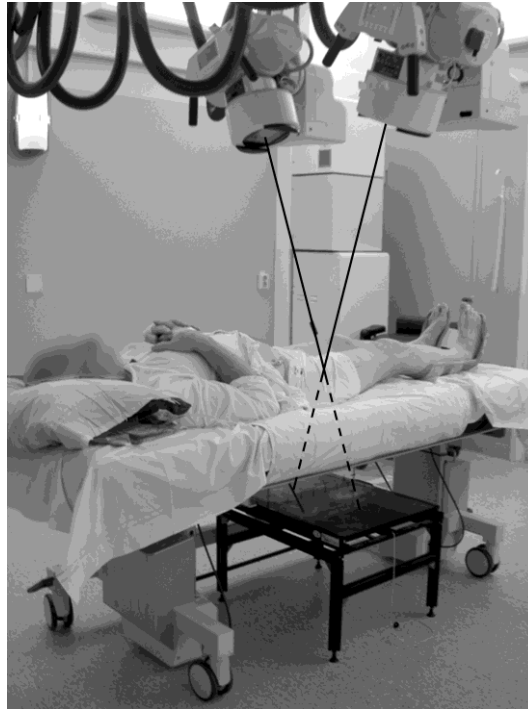


Figure 1: Patient in position for RSA examination with the two X-ray tubes above and the calibration cage beneath the patient

Marker-based RSA is when we mark implants and structural parts like bone with tantalum markers. Three is the minimum amount of markers to form an RSA segment to analyse micro motions of segments relative to each other at different time points. We normally implant up to 10 markers per segment as more markers give better results and due to the risk for loosening of markers. The markers must be fixed in place in order to form a sufficiently stable RSA segment to minimize the error of segment geometry between examinations at different time intervals. The error of segment geometry is named the mean error of body fitting, typically considered acceptable if less than 0.35mm(93). An RSA segment must have a proper spatial dispersion of markers in all three dimensions to increase the precision of measurements. We use the condition number (CN) to express the spatial dispersion.

CN=150 is an acceptable upper limit and CN of 1 denotes that all markers are ideally spread, for example, around a spherical object.

In our studies, we used a combination of marker- and markerless, i.e., model-based RSA. Using model-based RSA where prosthetic parts substitute as a segment, usually implies less accuracy and precision. However, it is motivated by the fact that RSA marker insertion upon manufacturing is often unavailable due to the need for CE marking procedures and therefore expensive as well as the increased challenge in identifying the markers(94).

Gait analysis

Clinical three-dimensional gait analysis allows the measurement and assessment of a wide range of variables in the gait cycle. It facilitates the identification of abnormal characteristics in the gait pattern. It gives complex interdependent data in the form of kinematic, kinetic, and temporospatial parameters. Kinematic parameters, which include the tracking of external markers placed on the patient, refer to the motion of a body or a system of bodies without consideration given to its mass or the force acting on it. Standard kinematic variables are hip flexion and extension, hip abduction and adduction, and pelvic tilt during walking. Kinetic parameters, which include the monitoring of patient-ground-forces, refer to the turnover, or rate of change, of specific factors in the body, commonly expressed as units of amount per unit time. Standard kinetic variables are hip flexion and extension moments and hip abduction and adduction moments. That is the tendency to cause rotation about a point or an axis. Temporospatial parameters are factors like walking speed, stride, and time in the single support phase, which portrays the ability to carry weight through one hip. We use these parameters to gain a better understanding of patients walking difficulties(95).

3D gait analysis can also give a single measure of the quality of a particular gait pattern, such as through the Gillette Gait Index (GGI), the Gait Deviation Index (GDI), and the Gait Profile Score (GPS). The GGI was initially referred to as the Normality Index (NI), and quantifies the difference between data from one gait cycle for a particular individual and the average of a reference dataset from people exhibiting no gait pathology. It incorporates temporal-spatial as well as kinematic parameters. However, it has several shortcomings, one being that it is specific to children with cerebral palsy. The GDI is a revised GGI index of overall gait pathology. It is based on kinematics from the pelvis and the hip in all three planes, the knee and ankle in the sagittal plane and foot progression in the transversal plane(96). We interpret GDI scores as follows: a value of 100 or higher indicates a typical gait pattern, while each 10-point decrement below 100 indicates one standard deviation (SD) from normal gait (e.g., a GDI score of 80 indicates 2 SD from normal

gait). The GPS is similar to GDI but can be calculated independently of the feature analysis, which adds to our understanding of clinical interpretation. However, it is more suitable for individual analysis of specific gait deviations. It reports in the form of deviations in degrees from what is considered a normal pattern as a whole and also in the form of the Movement Analysis Profile (MAP) concerning pelvis, hip, knee, and foot kinematics. The MAP summarizes much of the information contained within kinematic data. It provides useful insight into which variables are contributing to an elevated GPS, which makes it easier to identify variations in functionality on an individual bases, for example, concerning changes in the gait pattern pre- to postoperatively.

Aims

The overall aim of this thesis is to evaluate the importance of biomechanical restoration for prosthesis stability, prosthetic survival, and hip function and to explore tools for measurement and facilitation of these factors.

Specific aims

- **Paper I** – To examine whether there is a relationship between low hip-stem anteversion and stem migration and to quantify risk of prosthetic failure and revision.
- **Paper II** – To examine whether restoration of hip anatomy counteracts the postoperative migration of an uncemented stem. Moreover, to evaluate if stem-modularity makes their placement easier in accordance to their preoperatively planned position.
- **Paper III** – During the follow-up and data-processing for our study in paper II, we got some unexpected results regarding the modular design. At 5-year follow-up, we noted a compromised integrity of the modular stem with varus deformity in the neck-stem interface. Our aim in this paper is to investigate the cause of this unexpected phenomenon by measuring the movement of the head in relation to the tip point of the stem using RSA and rate level of deformation with whole blood ion levels of metal ions and ALTR formation.
- **Paper IV** – To analyze whether 3D is better than 2D templating in the prediction of prosthetic parts used during total hip arthroplasty.
- **Paper V** – To evaluate pre- and postoperative proximal femoral symmetry by semi-automated 3D CT measurements of FNA and the different offsets in the cohort described in paper II and to validate the software measurements by inter- and intraobserver agreement calculations.
- **Paper VI** – To quantify changes in hip anatomy and gait patterns one year after THA in patients with hip osteoarthritis using the same cohort as in paper II and to explore the relationship between change in hip rotation during gait and change in FNA, as well as the change in external hip adduction moments during gait and effects of change in FO/AO quota one year after THA.

Patients and methods

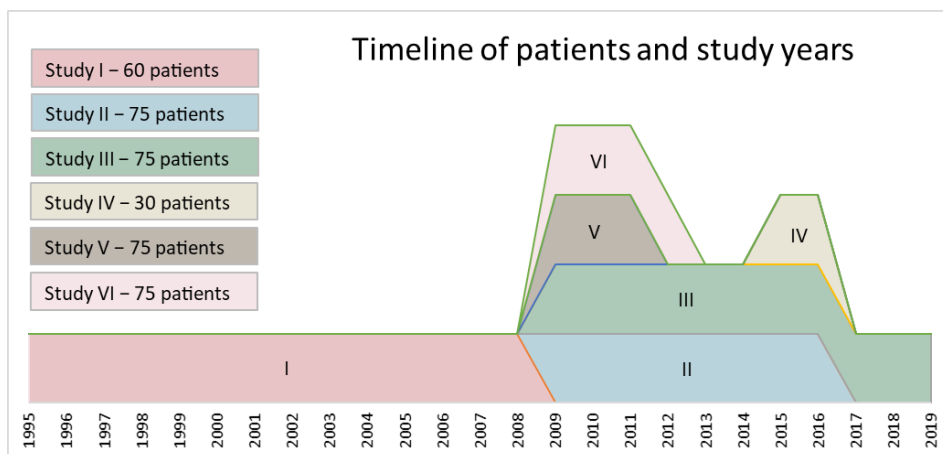


Table 1. Demographic data

Characteristics	Study I	Study II	Study III	Study IV	Study V	Study VI
Total number (n)	60	75	75	30	75	75
Number analyzed (n)	37	72/69	72/67	30/28	71	65
Male/female	28/32	48/27	46/26	19/11	45/26	44/21
Laterality (n)						
Right/left	28/62	41/34	39/33	18/12	39/32	34/31
Mean age at operation (yrs. (range))	67 (51–82)	59 (34–80)	59 (34–80)	58 (41–71)	59 (34–80)	59 (34–74)
Mean BMI at operation (kg/m ²)(range))	27 (20–36)	29 (20–36)	28 (20–36)	26 (18–35)	28 (20–36)	28 (20–36)
BMI, body mass index						

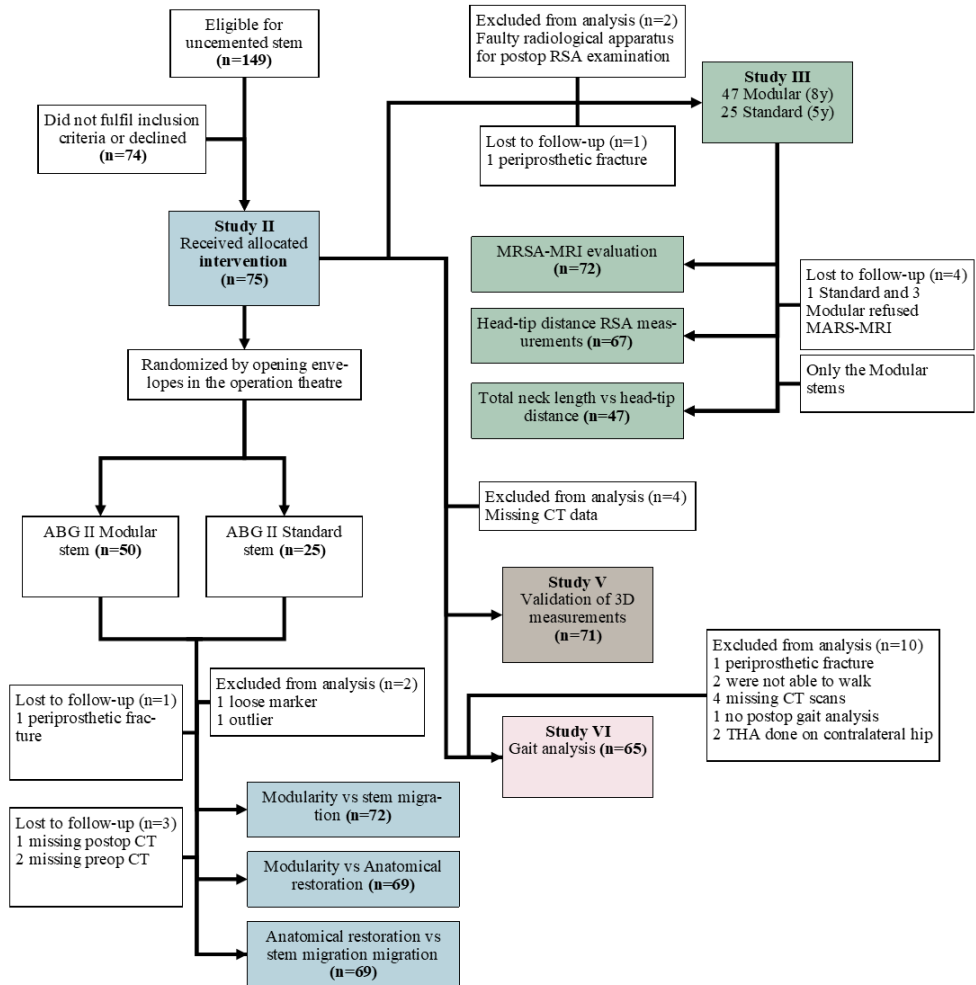
Patient cohorts and inclusion process

There were three different cohorts in total for all 6 studies in our project. However, studies II, III, V, and VI had the same cohort in common. For the demographics of the final selection for the different studies, see table 1.

The inclusion and exclusion criteria were the same for all studies. However, apart from our first study, we only considered patients with bone quality and morphology of the proximal femur suitable for an uncemented stem, i.e., type A and some type B femurs according to the Dorr classification(97). Patients who were < 75 years of age with primary unilateral osteoarthritis of the hip and were capable of understanding the conditions of the study with CT-scans, gait analysis, and RSA at follow up, and who were willing to participate for the duration of the prescribed follow-up were asked to enroll, and had to give their written informed consent to participation. Exclusion criteria were: previous major orthopedic surgery in the lower limbs, other lower extremity joint pain or severe back pain, rheumatoid arthritis, diabetes mellitus, neurologic disease, BMI>40, and other conditions affecting walking ability. We recruited participants from the THA waiting list at the department of orthopedics, Skåne University Hospital, Lund, Sweden. All enrolled participants provided written and verbal informed consent to participate in all parts of the study in accordance with the Declaration of Helsinki. For the inclusion process, see the Consort flow Diagrams.

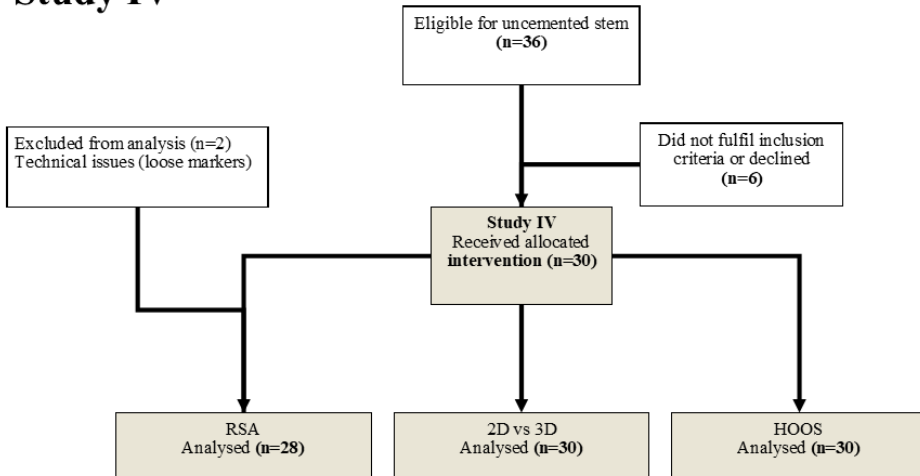
Consort flow Diagram

Study II, III, V and VI



Consort flow Diagram

Study IV



Implants

For the first study, we used the ScanHip system with the Optima and Classic II stems (Biomet, Bridgend, United Kingdom) intended for cemented use. Initially, we planned to use the Optima stem in all patients. However, during the study, its manufacture was discontinued and replaced by the slightly modified Classic II, which was considered easier to implant. Both stems had a matt surface, a collar, and a rounded stem shape. The Optima stem had a straighter shoulder and therefore was broader than the Classic II (Fig. 2). A total of 31 Optima and 29 Classic II stems were used.

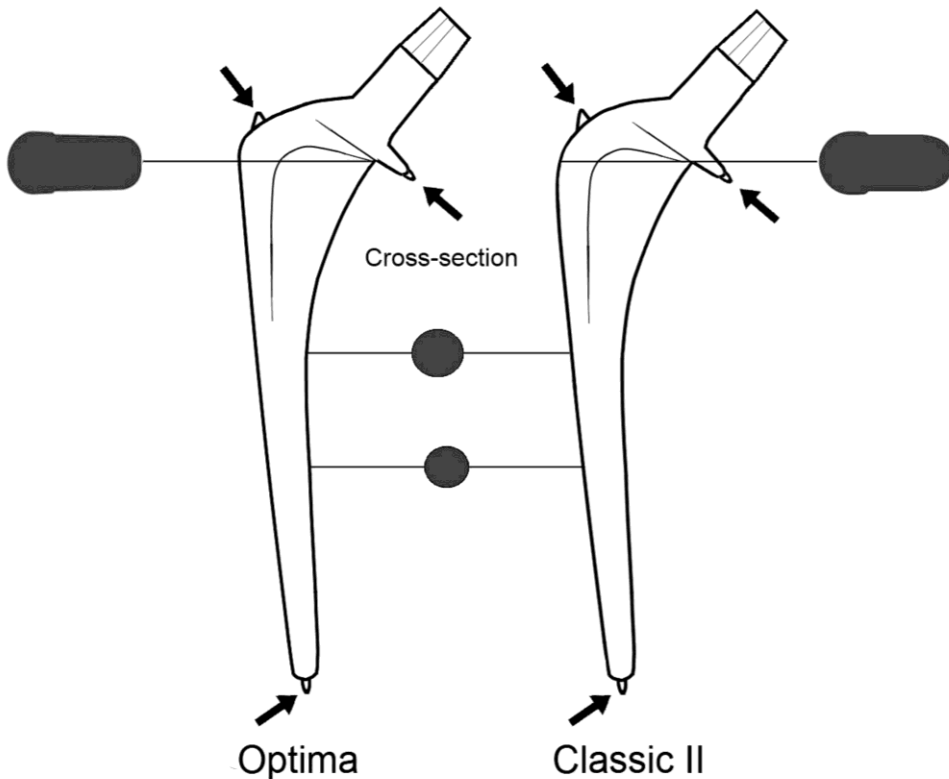


Figure 2: Diagrams showing the differences between the Optima and Classic II stems. The Optima stem had a straight shoulder and was, therefore, broader than the Classic II stem, which had a rounder shoulder to facilitate placement. Both stems were rounded in cross-section. The manufacturer supplied these stems with titanium towers, each with a tantalum marker attached to its tip at the prosthesis shoulder, collar and tip (arrows).

Studies 2, 3, 5, and 6, were based on the same cohort. For this cohort, we used 50 modular and 25 standard stems (ABG II modular[®] and monolithic[®] respectively with Trident[®] Acetabular system (Stryker Orthopaedics, Mahwah, New Jersey, USA)) (Fig. 3). The ABG II Hip Stem is an anatomical stem intended for cementless, press-fit application and therefore orients itself into the best proximal fit. The proximal region of the stem has a coating with PureFix[®] HA. The standard system includes left and right stems with eight body sizes ranging from size 1 to size 8 in which offset increases with size. The modular version came in three parts, i.e., a stem, neck, and head for the most suitable extramedullary anatomic fitting. It, therefore, had enhanced alignment abilities to allow improved range of motion and soft-tissue balance by various choices in neck length (short/long), version (anteverted, standard, retroverted), and CCD angle (125°/130°/135°) as well as different head length (-5mm/std/+5mm).



Figure 3: Anatomique Benoist Gerard (ABG) II system: Standard (monolithic) and Modular Stems used in this study II

In the fourth study, we operated all patients with Anato[®] hip (the redesigned ABG II stem) and Trident[®] Acetabular system (Stryker Orthopedics, Mahwah, New Jersey, USA) (Fig. 4). The Anato Stem has the same concept as the ABG II stem being an anatomical stem intended for a cementless, press-fit application and is designed for the best proximal anatomical fit. The proximal region of the stem is coated with PureFix HA. The system includes left and right monolithic femoral stems with neutral and anteverted neck options and eight body sizes ranging from size 1 to size 8 where offset increases with size.



Figure 4: Anato stem, Trident Hemispherical Acetabular Shell, X3 Polyethylene Insert and, LFIT CoCr Femoral head

Methods and tools of evaluation

Surgical procedures and randomization

The same posterolateral surgical approach with the patient placed laterally was used in all our studies. Before stem implantation, we marked the proximal femur with 9 to 10 tantalum markers (diameter 0.8 mm), of which we put 3 to 4 in the lesser trochanter region and 5 to 6 in the greater trochanteric region. In the first study, the stems came already marked by the manufacturer with one tantalum marker (diameter 1.0 mm) at the prosthesis shoulder, one on the collar, and one at the tip (Fig. 2).

Paper I

The operations were undertaken by eight surgeons in all, comprising both consultants and residents under supervision. The surgeons did not attempt to achieve a particular stem anteversion at surgery. However, the surgeons placed the stems in what seemed to be the most suitable position according to their judgment. Prechilled

Palacos bone cement with gentamicin (Schering-Plough, Brussels, Belgium) was used and mixed using the Optivac vacuum-mixing system (Biomet Cementing Technologies, Sjöbo, Sweden). We used a distal femoral plug in all operations as well as pulsatile lavage, retrograde cement filling, and cement pressurization via a proximal femoral seal.

Paper II, III, V and VI

We prepared 75 marked and numbered envelopes randomized for 50 modular and 25 standard stems. The latter was our control group. The surgeon then opened one of these envelopes in the operation room at the time of surgery. Two experienced hip surgeons performed the operations and attempted to restore the hip-anatomy based on measurements done on 2D radiographs with the healthy contralateral hip as reference. The ABG II is an anatomical and cementless stem, and therefore, the surgeons had little or no control over its orientation into the proximal bed of the femur. However, well in place, the surgeons had the option to use one of three neck versions (retroverted, standard, and anteverted) in order to mimic the contralateral hips anatomical orientation. Postoperative regimens allowed full weight-bearing immediately following surgery. Patients were encouraged to use an appropriate walking aid for 2 months to support normal gait patterns and avoid limping. The patients received rehabilitation according to standard practice at the hospital and, after that, in a primary care setting of the patient's choice.

Paper IV

Three experienced hip surgeons performed the operations and placed the stems according to the best proximal anatomical fit. They checked axial and rotational stability, aiming at symmetrical restoration of global offset, equal leg length based on soft tissue balance, and preoperative 2D templating using different neck length choices (-4, 0, +4, and +8) and the option of neutral or anteverted neck. The cup was positioned referring to the 2D templating and size estimated based on local conditions while reaming. Information only from the 2D templating was available during surgery.

Radiostereometry (RSA)

RSA values in studies I, II, and IV were expressed as migration (rotation and translation) about/along the three axes in an orthogonal coordinate system (6° of freedom), and referred to as transverse (x-axis), longitudinal (y-axis) and sagittal (z-axis). We considered distal translation (subsidence) and longitudinal rotation (both in/about the y-axis) as primary effect variables for how the stem migrates. We used a uniplanar RSA technique with the patient supine(93). The two Xray sources were fixed, mounted to the ceiling.

Paper I

We used a type-41 calibration cage (Tilly Medical, Lund, Sweden) and the UmRSA computer software version 5.0 (RSA Biomedical, Umeå, Sweden). The reference examination was performed within one week of the operation and served as the starting point for all further examinations. We carried out follow-up examinations at 3 and 6 months, and at 1, 2, 5 and 10 years, with a time tolerance of 5% to 10% at each interval. We used analog radiographs up until the 2-year follow-up. In contrast, at a 5-year follow-up and onwards, we used direct digital imaging, as the hospital had converted to a digital picture archiving and communications system (PACS).

Paper II

We used the same type-41 calibration cage (Tilly Medical, Lund, Sweden). However, a different software, the Model-based RSA computer software version 4.0 (MBRSA, RSAcore, Leiden, Netherland) with an elementary geometry shape (EGS) to add 2 fictive markers to the stem, one at the tip of the stem and one in the center of rotation in the head of the prosthesis. The EGS-hip analysis method includes accurate estimation of the positions of the head and the distal tip of the hip stem (94). The reference examination was performed on the first postoperative day and served as the reference for all further analyses. Follow-up examinations were carried out after 2 weeks, 3 months, and at 1, 2, and 5 years, with a time tolerance of 5% at each interval.

Paper III

This study had the same cohort as in paper II. Follow-up examinations were the same as in paper II with the added eight-year follow-up for the modular stems. Our primary outcome was the change in the distance between the center of rotation of the prosthetic head and the tip of the stem measured by successive RSA using postop as a reference (Fig. 5).

Paper IV

We used a type-43 calibration cage (Tilly Medical, Lund, Sweden) and the MBRSA 4.0 computer software version 4.0 (Leiden, Holland). We used model based RSA (MBRSA, RSAcore, Leiden, Netherland) for the stem and caput. RSAcore, Leiden converted CAD data from the prosthetic manufacturer for data compatibility with their MBRSA software. The reference examination was performed on the first day after surgery and served as the reference point for all further examinations. Follow-up examinations were carried out after 2 weeks, 3 months, and at 1 and 2 years, with a time tolerance of 5% to 10% at each interval.



Figure 5: We measured the head-tip distance reduction over time

3D CT techniques and measurements

Paper I

In study I, we measured stem anteversion on postoperative CT scans using a Toshiba Xpress HS single slice scanner (Toshiba Corp., Tokyo, Japan). We confined the slices to a section through the center of the femoral head, the middle of the lesser trochanter, and the middle of the femoral condyles at knee level. We performed measurements as described by Murphy et al(98) using a mathematical 3D correction adjusting for the actual positioning of the femur as described by Hermann and Egund(82). This technique had a precision of 1.6° for anteversion measurements.

Paper II, V and VI

For study II, we performed two separate CT scans pre- and postoperatively using a low-dose CT technique, with an effective radiation dose exposed to the patient equivalent to that of conventional radiography(99). We performed the CT on a multi-detector helical Brilliance 64 CT scanner (Philips, Eindhoven, The Netherlands). Helical CT was performed from the mid-pelvis, including the anterior superior iliac spine to about 6 cm distal to the lesser trochanter, and from directly

proximal to the femoral condyles to directly distal to the knee joint. Postoperative imaging covered the same area. We used a low-dose setting for the preoperative study, CT dose index by volume (CTDI_{vol}) at 4.8, and a medium-dose setting for the preoperative knee study (CTDI_{vol} at 4.2). In contrast, CTDI_{vol} was 16.4 for the postoperative hip study to compensate for the hip arthroplasty, but knee dose was unchanged(99). The images were archived in the local picture archiving and communication system (PACS).

We used measurements from one observer (SK) in study II and VI. For study IV, two observers blinded towards each other (MG, a radiologist, and SK, an orthopedic surgeon) performed measurements on pre- and postoperative 3D-CT examinations using a CT based 3D templating software (Ortoma PlanTM, version 1.0.0.26 (Ortoma AB, Gothenburg, Sweden). They made side-to-side comparisons of the AO, true-, and functional FO, and FNA between the non-affected and the osteoarthritic side on all patients. They repeated the same measurements postoperatively for surgical outcome evaluation. We validated the measurement technique by performing an interobserver agreement analysis on all pre- and postoperative measurements. For inter-observer agreement measurements, the two observers performed the above measurements on 71 pairs of hips on all pre- and postoperative studies, 284 measurements per observer. For intraobserver measurements, both observers repeated the measurements about 2 months later on both the pre- and postoperative CT using 15 randomly selected pairs of hips; 60 measurements per observer.

Paper IV

The CT examinations were performed 2 to 4 weeks before the operation and 2 weeks postoperatively. We used the same CT scanner as for study II.

Radiological evaluation and classification

Paper I

At 10 year follow-up, we obtained conventional hip radiographs of all 37 remaining patients. We then evaluated the radiographs for localized endosteal femoral osteolysis and radiolucent lines (RLLs). We defined osteolysis as a cystic lesion with endosteal scalloping not visible on the first (directly postoperative) radiograph. We measured the extent and width of any RLL and osteolysis at the bone-cement interface and assigned them to the different Gruen zones 1 to 7 on the frontal view, and zones 8-14 on the lateral view(100, 101). These measurements were performed digitally on calibrated computer screen images, but the visual definition of radiolucency was sometimes challenging to define. Therefore, in order not to overestimate the findings, we considered an RLL to be present if radiolucency was > 1 mm wide at the bone-cement interface. Using these measurements, we defined

“radiological loosening” as an apparent migration of more than 2 mm in combination with osteolysis and RLLs of more than 50% of the total bone–cement interface. Given the fact that subsidence can obscure otherwise distinct lucent zones around the bone-cement interface, our definition seems to be within safe limits. We graded the THAs according to their postoperative femoral neck anteversion into three groups using a modified Tönnis grade(102)(Table 2).

Table 2. Modification of the Tönnis grading system

Grade	Tönnis system		Our modification	
	Anteversión (°)	Description	Anteversión (°)	Description
Grade -3	< 10°	Severely decreased	< 10°	Low
Grade -2	10° to 14°	Moderately decreased	10° to 25°	Normal
Grade 1	15° to 20°	Assumed normal		
Grade +2	21° to 25°	Moderately increased		
Grade +3	>25°	Severely increased	> 25°	High

Paper III

We wanted to estimate the effect the different sizes of lever-arms had on the rate of reduction in head-tip distance. We, therefore, measured the lever arm gained by the combination of different component choices. We measured the length of a line from the head center to the point of its intersection with the longitudinal axis of the stem on calibrated templates (Fig. 6)

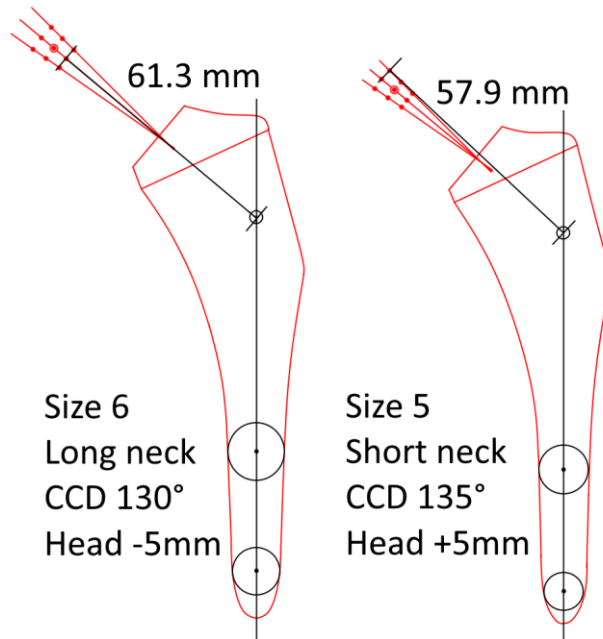


Figure 6: Examples of measurements of total neck length

Paper VI

For study VI, we did a radiographic classification of osteoarthritis according to the modified Kellgren Lawrence grade ranging from 0-4, where 0 represents no osteoarthritis and 4 severe osteoarthritis(103).

Templating

2D templating

2D templating is standard praxis in preparation for all our planned THA cases. It is a process that gives surgeons the means to choose the correct stem size, and in the case of the modular stems, with enhanced alignment abilities, to choose the most suitable modular neck for extramedullary anatomic fitting. Preoperative planning was done on calibrated digital plain radiographs using Sectra IDS7 PACS Orthopaedic Package™ (Sectra AB, Linköping, Sweden) (Fig. 7). We produced the X-rays in a standardized manner where we centered the anteroposterior view of the pelvis on the symphysis pubis, with toes touching to control femoral rotation. During the templating process, we used the anatomy of the contralateral healthy hip as a reference. In study II, the surgeons also relied on measurements previously done by a radiologist on 3D-CT scans, whereas, in study I and 4, only information from

the 2D templating was available during surgery. For study IV, the surgeons tried to predict the size and position of the stem and cup as well as neck length using -4 , 0 , $+4$, or $+8$ heads using 2D planning blinded towards the 3D templates done at least one week previously.

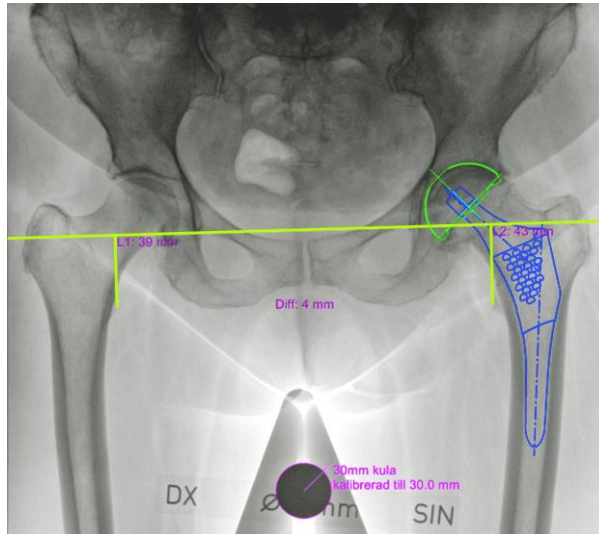


Figure 7: 2D templating

3D templating

For study II and in succession studies 5 and 6, based on the same cohort, we evaluated the pre- and postoperative 3D-CT examinations using a CT based 3D templating software (Ortoma PlanTM, version 1.0.0.26, Ortoma AB, Gothenburg, Sweden). We used the measurements for all these studies but included different parts. We used AO, true FO, GO, and femoral neck angle in these studies. Furthermore, we included functional FO in study V, and the FO/AO quota in study VI. The templating software assigned the pelvis and knees CT scan volumes to a combined 3D volume. Thick slab multiplanar reformations (MPRs) were provided in the orthogonal planes by the software (Fig. 8), and the reconstructed volume stepwise automatically rotated for alignment to the anterior pelvic plane, the sagittal plane and the anterior pelvic plane. The bi-ischial line between the teardrops on an AP thick slab MPRs defined the anterior pelvic plane(104). The line between the anterior superior iliac spines on the axial reconstruction defined the sagittal plane, and the line between the anterior superior iliac spines and the anterior point of the symphysis pubis on the lateral reconstruction defined the anterior pelvic plane.

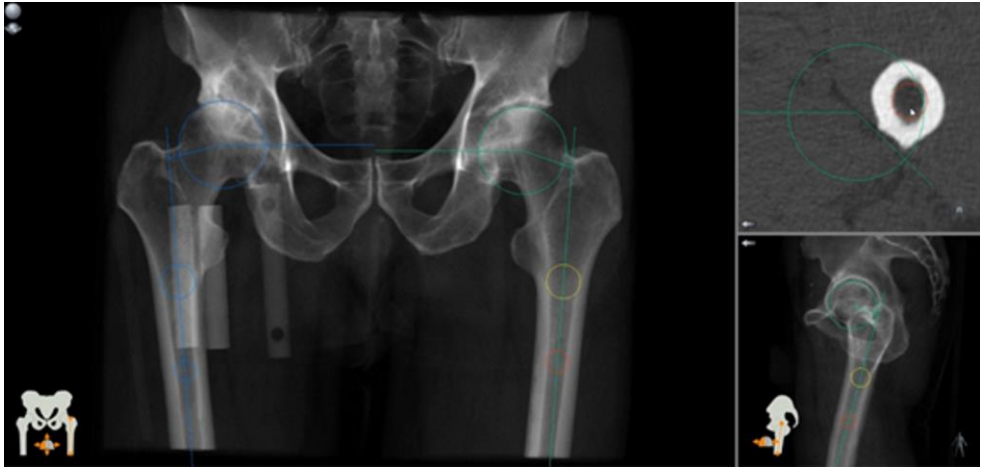


Figure 8: Screen capture showing the best-fit circles defining the femoral head, the definition of the long axis of the proximal femur, acetabular offset, and femoral offset (FO). We used the coronal reformation for the functional FO, and we measured the true FO in three dimensions. The external objects at the right hip are bone density phantoms.

The center of a best-fit sphere, intramedullary, on the axial MPR at the level of the distal part of the lesser trochanter and a best-fit sphere 6 cm more distal to the first, defined the long axis of the proximal femur (Fig. 8 and 9).

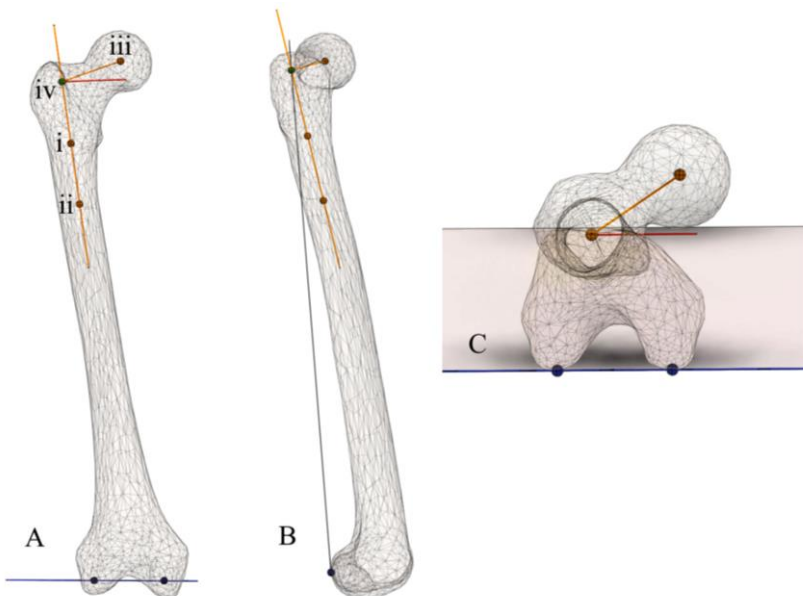


Figure 9: Schematic 3D illustration of the definition of femoral neck anteversion (FNA) in studies II–VI. Two points in the proximal femur define the long axis of the femur, i) at the inferior border of the lesser trochanter, ii) at a point about 6 cm distal in the femoral shaft. iii) the center of rotation of the femoral head

The line tangential to the posterior subchondral joint surface of both femoral condyles defined the condylar line. We adjusted these points in the craniocaudal direction on the lateral view to the most dorsal point of the femoral condyles. The condylar line and point iv (Fig. 9a) defined the condylar plane used for the calculation of the femoral neck anteversion (Fig. 9c). After assigning these points to the system, the software calculated the respective measurements. To see the definitions of the various variables measured, refer to the section of Definitions earlier in the thesis.

For study IV, where we compared 3D- to 2D templating, the 3D templating was performed at least one week before surgery using a 3D templating software, Ortoma[®] Hip plan, version 1.0.0.26 (Ortoma, Gothenburg, Sweden) (Fig. 10). One of the surgeons performed all 3D templates with the other two surgeons present for consensus. We tried to predict the size and position of the stem and cup as well as neck length using -4 , 0 , $+4$, or $+8$ heads with the contralateral healthy hip anatomy as reference(21). Furthermore, we measured the femoral neck anteversion, True FO, AO, and GO on pre- and postoperative CT scans.

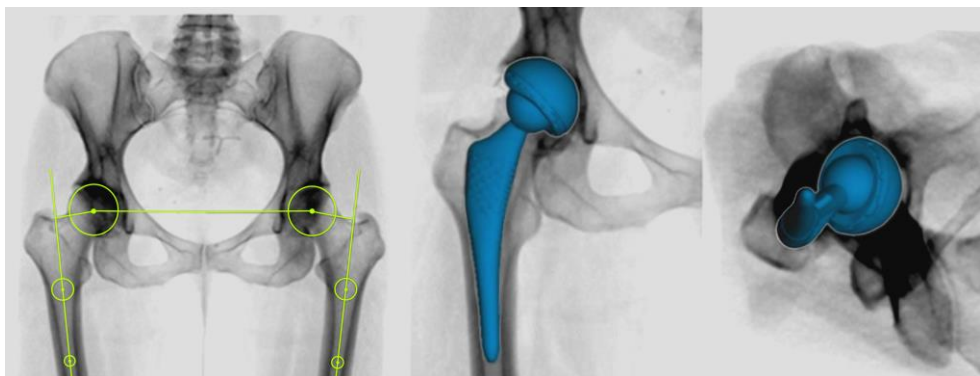


Figure 10: 3D templating

3D gait analysis

Two experienced physiotherapists conducted the three-dimensional gait analysis at the motion analysis laboratory in Lund, Sweden. They used a 6-camera Vicon MX40+ system (Vicon Motion Systems Ltd, UK) set at a capture frequency of 100 Hz and one OR6-5 force plate (Advanced Mechanical Technologies Inc, USA). The lab calculated joint rotations (kinematics), external joint moments (kinetics), and time-and-distance parameters using the Plug-In-Gait model (Vicon, Oxford, UK). We used The proCalc software (Vicon, Oxford, UK) for the extraction of data.

We selected parameters that might be affected by changes in the anatomical parameters measured by 3D-CT (Table. 3), and we calculated the Gait Deviation

Index (GDI) for the operated side to evaluate overall gait quality in the lower extremity.

Table 3. Gait analysis parameters evaluated when comparing changes in hip anatomy after THA

Kinematic parameters (joint rotations)
Mean trunk obliquity in stance (°)
Mean pelvic obliquity and rotation in stance (°)
Mean hip rotation in single stance (°)
Mean foot progression in single stance (°)
Kinetic parameters (joint moments)
Mean hip adduction moment in stance (Nmm/kg)
Maximal hip adduction moment (Nmm/kg)
1st peak(between initial contact and midstance)
2nd peak (between midstance and foot-off)
Temporospatial parameters (time-and-distance parameters)
Walking speed (m/s)
Time in single stance (s)

Participants walked barefoot on a 10-meter walkway and were instructed to walk on a self-selected speed. Patients did trial walks until they found their usual gait pattern whereafter three strides containing kinematic and kinetic data from each side were collected and subsequently analyzed. We used the mean value of these three strides for the statistical analysis.

ALTR assessment on MARS-MRI

Paper III

We evaluated all remaining patients that agreed to an MRI at 5 years for the occurrence of ALTR formations and graded the MARS-MRI findings. We used a 1.5 Tesla MRI system (MAGNETOM Avanto, Siemens AG, Healthcare Sector, Erlangen, Germany) for our ALTR evaluations. It used spine matrix and body matrix coils, running a protocol consisting of coronary T1 view angle tilting (VAT) + STIR VAT, sagittal T2 VAT, and axial T1 VAT. An axial T1 VAT, together with an axial subtraction image, was conducted after administration of intravenous contrast (19 ml Dotarem®). An experienced musculoskeletal radiologist at Skåne University Hospital analyzed all resulting 6 image sequences. He graded the findings using a modified version of J. Hauptfleisch et al. grading system (105) to suit our study better (Table 4).

Table 4. Modification of the Hauptfleisch grading system

Hauptfleisch system		Our modification	
		Type 0	No ALTR
Type I	Cystic ALTR with wall thickness <3 mm	Type I	Cystic ALTR with wall thickness <3 mm
Type II	Cystic ALTR with wall thickness >3mm	Type IIa	Cystic ALTR without solid parts
Type III	Solid ALTR	Type IIb	Cystic ALTR with a <50% solid part
		Type III	Solid ALTR

Whole blood ion levels

Paper III

The ABG II hip prosthesis has a titanium alloy (TMZF) stem and a Cobalt-Chromium (CoCr) head. The modular neck consists of the same CoCr alloy. Hence, we measured the levels of Cobalt, Chromium, and Titanium at the 5-year follow-up for both stem designs for comparison. At the 8-year follow-up, we did an additional measurement in order to correlate with the rate of stem deformation in patients operated with the modular stem. We obtained the metal ion concentrations by measurements on whole blood by SGAB Analytica, Luleå University of Technology, S-971 87 Luleå, Sweden (106).

Clinical evaluation and outcome questionnaires

Paper I

We used the self-administered quality of life questionnaire Short-Form (SF)-36(107), preoperatively, and at 1, 2, 5, and 10 years' follow-up, for clinical evaluation.

Paper II, III, and VI

All patients in the concerted cohort for these studies completed the Hip disability and Osteoarthritis Outcome Score (HOOS), Swedish version LK 2.0(108) with the subscale of VAS-pain and VAS-satisfaction for clinical evaluation, as well as the EuroQol- Five Dimensions EQ-5D(109) to evaluate health-related quality of life. The evaluations were done preoperatively and at 1, 2, and 5 years' follow-up. The patient-rated health scale, ranging from worst health 0 to perfect health 100, was used in the analysis(109).

Statistical analysis

Short explanation of the statistical analysis used throughout the thesis

Random intercepts model: All groups have the same slope as the overall line, which does not fit the real slope for each independent group so well.

Random slopes model: Allows each group line to have a different slope. So the random slope model allows the explanatory variable (X; independent)) to have a different effect for each group.

Mixed effect model regression

- Mixed models
 - Contain both fixed and random effects.
 - Individuals deviate randomly from the average (fixed) response
- Random-effects regression models, random coefficient models, random-regression models
 - Because of the random effect, the slope and intercept of each individual subject may be different.
- Multilevel models or hierarchical models
 - Incorporate two or more levels of random variation where one level is higher than the other
 - Repeated observations are clustered at the higher level of the subject.

Some add linear to distinguish them from nonlinear mixed-effects models.

Variance adjusted mixed model

Linear regression model: Fit a line through a set of points to make the line as representative as possible. To find how one set of data relates to another. The regression coefficient gives the gradient of the graph.

Multiple linear regressions: Multiple regression. Uses several explanatory variables to predict the outcome of a response variable. The goal of multiple linear regression is to model the linear relationship between the explanatory (independent) variables and response (dependent variable).

Logistic regression: It is a variation of linear regression that is used when there are only two possible outcomes. In other words, where each case in the sample can only belong to one of two groups (e.g., having a disease or not) with the outcome as the

probability that a case belongs to one group rather than the other. Model of binary outcome variables used to estimate odds ratios, primarily in case-control surveys. In linear regression, the coefficient b_1 represents the increase in Y for a unit increase in X . We are not so much interested in the meaning of b_1 in the logistic regression model, except to note that if the independent variable (X) is ordinal or metric, then you might be more interested in the effect on the odds ratio of changes of greater than one unit.

Fishers Exact Test: Test that gives valid results regardless of the size of the survey. It can be used to test differences in the proportion of positive outcomes in independent groups set up in crosstabs (cross tables).

Mann Whitney U-test: The non-parametric test for two independent groups equivalent to the standard t-test for two independent groups. Rather than comparing the values of the raw data, statisticians “rank” the data and compare the ranks. Useful if the median is a more meaningful mean, the mean. If the study groups are small and the standard t-test can not be used because the normal distribution can not be assumed, or if the outcome is measured on an ordinary scale, such as degree of symptoms or degree of disability after a trauma.

McNemar’s test: Tests used to test differences between two dependent proportions, for example, the proportion with contact allergy for two different metals tested on the same patient group.

Intraclass correlation coefficient (ICC): It is a comparison of how well people or tests agree. Typically it is used to look at how accurately a test can be repeated. The level of agreement can vary from zero to 1. Zero: There is no significant agreement – no more than would have been expected by chance. >0.5 : Good agreement. >0.7 : Very good agreement. 1: Perfect agreement.

Shapiro-Wilks test and Q-Q plots

T-test: Also known as Student’s t-test. A parametric test is used to compare the means of two groups. It tests the probability that the samples come from a population with the same mean value. A parametric test has an assumption that the data need to follow a certain distribution, i.e., the normal distribution.

Dependent (paired) sample t-test: More powerful as samples are matched regarding, i.e., age and sex. This eliminates variation between the samples. Used when the same item or group is tested twice, which is known as a repeated-measures t-test.

Independent (unpaired) t-test: Compares the means of two independent or unrelated groups to determine if there is a significant difference between the two. You use an unpaired t-test when you are comparing two separate groups with equal variance.

Signed-rank test: Wilcoxon signed-rank test. Non-parametric statistical hypothesis test used to compare two related samples, matched samples, or repeated measurements on a single sample to assess whether their population mean ranks

differ. Paired difference test. It can be used as an alternative to the paired Student's t-test when the distribution of the difference between two samples means cannot be assumed to be normally distributed. It can be used to determine whether two dependent samples were selected from populations having the same distribution.

Paper I

The studied outcomes were stem migration (translation and rotation along the y-axis) in relation to the extent of the postoperative anteversion, divided into three groups $< 10^\circ$, 10° to 25° and $> 25^\circ$. The two outcomes for translation and rotation were analyzed separately using two different statistical models. Of primary interest was the outcome at 10 years after surgery. However, because those patients who had experienced considerable stem migration tended to be revised and dropped out of the study before 10 years, data for the analysis could not be taken from the 10-year-measurements alone. In order to avoid the bias of including only 'moderate migrators,' data from the entire follow-up period were used for the analysis.

- We analyzed the relationship between postoperative anteversion and successive translation during the 10 years of follow-up. In order to account for the correlation structure and heteroscedasticity of the data, which contained repeated measurements on individuals with different migration patterns, we used a *random slopes and intercepts model*. Because the translation rate changed over time, the mean translation development in the model was described using a linear spline with a knot at 5 years. The approach differs only from the standard regression approach in how it describes the development of migration with time. Instead of attempting to describe the relationship as a straight line, assuming constant migration speed over the entire follow-up period, a linear spline is made up of several straight lines with different slopes that connect, describing a development scenario where the migration speed is only constant between specific time points, the knots. The knot for the model, as mentioned above, was chosen from the visual inspection of the data. In fitting our statistical model to the data, it became evident that some prostheses had migrated rather rapidly compared to the rest of the population, creating outliers in the study population data. When including these in the analyses, the data did not fit the statistical model of normality. Therefore, in order to facilitate analysis, these high-migrators were placed in a separate group. A corresponding indicator variable was added to the model, and their migration was estimated apart from that of the rest of the population. Consequently, in order to estimate the mean translation of the group with the least postoperative anteversion, where the 'high migrators' were present, a weighted mean of the 'high' and 'moderate' migrators in the group was used. We performed two analyses on the development of translation: one crude and one correcting for prosthesis size, stem type, patient weight, BMI,

and gender. The estimates produced from the analysis interpret as mean differences between anteversion groups at 10 years after the operation.

- The relationship between continuous posterior stem rotation and postoperative anteversion during the 10-year follow-up was analyzed in the same manner as for the translation, with one single exception. The outcome variable was log-transformed before applying the statistical model. We did this because the data were severely skewed and did not fit the statistical model. The estimates produced from this analysis are to be interpreted as mean ratios between-group rotations at 10 years after the operation.

We used STATA software version 12 (StataCorp LP, College Station, Texas), and all statistical tests of *mixed effect model regression* parameters were two-sided Wald tests and the standard p-value of < 0.05 was considered statistically significant.

Paper II

- **Figure 11a:** We used a *variance adjusted mixed model* to analyze migrating behavior in relation to stem type, where we treated patient ID as a random effect.
- **Figure 11b:** We used *logistic regression* to analyze postoperative anatomical symmetry. We were interested in whether better symmetry (where the non-operated leg was a reference) in anteversion, global offset, and FO/AO quota were significant factors to influence postoperative stem migration. When evaluating the impact of individual anatomical discrepancies on the probability of becoming at risk for increased postoperative stem migration, we chose to classify anteversion symmetry within the range of $-2,5^\circ$ to $+2,5^\circ$ discrepancy between hip sides. Likewise, we set the range for GO symmetry to $-2,5\text{mm}$ to $+2,5\text{mm}$ between sides.
- **Figure 11c:** We used *Fishers Exact Test* to evaluate the difference in anatomical restoration regarding stem type and examined distribution histograms for precision estimates.

We conducted all calculations in STATA s (IC v12 and v13).

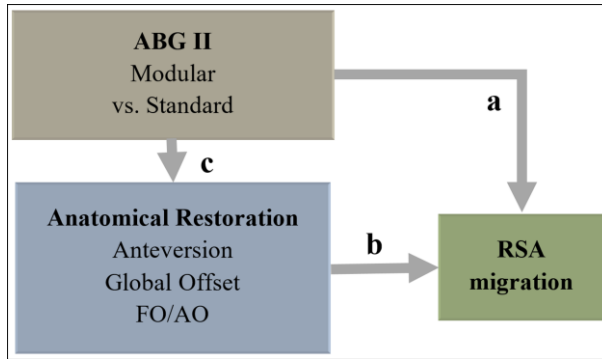


Figure 11: Overview of statistical analysis and variables

Paper III

- We used *estimates from a general linear mixed model* for the analysis of head-tip distance reduction, where the subject effect was taken into consideration and *estimates from a linear regression model* for the analysis of whole blood ion levels in relation to the rate of stem deformation.
- *Mann Whitney U-test* was used to compare the distribution for the different grades of ALTR as well as to test for differences between groups for the questionnaires VAS and HOOS.

We conducted all calculations in R v.3.5.2.

Paper IV

- We used *McNemar's test* for all statistical analyses.

We used the SAS Enterprise Guide (version 6.100.0.4025) for all statistical calculations.

Paper V

Continuous data were expressed as means and standard deviations (SD), and qualitative data as frequency and percentage.

We used *intraclass correlation (ICC)* with 95 % confidence intervals (CI) to analyze observer agreement. We translated the strength of observer agreement according to definitions proposed by Landis and Koch for kappa values(110), as:

Slight	0.00 – 0.20
Fair	0.21 – 0.40
Moderate	0.41 – 0.60
Substantial	0.61 – 0.80
Almost perfect	0.81 – 1.00

Further, Lee et al(111) stated that the lower 95 % confidence interval should be above 0.75 for an agreement to exist.

We conducted all calculations in R v. 3.5.1.

Paper VI

We used means and standard deviations (SD) or median and range or interquartile range (IQR) to describe demographics and disease characteristics.

We verified data normality using the *Shapiro-Wilks test and Q-Q plots*.

- We used a *paired sample t-test* to evaluate the differences between pre- and postoperative hip joint anatomy (CT measured) and variables derived from 3D gait analysis.
- We used an *independent t-test* to evaluate differences between postoperative CT measures and reference values from the contralateral side.
- We used the *signed-rank test* for identifying pre- and postoperative differences in HOOS pain and EQ5D VAS scores.
- We performed two *multiple linear regressions* to evaluate the associations between changed joint anatomy (THA) and changed gait pattern. Assumptions of linear relationship and multivariate normality were checked by scatterplots and by comparing the residuals vs. predicted values (i.e., the residuals had to be normally distributed around zero). We included all independent variables at the same time. The independent variables were as follows:

Change in FO/AO quota between pre and post evaluations

Change in trunk obliquity between pre and post evaluations

Change in pelvic obliquity between pre and post evaluations

Change in walking speed between pre and post evaluations

- In regression model 1, we used the change in mean hip rotation in single stance as the dependent variable. We included change in femoral neck anteversion, pelvic rotation, and walking speed between pre and post evaluations as independent variables.
- In regression model 2, we used the change in max external hip adduction moment in the first 50% of stance as the dependent variable.

Pain, subscale in HOOS, was initially included as an independent variable in both models but was excluded based on low response frequency (n=55).

However, pain was not a statistically significant variable in any model, and the result of the analyses were equivalent to pain excluded.

We performed statistical analyses using the Statistical Package for Social Science, version 22 (SPSS Inc, Chicago, IL; USA). A p-value below 0.05 was considered statistically significant.

Ethical considerations

The Regional Ethical Review Board at Lund University has approved the projects included in this thesis (Dnr 2009/6 and 2014/800) and it was carried out in compliance with the Helsinki Declaration of 1975, as revised in 2000 and registered 19th January 2012 in ClinicalTrials.gov Identifier: NCT01512550.

Results

Clinical evaluation

We regarded patient improvement as a result of THA in all study-cohorts, and this persisted throughout all different follow-up periods (Fig. 12 to 16).

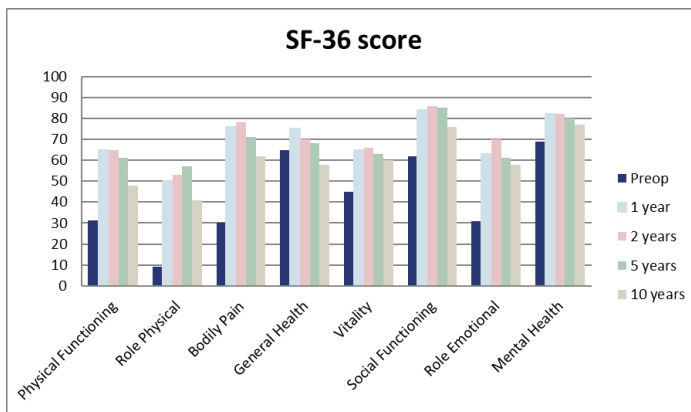


Figure 12: Results from the SF-36 outcome questionnaire for study I with a 10-year follow-up

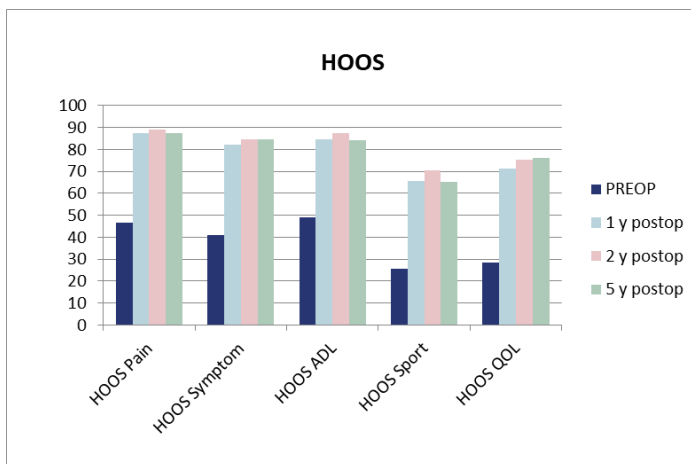


Figure 13:HOOS, evaluation of symptoms and functional limitations related to the hip for the cohort in studies 2, 3, 5 and 6 with a 5-year follow-up

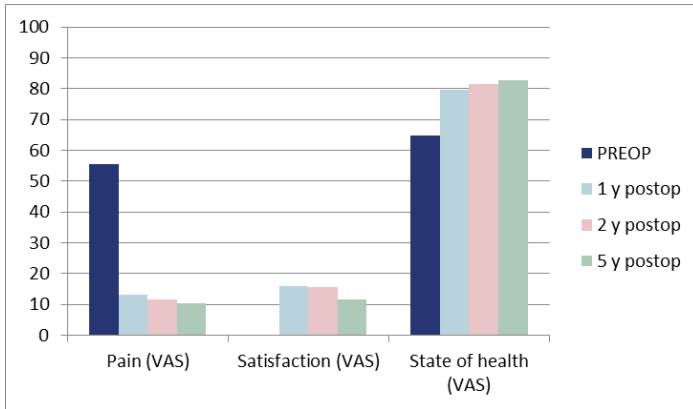


Figure 14: VAS, visual analog scale for the cohort in studies 2,3,5 and 6 with a 5-year follow-up. A low score for pain and satisfaction is good, while the high score in the State of health is excellent. Patients with a satisfaction score under 40 are considered satisfied

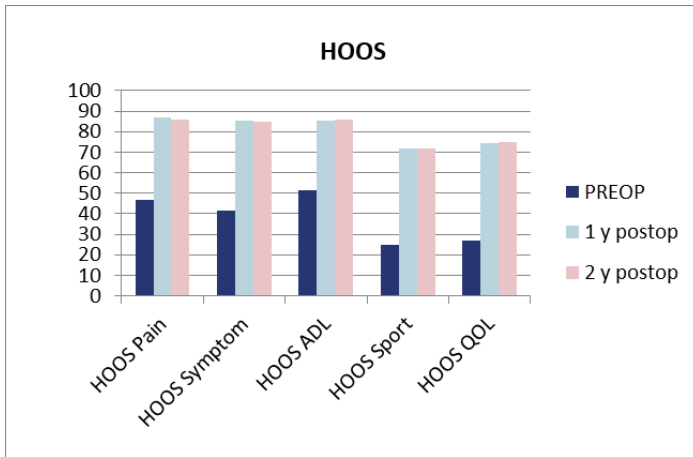


Figure 15: HOOS, evaluation of symptoms and functional limitations related to the hip for the cohort in study IV with a 2-year follow-up

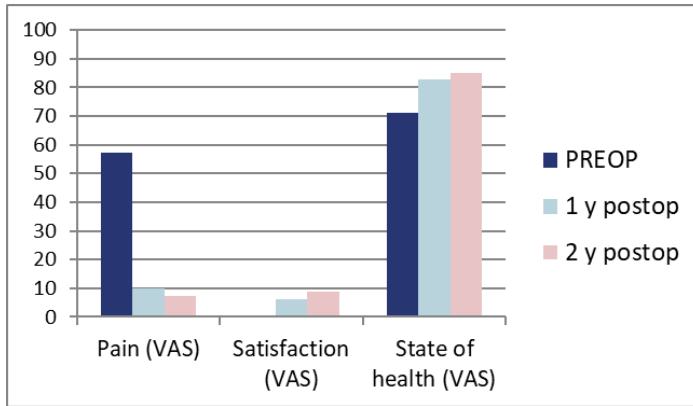


Figure 16: VAS, visual analog scale for the cohort in study IV with a 2-year follow-up. A low score for pain and satisfaction is good, while the high score in the State of health is excellent. Patients with satisfaction scores under 40 are considered satisfied

There were no significant differences in clinical evaluation and outcome scores between the three anteversion groups in study 1 (Table 2). There was no statistical difference between modular and standard stems preoperatively or throughout the 5-year follow-up in study II for neither the pain nor the satisfaction outcomes. The significant increase in whole blood Cobalt concentration and the reduction in Head-Tip distance analyzed in study III did not affect the hip-specific Hip Osteoarthritis Outcome Score (HOOS). In the same study, we found no correlation between either type or size of ALTR and pain or satisfaction scores at 5-year follow-up.

Validation of 3D CT measurements

Paper V

Observer agreements measured by ICC for the two observers were high. Observer agreement for 213 native hips, i.e., 71 pairs of hips on the preoperative CT and the 71 non-operated hips on the postoperative examination, was good with almost perfect ICC scores and narrow CI. Observer agreement for the 71 operated hips was equally good with almost perfect ICC scores and narrow CI without differences between pre- and postoperative results (Table 5). Thus, the results showed no increased difficulty in measuring postoperative hip examinations with a stem in place.

Table 5. Interobserver agreement assessed by ICC for the measured anatomical variables in 71 patients. Seventy-one hips on both sides preoperatively and 71 hips on both sides postoperatively were measured.

Measurements	213 non-operated hips		71 operated hips	
	ICC (95% CI)		ICC (95% CI)	
AO	0.94 (0.88 – 0.96)		0.97 (0.96 – 0.98)	
FNA	0.93 (0.90 – 0.95)		0.95 (0.93 – 0.97)	
True FO	0.94 (0.92 – 0.96)		0.96 (0.94 – 0.98)	
True GO	0.97 (0.96 – 0.98)		0.98 (0.96 – 0.98)	
Functional FO	0.96 (0.94 – 0.97)		0.97 (0.95 – 0.98)	
Functional GO	0.97 (0.97 – 0.98)		0.98 (0.96 – 0.98)	

FNA, femoral neck anteversion; ICC, Intraclass correlation coefficient; AO, Acetabular Offset; FO, Femoral Offset; GO, Global Offset

Intraobserver agreements were almost perfect for both observers, with narrow CI (Table 6).

Table 6. Intraobserver agreement assessed by ICC for measured anatomical variables in 15 randomly selected patients. Fifteen hips on both sides preoperatively and 15 hips on both sides postoperatively were measured.

	Observer 1			Observer 2		
	ICC (95% CI)			ICC (95% CI)		
	45 non-operated hips	15 operated hips	All 60 hips	45 non-operated hips	15 operated hips	All 60 hips
AO	0.94 (0.90 – 0.97)	0.99 (0.97 – 1.00)	0.96 (0.93 – 0.98)	0.96 (0.93 – 0.98)	0.97 (0.92 – 0.99)	0.97 (0.94 – 0.98)
FNA	0.97 (0.95 – 0.98)	0.95 (0.85 – 0.98)	0.97 (0.95 – 0.98)	0.94 (0.90 – 0.97)	0.95 (0.85 – 0.98)	0.95 (0.91 – 0.97)
TFO	0.97 (0.94 – 0.98)	0.93 (0.81 – 0.98)	0.96 (0.94 – 0.98)	0.93 (0.87 – 0.96)	0.92 (0.77 – 0.97)	0.93 (0.87 – 0.96)
FFO	0.98 (0.96 – 0.99)	0.96 (0.88 – 0.98)	0.97 (0.96 – 0.98)	0.96 (0.93 – 0.98)	0.98 (0.95 – 0.99)	0.96 (0.94 – 0.98)

FNA, femoral neck anteversion; ICC, Intraclass correlation coefficient; AO, Acetabular Offset; TFO, True Femoral Offset; FFO, Functional Femoral Offset

We compared the measurements from the pre- and postoperative CT of the non-operated hips to evaluate the robustness of the method, i.e., to determine whether repeated CT examinations and measurements on the same hip would yield comparable results. The ICC scores were almost perfect for both observers, with narrow CI (Table 7) and linear regression analyses showed a significant correlation for AO, true and functional FO, and FNA ($p < 0.001$; Fig. 17).

Table 7. Comparison of pre- and postoperative assessments in 71 operated hips by two observers by ICC.

	Observer 1	Observer 2
	ICC (95% CI)	ICC (95% CI)
AO	0.94 (0.91 – 0.96)	0.94 (0.91 – 0.96)
FNA	0.93 (0.84 – 0.96)	0.92 (0.88 – 0.95)
TFO	0.95 (0.93 – 0.97)	0.93 (0.89 – 0.96)
TGO	0.99 (0.98 – 0.99)	0.97 (0.96 – 0.98)
FFO	0.97 (0.95 – 0.98)	0.94 (0.90 – 0.97)
FGO	0.98 (0.97 – 0.99)	0.97 (0.94 – 0.98)

FNA, femoral neck anteversion; ICC, Intraclass correlation coefficient; AO, Acetabular Offset; TFO, True Femoral Offset; TGO, True Global Offset; FFO, Functional Femoral Offset; FGO, Functional Global Offset

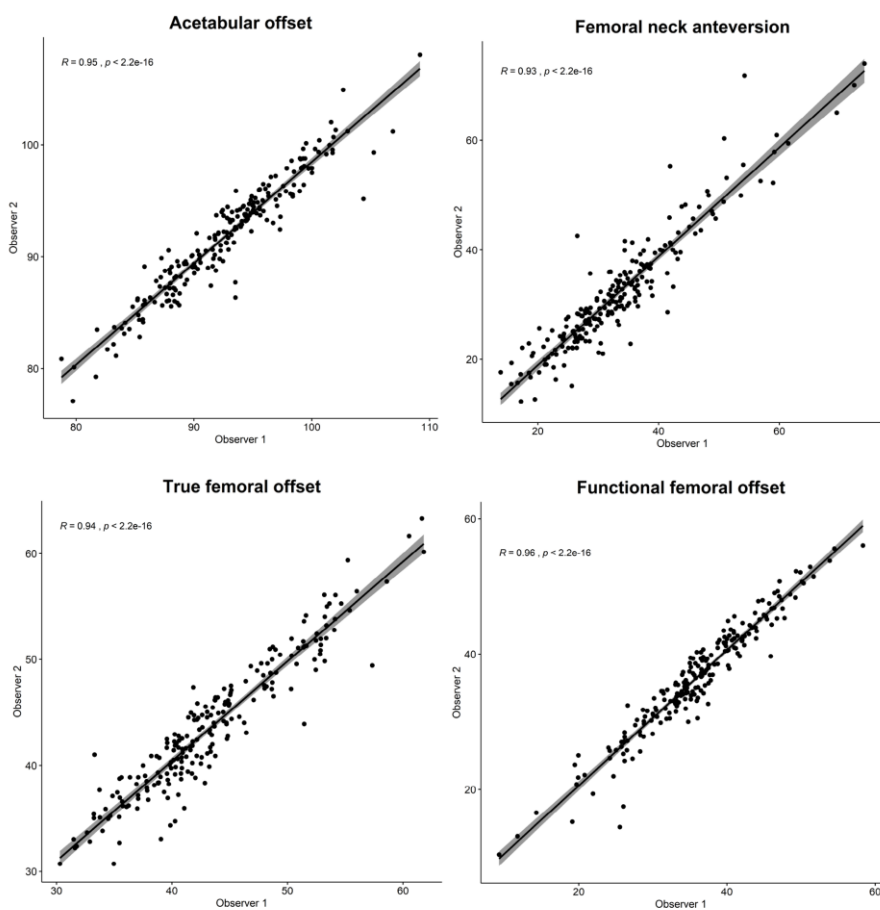


Figure 17: Correlation plots. Measurements done by two observers on 213 non-operated hips.

Preoperative Templating

Paper IV

3D templating showed a statistically significant superiority over 2D in the correct prediction of final stem sizes and neck lengths. However, there was no difference in cup size predictions. Furthermore, 2D tended to overestimate stem size and underestimate neck length (Table 8).

Table 8. Comparisons of proportions of correct sizes

Stem size	2D	3D	p value*
Underestimation	5	5	
Correct [§]	19	25	p=0.03
Over estimation	6	0	p=0.02
	29	30	
Accurate (within ± 1 size)	97%	100%	
Neck length			
Under estimation	14	1	p=0.001
Correct [§]	13	25	p=0.004
Overestimation	3	4	
	26	29	
Accurate (within ± 1 length)	87%	97%	
Cup size			
Underestimation	12	10	
Correct [§]	14	17	
Overestimation	4	3	
	27	29	
Accurate (within ± 1 size)	90%	97%	

[§] Correct: Implantation of size/length as planned

Total stems: 30

* p-value from McNemar's test comparing the proportion of correct sizes.

Modular components

Paper II

Stem size, neck length, neck angle, head length, neck version (anteverted, standard, retroverted), gender, and patient body weight did not influence the Reduction in Head-Tip Distance. We used the median neck-length to divide all modular stems

into two equal groups (long vs. short) (Table 9) and found a mean of 0.3mm (95% CI -0.0 – 0.6) greater reduction in Head-Tip Distance in the longer total neck lengths.

Table 9. Treatment data of the study population

Components used:	Modular (n=47)	Standard (n=25)
Size mean (range)	5 (1-7)	6 (4-8)
Short/long neck	23/24	
Retrov/std/antev neck	16/19/12	
CCD angle (125°/130°/135°)	37/6/4	
Head length, (-5/std/+5)	10/30/7	12/11/2
Total neck length, mm	57.8	57.9
Median (range)	(46.7–69.3)	(52.5–65.4)

Hip anatomy

Paper I

In study I, we measured the postoperative anteversion on the operated side. In ten patients the post-operative anteversion was $< 10^\circ$ (Tönnis grade -3), with a mean of 5° ($1^\circ - 9^\circ$); 30 patients were in the 10° to 25° group (Tönnis grades -2, 1 and +2) with a mean of 18° ($10^\circ - 25^\circ$); and 20 had $> 25^\circ$ (Tönnis grade +3) with a mean of 32° ($26^\circ - 43^\circ$). The mean post-operative anteversion for all stems was 20° ($1^\circ - 43^\circ$) (Fig. 18).

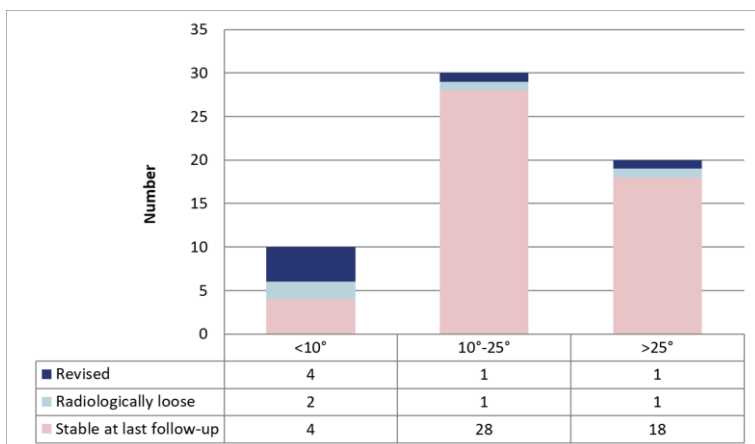


Figure 18: Chart showing the incidences of aseptic loosening in the low (< 10°), normal (10° to 25°) and high (> 25°) anteversion groups. At 10 years four stems were considered radiologically loose, two in group < 10°, one in group 10° to 25° and one in group > 25°. These patients were either too unfit to cope with revision surgery or did not experience sufficiently debilitating symptoms.

We measured the changes in hip joint anatomy after THA for the cohort analyzed in study VI (Table 1). Compared to preoperative values, the FO and FO/AO quota increased, while AO and GO decreased (Table 10). The distribution for postoperative FO differences between sides were:

- 74 % had a FO within ± 5 mm of the non-operated side (restored FO).
- 26 % had a FO more than 5 mm longer than on the non-operated side (increased FO).
- None had a FO more than 5 mm shorter than on the non-operated side (decreased FO).

Table 10. Preoperative values are for both sides, where the contralateral side is the reference. Postoperative values are for the operated side.

	Contralat. ref. values	Pre THA	Post THA	Diff. post vs. pre. THA side mean [95% CI]	Diff. post vs. contralateral mean [95% CI]
Anteversion (°)	33.8 (10.2)	33.7 (10.0)	33.7 (9.6)	0.1 [-1.7, 1.9]	
Acetabular offset (mm)	91.9 (5.0)	95.0 (5.2)	89.3 (4.3)	-5.6 [-6.5, -4.8]	
Femoral offset (mm)	44.0 (6.2)	43.5 (6.6)	46.7 (6.2)	3.2 [2.2, 4.2]	
Global offset (mm)	135.9 (9.2)	138.5 (9.6)	136.1 (8.1)	-2.4 [-3.4, -1.5]	
FO/AO quota	0.48 (0.06)	0.46 (0.07)	0.52 (0.07)	0.06 [0.05, 0.08]	0.04 [0.02, 0.07]

Pre- and postoperative values as mean (SD). Differences between pre- and postoperative values and between postoperative and contralateral values as mean differences and 95% confidence intervals. Statistically significant differences are highlighted in bold. CT, computed tomography; CI, confidence interval; FO, femoral offset; AO, acetabular offset.

We measured the differences in hip joint anatomy pre- and postoperatively for the cohort analyzed in study V (Table 11 and 12). Preoperative AO was 2.5 mm larger on the osteoarthritic hip compared to the healthy side. The increase in AO corresponded to a larger true and functional GO of 2.2 mm and 2.6 mm, respectively. There were no preoperative differences in true and functional FO (Table 11, Fig. 19).

Table 11. Preoperative differences between non-arthritis and osteoarthritic hips in 71 patients. Combined data for two observers

	Mean (95% CI)
Femoral anteversion angle (°)	-0.86 (-2.14 – 0.42)
Acetabular offset (mm)	2.46 (1.97 – 2.95)
True femoral offset (mm)	-0.26 (-0.76 – 0.25)
True global offset (mm)	2.20 (1.52 – 2.88)
Functional femoral offset (mm)	0.19 (-0.53 – 0.91)
Functional global offset (mm)	2.65 (1.83 – 3.47)

CI, Confidence interval. Statistically significant differences are highlighted in bold

Postoperative AO was 2.0 mm smaller on the now operated side compared to the healthy side. However, the true and functional FO had been concomitantly increased and was now 2.5 mm and 1.4 mm greater than on the healthy side, respectively. The appropriate reduction in AO and the increase in FO resulted in postoperative GO symmetry between sides (Table 12, Fig. 19). There were no significant side-to-side differences in FNA pre- or postoperatively (Table 11 and 12).

Table 12. Postoperative differences between non-arthritis and osteoarthritic hips in 71 patients. Combined data for two observers

	Mean (95% CI)
Femoral anteversion angle (°)	0.52 (-1.65 – 2.68)
Acetabular offset (mm)	-2.05 (-2.58 – -1.52)
True femoral offset (mm)	2.46 (1.82 – 3.10)
True global offset (mm)	0.41 (-0.29 – 1.10)
Functional femoral offset (mm)	1.35 (0.47 – 2.24)
Functional global offset (mm)	-0.70 (-1.61 – 0.26)

CI, Confidence interval. Statistically significant differences are highlighted in bold

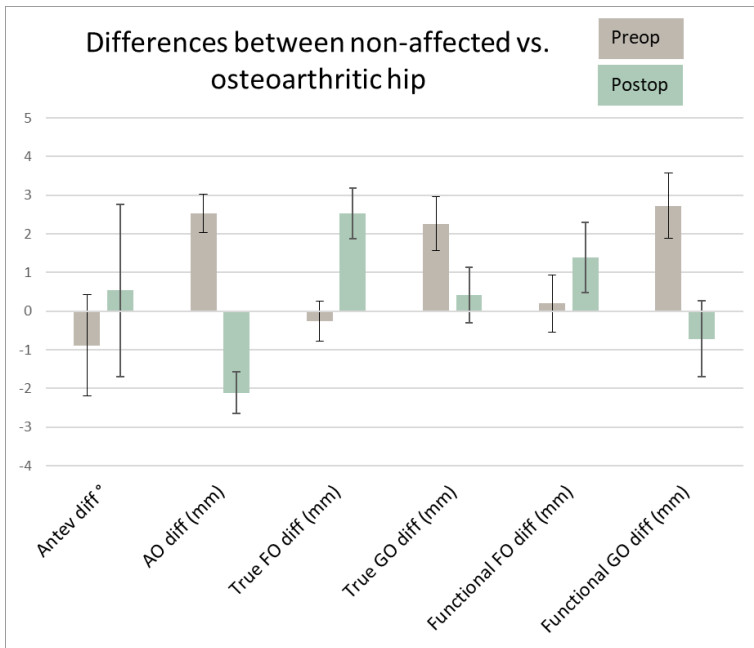


Figure 19: Bar chart showing the difference in measurements between the non-affected side and the side planned for THA in grey and after THA in green.

For comparison, the changes in hip joint anatomy after THA for the cohort analyzed in study IV were as follows presented as mean (range):

- Preoperative FNA: 35° (14 – 56°)
- Postoperative FNA: 28° (6 – 54°)
- FNA on the contralateral side: 33° (10 – 56°)
- Preoperative GO: 136mm (124 – 148mm)
- Postoperative GO: 133mm (117 – 146mm)

Gait pattern

Paper VI

We measured the changes in gait patterns one year after THA. The quality of overall gait pattern, walking speed, and time spent in single stance increased significantly (Table 13).

Table 13. 3D gait analysis parameters, pre- and postoperative data from the operated side.

	Pre	Post	Diff.post vs. pre Mean [95% CI]
Overall gait pattern			
Gait Deviation Index	81 (12)	90 (10)	8.9 [5.7 – 12.1]
Time and distance parameters			
Walking speed (m/s)	1.02 (0.2)	1.14 (0.2)	0.13 [0.1 – 0.2]
Time in single stance (s)	36.2 (3.3)	38.0 (1.7)	1.8 [1.1 – 2.5]
Gait variables hypothesized to be associated with femoral neck anteversion			
Hip rotation (°)	0.3 (6.8)	0.3 (5.4)	0.0 [-1.7 – 1.8]
Pelvic rotation (°)	0.8 (3.6)	-0.5 (2.5)	-1.3 [-2.1 – -0.4]
Foot progression (°)	-10.0 (7.2)	-5.1 (6.1)	4.9 [3.8 – 6.1]
Gait variables hypothesized to be associated with femoral and acetabular offsets			
Hip add mom avg. (Nmm/kg)	350 (88)	389 (88)	40 [18.7 – 60.5]
Hip add mom peak 1 (Nmm/kg)	575 (134)	616 (122)	40 [9.3 – 71.6]
Hip add mom peak 2 (Nmm/kg)	543 (120)	600 (133)	57 [27.6 – 85.5]
Trunk obliquity (°)	-3.9 (2.4)	-3.0 (2.3)	0.9 [0.3 – 1.5]
Pelvic obliquity (°)	2.7 (2.7)	2.1 (2.2)	-0.6 [-1.3 – 0.1]
Hip adduction (°)	0.2 (3.1)	1.4 (3.1)	1.2 [0.2 – 2.1]

Pre- and postoperative values as mean (SD). Difference between post- and preoperative values as mean difference and 95% confidence intervals. Statistically significant differences are highlighted in bold. CI, confidence interval; add, adduction; mom, moment; avg, average

On the operated side, hip rotation during gait changed equally in internal and external directions leading to a statistically non-significant change on the group level. On the operated side, the pelvis segment became more externally rotated, and the foot segment became less externally rotated during stance. External hip adduction moments increased significantly, and participants walked with less trunk obliquity (i.e., less lean over the operated side).

Relationship between change in hip anatomy and gait pattern

The change in hip rotation during gait after THA was associated with change in FNA, in the same direction, and with pelvic rotation, in the opposite direction, but not with change in walking speed (Table 14). The increase in hip adduction moment during gait was not associated with change in FO/AO quota but with less trunk lean and pelvic obliquity and an increase in walking speed (Table 14).

Table 14. Model 1. Multiple linear regression analysis, change in hip rotation during walking after THA defined as the dependent variable.

n=65	Unstandardized B	p-value	95% CI	R ² model
Change in hip anteversion	0.34	0.003	[0.12 – 0.57]	0.240
Change in pelvic rotation	-0.69	0.004	[-1.15 – -0.23]	
Change in walking speed	0.001	0.758	[-0.01 – 0.01]	

Model 2. Multiple linear regression analysis, change in max hip adduction moment (1st peak) during walking after THA defined as the dependent variable.

n=65	Unstandardized B	p-value	95% CI	R ² model
Change in FO/AO (quota)	4.02	0.985	[-416 – 424]	0.435
Change in trunk obliquity	17.39	0.001	[7.01 – 27.78]	
Change in pelvic obliquity	17.98	<0.001	[8.81 – 27.13]	
Change in walking speed	0.23	0.002	[0.08 – 0.37]	

Statistically significant differences are highlighted in bold. The Unstandardized B represents the amount by which the dependent variable changes if an independent variable changes by one unit, keeping other independent variables constant. n, number; THA, total hip arthroplasty; CI, confidence interval; FO, femoral offset; AO, acetabular offset.

Radiostereometric analysis

Paper I

The mean migration rates after each follow-up period are summarised in table 15 and classified into anteversion groups.

There was a strong relationship between the immediate postoperative anteversion and subsequent posterior stem rotation. This relationship could be seen as early as 3 months after THA and continued to develop during the whole follow-up period. At 10 years, all except two stems, both in the > 25° group, had rotated into retroversion (anteverted by 0.3° and 0.8°, respectively). At 10 years the < 10° group had a significantly higher mean retroversion of 15.1° (2.5° to 43.1°) compared with 4.7° (1.1° to 17.8°) in the 10° to 25° group and 5.4° (-0.8° to 20.3°) in the > 25° group (Table 15).

Distal stem migration was in agreement with the findings of rotational migration, with significantly more mean subsidence for the < 10° group at the 10-year follow-up (2.7 mm (0.3 to 10.4) compared with 0.5 mm (-0.3 to 1.7) and 0.4 mm (-0.5 to 1.2), respectively) (Table 15).

Table 15. Results of radiostereometric analysis

		Mean migration (median)					
		3 months	6 months	1 year	2 year	5 years	10 years
		Rotation (°)					
x-axis							
<10°		0.15 (0.09)	0.21 (0.18)	0.23 (0.15)	0.48 (0.38)	1.39 (0.89)	1.38 (0.64)
10° to 25°		-0.12 (-0.07)	-0.07 (-0.06)	-0.11 (-0.04)	0.03 (0.01)	0.45 (0.44)	-0.19 (-0.13)
>25°		-0.02 (0.03)	0.08 (0.07)	0.07 (0.10)	0.18 (0.22)	0.64 (0.63)	-0.19 (-0.09)
y-axis							
<10°		1.08 (1.11)	2.04 (1.83)	3.64 (2.54)	5.53 (3.87)	11.11 (6.24)	15.11 (8.87)
10° to 25°		1.00 (0.77)	1.24 (1.19)	1.98 (1.50)	2.51 (1.73)	3.84 (2.45)	4.67 (3.36)
>25°		0.28 (0.30)	0.73 (0.65)	0.73 (0.73)	1.24 (1.09)	2.34 (2.33)	5.3 (4.63)
z-axis							
<10°		-0.13 (-0.12)	-0.20 (-0.15)	-0.39 (-0.28)	-0.64 (-0.55)	-1.20 (-0.79)	-1.97 (-1.30)
10° to 25°		-0.02 (-0.04)	-0.11 (-0.12)	-0.23 (-0.19)	-0.24 (-0.21)	-0.39 (-0.31)	-0.69 (-0.39)
>25°		-0.06 (-0.05)	-0.07 (-0.06)	-0.10 (-0.11)	-0.10 (-0.18)	-0.18 (-0.31)	-0.23 (-0.37)
		Translation (mm)					
x-axis							
<10°		0.04 (0.03)	0.06 (0.06)	0.17 (0.18)	0.25 (0.13)	0.00 (0.03)	-0.04 (0.07)
10° to 25°		0.04 (0.05)	0.07 (0.05)	0.10 (0.07)	0.15 (0.07)	0.17 (0.13)	0.29 (0.17)
>25°		0.00 (0.02)	0.04 (0.01)	0.80 (0.05)	0.18 (0.12)	0.19 (0.19)	0.56 (0.43)
y-axis							
<10°		-0.18 (-0.17)	-0.26 (-0.27)	-0.48 (-0.43)	-0.84 (-0.59)	-1.89 (-0.81)	-2.71 (-0.91)
10° to 25°		-0.06 (-0.06)	-0.14 (-0.11)	-0.16 (-0.16)	-0.32 (-0.26)	-0.45 (-0.42)	-0.51 (-0.36)
>25°		-0.05 (0.02)	-0.13 (-0.09)	-0.12 (-0.11)	-0.25 (-0.25)	-0.38 (-0.43)	-0.39 (-0.47)
z-axis							
<10°		-0.20 (-0.20)	-0.38 (-0.23)	-0.94 (-0.49)	-1.50 (-0.77)	-3.28 (-1.95)	-3.24 (-2.04)
10° to 25°		-0.18 (-0.18)	-0.28 (-0.21)	-0.47 (-0.31)	-0.74 (-0.39)	-1.43 (-1.21)	-1.20 (-1.00)
>25°		-0.04 (-0.04)	-0.14 (-0.18)	-0.13 (-0.11)	-0.43 (-0.25)	-1.16 (-1.08)	-1.61 (-0.88)

Inspection of the RSA results can predict aseptic loosening as early as one year post-operatively. As shown in figure 20, the < 10° group consisted of two subgroups. Subgroup A contained two stems with consistently very high migratory values throughout the 10-year follow-up period. These two stems had retroversion of 42° and 43° and distal translation of 9.2 mm and 10.4 mm, respectively, at 10 years.

Subgroup B contained the remaining 8 stems in the $< 10^\circ$ group, with a mean retroversion of 8° (2.5° to 17.6°) and a mean distal translation of 1 mm (0.3 to 2.4).

Excluding subgroup A, the stems in the $< 10^\circ$ group had retroverted twice as much as stems in the 10° to 25° group ($p = 0.146$) and 2.5 times more than the $> 25^\circ$ group ($p = 0.068$). Stems in the $< 10^\circ$ group had subsided 0.46 mm more than stems in the 10° to 25° group ($p = 0.086$) and 0.66 mm more than in the $> 25^\circ$ group ($p = 0.020$) (Table 16).

When the two high-migrating stems (subgroup A) were included in our statistical model the $< 10^\circ$ group had rotated into retroversion 3.2 times more than stems in the 10° to 25° group ($p = 0.008$) and 4.1 times more than in the $> 25^\circ$ group ($p = 0.003$). Furthermore, stems in the $< 10^\circ$ group had subsided 3.2 mm more than stems in the 10° to 25° group ($p < 0.001$) and 3.4 mm more than in the $> 25^\circ$ group ($p < 0.001$) (Table 16). The significant differences remain when adjusting for all covariables.

There was no significant difference between the 10° to 25° group and the $> 25^\circ$ group when comparing translation and rotation along the y-axis ($p = 0.327$ and $p = 0.535$, respectively).

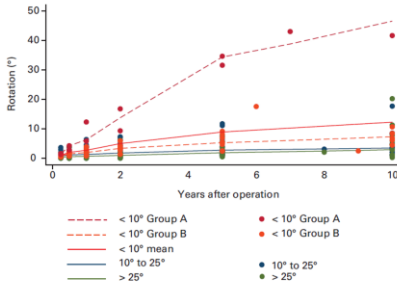


Fig. 4a

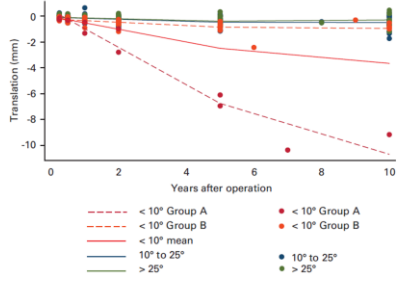


Fig. 4b

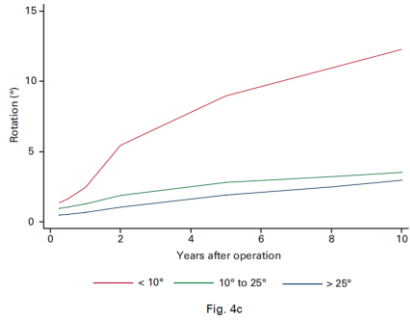


Fig. 4c

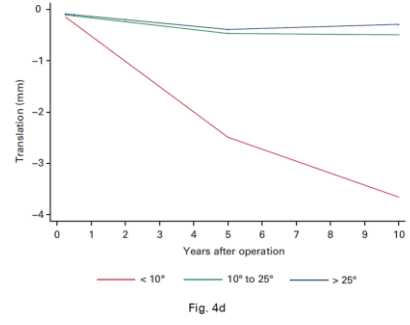


Fig. 4d

Figure 20: Figure 20a – a graph showing the values of stem retroversion by anteversion group (< 10°, low; 10° to 25°, normal; > 25°, high) across the 10-year follow-up. The low anteversion group is divided into subgroup A (two stems with consistently high results) and B (the remaining 8 stems). Figure 20b – graph showing the stem subsidence by anteversion group (including the subgroups A and B of the < 10° group). Figures 20c and 20d – these graphs show the mean retroversion (c) and subsidence (d) of the stems in all groups without subgroup analysis. All graphs are corrected for dropouts, including radiostereometric analysis pre-revision and loss to follow-up.

Table 16. Posterior rotation around the y-axis at 10 years (Low (< 10°); Normal (10° to 25°); High (> 25°); CI, Confidence interval)

	Posterior stem rotation (y-axis)		Distal translation (y-axis)		
	Ratio* (95% CI)	p-value	Difference† (95% CI)	p-value	
High/Normal	0.80 (0.39 to 1.64)	0.535	Normal – High	0.20 (-0.20 to 0.61)	0.327
Low‡/Normal	2.00 (0.79 to 5.03)	0.146	Normal – Low‡	-0.46 (-0.98 to 0.07)	0.086
Low‡/High	2.50 (0.94 to 6.70)	0.068	High – Low‡	-0.66 (-1.22 to -0.10)	0.020
High/Normal	0.80 (0.39 to 1.64)	0.535	Normal – High	0.20 (-0.20 to 0.61)	0.327
Low§/Normal	3.23 (1.35 to 7.72)	0.008	Normal – Low§	-3.16 (-3.65 to -2.68)	< 0.001
Low§/High	4.06 (1.60 to 10.3)	0.003	High – Low§	-3.37 (-2.84 to -3.89)	< 0.001

* estimates produced from this analysis are to be interpreted as average ratios between groups

† estimates produced from the analysis are to be interpreted as mean differences between groups

‡ not including stems with high migration

§ including stems with high migration

Adjusting for the covariables weight, BMI, gender, stem size, and stem type did not affect the significant differences between the groups. However, the multiple linear mixed-effects model used to correct for these aforementioned covariables showed that the Classic II stem significantly increased the translation (95% confidence interval (CI) 0.007 to 0.159; $p = 0.033$), and small stem size significantly increased both stem translation and retroversion (95% CI 0.051 to 0.232; $p = 0.002$ and 95% CI 0.340 to 0.799; $p = 0.003$, respectively).

Paper II

The mean migration rates after each follow-up period are summarised in table 17 and further divided into subgroups of stem types.

The whole group showed a statistically significant mean early stem subsidence of 1.00 mm and average stem retroversion by 1.03° within the first 3 postoperative months ($p < .0001$ and $p < .0001$ respectively). After that, until the 5-year follow-up, the stems rotated slightly further to an average of 1.47° ($p < .0001$), while no more subsidence occurred after 3 months ($p = 0.09$) (Fig. 21, Table 17).

Table 17. Results of RSA

		Mean stem migration (Stdev) in relation to direct postoperative reference examination						
		Early migration			Late migration			
		2 weeks	3 months	p-value [‡]	1 year	2 years	5 years	p-value [§]
Rotation (°)	X-axis							
	All stems	0.15 (0.52)	0.15 (0.65)	0.13	0.09 (0.67)	0.17 (0.61)	0.27 (0.79)	0.01
	Modular	0.12 (0.52)	0.11 (0.65)	0.54	0.01 (0.67)	0.12 (0.61)	0.16 (0.79)	0.18
	Standard	0.21 (0.49)	0.24 (0.72)		0.27 (0.72)	0.28 (0.66)	0.51 (0.68)	
	Y-axis							
	All stems	0.66 (1.27)	1.03 (1.51)	<0.001	1.05 (1.41)	1.23 (1.60)	1.47 (1.70)	<0.001
	Modular	0.61 (1.27)	1.07 (1.51)	0.35	1.11 (1.41)	1.32 (1.60)	1.56 (1.70)	0.93
	Standard	0.76 (1.49)	0.95 (1.67)		0.92 (1.61)	1.03 (1.97)	1.25 (2.02)	
	Z-axis							
All stems	-0.56 (0.57)	-0.69 (0.68)	<0.001	-0.70 (0.71)	-0.75 (0.77)	-0.82 (0.77)	<0.001	
Modular	-0.55 (0.57)	-0.69 (0.68)	0.74	-0.69 (0.71)	-0.76 (0.77)	-0.81 (0.77)	0.62	
Standard	-0.60 (0.70)	-0.69 (0.82)		-0.72 (0.83)	-0.74 (0.95)	-0.84 (0.89)		
Translation (mm)	X-axis							
	All stems	0.16 (0.25)	0.18 (0.26)	<0.001	0.18 (0.27)	0.20 (0.29)	0.23 (0.30)	0.001
	Modular	0.14 (0.25)	0.18 (0.26)	0.50	0.16 (0.27)	0.19 (0.29)	0.21 (0.30)	0.15
	Standard	0.21 (0.29)	0.19 (0.32)		0.22 (0.33)	0.21 (0.39)	0.28 (0.33)	
	Y-axis							
	All stems	-0.76 (0.83)	-1.00 (1.10)	<0.001	-1.00 (1.12)	-0.89 (1.21)	-0.92 (1.11)	0.09
	Modular	-0.70 (0.83)	-0.88 (1.10)	0.17	-0.88 (1.12)	-0.84 (1.21)	-0.86 (1.11)	0.77
	Standard	-0.90 (0.89)	-1.25 (1.21)		-1.25 (1.22)	-1.01 (1.49)	-1.05 (1.07)	
	Z-axis							
All stems	0.01 (0.26)	0.03 (0.34)	0.22	0.06 (0.42)	0.02 (0.40)	0.01 (0.44)	0.66	
Modular	0.00 (0.26)	-0.02(0.34)	0.02	-0.03 (0.42)	-0.04 (0.40)	-0.09 (0.44)	0.03	
Standard	0.03 (0.23)	0.14 (0.43)		0.25 (0.51)	0.14 (0.53)	0.23 (0.48)		

[‡] P-values for estimates of changes before 3 months representing the period when the stem settles in place.

[§] P-values for estimates of changes from 3 months after surgery during which osseous integration and stabilization should have occurred.

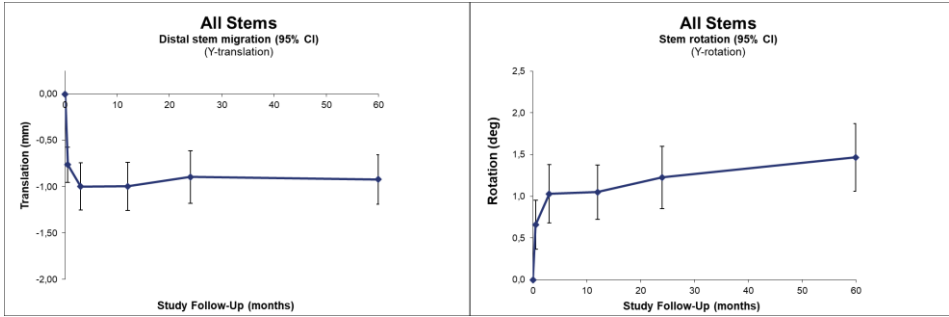


Figure 21: Line Charts with 95% Confidence Intervals

ABG II Modular vs. Standard

Comparing the modular and standard designs, we found no difference regarding neither retroversion nor subsidence (Fig. 22, Table 17).

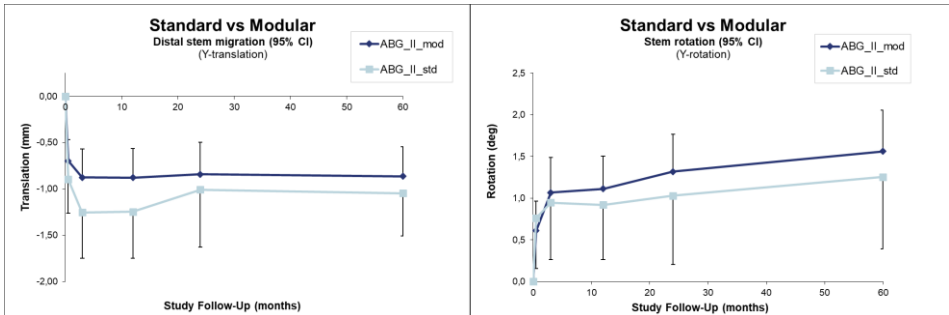


Figure 22: Line Charts with 95% Confidence Intervals

Postoperative anatomical symmetry

Postoperative stem anteversion and FO/AO quota had no impact on late postoperative stem migration.

We found no differences in postoperative stem migration related to how well hip symmetry was restored concerning anteversion and GO.

Stem type vs. symmetry

When comparing different stem types, there was no difference regarding symmetrical anteversion restoration ($p=0.20$) nor symmetrical GO restoration ($p=0.32$). However, compared to the modular stem, the standard stem had a tendency towards a lower GO on the operated side compared to the contralateral side ($p=0.00$).

Paper III

For the modular group, at five years, the mean change in head-tip distance was -0.75 mm (range: -1.64 – 0.14 mm), equivalent to -0.15 mm/year. For the standard group, the change was only -0.09 mm, (range: -1.07 – 0.33 mm) or -0.02 mm/year. We then continued to follow the modular group, and at 8 years, the mean change in head-tip distance was -1.21 mm (range: -1.94 – -0.10 mm) or still at the same pace of -0.15 mm/year. This head-tip distance reduction was significant overtime for the modular group ($p < 0.001$) but not for the standard group ($p = 0.25$). There was a significant difference in head-tip distance between the modular and standard groups from the 2nd year follow-up onwards, and by the 5-year follow-up, the difference was 0.66mm (Fig. 23). No statistical comparison could be made at 8 years, as we only followed the standard group for five years.

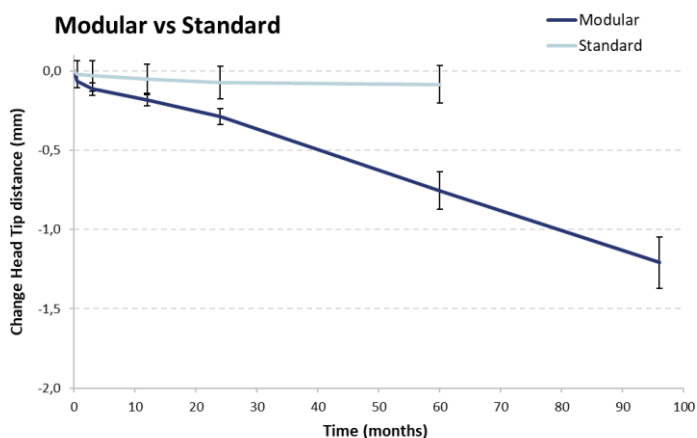


Figure 23: Mean values with 95% CI of the Reduction in Head-Tip Distance in mm for different Follow-Up moments in months up to 5 years for the standard design and up to 8 years for the modular version

The head position changed over time in the general direction of the tip of the stem and resulted in a reduction in Head-Tip Distance. This movement was evident in modular stems but not in standard stems (Fig. 24).

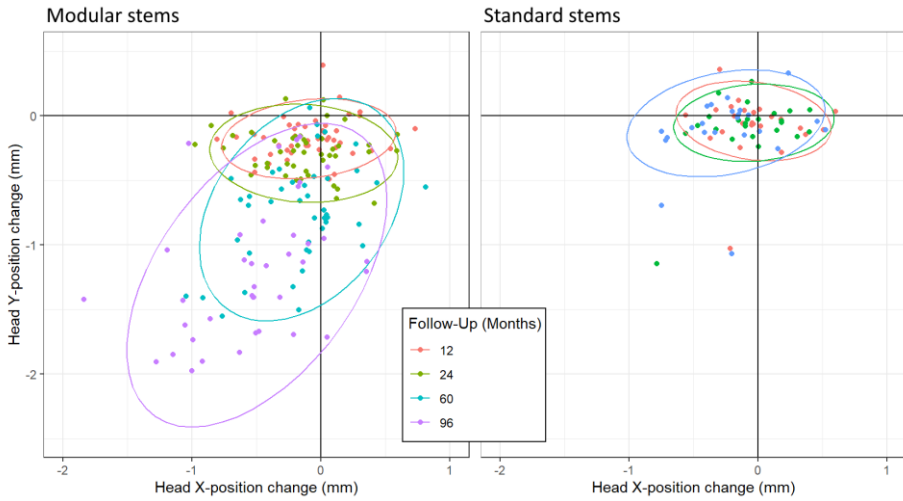


Figure 24: change in position of the hip head relative to the post-op situation in X-direction (perpendicular to the hip-stem axis) and Y-direction (along the hip-stem axis), for 1, 2, 5 and 8 years postoperative follow-ups. The ellipsoid presents the 95% confidence interval of the head position change for each follow-up moment

Paper IV

We summarized the mean migration rates for all stems after each follow-up period in Table 18. The results showed statistically significant mean early stem subsidence of 0.55 mm and average stem retroversion by 0.91° within the first three postoperative months ($p < .0001$ and $p < .0001$, respectively). After that, we noted no statistically significant migration ($p = 0.73$ and $p = 0.05$, respectively) (Fig. 25).

Table 18. Results of RSA for all 28 stems

	Mean migration (Stdev)			
	2 weeks	3 months	1 year	2 years
Rotation (°)				
x-axis	0.18 (0.36)	0.22 (0.53)	0.27 (0.47)	0.27 (0.45)
y-axis	0.56 (0.60)	0.91 (1.08)	1.01 (1.14)	1.14 (1.26)
z-axis	-0.51 (0.38)	-0.69 (0.61)	-0.72 (0.65)	-0.77 (0.63)
Translation (mm)				
x-axis	0.18 (0.18)	0.22 (0.24)	0.21 (0.25)	0.23 (0.25)
y-axis	-0.35 (0.29)	-0.55 (0.57)	-0.55 (0.55)	-0.47 (0.58)
z-axis	0.00 (0.25)	0.03 (0.39)	-0.02 (0.27)	0.05 (0.27)

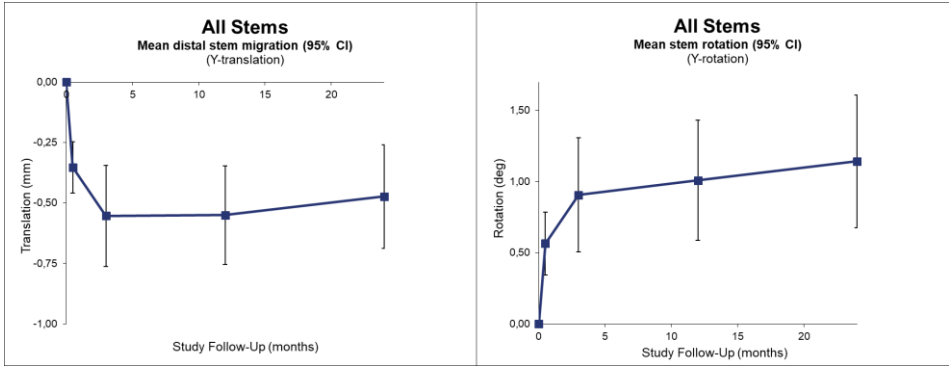


Figure 25: Line Charts with 95% Confidence Intervals

Metal ion measurements

Paper III

We found a statistically significant difference between standard and modular designs for all metal ion results at a 5-year follow-up with higher levels for the modular group. Cobalt, Chromium, and Titanium whole-blood concentration measurements at five and 8-year follow-up can be viewed in table 19.

Table 19. Metal ion levels at 5 and 8-year follow-up for stem designs

		5 year [€]	8 year [€]
Modular	Cobalt	4.9 (4.1–5.7)	4.8 (4.3–5.3)
	Chromium	1.8 (1.5–2.0)	1.3 (1.0–1.6)
	Titanium	1.3 (1.1–1.5)	1.2 (1.0–1.5)
Standard	Cobalt	1.0 (0.7–1.4)	
	Chromium	0.9 (0.4–1.4)	
	Titanium	0.8 (0.6–1.0)	

€ Mean values in µg/l (95% CI)

According to estimates from our linear regression model for the modular stem, a 1 mm reduction in Head-Tip Distance corresponds to 1.9 µg/l increase in whole blood Cobalt concentration at 8 years' follow-up ($p < 0.001$) (Fig.26). There was no significant correlation between reduction in Head-Tip Distance and whole-blood concentration of Chromium or Titanium ($p = 0.356$ and 0.599 , respectively). The metal ion concentrations (Co, Cr, and Ti) leveled out after the 5-year follow-up.

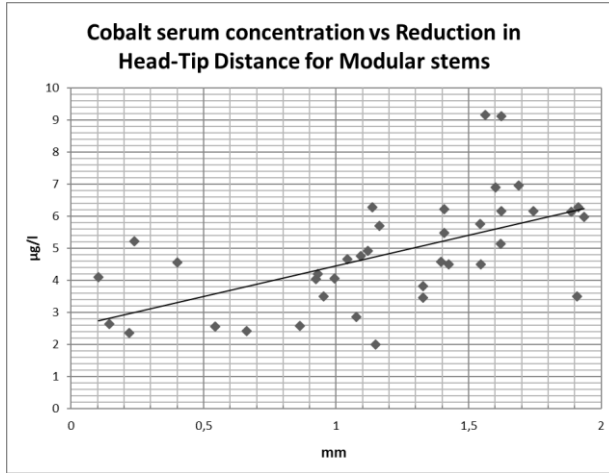


Figure 26: Estimates from our linear regression model showing Cobalt whole blood concentration vs. Reduction in Head-Tip Distance at 8-year Follow-up

ALTR assessment on MARS-MRI

Paper III

There were no statistically significant differences in grade of ALTR between stem design (table 20), nor was there any correlation between the level of any of the metal ions and grade of ALTR.

Table20. ALTR grades assessed on MARS-MRI

Grades	Modular (n=45)	Standard (n=22)
0	19 (42%)	13 (59%)
1	10 (22%)	2 (9%)
2	2 (4%)	0 (0%)
3	6 (13%)	1 (5%)
4	3 (7%)	5 (23%)
Missing	5 (11%)	1 (5%)

0 = no ALTR; 1 = cystic ALTR with a wall thickness of less than 3 mm; 2 = Cystic ALTR with a wall thickness of more than 3 mm and without any solid parts; 3 = Cystic ALTR with a wall thickness of more than 3 mm with a solid part, but comprising less than 50% of the total ALTR area; 4 = solid ALTR.

Revisions

In the $<10^\circ$ group in study I, 4 out of 10 stems had been revised at 10 years with additionally 2 stems radiologically loose. In the “normal” 10° - 25° anteversion group, there were 1 revised and 1 loose of 30 stems and in the $>25^\circ$ group 1 revised and 1 loose of 20 stems. The reason for revision was, in all cases, aseptic loosening (Fig. 18).

In study III, at the 8-year follow-up, 8 modular stems had been revised. Same cohort as for studies II, V, and VI. One because of hip pain and discomfort in combination with raised metal ion levels and MRI signs of ALTR. One revision was due to loosening of the stem, and two revisions were due to loosening of the cup where the decision was made to revise also the well-fixed stems. Three stems were revised because of PPF with adequate trauma and one because of late periprosthetic infection. None of the modular necks showed signs perioperatively of loosening from the stem, and they had to be dismantled with force. However, in all cases, the metal on both stem and neck in the junction area showed signs of corrosion with black discoloration in some degree (Fig. 27). One of the hips in the standard group was revised before the 5-year follow-up because of periprosthetic infection (Table 21).

For the cohort in study IV, there had been no revisions up to the 2 years RSA follow-up.

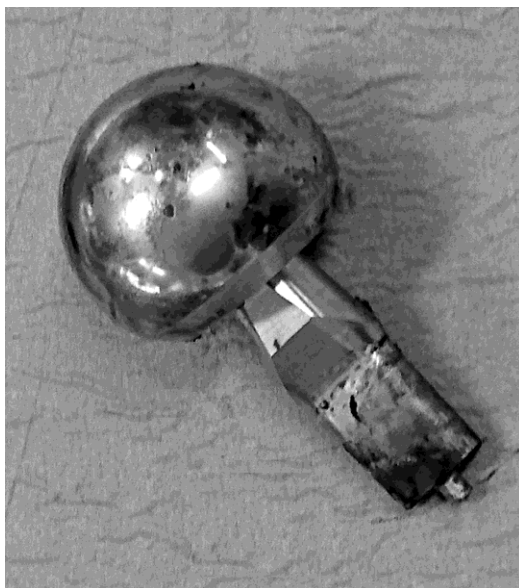


Figure 27: ABG II modular head (LFit) and neck after revision with corrosion on the neck part engaged in the stem/neck junction

Table 21. Time to and cause for revisions

	Years to revision	Cobalt [‡]	Chromium [‡]	Titanium [‡]	ALTR grade [§]
Modular					
Infection	1.9	n/a	n/a	n/a	n/a
Loose cup	3.6	3.3	1.0	1.7	n/a
Loose cup	4.3	3.8	1.7	0.5	n/a
PPFF [€]	5.8	3.0	0.9	2.8	4
PPFF	6.4	5.4	1.9	0.5	0
ALTR [€]	6.4	8.2	2.4	1.3	3
PPFF	7.1	9.3	1.8	0.5	1
Loose stem	7.8	4.8	1.1	0.5	1
Standard					
Infection	1.4	n/a	n/a	n/a	n/a

ALTR: Adverse local tissue reaction

PPFF: Periprosthetic femoral fracture

[€]ALTR type 3. Skin reaction with proved hypersensitivity to Cobalt. Accompanying groin pain

[£]Accompanying groin pain before PPFF.

[‡] Serum concentrations before revision surgery (µg/l)

[§]At five years follow-up

General discussion

In general, postoperative improvements were seen in gait pattern, pain and health-related quality of life for all our study groups. However, what is the benefit, if any, of rigorous anatomical restoration? Moreover, does it matter? In this thesis, we explored parameters that, in our opinion, had high potential for further improving an already successful THA operation technique by carefully restoring individual anatomy for correct biomechanics and hip function. We have shown that for cemented stems, the FNA plays a role, but we have not been able to show the same phenomenon using uncemented stems. In contrast, uncemented stems seem to be more torsionally stable, whereas, on the other hand, cement allows for a certain degree of creep within its mantle. Also, we have shown that changes in FNA does affect some traits of gait. We have not, however, had significant success in finding clarity if factors such as FO, AO, and GO has anything to do with prosthetic survival or hip function in general.

THA is already a very safe and effective surgical interventions for relieving pain and improving physical function caused by arthritis. The lack of significant clinical value throughout some of our studies might be attributed to the fact that there is not so much more to gain from further improvements in prosthetic design or surgical technique. In many ways, this could be seen in the lack of distribution of our surgical outcome values as the majority of our study subjects had their anatomy adequately restored during the operation.

Measurements of anatomical variables

Offset measurements have traditionally been done on AP pelvis or hip radiographs(8), where femoral rotation(80) and flexion(81) have been shown to influence measurements. To bridge between 2D and 3D measurements, we measured functional as well as true femoral offset (see definitions). We can only measure the latter using 3D based measuring techniques. In contrast, the former always underestimates the true femoral offset due to the missing dimension in AP based measurements. Also, mean FNA values vary greatly between studies because of the different definitions of which they are based. For example, there are four different methods to define the femoral condylar axis(112, 113). In studies 2 to 6, we used the most posterior points of the femoral condyles to define the condylar

line. Our FNA measurements are not identical to the most used one definition by Billing(114).

Back in the year1954, Billing defined FNA based on a line defined by two points, namely the long axis of the femur. These points were the center of the knee and the center of the base of the femoral neck. We used his definition in our first study. However, in our successive studies (II-VI), we measured FNA relative to the long axis of the femur proximally, to better correspond to the true insertion site and final position of a femoral prosthetic stem, and not having to compensate for the physiological bowing of the femoral shaft at templating. The placement of the proximal point in the long axis has been unclear. Despite a detailed description of the geometry of the proximal femur, Billing did not define this point(114). Murphy(98) identified it as “a centroid of a cross-section of the femur at the base of the femoral neck” on an axial CT section “3 percent” distal to the middle of the lesser trochanter. We simply defined it as the middle of a circle fitted in the femoral shaft at the lower level of the trochanter minor. We described the condylar plane as the posterior intercondylar line projected through the point of intersection of the proximal long axis line and the line for the true FO measurement. Our way of measuring FNA gives, in general, a 15° higher FNA as explained by figure 28.

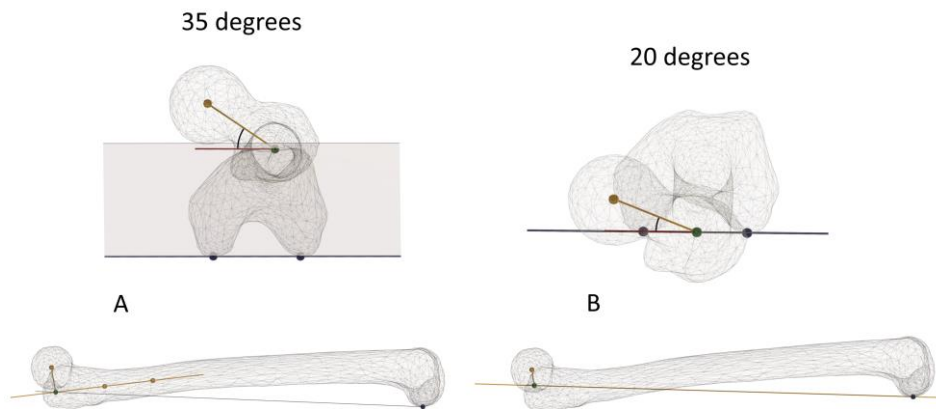


Figure 28: Femoral neck anteversion (FNA) is different depending on the choice of the long axis of the femur. A: In the cohort used for study II, the proximal part of the femur was chosen for the long axis definition since that corresponds to the length of the femoral stem in hip arthroplasty. B: In previous descriptions, e.g., by Billing and Murphy et al., the long axis was defined by a point in the knees and a point in the proximal femur, giving a different measurement value of FNA, as shown in the above example.

In osteoarthritis, reactive bone formation in the acetabular socket often leads to an increase in AO but with no effect on FO or FNA. This lateral migration of the femoral head could be seen in our study subjects, whereas GO had slightly increased due to the successive lateral migration of the femoral head.

Increased anteversion, especially in combination with a larger FO, raises stresses within the cement mantle around the stem(115). However, this relates only to the bending stresses that mainly load the calcar, but does not take into account the internal rotational torque that is high when loading a hip in flexion(51). During hip loading in flexion, anteroposterior loading relative to the femoral axis is transformed via the lever arm to the stem as a rotational torque. The internal torque increases with an increased lever arm due to low anteversion and larger FO (Fig. 29). The ability of a stem to withstand compression-bending forces far exceeds its resistance to a rotational torque.

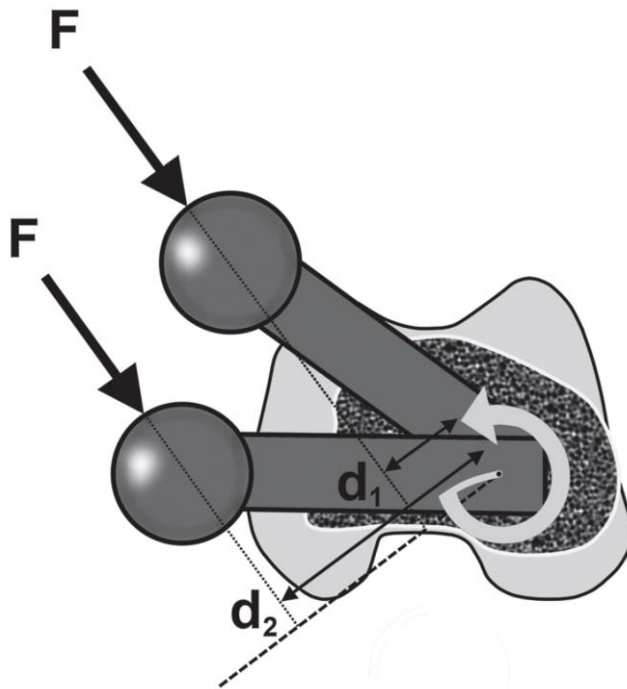


Figure 29: Diagram of a hip prosthesis from above at two different levels (dark grey, minor trochanter level; light grey, epicondylar level), showing the mechanism of internal rotational torque. Torque (circular arrow) = Hip joint reaction force (F) \times Lever arm (d). The hip joint reaction force (F) is transformed via the lever arm to the stem as rotational torque. A reduced anteversion angle in a hip loaded in flexion will increase the internally rotating torque because of the relatively longer lever arm (d_2). A shorter lever arm (d_1) results in less torque.

Therefore, the stem should not be placed in a too low anteversion, whereas the more significant problem regarding FO is that a too-small FO is associated with increased acetabular polyethylene wear(33), and improving lever arm biomechanics by increasing FO reduces the load transferred to the cup(44). We, therefore, believe there are more benefits in enlarging the FO than vice versa. Apart from that, we assumed that an endoprosthesis could better withstand various load factors and function better if positioned according to the original anatomy.

Our surgical aim in studies 2 to 6 was to decrease the enlarged AO by medializing the cup while consequently increasing the FO to restore symmetry in GO(4). In general, we want to avoid a decreasing FO, as it could lead to decreased abductor strength, limping, and increased polyethylene wear(43). As a result, we found that postoperatively the GO was adequately restored. The result was a significant increase in the FO/AO quota, potentially improving the biomechanical prerequisites for the hip abductor muscles(35, 44). On the group level, the average FNA was unchanged after THA. It has been suggested that approximately 15-25° is a “safe zone” for FNA. The higher FNA angles presented in our studies (2 to 6) are an effect of our alternative anteversion CT measurement technique, and therefore translates as a “safe zone” of about +15° or 30-40° for FNA (Figure 28).

Intra- and interobserver variability

The inter- and intraobserver agreements for our measurements (AO, true FO, functional FO, and FNA) were generally near-perfect with narrow CI. Measures on repeated CT examinations were close to identical with high observer agreement rates consistent with other studies reporting on CT assessment of measurements using 3D images. In our opinion, it does not matter how anteversion measurements are done. However, the measurements must be simple, consistent, and reproducible. We believe that our way of measuring anteversion better takes into account the local anatomy and therefore relates better to the surgeons during stem placement.

Stem stability

Distal migration up to 10 years may represent normal subsidence and stabilization within the cement mantle for some stem designs like the Exeter(116). However, for prostheses not designed to subside within the cement mantle, continuous migration is likely to be indicative of detrimental results(54, 117).

The ScanHip used in study I had a rounded stem-design to allow for an even cement mantle to avoid stress risers leading to cement fractures thought at the time to be the leading cause for aseptic loosening. Consequently, the rotational stability of the stems was not considered(52). Nevertheless, it provided us with a good model for identifying the phenomenon of posterior rotation of the stem.

The uncemented ABG II and Anato stems showed an early stabilization after an initial rotation into slight retroversion while subsiding. The lack of significant clinical value throughout some of our studies might be attributed to the excellent stability of these uncemented stems. Cemented stems seem to show more creep over

time, which would have been helpful when trying to access the influence of deviant anatomical parameters on stem migration.

Hip anatomy and stem orientation vs. stem migration

For Optima and Classic II stems in study I, the initial rotational position of the prosthesis within the femur affected the degree of later posterior rotation and significantly influenced the longevity of the implant. We suggest that the rotational position of the stem may be a fundamental factor in determining prosthetic survival in total hip replacement. Less than 10° of stem anteversion seems deleterious due to a significant increase in retroversion and subsidence experienced in that group. Our results suggest that rotatory forces are essential in terms of prosthetic loosening, and therefore axial loading should not be considered in isolation. Posterior rotation of the stem is associated with subsidence within the cement mantle, and thereby appears to be a fundamental initial mode of stem loosening. Prosthetic anteversion, therefore, needs to be optimized to withstand the stress of stem torsion caused by the reaction force on a flexed hip.

For the uncemented stems in the cohort used for study II and successively study V and 6, our results show a generally good symmetrical anatomical restoration and a benign migratory behavior with early stabilization for both types of the ABG II stem. Further, there was no indication that neither anteversion- nor GO symmetry influenced postoperative migration. It, therefore, seems to be of no importance whether we choose a modular or a standard stem concerning postoperative stem migration. We believe that biomechanical restoration and correctly placed prosthetic components are essential and will probably counteract postoperative stem migration, increase the function perceived by the patient and reduce lameness. We should always try to optimize the surgical result, and being well prepared by thorough preoperative planning is an important measure.

Hip anatomy vs. changes in gait patterns

We continued to evaluate the functional benefit of anatomical restoration by analyzing our study subjects in study II further with data obtained from 3D Gait Analysis. Study VI, therefore, aimed to describe the change in hip anatomy after THA and to evaluate the subsequent change in gait pattern one year after THA in individuals with hip osteoarthritis. As expected, for this type of intervention, the THA resulted in substantially improving the quality of life for our study group, due to less perceived pain and improvements in gait. For our patients, the general increase in hip adduction moment resulted in less trunk and pelvic obliquity and

increased speed of walking. An increase in external hip adduction moments was seen and was associated with a more upright walking position and faster walking speed. However, our modification in the FO/AO quota did not impact the adduction moment during gait. Increased anteversion was accompanied by reduced pelvic rotation and inward rotation of the hip during walking. This means that if the femoral stem is placed in more anteversion, the patient tries to improve the lever arm for the abductors by rotating the hip inward.

In agreement with previous research, walking speed and gait pattern improved one year after THA. However, some gait deviations persisted, shown in this study by the postoperative GDI score of 90 (preoperative GDI score 81)(32, 88, 118). The GDI is a summary score of gait deviations compared to that of a healthy reference group, taking the pelvis and lower extremity kinematics into account. After surgery, the participants walked more upright with less trunk lean over the operated side, indicating an increased ability to load the affected hip, which is not reflected in the GDI value. The more upright gait found in this study could, at least in part, be an effect of improved strength due to anatomical restoration of GO and hip rotational center after THA. The importance of sufficient strength of the hip abductor muscles following THA has been widely discussed and agreed upon, including the effect of surgical approaches, compensatory movements and anatomical restorations(34, 35, 47, 48, 87, 88, 119, 120). The same posterolateral surgical approach, which does not significantly impact abductor strength, was used in all our studies. As earlier stated, the participants walked more up-right and faster after THA, which seems to have a greater impact on the external hip adduction moments during gait than the changed FO/AO quota. However, no individual had a shorter FO on the operated side compared to the non-operated side. This indicates that all individuals had a restored or increased FO, making it challenging to assess the possible adverse effects of a short FO on hip moments. Our results are in line with those of van Drongelen et al. (2019). They evaluated 22 individuals pre- and post THA with biplanar radiographic examinations and 3D gait analysis and found no correlation between FO and hip adduction moments(49).

We showed that the change in FNA had an impact on hip joint rotation during walking in an equivalent direction. Meaning that if we place the THA in a more anteverted position; the patient is more likely to experience an increase in internal hip rotation during walking. Estimating the exact relationship between the amount of change in FNA and the consequent change in hip rotation during walking would be of great value for surgical planning. However, although 3D gait analysis is considered the gold standard for measuring gait and CT, the gold standard method for measuring FNA, such a direct relationship, is very difficult to establish. The ability of the gait analysis model to accurately define the hip rotation center is of particular concern, as is the lower reliability of transversal plane rotation kinematics compared to the sagittal and frontal plane kinematics(121, 122). We also determined that change in hip rotation during gait was related to change in pelvis rotation in the

opposite direction. This relationship is not unexpected since the rotations of the hip joint and pelvis segment are linked. As an example, the internal rotation of the pelvis during stance is typically accompanied by external rotation of the hip in order for the individual to maintain a straight line of progression. The hip rotations are defined and reported according to their relation to the pelvis segment in the biomechanical model used, resulting in a negative correlation between the hip and pelvic rotations. The understanding of the relationship between change in FNA and change hip rotation during gait is further complicated by compensatory movements, pain, and muscular weakness. Therefore, in order to estimate the exact relationship, further studies are needed.

Modularity – risks and benefits

The two stem types in the cohort for study II, 3, 5, and 6 showed equal potential in restoring anteversion- and GO symmetry within the range of $\pm 2.5^\circ$ and $\pm 2.5\text{mm}$ between sides. The ABG II stem design is for close anatomical proximal fit in the femur, which makes the stem version difficult to direct without modular options. Further, the standard stem has an offset that increases with size but limits the possibility for achieving a predetermined stem orientation. A monolithic (standard) system with different offset and anteversion choices can compensate for the increased capabilities of a modular system to provide surgeons with options regarding anatomical restoration. With these increased options, we believe that a reliable preoperative template plan can give sufficient precision and accuracy in stem positioning regardless of what stem used.

Stryker recalled the modular version of the ABG II system in June 2012 due to the potential for fretting and corrosion at the stem-neck junction (70). In our study, the head-tip distance reduced significantly for the modular group for all follow-up moments at a constant rate equivalent to 0.15 mm/year. This reduction corresponds to a varus deformation of the stem, of which there were none in the standard stem group. This deformation correlated with the level of Cobalt concentration, and at examining the revised stems, we could see signs of corrosion. We, therefore, suspect that the head-tip distance reduction was caused by corrosion at the neck-stem interface. At the same time, only a tiny adaptation probably occurred in the head taper connection, the latter also seen in the standard stem group.

The increased modification possibilities of modular stems with different neck options have previously been deemed valuable for ROM, soft tissue balance and to minimize leg length discrepancies (24-27). However, there have also been reports on disadvantages related to the additional neck-stem interface when using modular stems. Some have reported on fractures of the modular femoral neck (123, 124), and others have reported on ALTR to the metal debris caused by corrosion-related to

titanium-cobalt-chromium interfaces in modular stem junctions (72, 125, 126). Pivec et al. evaluated 202 ABG II Modular stems and reported a 2.9% revision rate up to 2-year follow-up for reasons unrelated to corrosion and 30.1% revision rate because of corrosion-related symptoms before 2 years (127). Restrepo et al. reported a 13% revision rate at a 2-year follow-up for the ABG II Modular stem (128). In our study, 8 out of 50 patients (16%) operated with modular stems have now been revised 8 years after surgery. Although only one of these revisions was directly related to discomfort in association with corrosion at the neck-stem junction, another patient already had severe MRI verified ALTR with accompanying groin pain before the incidence of PPF, which resulted in its revision. This high rate of revisions has raised general concerns, and it was, in hindsight, a correct decision made by Stryker to voluntarily recall the ABG II Modular prosthesis in June 2012 as soon as concerns arose due to the potential for corrosion at the neck-stem junction.

We are the first to report on the steady rate of Head-Tip Distance reduction in ABG II Modular stems, and we are not aware of that this phenomenon has been described for any other modular hip stem design before. We found, as expected that the modular ABG II prosthesis does release more metal ions into the surrounding tissue compared to the standard ABG II. This type of metal release seems to be the case for all modular stems and confirmed by other studies (129).

There was, interestingly, no correlation between elevated metal ion levels and type of ALTR in MRI. We expected that higher metal ion levels, especially Cobalt, would result in more ALTR, as reported in other studies (75, 126, 130), although this was not the case in our study. For example, we have a patient with a relatively high Co level of 8,9 µg/l and no ALTR at all. This result raises the question if ALTR is a physiological reaction to the metal ions or a more complicated process dependent on other variables such as genetics and individual allergic sensitivity to metals.

It was not our original intent in study II to evaluate ALTR or metal ion release from modular stems, but rather to evaluate the outcome of modularity as used to achieve a more anatomical restoration of the hip. During that study, the problems with our RSA measurements became apparent diverging our attention towards the unexpected varus deformity of the modular stem and concomitant metal ion release. We have a relatively high rate of revisions. However, only 2% were directly related to discomfort in association with corrosion at the neck-stem junction, and the remaining patients are doing clinically well without any suspicious radiographic findings. The revised necks were all firmly attached to the stem body, and they did not seem to be loose, whereas it took a relatively high force to separate the necks from the stem with the available instrument used for that purpose.

A slow deformation caused by the ongoing corrosion process might not be so harmful in itself, but how long can it continue? As of yet, we are unable to make

any conclusions about the outcome in the long-term. Hopefully we can see in the future follow-ups, what is already being indicated by our results, a leveling out of whole blood ion concentrations. This leveling out might be an indicator of a steadier state at the neck-stem junction. A far worse scenario is continuing varus deformity with modular-neck fractures or dislocation of the neck-stem junction.

We contemplated if different combinations of CCD angles, neck-lengths, head-lengths could lead to different amounts of forces acting on the neck-stem interface. We thought that a stem combination of, e.g., CCD 125°, long neck, +5mm head, and small stem should be more susceptible to Head-Tip Distance reduction than a stem combination of CCD 135°, short neck, -5mm head and large stem. This hypothesis was not true for our study group at the 8-year follow-up but might be revealed in the future as we continue our observations of this group of patients.

Finally, the increased burden keeping track of all the boxes and tools for the various parts that a modular prosthesis entails could be seen by some as a disadvantage to its use. In our group of 47 patients with modular stems, we used 13 different combinations of modularity, not counting stem sizes and 27 different combinations of modularity, including stem sizes.

The role of 3D templating

3D templating software is superior to 2D templating because it gives much more information, for example on the hip version. Likewise, the conception of true femoral offset can be improperly assessed during 2D templating (79). Our data suggest that 3D templating is better in predicting stem size and neck length. Further, there is a tendency to plan for a too big stem during 2D templating. 3D comes out better in that regard, probably because it is possible to view the margins of proximal hip bone structure in more detail on 3D reconstructed images making the overestimation of stem size completely avoidable. Using this particular stem type in which offset increases with size, the tendency to choose a bigger stem during 2D templating, predisposes us to compensate the increased offset with templating for a smaller neck length than was eventually used perioperatively. We could avoid this using 3D templating because of a better view of the proximal femur anatomy. In general, regardless of the templating technique, the correct prediction rate was not as good for cup sizes as it was for stem sizes and neck lengths. During acetabular preparation, the surgeon will ream more or less through the subchondral bone plate based on local findings. In contrast, the size of uncemented stems will be limited to the anatomical fit and fill of the proximal femur(131). It is essential to predict correct stem size as it influences leg-length and offset predictions, whereas cup sizes will not. Accurate stem size predictions are also essential to avoid perioperative fractures. It is also essential to be able to rely on preoperative templating to avoid

choosing a too small stem size for the actual anatomy. As might happen when the femoral broach is not placed correctly during reaming, and the tip collides with the lateral cortex of the femoral shaft preventing any further distal reaming.

The mean postoperative anteversion was lower compared to the healthy hip. We used three anteverted and 27 neutral stems. Therefore, in retrospect, we should have used more anteverted versions of the stem. However, individual anteversion is challenging to estimate during surgery. Probably Computer-assisted surgery (CAS) based on 3D templating might be of value for improving accuracy in restoring individual anteversion.

To our knowledge, there have only been two previous studies on comparing 3D templating with 2D templating in predicting implant size for uncemented THA(91, 92). Sariali et al. reported a significant difference in prediction rate for the benefit of 3D templating (combined for stem and cup size 96% for 3D vs. 16% for 2D) while Schiffner et al. reported a statistically significant difference advantageous for 3D but without clear clinical relevance.

We perform 3D templating on a reconstructed CT scan that allows the user to correct for pelvic, hip, and leg orientation before templating. In this way, one may template on an already symmetrical hip. It also allows the user to see the true femoral offset and anteversion.

From our study and others, it seems that with 3D, one can make better judgments regarding types, sizes, neck-lengths, offsets, anteversions, and cup inclinations of prosthetic components to be able to apply the ones best suited for the individual hip anatomy. It also supplies us with a tool for improved oversight of the potential need for bone grafting and osteophyte removal and impingement.

Strengths

The inclusion of surgery undertaken by 8 different surgeons in study I potentially increased the variation in stem anteversion, better-reflecting hip surgery practice in general. The surgeons were not aware of the aim of the study, and so we assume that this spread of anteversion reflects common practice.

The preoperative CT measurements done by a radiologist for study II functioned as a guide for the surgeons during 2D templating and surgery. He did not have access to the CT based 3D templating software (Ortoma Plan™), which we later used to measure our anatomical parameters. Thus, we were blinded in our later measurements regarding these preoperative measurements. Other assets for study II was that the observer, an orthopedic surgeon, made all radiological measurements based on Ortoma Plan™, was not involved in patients' clinical follow-up and did not take part in their management.

There have been concerns defining appropriate and reproducible anatomical landmarks for 3D-CT measurements in the varying dimensions and contours of the anatomical structure in the proximal femur(82, 98). We, therefore, decided to place the proximal reference point at the lower level of trochanter minor. The center is easily reproduced at this level, where the medullary canal becomes circular. We also believe this better represents the longitudinal axis of the stem.

Paper III is unique in the sense that we can measure the head-tip movement with RSA and suggest it as a valuable tool for measuring the integrity of a modular implant. If we had been specifically looking for this phenomenon, we would have noticed the difference within the first 2 years from surgery.

A high radiation dose has hampered the use of CT. However, the reduced dose CT protocol used in studies 2-6 gives a substantial dose reduction compared with standard CT while maintaining sufficient image quality(99). Low-dose CT was equal to the dose from radiography and, therefore, a comparable level of risk to radiography with the added benefit of 3D templating. Nowadays, there is better availability and lower costs for CT scans and, therefore, a viable option for preoperative templating. Nevertheless, this may not apply to all countries, and costs may vary.

The strength of study VI includes the large group of participants in comparison to other studies evaluating 3D gait after THA. Also, the increased precision in measurement is offered by CT scans and 3D gait analysis.

To the best of our knowledge, no other studies have used the FO/AO quota to quantify the ratio between the two lever arms acting around the hip joint. We believe this ratio to be a useful measure of the balance between the lever arms, with the added benefit of being relative and comparable between individuals, regardless of pelvis size.

Limitations

Long-term follow-up has limitations owing to the loss of subjects, which compromises statistical precision. It was especially true for study I, and for this reason, we have used a mixed model analysis to be able to include RSA data from the whole follow-up period into our statistical model.

Although 3D-CT makes it possible to measure the leg-length-difference by taking into account points in the hip, knee, and ankle, we did not include the ankle in our CT analysis. Therefore we could regrettably not include LLD in our studies. In general, we used an early beta version of the measurement-software, which in later versions included LLD measurements.

In the design of study II, we overestimated the effect that anatomical parameters would have on the stem movement. Therefore, the study design was underpowered for detecting the minor effect that anatomical parameters possibly have on postoperative migration of uncemented stems.

With the surgical aim of achieving better symmetry between hips, we could argue that a limitation of this study is the lack of divergence in anatomical restoration. This fact, with the addition of the good stability of the stem used, makes it hard to find any clinically important differences regarding stem migration. Based on our data, we cannot conclude to what degree we must restore symmetry to gain adequate stability for prosthetic parts. A limitation for study VI was that the FO was restored or increased in most of the participants. Thus the impact of a decreased FO or the FO/AO quota on gait pattern cannot be determined.

The theory that ALTR is a result of a type IV hypersensitivity reaction(132, 133) is supported by the changes in leukocyte count (especially T-cells) in patients with metal-on-metal prostheses (134, 135). This theory remains controversial, since others suggest that true hypersensitivity is rare and that excessive metal wear debris generated at MoM articulations is the cause of ALTR in the majority of cases(136). As we did not measure lymphocyte count, we cannot do more than theorize about T-cells being generally involved in our ALTR cases.

We were surprised by the lack of statistically significant differences in grade of ALTR between stem designs. In study III, the standard group had more cases than the modular group with ALTR grade 4 (Table 20). None of these five standard cases reported any discomfort and scored relatively high on clinical outcome scores. One explanation might be that it is in general challenging to grade these findings on MRI. For example, a thickened capsule without actual local reaction is likely to result in a higher grade in ALTR. We, therefore, conclude that our MRI settings and evaluation were potentially inadequate for ALTR grading. Hopefully, there will be progress in the MARS-MRI technique in the forthcoming follow-ups.

Another limitation of study III is that we lack patient-reported outcome measures for the 8-year follow-up. It was an accidental administrative mistake that we did not send out these questionnaires for the modular stem patients at 8-years, but we will continue to do so in later follow-ups.

A limitation of study IV was the potential risk that the 2D templating would be influenced by and be prone to imitate the previously done 3D templating outcome even though the latter was performed at least one week before surgery. Only one surgeon performed all 3D templates, which some might consider a limitation, in that variability between the plans created by different surgeons, could not be evaluated. Nevertheless, this evaluation has already been done for the cohort in study II and presented in paper V. Also, the other two surgeons were present for consensus during the 3D templating. In contrast, each surgeon performed their 2D templating directly preoperatively. A further limitation in study IV, was that while using an

early version of the 3D templating software, we did not have accurate leg-length measurement capabilities.

Since previous studies have used slightly different techniques and measuring points for FNA, the comparison of measurements between studies is difficult (Fig. 28). The most crucial issue, however, is to develop a measuring method with high reproducibility and low observer variation, such as we have done for our measurements, described in paper V.

The limitation of study V is mainly a small number of observers. However, the high ICC and narrow CI showed high inter- and intraobserver agreements. There was no reference standard for the measurements, but due to the use of different reference points for measurements in the literature, this was impossible to find.

Leg length discrepancy after THA has been debated as a cause of gait deviations(137). In study VI, we did not include this factor since leg length was measured on CT scans at the pelvis level, not taking the length of the total leg into account. For research purposes, we will include CT measured leg-length in future studies. Also, we should consider the inclusion of the height of the hip rotation center since a high center of rotation decreases the lever arm and increases the force of the abductor muscles needed to balance the pelvis during walking(138).

Summary and conclusions

Background

Inferior placement and sizing of a hip prosthesis increase the risk of mechanical failure and early loosening. Can we avoid detrimental stem orientation by restoring the original hip anatomy, and will it benefit function and increase survival of total hip arthroplasties? Preoperative hip templating can anticipate the size and position of the planned implant but is three-dimensional (3D) templating better than the commonly used 2D templating for predicting stem and cup size and neck length? To be able to measure and evaluate hip anatomy pre- and postoperatively after total hip arthroplasty, we need a validated tool of measurement. We used a semiautomated 3D templating software based on low-dose CT scans for proximal hip anatomy evaluation. We collaborated in the development and validation of these measurements. We wanted to evaluate the effect of change in hip anatomy on change in gait pattern as this is not well described in current literature. Apart from this, we report an unexpected finding during a study comparing the migration of modular vs. standard hip stems.

Patients and methods

In paper I, we assessed the relationship between direct postoperative stem anteversion and the resulting rotational stability, measured with repeated radiostereometric analysis over 10 years. The study comprised 60 cemented total hip replacements using one of two types of matt collared stem with a rounded cross-section. We divided the patients into three groups depending on their measured postoperative anteversion ($< 10^\circ$, 10° to 25° , $> 25^\circ$).

In paper II, Seventy-five patients with primary unilateral hip osteoarthritis operated with an uncemented anatomical stem were randomized for either standard or modular stems. We used 50 ABG II stems with modular necks and 25 standard stems (control group). We measured the symmetry in hip anatomy between healthy and operated side. We measured the anteversion, global offset, and the femoral offset/acetabular offset (FO/AO) quota. Moreover, we performed measurements using a CT-based 3D templating and measuring software. Migratory behavior of the stems was then measured postoperatively with repeated radiostereometry (RSA) examinations over five years. At 5-year follow-up, we noted a compromised

integrity of the modular stem with varus deformity in the neck-stem interface. To investigate this phenomenon unknown in the current literature, we analyzed changes in head-tip-distance with radiostereometry up to 8 years, as well as whole-blood ion-concentration and MRI findings in paper III.

In paper IV, we included 30 patients with primary unilateral hip osteoarthritis operated with an uncemented anatomical stem and cup. 3D templating, based on low-dose CT-images, was performed one week before surgery and 2D templating on the day of surgery. We predicted the size, neck-length, and position of the components based on contralateral hip anatomy. Only the information from the 2D templating was available during surgery, and we based the final selection of prosthetic parts on the best anatomical fit during surgery.

In paper V, two observers used a digital 3D templating software to measure anatomical parameters. True- and functional femoral offset, acetabular offset, and femoral neck anteversion. We calculated observer agreements using intraclass correlation. Hip measurements were compared in each patient and between pre- and postoperative measurements.

In paper Paper VI, Sixty-five individuals with primary hip osteoarthritis, scheduled for THA, were analyzed in this prospective intervention study. Participants were evaluated pre- and one year postoperatively with computed tomography-scans, three-dimensional gait analysis, and patient-reported outcome measures. We performed multiple linear regressions to evaluate the association between change in joint anatomy and change in gait patterns after THA.

Results

Paper I: There was a strong correlation between direct postoperative anteversion and later posterior rotation. At one year, the $< 10^\circ$ group showed significantly more progressive retroversion together with distal migration, and this persisted to the 10-year follow-up. In the $< 10^\circ$ group, four of 10 stems (40%) had been revised at 10 years, and an additional two stems (20%) were radiologically loose. In the 'normal' (10° to 25°) anteversion group there was one revised (3%) and one loose stem (3%) of a total of 30 stems, and in the $> 25^\circ$ group one stem (5%) was revised and another loose (5%) out of 20 stems.

Paper II: Both stem types showed an early (within 3 months) good stabilization after an initial slight rotation into retroversion and subsidence. There were no significant differences in RSA migration between modular and standard stems. Postoperative anteversion and FO/AO quota had no impact on stem migration. The standard stem tended to result in insufficient global offset (GO), whereas the modular stem did not.

Paper III: The head-tip-distance decreased continuously by 0.15mm per year resulting in 1.21mm (95%CI 1.0 – 1.4) at 8-years for modular stems. The reduction in head-tip distance correlated significantly to the increase in whole-blood Cobalt concentration at 8-years but not to the MRI-grading. The standard stems had no such findings.

Paper IV: 3D templating was superior in the correct prediction of final stem size and neck-length ($p=0.03$ and $p=0.00$, respectively). 2D templating overestimated stem-size and underestimated neck-length. There was no statistically significant difference regarding cup size predictions.

Paper V: Inter- and intraobserver agreements were near-perfect, ranging between 0.92 and 0.98 with narrow confidence intervals (0.77-0.98 – 0.94-0.99).

Paper VI: Quality of overall gait pattern improved, and participants walked faster and with less trunk lean over the affected side. Femoral neck anteversion and hip rotations during walking changed equally in external and internal directions after THA. Change in hip rotation during walking was associated with change in femoral neck anteversion in the same direction. An increase in external hip adduction moments was, on the other hand, not associated with change in FO/AO quota but with a more upright walking position and increased walking speed.

Conclusions

Paper I: Our results strongly suggest that the rotational positioning of the femoral component during surgery is decisive for the degree of later posterior rotation, subsidence, and eventual aseptic loosening. The ideal rotatory position may be sensitive to factors like prosthesis design, stem size, and femoral offset. However, anteversion of $< 10^\circ$ appears to have a detrimental aftermath for prosthesis survival.

Paper II: The modular stem gave proper symmetrical anatomical restoration and, like the standard version, a benign migratory behavior. However, modular stems may allow better precision in GO reconstruction. Anteversion, GO, and FO/AO quota had no significant impact on stem migration. It, therefore, seems to be of no importance whether we choose a modular or a standard stem with regard to postoperative stem migration for this stem type. We overestimated the effect anatomical parameters have on stem movement. Hence we believe the study to be underpowered.

Paper III: There is a corrosion-related ion release from neck-stem interfaces of ABG II modular stems. In particular, cobalt ions. It is leading to progressive varus deformation about the neck-stem junction. However, the ion-concentration seems not to correlate with ALTR, and up to 8 years, and we have not yet seen a definite clinical problem, but further follow-up is needed.

Paper IV: 3D templating, based on low-dose CT-scans, is superior to 2D when estimating stem size and neck length. Further improvements in the accuracy of preoperative templating has clinical benefits, i.e., decreased implants needed on the back table, improved efficiency in the operation room, and improved patient outcomes. Furthermore, it serves as bases for computerized navigational instruments and robotic surgery.

Paper V: Using low-dose CT with 3D measurements with a templating software yielded excellent repeatability of measurements with near-perfect observer agreement. The study supports the use of 3D data sets for measurements in the pre- and postoperative evaluation in THA. The results from the current study further support the use of 3D data sets. With the use of 3D data sets, we practically eliminate the need for exact patient positioning.

Paper VI: One year after THA, the GO was adequately restored despite the medialization of the center of rotation due to increased FO and a decreased AO. Postoperative improvements were seen in gait pattern, pain and health-related quality of life. Change in hip rotation during walking was associated with change in FNA in the same direction and with a change in pelvic rotation during gait in the opposite direction. An increase in external hip adduction moments was not associated with change FO/AO quota but with a more upright walking position and increased walking speed. The findings of this study suggest that biomechanical restoration during THA does impact postoperative gait pattern, and, in addition to known factors such as FO, we also must take into consideration the height of the hip rotation center, and leg length discrepancy, the FNA.

Clinical implication

FNA should be measured preoperatively to find patients with increased risk of stem failure because of reduced anteversion relative to the native femoral neck. The true FO measurement is also only reliable using 3D measurements. Furthermore, CT is done without exposing the patient to more radiation than during a routine radiographic examination. These CT based measurements are much more reliable than measurements done on conventional radiographs, especially for FNA, true FO, and leg-length measurements.

Changing FNA, had an impact on hip joint rotation during walking in an equivalent direction. This means that if the THA is placed in more anteversion, the patient is likely to experience an increase in internal hip rotation during walking. Estimating the exact relationship between the amount of change in FNA and the consequent change in hip rotation during walking would be of great clinical value for surgical planning. However, although 3D gait analysis is considered the gold standard for measuring gait and CT, the gold standard method for measuring FNA, such a direct relationship, is very difficult to establish.

Standard definitions and universally easy to use measuring techniques that show consistent and reproducible measurements are essential when comparing different study outcomes. We believe that our way of measuring anteversion, although resulting in about 15° higher values, takes better into account the local anatomy and therefore relates better to the surgeon during stem placement.

Careful preoperative planning is vital for consistent and sound surgical outcomes. There is a higher value in preoperative templating if surgeons know that their measurements are correct. Therefore, improvements in the accuracy of preoperative templating has clinical benefits, i.e., decreased implants needed on the back table, improved efficiency in the operation room, and improved patient outcomes. Furthermore, it serves as bases for computerized navigational instruments and robotic surgery.

We are inclined to recommend awareness when using modular implants in primary THA. In our opinion, it is better to avoid them and use monoblock prosthetic systems instead that have the option of choosing different offsets within each stem size. Our experience from the unexpected findings with the modular concept emphasizes the importance of the stepwise introduction with clinical studies of new concepts and designs onto the general market(139).

Future research

We have been involved as consultants in the development of the 3D templating software used during our studies. The project is ongoing within our research group, where we help to develop standard reference points for measurements in the hip, knee, and ankle in order for the concept to become cohesive when measuring anatomical variables in different parts of the lower extremities.

For practical purposes, the process must be simplified and refined to lessen the time spent during 3D templating. Artificial intelligence (AI) has been implemented into the software bringing the automatic templating procedure down to about one minute. The potential of AI is used to facilitate an otherwise complicated process. The system has integrated reliable measurements for true FO, AO, GO, HCR, leg-length measurements, FNA, and cup anteversion and inclination.

Our next project will be a study to evaluate if a CT based method can replace RSA in postoperative migration analysis of prosthetic parts, where the preliminary results are promising.

We will continue to follow our patients operated with the ABG II modular stem with RSA and metal ions in the blood and, when needed, MRI.

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The importance of biomechanical restoration for total hip arthroplasty



Sverrir Þór Kiernan was born and raised in Iceland. He received his medical degree at the University of Iceland. He later moved to Lund in 2005 to continue his specialist studies at the Orthopedic Department at Skåne University Hospital, Lund, Sweden. Since 2009, Sverrir has been a specialist in orthopedics. He works at Skåne University Hospital, where he is part of the Orthopedic Department's joint arthro-

plasty unit. This thesis's main objective was to evaluate the importance of improved biomechanical restoration for THA's function and survival and to find ways of achieving this improvement. We used radiostereometry (RSA), low dose computer tomography (CT) for 3D measurements, 3D templating, prosthetic modularity, and 3D gait analysis, together with patient-reported outcomes.

