Reverse hybrid Total Hip Replacement: Wear, fixation and bone remodeling

Thesis

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Vær forberedt på alt, ikke sverg på noe, og ikke bli forundret over noe.

Arkhilokhos

Contents

Abstract

Reverse hybrid total hip replacement: Wear, fixation and bone remodeling

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Over the last decade there has been a shift towards more reverse hybrid and cementless Total Hip Replacement (THR) in Norway. Highly cross-linked polyethylene has been introduced as a bearing material to improve the longevity of THR. Different highly cross-linked polyethylenes from various manufacturers have been released to the market without proper clinical documentation. The main aims of this thesis were to document the reverse hybrid method and to measure wear in a cementless THR with a new E-vitamin infused highly cross-linked polyethylene.

Paper 1: 3963 hips of 3630 patients operated with the reverse hybrid method were compared to 37666 hips with the 10 most commonly used cemented THR. This national register study included patients from January 2000 to January 2010. Reverse hybrids showed equal survival compared to all cemented implants up to 10 years. We found no difference between the 2 methods for all ages and for ages less than 60. The reverse hybrid group had a 3.6 (95% CI: 1.9-6.9, p<0,001) fold higher risk ratio (RR) of periprosthetic femoral fracture compared to the cemented group. 5 years survival with periprosthetic fracture as endpoint was 99.6 % versus 99.85 %.

Paper 2: In a prospective randomized trial between a reverse hybrid THR and a cemented THR we found only minor differences after 2 years. Conventional radiographs, RSA (Radiostereometric analysis), DXA (Dual Energy X-ray Absorptiometry) and clinical scoring were used to compare the 2 groups. Analysis of migration of the stems, bone remodeling around the cup and wear of the all polyethylene cup showed no difference between study groups. The cementless stems had more bone loss in Gruen zone 1. Wear of the conventional all poly cup, including bedding-in, was high and comparable with other studies of this non cross-linked cup.

Paper 3: Two methods were compared to measure wear of the cemented polyethylene cup. The results showed that tantalum markers in the periacetabular bone overestimated wear compared to tantalum markers in the polyethylene. The cup migrated both in vertical and in total 3D directions, partly explaining the overestimation of wear when tantalum markers were used in the periacetabular bone. We conluded that wear measurements using markers in the periacetabular bone were inferior to the traditional method, and should not be used as the reference segment.

Paper 4: The main aim of this study was to investigate the wear difference between 32 and 36 mm ceramic heads articulating against an E-vitamin infused highly cross-linked polyethylene, in a cementless THR. Patients aged between 50 and 65 years and with primary osteoarthritis were included. Markerless RSA showed very low wear, including bedding-in, of 0.04 mm and 0.18 mm in the vertical and total 3D directions respectively. No statistically significant difference in wear for the total material from 3 months to 2 years was found, indicating that most of the wear measured is the effect of bedding-in. A statistically significant difference, with less wear for 36 mm heads, in the total 3D direction was found. The bedding-in appeared to be less for 36 mm heads and the mean difference between the 2 head sizes at 2 years was below the accuracy of the measuring method. In addition the 95% CI of the mean difference included zero. Therefore we concluded that the finding was uncertain. In addition the clinically important wear threshold regarding highly cross-linked polyethylene is not known. Long-term follow-up of this trial will be interesting to evaluate the wear properties of this polyethylene and to determine any differences between the 2 head sizes.

In summary we found that the reverse hybrid hip replacement performed well compared to cemented hip replacement in a national register study with up to 10 years follow-up. In a prospective clinical trial, with 2 years follow-up, only minor differences between reverse hybrid and cemented THR were found. The E-vitamin infused highly cross-linked polyethylene showed low wear, including bedding-in, with 2 years follow-up. Finally, we showed that polyethylene wear measurement using periacetabular bone markers was inferior to wear measurements using markers in the polyethylene.

Abbreviations

CIRRO - Center for Implant and Radiostereometric Research Oslo
HA - Hydroxyapatite
UHMWPE - Ultra high molecular weight polyethylene
HDPE - High density polyethylene
PMMA - Polymethylmethacrylat
mm - Millimetre
μm - Micrometre
RH - Reverse hybrid
MoM-Metal on metal
CoC-Ceramic on ceramic
CV - Coefficient of variation
CI - Confidence interval
SD - Standard deviation
ROI - Region of interest
HHS - Harris hip score
OHS - Oxford hip score
RCT - Randomized controlled trial
RSA - Radiostereometric analysis
CN - Condition number
ME - Mean error
MTPM – Maximal total point motion or Maximal 3 dimensional movement
DXA - Dual energy X-ray absorptiometry
BMD - Bone mineral density
THR - Total hip replacement
TKR - Total knee replacement
Ti - Titanium
Al_2O_3 - Aluminium oxide
$BaSO_4$ - Barium sulphate
EtO - Ethylene Oxide
kGy - kilogray
Mrad - Megarad
IQR - Interquartile range
NAR - Norwegian Arthroplasty Register
NARA - Nordic Arthroplasty Register Association
UCLA- University of California Los Angeles
ZTA- Zirconium toughened alumina matrix
3D - 3 dimensional
RR – Risk ratio

Acknowledgements

Rolv Mjaaseth introduced me to the field of orthopaedics when I started as a resident in the Orthopaedic Department of Telemark Hospital in Skien. Rolv and his team of consultant orthopaedic surgeons patiently taught me both trauma and elective orthopaedic surgery. His support and the good atmosphere in this department was one of the main reasons I continued the education to become an orthopaedic surgeon.

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List of papers

Paper 1

Einar Lindalen, Leif I Havelin, Lars Nordsletten, Eva Dybvik, Anne M. Fenstad, Geir Hallan, Ove Furnes, Øystein Høvik, Stephan M. Röhrl

Is reverse hybrid hip replacement the solution?

3963 primary hip replacements with cemented cup and cementless stem, from the Norwegian Arthroplasty Register. Acta Orthopaedica 2011;82(6):639-645

Paper 2

Einar Lindalen, Jon Dahl, Lars Nordsletten, Finnur Snorrason, Øystein Høvik, Stephan M. Röhrl

Reverse hybrid and cemented hip replacement compared using radiostereometry and dual energy X-ray absorptiometry.

43 hips followed for 2 years in a prospective randomized trial. Acta Orthopaedica 2012; 83 (6): 592-598

Paper 3

Einar Lindalen, Lars Nordsletten, Stephan M. Röhrl

Segment choice and cup stability influence wear measurements using radiostereometric analysis. A radiostereometric study comparing wear measured by markers in the polyethylene with markers in the periacetabular bone. Clinical Biomechanics 2012; 27(5): 511-514

Paper 4

Einar Lindalen, Lars Nordsletten, Øystein Høvik, Stephan M. Röhrl

Low wear of E-vitamin infused highly cross-linked polyethylene. 2 year RSA results from a randomized controlled trial using 32 and 36 mm ceramic heads. Submitted

Introduction

An x-ray of a healthy hip is shown in figure 1, and an x-ray of an arthritic hip is shown in figure 2. Typically narrowing of the joint space, cyst formation, osteophytes and sclerosis are present. The hip joint is a ball and socket joint, lined with cartilage and a limbus in the periphery. The joint is embedded inside the capsule. Different muscles act to stabilize the joint.

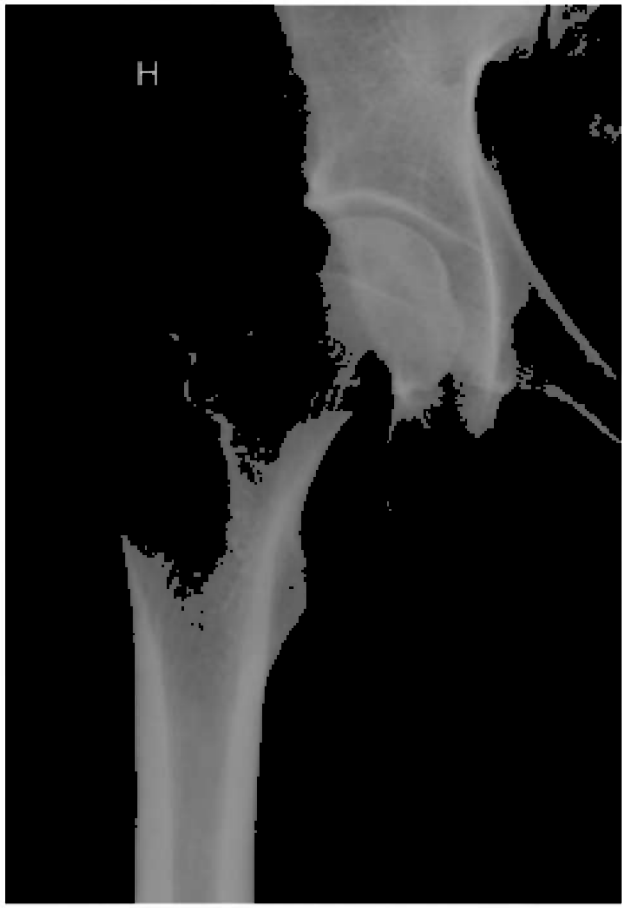

Figure 1

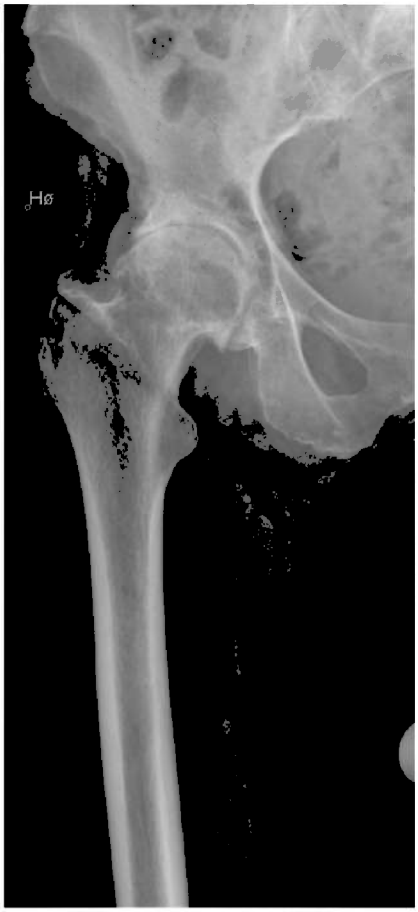

Figure 2

An x-ray of a total hip replacement (THR) is shown in Figure 3. The THR shown consists of a cementless femoral stem, a modular head and a cemented acetabular component of polyethylene. The small balls in the acetabular bone, cup and proximal femur are tantalum markers used in one of the randomized controlled trials (RCT) in this thesis.

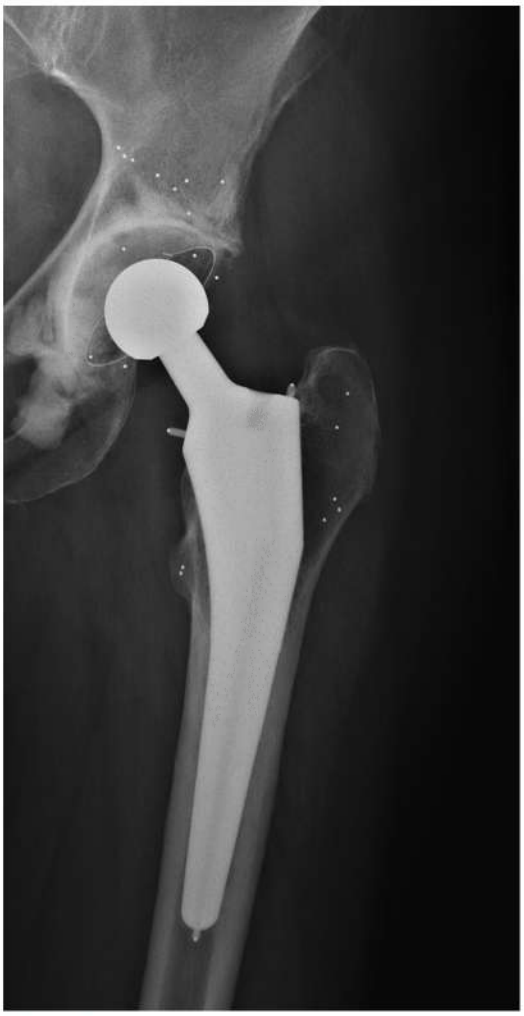

Figure 3

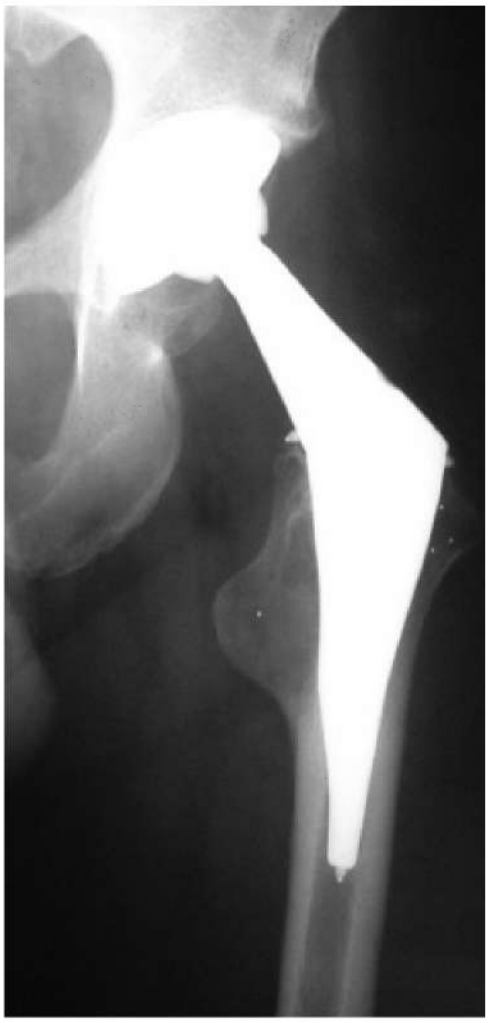

Figure 4 (Permission from Arild Aamodt)

Hip prostheses have different designs, like the hemiprosthesis often used after femoral neck fractures in the elderly, hip resurfacing arthroplasty, conventional cemented or cementless THR, or a combination of such implants. Even custom-made (individual matched) THR is available [1]. In Figure 4 a custom-made stem of a THR is shown. Most prostheses today are modular, which means that they are constituted of different parts that are assembled during the operation.

Degeneration of the hip joint leading to arthritis may develop into severe pain, stiffness and compromised function. If conservative treatment can no longer relieve pain and restore function, surgical intervention may be the solution. In some instances, joint conserving surgical approaches may be appropriate, but for end-stage osteoarthritis a total hip replacement is a well-documented method.

History

Historically, different surgical treatment options for end stage arthritis have been investigated. Early attempts at total joint arthroplasty credited to Gluck and Pean have been described in an abstract by Fisher et al. [2].

Philip Wiles is recognized as the first surgeon to implant a total hip arthroplasty in 1938. He used a metal on metal articulation [3]. Marius Nygaard Smith Petersen from Grimstad, Norway, investigated different materials for his ”mould arthroplasty”. Glass, celluloid and pyrex were tried until he finally started to use Vitallium (cobalt chrome) in 1938 [4]. There is a reported case of ultra long follow-up of this concept, after 56 years [5]. The Judet brothers developed a femoral prosthesis with a stem passing into the colli femoris [6]. This prosthesis was made of acryl, but due to breakage of the acrylic rod this prosthesis was later reinforced with steel to strengthen the stem that passed into the colli femoris. Problems with the remaining part of the head of the femur after implantation of this prosthesis led to the development of e.g. the Moore stemmed prosthesis. This prosthesis was a mono-block type of hemiprosthesis. Good results were reported, especially for fractures, but the results using this technique with osteoarthritis were not so good [7]. Thigh pain was reported in some cases using this cementless prosthesis [7].

McKee and Farrar described the development of a cementless total hip replacement of stainless steel from 1951 in Norwich [8]. Their experience with this concept led to the use of the Thompson cementless femoral stem combined with an acetabular component that was fixed to the acetabular roof with screws from 1956. They also believed that this metal on metal (MoM) articulation would perform better using cobalt chrome [8]. After Charnley documented the fixation of the Thompson prosthesis with cement in 1960, they started to also cement the acetabular component in order to improve fixation [8]. Ring worked on a more stable fixation of the acetabular component and he used a modified Moore stemmed prosthesis. His concept was used from May 1964 and he modified the concept during the first year. In November 1968 he presented encouraging 4-year results [9]. He was sceptical to the use of cement and thought that it could increase the risk of infection.

Charnley, in his article “The bonding of prostheses to bone by cement” in 1964, refers to Haboush who in 1953 described the possibility of anchoring long stemmed metal prostheses with cement [10]. In 1960 Charnley published a paper that described the fixation of the femoral

prosthesis with two-component acrylic cement [11]. He also found that the cement could be made visible on normal x-rays with the addition of Barium-Sulphate. He originally used a cemented Moore prosthesis and a Teflon socket [12].

Due to wear and tissue reactions to the Teflon, he eventually developed the "low friction arthroplasty" with a head of 22 mm and a cemented cup of high density polyethylene (HDPE). The femoral stem was made of stainless steel (Figure 5). He used this concept from 1962 and he presented the results of these operations in 1972 [13]. The low friction arthroplasty revolutionized the treatment of osteoarthritis and to the present day many surgeons have implanted the Charnley prosthesis with good long-term success [14-17]. In the report from the Norwegian Arthroplasty Register (NAR) in 2008, the Charnley prosthesis was still one of the most used prosthesis in Norway [18].

Figure 5: Charnley monoblock stem

The experience of different registries regarding fixation of total hip replacement

In different countries the use of cemented and cementless implants varies. In the 2012 report from the NAR, the fixation used for primary THR for all ages showed that cemented implants still dominate. In the last decade the use of cemented THR in this register has decreased and the use of cementless and reverse hybrid THR have increased. For ages under 60, cementless and reverse hybrid THR combined dominate, while for ages over 60 an almost even distribution between cementless and reverse hybrid against cemented THR is found [19]. During the last decade cemented implants have decreased and cementless implants increased in the Australian registry also. Only 5.7 % are cemented implants and 63.3 % are cementless in this register [20]. Even in The Nordic countries there are differences regarding fixation, but cemented implants traditionally dominate [21]. In the Swedish Registry cemented implants clearly dominate in 2011, but during the last decade there has been increased use of

cementless and reverse hybrid THR also in this register. In the same period cemented THR has declined [22]. In the report from the National Joint Registry for England and Wales in 2012, 36% were cemented while 41% were cementless THR. Hybrid THR constituted 17% and of these only 15% were reverse hybrid while, 86% were standard hybrid THR. From 2005 there has been a decline in the use of cemented THR while cementless THR has increased [23]. There seems to be no consensus which method provides the best fixation, but the trend in some countries is pointing towards increased use of cementless implants.

Cemented

In the early 1970´s cemented fixation expanded after the results presented by Charnley [13]. Cemented THR has generally been documented with good results [21, 24, 25], and generally cemented stems of stainless steel or cobalt chrome have performed well [15, 17, 24, 26]. However, even if some implants showed good results attempts were made to improve the longevity, but even small changes may affect the survival of the implant. An example is the matt surface Exeter stem. This stem had inferior results compared to the polished version [27]. The Spectron stem has been modified since its introduction in 1983. The first type was a mono-block prosthesis with a 32 mm head. This prosthesis has been documented both in a clinical randomized trial and in a register study [26, 28]. Later this prosthesis was modified with a proximal grit blasted area and with different offsets and stem sizes. Differences in survival with increasing off-sets and with smaller stem sizes has been found [29]. Report about early loosening and severe metallosis has also been presented for this prosthesis [30]. In the NAR, this prosthesis combined with the cemented Reflection all poly cup has inferior results compared to some other implants [24]

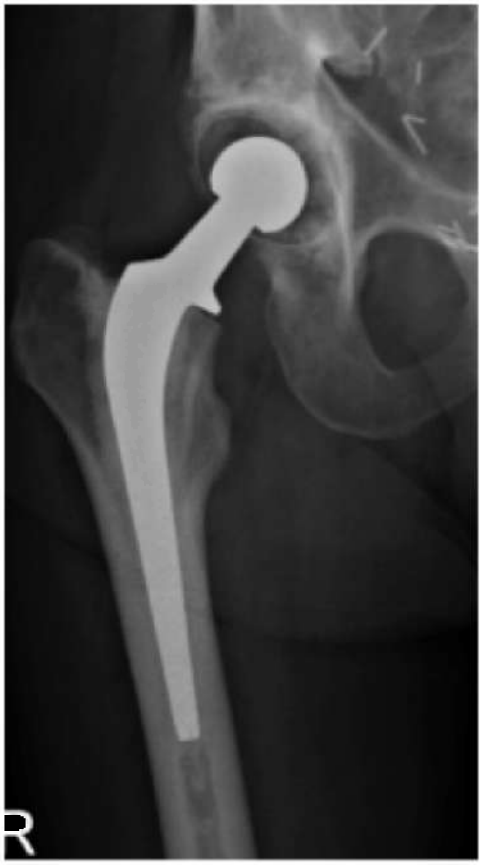

Figure 6: Cemented Spectron EF stem and Reflection all poly cup

It is interesting, although perhaps not for the patients, to see how small modifications can interfere with the

results of cemented prostheses. Therefore we should always bear in mind that small changes to a documented prosthesis may affect the results in an inferior direction.

Generally, cemented all polyethylene acetabular cups have performed well and, in comparison to cementless sockets using UHMWPE, they have a better survival record in several register studies [25, 31, 32]. The cemented Spectron metal backed cup has however shown inferior results compared to the cemented Charnley cup, and high failure rates have also been found in an independent series [26, 33].

In a register study some cementless stems provided better survival in ages below 60 compared to some cemented ones [25]. Several register studies using UHMWPE have documented lower revision numbers for all cemented implants compared to cementless implants [25, 32, 34]. This has mainly been due to revision of cementless acetabular cups, and osteolysis and wear have been the major causes for such revisions [35, 36]. With the introduction of highly cross-linked polyethylene this may change, but it is too early to make this conclusion.

Cementless

Early in the 1970´s cemented fixation expanded after introduction by Charnley, but due to cases of loosening requiring revision surgery, the development of cementless implants continued. The purpose was to ensure fixation without the use of polymethylmethacrylat (PMMA). Jones and Hungerford [37] introduced the term "cement disease" and over the last decades the debate in pros and cons in using cement in comparison to cementless implants persisted. In a cementless THR the surgeon inserts the acetabular and femoral component with an initial primary stability. A press fit design, with or without additional screw-fixation, pegs and fins for the cup, or a threaded cup may be used. A forthcoming biological ongrowth of bone then secondarily stabilize the components with osseointegration [38]. In an animal study the primary stability was found to be important to ensure secondary biological fixation [39]. The metal alloy may be coated or not, and may have hydroxyapatite (HA) on top of the metal. A very thin electrochemically deposited HA, Bonemaster®, has also been developed. This coating was recently documented in a prospective randomized trial [40]. The thickness of the Bonemaster coating is about 5 μm, while HA used without this technique may have a thickness from 50-60 μm (e.g. Taperloc) to 150 μm (e.g. Corail). The sealing effect of HA was documented in different animal studies [41-43], and clinical studies also proved less initial

migration with HA applied to the surface of the implant compared to an implant without HA [44, 45]. In contrast a register study investigating HA coating on identical stems did not show any difference in survival with up to 10 years of follow-up [46]. However, concern about HA was raised. The possibility that the HA particles might separate and become trapped in the joint and lead to third body wear was proposed [47]. The thickness and composition of the HA may be important to its performance. It was suggested that thick HA coatings may more easily delaminate and cause particle-separation that may reach the joint space, leading to third body wear [47]. Porous coated cementless titanium stems (Ti-6Al-4V) with and without HA have good long-term documented survival [48-51]. The Corail stem, one of the most commonly used cementless femoral stems in the Norwegian and Australian joint registries, has shown excellent long-term survival [50].

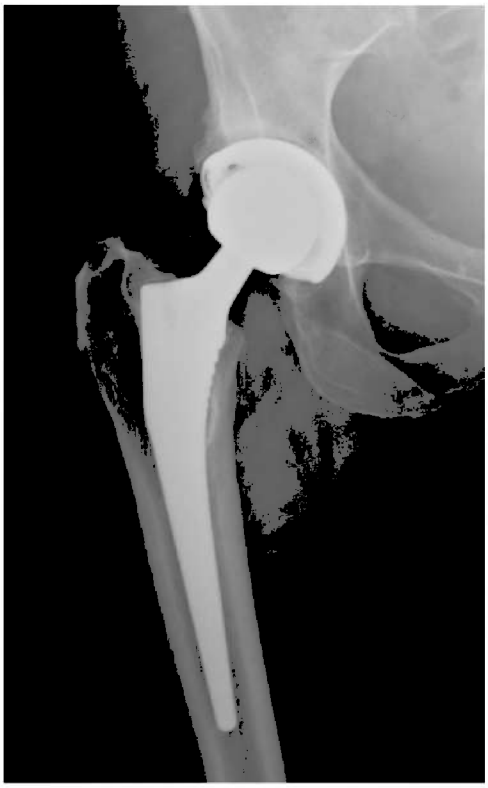

Figure 7: Corail cementless stem and Exceed ABT cementless shell

Durability of cementless stems without thigh pain, and reliable fixation making revision surgery possible without excess bone loss is desirable. Good long-term survival of early cementless stems has been documented, but there have also been reports of difficult revisions [52], and some have been affected by thigh pain [53, 54]. In a randomized trial between a cemented and cementless stem, thigh pain was more frequent with the cementless stem [55]. Thigh pain was not absent with the cemented stem, indicating that this problem is not exclusively related to cementless implants. The diversity of cementless implants has also delivered widely different clinical results. In the Norwegian Arthroplasty register some cementless femoral stems had inferior results [50]. Porous coated titanium femoral stems (Ti-6Al-4V) gave generally good results with a low number of revisions due to aseptic loosening, and some cementless femoral stems had better survival in a register study compared to cemented stems in patients aged below 60 [25]. Independent reports showed good long-term results for certain cementless stems [48, 51, 53, 56]. Cementless titanium stems may initially migrate into retroversion and subside, and thereafter stabilize. This has been documented using RSA for certain well documented stems [40, 57].

Some cementless acetabular components with HA had inferior results compared to those without HA [58-60]. Önsten et al. [61] found no difference in wear comparing a cementless HA-coated cup with a cemented all polyethylene cup. A RSA study did not find any advantage with HA, comparing the stability of cups with and without HA during 5 year follow-up [62]. In a register study cementless cups with HA performed worse than a cemented cup [31]. The advantage of HA on porous coated cups made of titanium is therefore questionable. Compared to cementless cups using conventional UHMWPE, the survival of cemented cups in a register study was generally better [25]. Osteolysis and wear have been the main reasons for revision surgery of cementless cups [35, 36], but the performance of some cups have been good with few revisions due to aseptic loosening [35]. Huk et al. [63] performed histological and retrieval studies of cementless cups with additional screw holes . They found that these modular cups provoked backside wear and that wear particles may be transported through the screw holes. Metal fretting in conjunction with these holes was also described. The idea of creating cups with good primary stability by under-reaming and having no screw holes was suggested. The Reflection cementless cup was designed to minimize backside wear. The central hole used to insert the cup was closed using a central hole-cover screw. This cup with a polished inner surface showed good results in a register study [35] and in a clinical study with aseptic loosening as endpoint [64]. While fixation was good, metal backed acetabular cups using UHMWPE have not shown satisfactory long-term results in a register study due to wear, osteolysis, aseptic loosening and dislocation [35]. However these results may indicate that better results for porous coated titanium cups might be achieved using wear resistant bearings.

Hybrid

In 1989, Harris and Maloney suggested using the hybrid concept to improve long-term durability and to reduce loosening [65]. In a hybrid THR a cemented femoral stem is combined with a cementless acetabular socket, but due to inferior results for cementless sockets, the NAR could not support the use of hybrids with cementless UHMWPE sockets and cemented femoral stems [25].

Reverse hybrid

Due to good results for some cementless femoral stems, the concept of reverse hybrid (also known as inverse hybrid) THR was suggested [25, 66]. The documentation for this concept was sparse. However, McNally presented good results for a HA coated Furlong cementless stem in

combination with a cemented UHMWPE cup at 10-11 years [67]. We have not seen any register studies or RCTs comparing this method against all cemented THR, and the scarce documentation was the impetus for our research.

Modularity

The development of modular prostheses has made the selection of different bearing materials and head sizes possible. New materials like highly cross-linked polyethylene reached the market in the late 1990´s [68], and in that period the use of metal on metal was reintroduced in hip resurfacing [69]. In the National Joint Registry for England and Wales the use of stemmed metal on metal with large heads, in the last decade, have been documented [23]. Modularity makes it possible for the surgeon to easily choose a new bearing material using the same cementless shell and stem.

The cementless acetabulum may have different inserts like metal, polyethylene or ceramics as bearing materials. The femoral stem typically comes with a modular caput, choosing between different sizes in diameter, and the taper makes it possible to add different heads, adjusting length and offset. In revision surgery it is also possible to adjust to some extent with heads providing different angles. Modular necks have been introduced not only for revision surgery but also for primary THR. Long-term results are absent, but short to medium term register results show inferior results for modular necks so far [20]. In a recent paper concern was raised that corrosion may occur in modular necks with adverse periprosthetic reaction leading to revision surgery [70].

Figure 8: Corail stem, Biolox Delta ceramic head, E-poly liner and the Exceed ABT shell

Theories about the process of lucency, osteolysis and loosening

A prerequisite for retaining prosthesis components in the long-term is that the cells around the implant tolerate the material used. In 1963 Charnley warned in a letter to an editor against tissue reactions of abraded "Teflon" particles [71]. He described granulomatous masses with reactions to adjacent bone. In this letter he also wrote that he had implanted a specimen of high-density polyethylene and 2 specimens of "Teflon" subcutaneously in his thigh. While reacting to the "Teflon" he had no signs of biological reaction to the high-density polyethylene. Charnley discovered that low-grade infection may cause loosening of implants [13], but we also know that loosening of implants can occur without infection: aseptic loosening. Jasty et al. [72] proved that there could be localized osteolysis with macrophages and foreign body giant cells around stable cemented implants without infection. In 4 reported cases with the use of cemented cobalt chrome stems and stainless steel stems they found no polyethylene wear debris in the localized lytic areas. Willert et al. [73] examined osteolytic areas adjacent to the artificial joint and found granulomatous masses with foreign body reaction and large amounts of polyethylene debris with nearly no metal or cement debris. Aggressive granulomas were described in cemented THR and it was thought to be a partial reaction to the cement and therefore called "cement disease" [37]. Willert thought that any material could produce wear-debris and that a reaction to this with phagocytosis, and a subsequent foreign body reaction, could occur. Therefore the main goal was to reduce wear to a minimum [73]. Santavirta et al. [74] also found such lesions in cementless THR and proposed that this could be a reaction to wear and polyethylene particles. According to these teories, suggested by Willert and Santavirta, reaction to polyethylene particles may lead to the formation of foreign body granulomas with subsequent osteolysis around well-fixed implants, both cemented and cementless [73, 74]. Wang et al., in an in vitro study, showed that metal particles could also influence macrophage activation [75]. A theory of equilibrium between removal of particles and resorption of bone was proposed. This theory proposes that if the amount of wear particles exceeds the amount which is removed via the perivascular lymph spaces, this may lead to further reaction and bone resorption [76]. In laboratory studies different reactions to particulate debris were reported, from bio-inert materials like ceramics, and more bio-active particles of polyethylene [77]. Particles generated from highly cross-linked polyethylene may differ from that of UHMWPE, and metal particles may again be different from polyethylene particles in size and shape [77]. Particles from highly cross-linked polyethylene may have stronger biological activity than particles from UHMWPE, but in an in vitro study the total volume of these particles was lower than the volume from UHMWPE, indicating that total biological

activity would be lower for highly cross-linked polyethylene [77]. The complete explanation regarding loosening of hip prostheses could be multifactorial. Sundtfeldt et al. [78] discussed these different theories with references to the current literature. Schmalzried proposed the theory of effective joint space. A model that describes the "joint space" with particulate debris and the inflammatory reaction that occurs along its path [79]. The effective joint space may disseminate along the implant cement interface or along the cement bone interface. Furthermore, the high-pressure theory of Aspenberg and Van der Vis was presented [80]. This theory is based on papers measuring higher fluid pressure around implants in a rabbit model, and it was proposed that this fluid pressure could contribute to further osteolysis and loosening of implants [81, 82]. Robertsson et al. measured preoperative intracapsular pressure and investigated the capsular distension in some aseptically loose hip implants. They concluded that the intracapsular pressure is usually elevated in hips with loose implants.[83]. Other contributing factors, discussed in the review by Sundfelt et al., have been the stability of implants, where micro motion is thought to be a factor involved in the loosening process, stress shielding and finally the sealing of the interface between the bone and prosthesis or cement. Remaining endotoxin without infection was also proposed as a cause for activating cells that in turn may cause osteolysis [78].

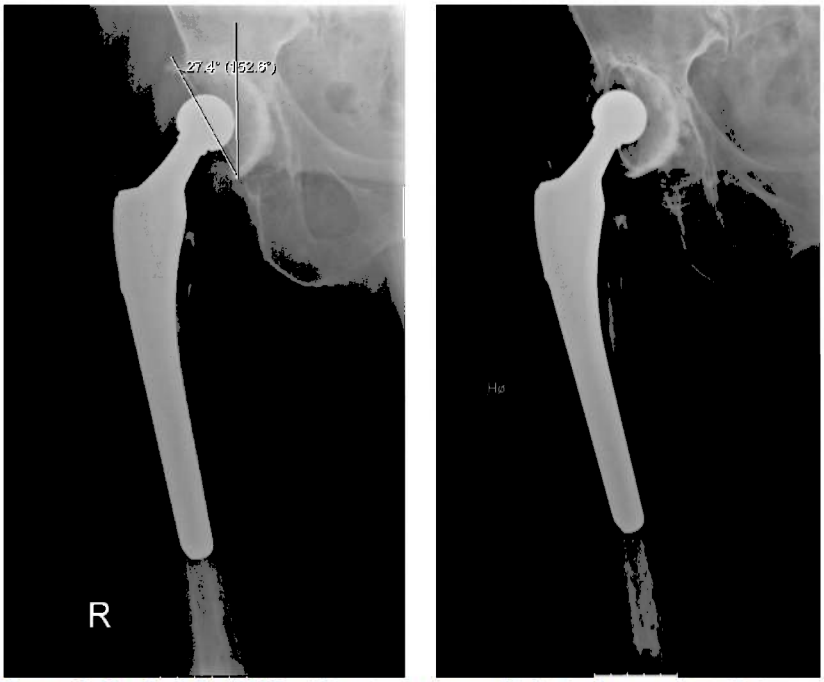

Figure 9: On the left a THR with a steep cup, and inferior lucency/osteolysis behind the cup. Approximately 4 years later (on the right) we found loosening of the cup and subsidence and loosening of the stem.

Bearing materials

Different bearing materials have been used in THR. A short introduction to, and results of these materials will be presented.

Polyethylene

Ethylene gas is the precursor of UHMWPE and polymerization of this gas leads to ultra-long chains of the polyethylene. Under electron microscopy the polyethylene chains may be oriented in different shapes, and areas are often termed as amorphous regions or crystalline regions [84]. UHMWPE used in THR is made from different resins. These resins are often labelled GUR (with subsequent 4 digits). GUR resins are trademark of Ticona, the largest polyethylene supplier of orthopaedic implants. GUR is an abbreviation for "Granular", "UHMWPE" and "Ruhrchemie" according to Kurtz et al. [84]. There are different resins from other manufacturers. The polyethylene resins come in powdered form. The resin powder is then compression moulded or ram extruded to form a solid polyethylene stock, before the final design is determined using a machining process applied by the manufacturer. Hot isostatic compression of ArCom (Biomet) UHMWPE is also described, and finally one could use direct compression moulding of the UHMWPE [84]. The properties of the final component may be further affected by the method of sterilization, the degree of (e.g. gamma) irradiation, or addition of different substances (e.g. Vitamin E).

With the understanding that wear may cause tissue reaction a main goal in THR has been to reduce wear. In the 1970`s a carbon reinforced polyethylene -POLY II- was introduced to the market. In tibia bearings used in Total Knee Replacement (TKR) this polyethylene showed increased wear at the surface [85]. Another polyethylene, Hylamer, was introduced in the early 1990's. This polyethylene was thought to have better mechanical properties with less wear. Later this polyethylene was withdrawn from the market and a long-term study showed that revision was more prevalent for Hylamer than with UHMWPE [86]. In a randomized trial using RSA with 5 year follow-up the wear rates for Hylamer was higher compared to a conventional UHMWPE, with both stainless steel and Zirconium heads [87]. However it should be pointed out that there have also been studies with low wear rates of this material, and studies with comparable results with UHMWPE. These different results were discussed in a paper by Kurtz et al. [84]. Small changes in the manufacturing process may result in changes in the

mechanical properties of the polyethylene. In 2003 Digas et al. [88] published a paper showing increased early wear regarding an Ethylene oxide (EtO) sterilized UHMWPE. The philosophy of using EtO was that this would not lead to the development of free radicals. Terminal gamma sterilization has shown to form free radicals, and thereby to a certain extent perform cross-linking of the polyethylene. A Register study later showed an increase in revision rates for the Reflection all poly cup in combination with the cemented Spectron EF femoral stem, and other RSA studies confirmed high wear rates with this polyethylene [24, 62, 89]. By reducing the O_2 environment and performing gamma sterilization in an inert environment, the oxidation of free radicals may be diminished [90].

Cross-linking of the polyethylene increases wear resistance in the long-term [91, 92]. Groobelaar, Oonishi and Wroblewski documented low wear rates of early cross-linked polyethylenes [93-95]. According to Kurtz et al. both Oonishi and Groobelaar used gamma irradiated cross-linked Hostalen RCH 1000C in their acetabular components. Wroblewski used a Cilane cross-linked HDPE [84]. In the 1990`s the first commercially highly cross-linked polyethylene entered the market [68]. Even if the wear has been reduced, the long-term reaction to the polyethylene and the wear particulate debris amount is uncertain. An in vitro study indicated smaller wear particles with higher biological activities, but the total volume of such particles was possibly lower indicating lower biological activity compared to conventional UHMWPE [77]. Another concern has been the irradiation of the polyethylene that will split the long polyethylene chains. This process is necessary to cross-link the polyethylene chains. As a side effect, after cross-linking, this process will generate free radicals that may become trapped in the polyethylene. These free radicals can react with oxygen in vivo and may over time alter the mechanical properties [96]. Reduction of free radicals is therefore desirable. Therefore a main goal has been to eliminate these free radicals without compromising the mechanical properties of the polyethylene. Heating the polyethylene will reduce the amount of free radicals [97]. The dilemma is that the thermal treatment of the polyethylene at or above the melting point is effective in disposing free radicals but may alter its mechanical properties[98], and heating the polyethylene below the melting point may not remove all free radicals [99].

Today cross-linked polyethylene has shown extremely low wear compared with conventional polyethylene up to 10 years follow-up [68, 91, 92, 100]. The latest generation of highly cross-linked polyethylene has tried to exhibit good mechanical properties after cross-linking with a low amount of free radicals, and without re-melting the polyethylene. X3 (Stryker®) has been

sequentially annealed and gamma irradiated in three steps. Another approach to reduce free radicals is to add an antioxidant in the manufacturing of the polyethylene. E-Poly™ (Biomet®) cross-linked polyethylene is irradiated and processed below the melting point. Vitamin E is added as an antioxidant to reduce the level of free radicals [101]. Vitamin E contains an OH-group and will act as an antioxidant by donating a hydrogen atom from this OH-group in the ring structure [102]. Finally the polyethylene is sterilized by irradiation. This polyethylene is available for use in THR. Laboratory results have shown promising results, but published clinical trials are absent [101, 103-106]. At present there are even different resins with incorporated vitamin E. A dilemma with E-vitamin infused resin is that this may inhibit cross-linking in the irradiation process[107]. E-poly is therefore gamma irradiated before it is infused with vitamin E.

In the Australian Register, cross-linked polyethylene had better survival compared to conventional polyethylene using a metal head. The same register found that using metal on highly cross-linked polyethylene had no effect on survival when comparing the use of heads under 32 mm or over 32 mm. Furthermore they found no difference in survival between UHMWPE and highly cross-linked polyethylene when a ceramic head was used. [20]. Both wear and osteolysis are favoured by highly cross-linked polyethylene, compared to conventional UHMWPE [68]. However, a study by a Swedish research group, at 10-year follow up, did not see any differences in loosening of cemented implants, even if the wear of highly cross-linked polyethylene was significantly lower compared to UHMWPE [91]. A study comparing highly cross-linked polyethylene with UHMWPE with up to 8 years follow-up found less wear and osteolysis in the highly cross-linked group [100]. We are now in the second decade of cross-linked polyethylene use and new long-term follow-up studies are expected to show if these articulations will surpass UHMWPE in the long-term. In the last decade use of highly cross-linked polyethylene has increased and in the annual NAR report of 2012, highly cross-linked polyethylene is used more often than UHMWPE in Norway [19].

Ceramic on ceramic

Boutin is said to be the first to implant a Ceramic on Ceramic (CoC) bearing in 1970 [108]. Jeffers and Walter published a systematic review of ceramic on ceramic bearings and found that CoC has shown very low wear rates, but some of the early ones had loosening of the cup as a frequent cause of revision, and fracture of the ceramic was also reported [109]. Histologic

samples obtained during revision of such prostheses revealed small (1-3 μm) ceramic particles inside macrophages taken from the joint capsule. Radiologically, the reaction to these particles with subsequent cystic formation and osteolysis was not as extensive as for metal on polyethylene [109, 110]. Low biological response and low wear rates of CoC have been documented in an in vitro study [77]. Fracture of the components has been considered a serious problem and may complicate revision surgery [111]. The fracture risk was suggested to be around 1 per 2000 over a 10 year period [108]. The manufacture of the alumina-alumina couple has developed over the years and probably resulted in a lower fracture risk. There has been some concern about squeaking and this phenomenon may be multifactorial, but the design may play a role [112]. Liner chipping and liner dissociation combined with fracture are known side effects of this articulation [109]. All these factors have been arguments against this method and may explain why ceramic or metal on polyethylene is used on a larger scale. The placement of the shell in relation to the stem is also crucial to avoid impinging the stem with the edge of the shell [109]. Ceramic on ceramic bearings may be more technically demanding than using metal or ceramic on polyethylene.

A frequently used ceramic in THR is alumina (Al2O3). Zirconium (ZrO2) and Oxinium (Zr2.5Nb) are other options with a ceramic surface. Well-known alumina such as Biolox and Biolox forte (CeramTec) preceded the latest generation, Biolox delta. This material is stabilized with zirconium, strontium aluminate and chromium oxide. This material is supposed to be harder and have a greater resistance to fracture.

In a 2012 register study from the National Joint Registry for England and Wales CoC bearings performed well [113].

Metal on metal

The concept of metal on metal has gained increasing popularity over the last 2 decades. In stemmed prostheses the taper/head junction, also called the trunion, may be the source of metal fretting and corrosion [114]. While metal on metal has shown poor results, especially for large heads, ceramic on ceramic has shown good results, also using larger heads, in a register study [113]. The metal on metal articulation on stemmed prostheses is no longer recommended [113]. Long-term response to metal wear debris, with possible elevated metal ion levels in the blood or peripheral organs, has so far not been fully determined.

Reduced use of metal on metal is reported in some registries in the last few years, probably due to the documentation aforementioned [20, 23] .

Head materials

Alumina ceramic heads may be used in articulations with polyethylene. The risk of fracture has diminished since the first generation, but this complication has been a major concern against the use of such heads. Fracture of ceramic heads may complicate revision surgery as aforementioned. Small ceramic particles may provoke third body wear both to the head material and to the polyethylene after revision due to ceramic fracture [115].

A 10 year RSA study confirmed statistically significant reduced wear for alumina heads compared to cobalt chrome using UHMWPE [116].
An in vitro study showed lower wear rates with ceramic against cross-linked polyethylene compared to metal heads [77]. This finding may indicate that ceramic heads with less wear may be an advantage in the long-term, and for young patients with a long life span. However, long-term clinical studies are not available to make this conclusion.

Both steel and cobalt chrome heads against UHMWPE have been used for several years with reliable results in THR [24]. Zirconium femoral heads were in clinical use until 2001. This material was recognized as being stronger than regular alumina ceramics, but may undergo phase transformation with subsequent volume change [117]. The wear properties of this material have been investigated. A RSA study proved increased annual wear rate compared to cobalt chrome articulating against UHMWPE, at five years follow up [87]. According to Kurtz et al. the manufacturer of this material changed the manufacturing process in 1998 [117]. This may have resulted in the high number of fractures reported to the company. This led to withdrawal of these zirconium heads from august 2001 [117].

Oxinium consists of a niobium alloy of zirconium [118] which is heated in the presence of air, and this process converts the surface to a zirconium oxide ceramic [117]. This bearing material is meant for hard on soft bearings and should not phase transform [117]. Oxinium heads in THR have not shown any advantage compared to cobalt chrome in a RSA study with 2 years follow-up [89]. Some reports have described surface damage to Oxinium femoral heads, after dislocation, with secondary seriously abrasive wear [119, 120].

Wear measurements

Polyethylene wear is proposed to be a continuous process where polyethylene particles are released during hip movement. Wear is classified as adhesive, abrasive, fatigue, fretting, erosive and corrosive [121]. As wear is proposed to be a major factor limiting prosthesis survival, the assessment of wear is crucial in documenting different bearings.

Polyethylene liners or cemented polyethylene cups may be inspected after they have been explanted during revision surgery or removed from deceased patients. Such retrievals may be investigated directly with measuring tools to estimate the wear.

In vivo wear measurements are performed using different radiological methods. When performing in vivo wear measurements the penetration of the head into the acetabular component reflects not only the wear but also the bedding-in of the polyethylene. Bedding-in (also called creep) may be the effect of both plastic deformation on the articular side and seating of the liner into the shell [122]. Therefore the true wear rate is measured after the bedding-in period with multiple measurements at different time intervals.

Griffith measured wear on conventional radiographs with reference to the marker in Charnley cups [123]. A prerequisite for this method was that radio-opaque cement had to be used. Livermore presented a method to estimate wear using conventional radiographs [124]. An initial scan taken postoperatively was compared to x-rays taken at later follow-up. The centre of the head was located by the use of concentric circles in one mm increments of radial length. The direction of wear was estimated with the use of a compass to measure the shortest distance from the centre of the head to the outer border of the cup. With a calliper he measured the distance along the wear direction from the outer border of the head to the outer border of the cup and cement interface.

Different techniques have been developed over the years. The RSA method described by Selvik [125] was initially developed to examine movement of different defined “rigid bodies” in the skeleton. Baldursson used RSA and performed the first wear measurements with tantalum markers in the polyethylene [126]. RSA has been used in several clinical studies and validated in in-vitro studies [61, 92, 127-129]. Initially wear measurements were done manually, but today there are several computer assisted methods available. Martell Hip Analysis suite 7.14, Rogan HyperOrtho, Rogan View Pro-X and Roman v1.70 are examples, and in a study by Geerdink

these methods have been compared [130]. Bragdon et al. found that the Martell method overestimated wear in comparison to RSA with cementless cups [131]. However, comparing these techniques the authors found no difference in wear rates between 2 and 5 years follow-up. RSA has also been refined with digital automatic measurements [132, 133]. RSA has been proved to be both accurate and precise [89, 127, 134, 135]. Initially markers in the polyethylene were used as a reference segment, and the point motion of the head's centre in the polyethylene is used to measure the bedding-in and wear rate. Marker-less methods using RSA have also been developed. One technique is to use the outer border of a hemispherical shell as the reference in relation to the centre of the head. This method has been validated by Børlin et al. [134]. Another method is to use a model based RSA, also without the use of tantalum markers [135]. With its high precision and accuracy the RSA method is the gold standard. Especially when measuring low wear-rates, short follow-ups and having a small sample size, this method is to be preferred [129, 135].

Motivation for this thesis

The objective of the current thesis was to study total hip replacement with a special focus on the reverse hybrid method. Our main objective regarding the research was to document this method to possibly prevent unnecessary revision surgery. Polyethylene wear has been a major cause of revision surgery. Our interest in this topic is therefore reflected in 3 of the 4 papers. In paper 4 we performed a clinical trial with a new E-vitamin infused highly cross-linked polyethylene, a new bearing material not yet clinically evaluated.

Paper 1

Main objective: To evaluate short to medium term results of the reverse hybrid method and to compare this method to all-cemented total hip replacement using data from the Norwegian Arthroplasty Register.

An observational national register study.

Paper 2

Main objective: To compare a reverse hybrid THR with a proximally HA coated stem to a cemented THR using the same cemented cup in a prospective randomized controlled trial.

A prospective randomized clinical trial.

Paper 3

Main objective: To estimate polyethylene wear using the traditional RSA-method with tantalum markers in the polyethylene and compare it to a method where the penetration of the head is estimated using tantalum markers in the periacetabular bone. The main goal was to investigate if there were significant differences in wear estimates between the two methods, and to see if migration of the acetabular component could affect the wear measurements.

Evaluation of wear-measurements with two methods of RSA using a paired sample

Paper 4

Main objective: To evaluate the wear of an E-vitamin infused highly cross-linked polyethylene in vivo, and to examine whether there is difference in wear between 32 and 36 mm heads in a cementless THR.

A prospective randomized clinical trial.

Ethics

In paper 1, patients gave informed consent to participate with information to the NAR regarding their THR. This national register is well established and no ethical approval is required when using data on primary and revision surgeries.

The clinical trial in paper 2 was conducted in accordance with the Helsinki Declaration and approved by the Regional Ethics Committee (REK) South-East, Norway. We also registered the trial with Clinical Trials.gov Identifier: NCT00526539. All patients gave informed consent to participate in the study and the informed consent was approved by the REK.

In paper 3 we used wear measurements and micro-migration of prosthetic components from the clinical trial described in paper 2. Therefore no additional ethical approval was required.

We established RSA in Lovisenberg Diaconal Hospital prior to the conduction of the clinical trial described in paper 4. Permission was obtained from the Norwegian Radiation Protection Authority. The study was also conducted in accordance with the Helsinki Declaration and approved by the Regional Ethics Committee (REK) South-East, Norway. The study was registered with Clinical Trials.gov Identifier: NCT00804388. All patients gave informed consent to participate in the study and the informed consent was approved by the REK.

Patient study groups

Paper 1

We used data from the Norwegian Arthroplasty register. In this register patients are asked to contribute data to the register, prior to surgery. A written consent is obtained and the surgeon fills out a form after implantation or revision of a THR. There have been some modifications to the forms and those used in paper 1 are shown in the appendix. On the backside of each form there are guidelines on how to use it. The register was established in September 1987 [136] and several scientific papers have originated from this register. The degree of completeness regarding this register was found to be high [15, 137, 138]. In paper 1, 3963 hips in 3630 patients were included, from December 31, 1999 through December 2009, in the RH group. In the cemented group 37666 hips from the 10 most commonly used prosthesis combinations in the same time period were included. This was an observational national register study and we observed skewness in follow-up, age and male/female ratio between study groups. These could be biases and have to be taken in consideration when analysing the data.

Paper 2

All patients were included and operated on at Lovisenberg Diaconal Hospital. Written consent was obtained before inclusion. In this study the upper age limit was set at 75 years. We excluded patients with rheumatoid arthritis, former surgery, high offset, and dysplasia. We initially planned to include 60 hips. 52 hips (51 patients) were included and 43 hips (42 patients) were followed for 2 years. During the study we had periods where we did not have all sizes of study prosthesis. The inclusion period was prolonged and we had difficulties in perceiving a complete flow chart with eligible patients and patients not willing to participate. After including the patients the rest of the flow chart was complete. One patient withdrew from the follow-up. Other missed data constituted with exclusions of patients and missed data regarding DXA and RSA analysis as shown in the flow chart in the appendix.

Paper 3

We obtained the required data for this study from those patients included and operated on in paper 2. From that randomized controlled trial 31 patients had enough tantalum markers in the polyethylene and in the periacetabular bone to make it possible to measure point motion according to both segments in the same patient.

Paper 4

All patients were included and operated on at Lovisenberg Diaconal Hospital. 50 hips (49 patients) were randomised to receive 32 or 36 mm heads of Biolox delta ceramics.
The age of these patients was between 50 and 65 years, to have a group of patients with the same approximate age, to investigate this new material in a cohort of young patients. With a homogenous age between the groups we hoped that this would reduce the activity bias between study groups. All patients had primary arthritis, and we excluded patients with rheumatoid arthritis, systemic inflammatory disease and former surgery. Demographic data was similar between study groups although there was a non-statistically significant tendency towards more females in the 32 mm group. All, but two patients attended follow-up, and just one RSA examination was excluded due to poor quality of the RSA scan taken postoperatively. The flow chart is shown in the appendix.

All patients in paper 2 and 4 attended clinical and radiographic follow-up at Lovisenberg Hospital, while the RSA and DXA analyses were performed at Oslo University Hospital. In paper 2 all DXA and RSA scans were performed at Oslo University Hospital. In paper 4 all RSA scans were performed at Lovisenberg Diaconal Hospitals.

Methods

X-ray evaluation

In study 2, 3 and 4 all patients were evaluated with radiographs preoperatively. Templating was not used as a routine in either study 2 or 4**.** All patients had a postoperative radiograph of the hip during the hospital stay, followed by x-rays at 3 months and at 2 years. At the 2 year follow-up we obtained anteroposterior pelvic x-rays and an x-ray of the operated hip with a Lauenstein projection. These x-rays provide the possibility to evaluate the different Gruen zones [139], and also to evaluate osteolysis on the lateral projection of the femur. Cup placement was evaluated on the anteroposterior pelvic projection. We now routinely obtain a lateral view with the possibility to evaluate the aforementioned parameters. At 2 years, we registered the position of the cup, stem, osteolysis and lucency using M-desk version 3.0 (UmRSA Biomedical). This system uses the x-ray from a pelvic view (Figure 9). With this system it is

possible to measure inclination of the cup, the position of the stem and lucency around the cup/stem. Different distances in relation to the centre of the prosthetic head can be measured. The distance from the distal sacroiliac joint, from the Kohler line, the height above the tip of trochanter, the offset and the distance from the tuber line may all be calculated in relation to the centre of the head. These lines are shown below (Figure 10).

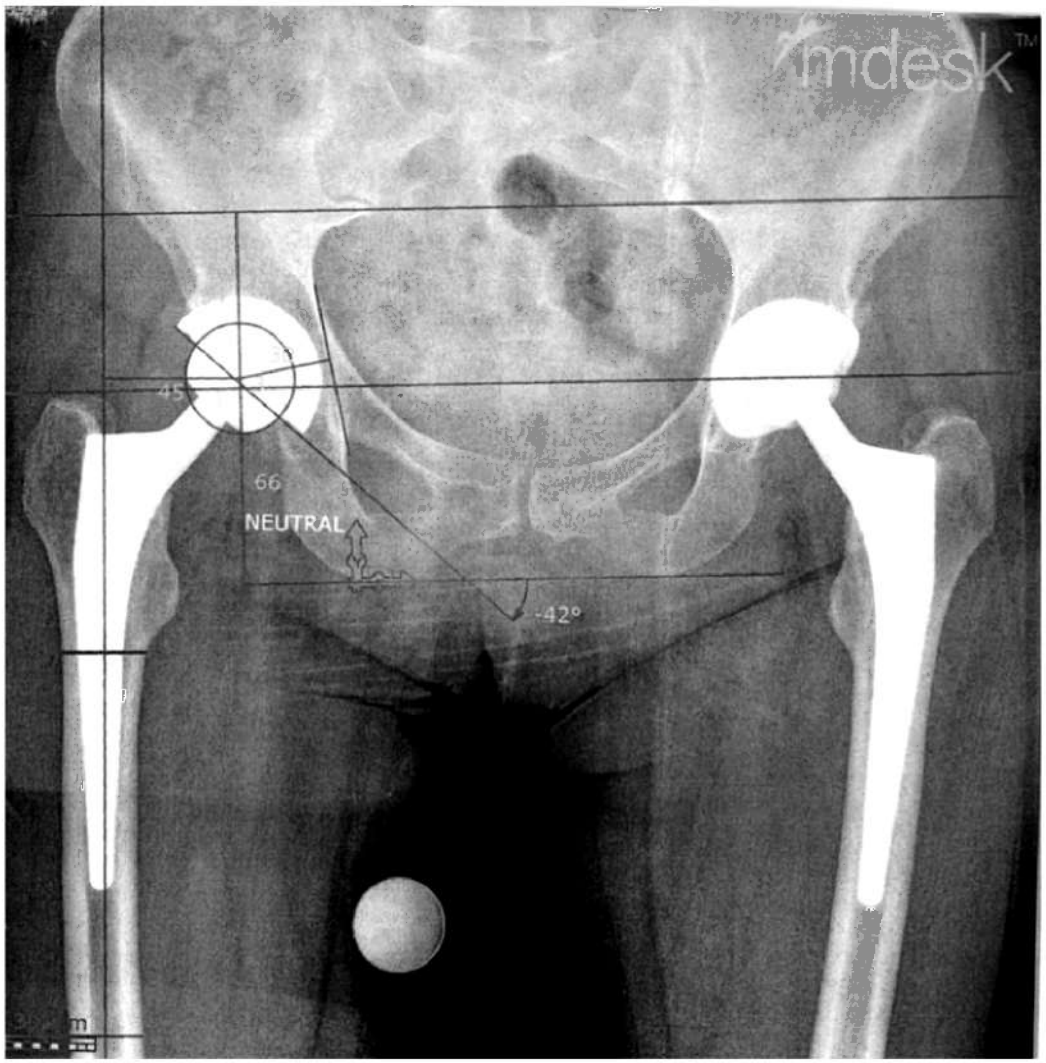

Figure 10: An X-ray and different reference points and measured distances using M-desk

Radiostereometry (RSA)

Radiostereometric analysis has been used in THR surgery to measure 3-dimensional micro-motion of implants and wear of the polyethylene [61, 62, 125, 127, 129, 131]. RSA has evolved from a manual tool to digitized radiographs and digital measurements [133]. RSA is often based on the insertion of tantalum markers in the bone, the polyethylene or markers attached to prosthesis components. Tantalum markers come in different sizes of 0.5 mm, 0.8 mm or 1 mm [135]. Using two x-ray tubes with simultaneous exposure, and a calibration cage placed underneath the patient, stereo radiographs are taken. The calibration cage defines the three dimensional coordinate system. In addition to the spherical tantalum markers, the centre of the head and the centre of a hemispherical cup can be used as reference points. At least 3 defined markers are used to define a rigid body, and they must be identified in both configurations (both films taken by the stereo x-ray). These markers define a rigid body with a centre.
Markerless RSA uses the outline of a hemispherical cup and the centre of the femoral head [128, 134]. The point motion of the femoral head is measured in relation to the segment defined by computer-selected points on the hemisphere of the cup and cup opening [134]. One of the advantages of RSA is the possibility to perform clinical trials with a limited sample size [135]. This can be done because of the high accuracy of RSA. Software programs from different companies can be used in the analysis. RSA is demanding and expensive to use and therefore better suited to clinical trials than to routine in an orthopaedic department. With increasing use of RSA there have been some efforts to standardize methods [129, 135, 140]. Standardization may be useful in the interpretation of RSA results.

RSA with a calibration cage and the x-ray set up is shown in figure 11. Calibration cages may be uni- or biplanar [135]. The x-ray set up may be a mobile unit and a fixed unit, or a completely fixed set up with two x-ray tubes.

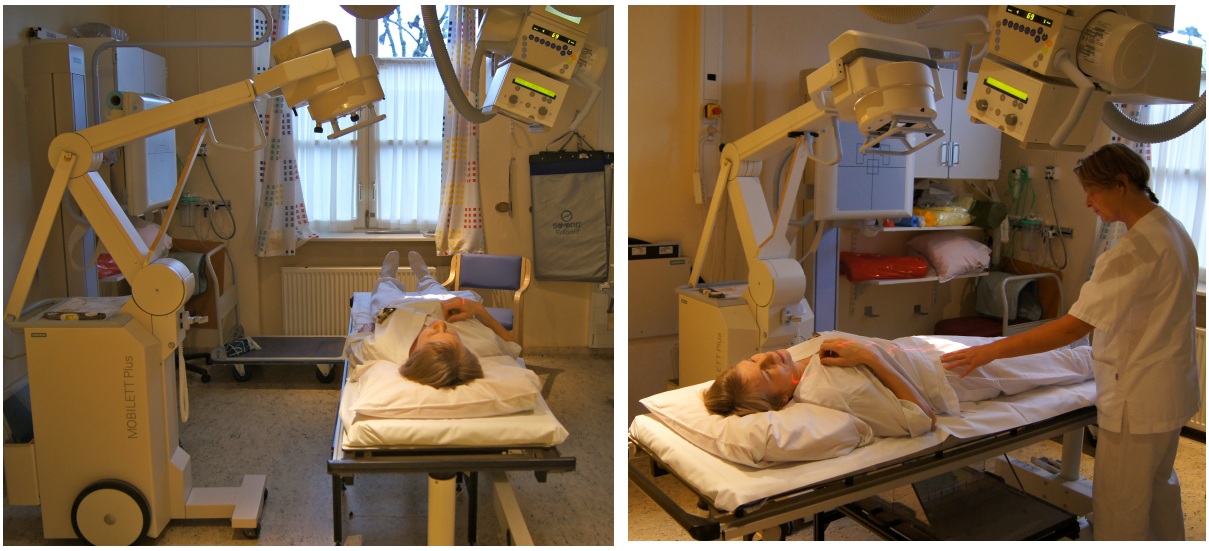

Figure 11: Siri and Berit demonstrating the RSA set up with a mobile and fixed x-ray tube. In the picture to the right we can see the calibration cage placed under the patient.

The stability of the markers is measured according to the mean error. The mean error is recommended to be lower than 0.35 mm [135]. The condition number describes the distribution of markers. Low condition numbers represent good distribution of markers, while high condition numbers represent poor distribution. Valstar et al. propose using condition numbers below 150 [135].

Movement can be expressed as translations (movement along axis) or rotations (movement around axis). Movement can also be expressed as MTPM (Maximal Total Point Motion or 3 dimensional movement). Movement can be expressed using both positive and negative values (signed) or absolute values (unsigned) [135, 140]. As Valstar points out, unsigned values are not normally distributed which may imply some methodological problems [135].

In this thesis we used RSA in 3 of 4 papers. Recently a study by Kibsgård et al. [141] evaluated the accuracy and precision of RSA in our department. This was done on a model estimating movement in the sacroiliac joint. Ideally it would also have been done for wear measurements in our laboratory.

The precision of the measurements in our studies was calculated by double examinations and expressed as an absolute mean plus 2 times standard deviation (SD) to cover the 95%

confidence interval (CI) [62]. Another formula was described in a paper by Ranstam et al. [142]. The difference between these two calculations is essentially that we used the absolute difference between double examinations, while the other formula calculates the precision with respect to zero.

We used a fixed system for RSA set up in paper 2 and 3. In paper 4 we used one fixed x-ray tube and one portable. Radiographs were taken with the patients in the supine position using a calibration cage number 43. All scans were digitized and analysis was done with UmRSA digital measure 6.0 (RSA Biomedical, Umeå, Sweden).
In paper 2 RSA was used to estimate micro-motion of both the cup and the stem. Wear was also estimated using the centre of the head, with measurement of its penetration into a reference segment defined by markers in the polyethylene. In paper 3 we compared two methods of RSA measurement of wear. Patient and data for this study were taken from the study described in paper 2. In Paper 4 we used the markerless method for measuring wear of the polyethylene liner in a cementless hemispherical shell.

Dual energy X-ray absorptiometry (DXA)

Dual energy x-ray absorptiometry (DXA) estimates bone mineral content in bone as described by Dunn et al. [143]. In THR, DXA has been used to estimate change in bone mineral density (BMD (g/cm^2)) around both cemented and cementless implants [40, 144-147]. Bone remodeling can be measured as a change in bone mineral density by repeated scans with respect to the initial scan postoperatively. Different regions of interest (ROI) have been defined on the acetabular side [145-147]. On the femoral side the 7 Gruen zones are typically used [40, 139]. The different ROIs may be copied and used on later scans in the same patient.

DXA can discriminate between soft tissue, bone and metal implants. Bone cement may be difficult to discriminate from dense bone or prosthesis. Manual removal may be used after the initial digital scan using the paint facility. Using this manual tool the operator can adjust for example the bone cement interfaces, prosthesis cement interface or prosthesis bone interface.

The precision of each ROI is often given as a CV %. A CV % illustrates the repeatability for the measurements in the certain ROI.

To calculate the precision in our study the patients went through 2 scans at each follow-up. Between the scans they stood up and were repositioned. We tried to standardize the position by using a foot brace and the patient's scans were taken with the patient in the supine position. In the present thesis we estimated the CV % with the formula [145, 147]:

$$CV\ \% = 100 \times [(\delta/\sqrt{2})/\mu]$$

δ is the standard deviation of the differences between the paired BMD measurements, and μ is the mean of all BMD measurements for each ROI.
We used the same DXA-machine on all patients in study 2.

Several models have been described regarding the selection of different ROI´s around the cup. Wilkinson described a 4 ROI model, Field et al. used modified Charnley DeLee zones and Digas et al. used a 5 ROI model [145-147]. The 4 ROI model described by Wilkinson is also validated using a cadaver model. We used the modified Charnley DeLee zones. We chose this model because we have the possibility to measure 3 different zones adjacent to the cup, and also split the area superior to the cup into two zones, while Wilkinson et al. just had one zone covering the area adjacent and superior to the cup.

Clinical score

We used the Harris and Oxford hip scores [148, 149]. These scoring systems have been used in clinical trials and are well established. In paper 4, at 2 years, we used the UCLA (University of California Los Angeles) score to measure activity between study groups [150]. Activity score was not measured in paper 2 and we have pointed out that this could be a possible bias. Wear has been shown to be a function of activity [151]. In retrospect it would have been desirable to also have an activity score at 2 years follow-up in study 2. If this cohort attends a later follow-up we will take an activity score.

Implants used

We performed 2 randomized clinical trials. In paper 2 we compared a reverse hybrid THR with a cemented THR. In both cases we used a cemented Reflection all poly cup (Smith and Nephew). The stem in the reverse hybrid THR was the cementless Taperloc (Biomet) made of Ti-6A1-4V (Figure 12). The stem had proximal plasma sprayed HA coating on top of the porous metal coating. The HA coating was 55±15 µm thick and had a crystallinity of 50-70 %. The Taperloc had tantalum balls attached to the tip, at the calcar-region and at the neck. For study purposes we had sizes 7.5, 10, 12.5, 15 and 17.5 in standard offset.

Figure 12: The Spectron EF (left) and the Taperloc (right) with tantalum markers. These stems were used in study 2.

The cemented stem was the Spectron EF (Smith and Nephew). This stem had tantalum balls attached to the tip and to the calcar region. A metal piece with a cone and a tantalum marker was attached to the neck during surgery. We had all available sizes of this stem in standard offset (Figure 12). In both groups we used a head of cobalt chrome with a diameter of 28 mm. Heads on the Taperloc stem was manufactured by Biomet while heads on the Spectron EF stem came from Smith and Nephew. The reason for this was that the 2 stems had different taper dimensions.

The cemented all polyethylene Reflection cup was manufactured from a GUR 1050 resin and ram extruded. Made of UHMWPE, it has ridge in the radial direction, grooves in the polar direction and a peripheral flange. The cup had cement-equalizing pods and a wire marker along the cup equator. This wire might help to provide information on the cup placement. The cup was sterilized by ethylene oxide.

Figure 13: Corail/Exceed ABT

The PMMA used was Palacos R+G from Heraeus, Hanau, Germany. We used a third generation cementing technique with puls lavage and pressurization of the cement before insertion of the components. In the acetabulum we created anchoring holes for the cement, and in the femur we used a cement restrictor of polyethylene. The reason for choosing these components was that at the time of the study we used the cemented Spectron EF stem in conjunction with the Reflection cemented all poly cup in our department. We also used the Taperloc stem without HA in conjunction with the cemented Reflection all poly cup. The Taperloc stem with HA was used in the study because we aimed to investigate if a HA coated cementless stem would cause more wear than a cemented stem using the same all poly cup.

In paper 4 we used a cementless Corail stem. The Corail (Depuy) cementless stem is made of Ti-6Al-4V, is fully coated with an approximately 155 μm thick hydroxyapatite (HA) coating and has a taper dimension of 12/14 (Figure 13).

On the acetabular side we used the Exceed™ABT (Biomet) shell, made of Ti-6A1-4V. The shell is hemispherical and has a porous coating with a rim flare and was inserted after under-reaming by 1-2 mm. The porous coating was without HA (Figure 12). We used the Exceed™ ABT shell with sealed screw holes and the apical hole, used to seat the shell into the acetabulum, was supplied with a blanking screw. We decided to use a minimum polyethylene thickness of 5 mm. With that minimum thickness of polyethylene, outer diameters of the shell of 50 and 52 mm could only fit liners with 32 mm heads. With an outer diameter of 54 mm or more, the liner could accommodate both 32 and 36 mm heads. The polyethylene liner used in this particulate study was a highly cross-linked polyethylene infused with E-vitamin.

The E-poly (Biomet) was manufactured from ArCom® barstock as the starting material. This material constitutes both GUR 1020 and GUR 1050 resins and is manufactured using a hot-isostatic compression moulding process. The ArCom barstocks are machined, packed and gamma irradiated with 100kGy (10Mrad). Vitamin E is infused after this process and the components are then machined to final shape, cleaned and packed with final gamma sterilization. Processing is done below the melting temperature (Information from Biomet Biomaterials Laboratory, Warsaw, IN).

The femoral head used in this study was a Biolox® delta head produced by Ceram Tec A.G., for DePuy. One study group received a 36 mm head while the other group received a 32 mm head.

This alumina head is sometimes called Zirconia-Toughened Alumina Matrix Composite (ZTA) due to the fact that the alumina matrix is reinforced by zirconia, strontium aluminate and chromium oxide [117]. Both the head and the stem came from DePuy, while Biomet produced the Exceed shell and liner.

Statistics

In the register study we estimated Risk Ratio (RR) with 95% confidence interval (CI). We used Cox regression analyses, with adjustments for age (< 50, 50–59, 60–69, 70–79 and > 80), sex, and diagnosis (osteoarthritis (OA), inflammatory arthritis, and others). Plots with scaled Schoenfeld residuals were made for each covariate and judged by a statistician. This was done to test that the Cox proportional hazard model was fulfilled. The Kaplan-Meier method was used to estimate the survival probabilities for the prostheses, with 95% confidence interval (CI). In the register study we included bilateral hips as Ranstam and Robertsson have discussed statistical analysis regarding arthroplasty register data and found a negligible effect on survival rates including bilateral hips [152]. When less than 20 hips remained at risk, survival probabilities were not calculated. The reverse Kaplan-Meier method was used to calculate the median follow-up [153].

In paper 1, 2 and 4 we used the Chi-squared test to look for binary outcomes between study groups. In studies 2 and 4 we also used the Fisher exact test to look for differences between two groups with binary outcomes.

The non-parametric Mann-Whitney U test was used in all 4 papers to test for differences between study groups. In paper 2 and 4 the sample sizes were not so large and RSA values may not be normally distributed. According to Valstar 3D migration is not normally distributed since absolute values are used. This was the main reason for choosing this test and why we also used the non-parametric Wilcoxon signed rank test to look for differences between wear measurements in paper 3. The non-parametric Wilcoxon signed rank test was also used to look for differences at different time intervals.

Prior to performing a randomized study it is important to estimate the sample size to avoid, for example, type 2 errors. This means that even if we do not prove differences between study groups, the sample may be too small to detect such differences. In paper 2 we did not perform a sample size calculation but relied on earlier RSA estimates and studies [129]. Due to a lower final sample size than we had planned, this may be a weakness of this study. We used the effect size with the mean difference (95% CI) between study groups. This was to check if the 95 % CI of the mean difference was below the likely, clinically important wear threshold of 0.1 mm/y [154].

In paper 4 we performed a sample size calculation before study start. Focusing on wear, we found that 17 patients in each group would be appropriate to detect a difference of 0.1 mm (SD: 0.1) with an alfa of 0.5 and a power of 80 %.

In paper 3, with the use of boxplot from SPSS, we detected outliers defined to have values from 1.5 to 3 inter-quartile ranges (IQR) from the median value, and extreme values defined as values above 3 IQR from the median.

In all 4 papers, p-values less than 0.05 were considered to be statistically significant.

Main results

Paper 1

The survival comparing reverse hybrid with all cemented THR was equal for the total material at 5 and 7 years, and also for age below 60 years. In sub analyses of the total material, using the endpoints revision due to deep infection, dislocation, aseptically loosened stem, and aseptically loosened cup, no statistically significant differences between cemented and reverse hybrid THRs were found. We found a 3.6 ((95% CI: 1.9-6.9), p<0,001) fold higher risk for revision due to periprosthetic femoral fracture in reverse hybrid THRs, but the survival for the two groups were 99.6 % and 99.85 % at 5 years with this endpoint, indicating that this complication is rather infrequent. We performed analyses of the different cup/stem combinations in the reverse hybrid group with all revisions as the endpoint at 3 and 5 years. No statistically significant differences were found. No statistically significant difference regarding deep infection between cemented and reverse hybrid THR was found. Ninty-seven % of the cementless stems had HA.

Paper 2

Mean wear including bedding-in for the total material was 0.33 mm (95% CI: 0.28-0.37) in the vertical direction and 0.39 mm (95% CI: 0.34-0.44) in total 3D, at 2 years follow-up.
Mean cup rotation around the x-axis was 0.13° for the cemented group, and -0.24° for the RH group (p=0.03). Cup migration in the other axes, stem migration and wear were similar between study groups.
Bone remodeling around the cup was also similar between the groups, while bone loss in Gruen zone 1 was 18% for the cementless stems compared to an increase of 1.4% for the cemented ones (p<0.001). Bone loss was similar in the other Gruen zones.

Paper 3

Mean proximal wear was 0.34 mm (95% CI: 0.29–0.38) when we used the polyethylene as the reference segment, and 0.52 mm (95% CI: 0.38–0.65) using the periacetabular bone as the reference segment. Therefore, mean proximal wear was overestimated by 53 % when using the periacetabular bone as the reference segment. Mean cup migration in the y-axis was 0.14

mm (95% CI: 0.02–0.26). Mean total 3D migration of the cup was 0.36 mm (95% CI: 0.23–0.50). Subtracting the individual vertical migration of the cup in each case, we estimated the wear to be 0.38 mm (95% CI: 0.31–0.44 and p = 0.021 compared to wear with markers in the polyethylene). Therefore, correcting for the vertical movement of the cup, wear was still overestimated, but only by 0.04 mm. Cup migration seemed to influence the wear calculations leading to an overestimation of wear when markers in the periacetabular bone were used as a reference segment.

Paper 4

Wear (95% CI) for the total material, including bedding-in, in the proximal and total 3D direction was 0.041 mm (0.015-0.066) and 0.177 mm (0.155-0.200), respectively. The mean annual wear rate in the vertical and total 3D direction from 1 to 2 years was 0.030 mm (0.002-0.058) and 0.015 mm (-0.018-0.047). We found no statistically significant difference in wear from 3 months to 2 years in vertical and in total 3D direction regarding the total material. In the vertical direction, we found no statistically significant difference in wear comparing 32 and 36 mm heads. A small, yet statistically significant difference with less wear for 36 mm heads (mean difference (95% CI) of 0.037 mm (-0.008-0.082) p = 0.045), was found in the total 3D direction. The bedding-in period (plastic deformation, seating of the liner, interposition of blood or tissue) was assumed from our data to take place during the first 3 months postoperatively. In this period the bedding-in seemed reduced for 36 mm heads (Figure 14). No clinically adverse effects of the polyethylene were found.

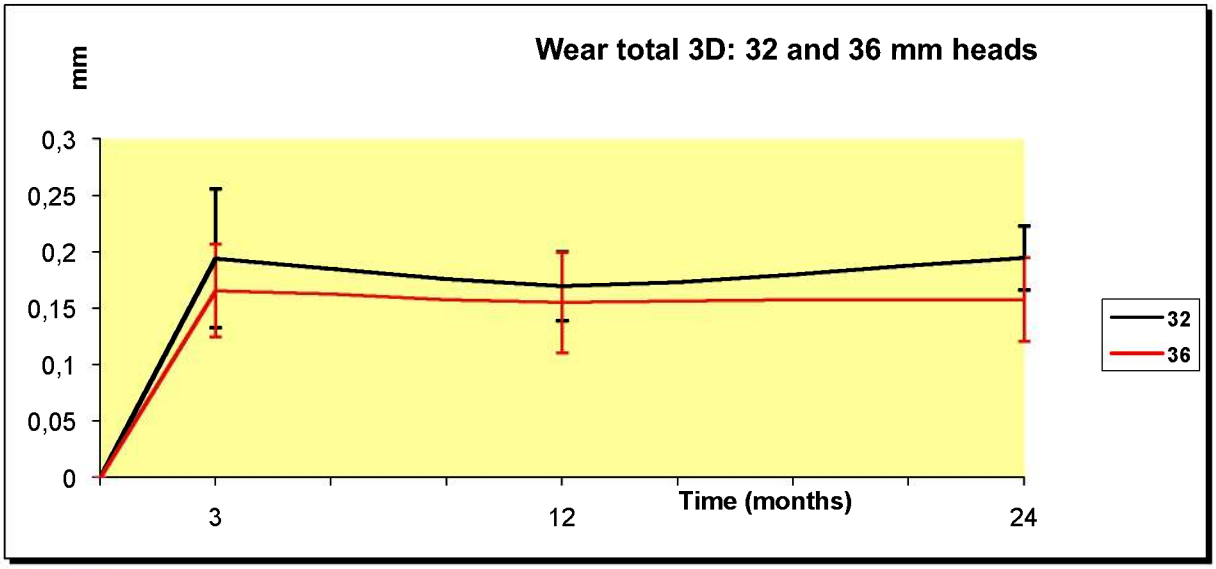

Figure 14

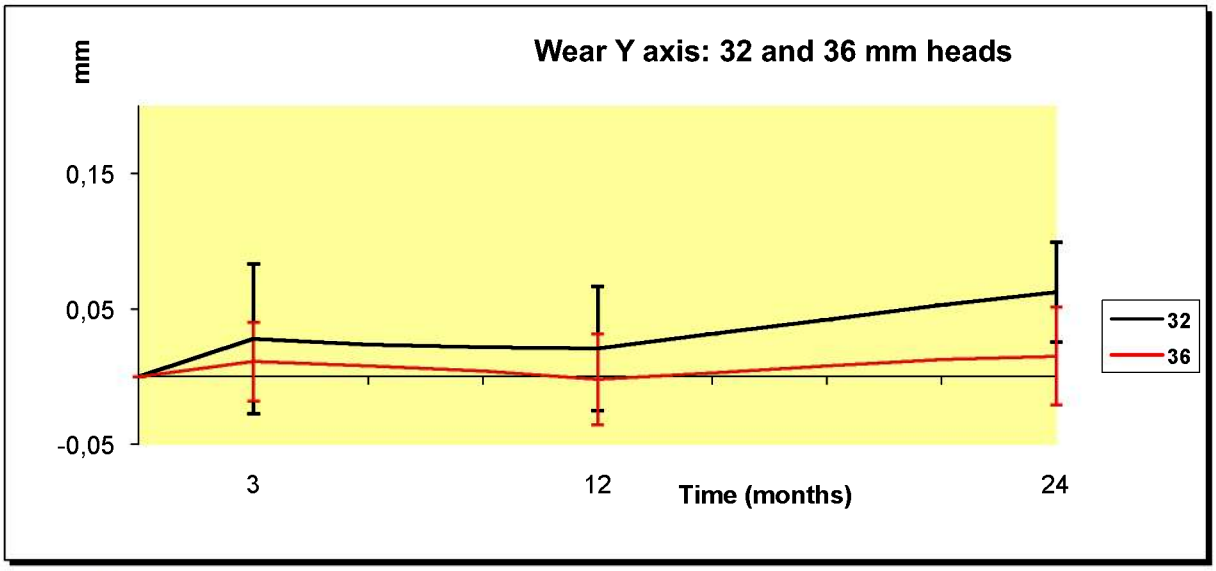

Figure 15

Figure 14 and 15: Graphic presentation of wear for the 32 and 36 mm heads in the vertical (y-axis) and the total 3D direction (Mean (95% CI)). n=24/24 at 3 months, n=25/22 at 12 and 24 months.

Discussion

General discussion

Given the main aim to investigate the reverse hybrid method, the randomized controlled trial and the register study complement each other. A register study on a specific method of THR will often reflect the performance of different surgeons with different skills. Different prosthesis combinations are used, and in paper 1 we noticed that prosthesis components from different companies were also mixed. Register studies have larger numbers of cases compared to clinical trials. A randomized trial will often compare two or more methods (treatment options) and often with a selected group of surgeons. With just one or two surgeons in a trial, these surgeons are often very skilled and well trained. With an improper selection of surgeons and a small sample size, a poor surgeon may skew the results if this surgeon operates more patients in one of the study groups. In contrast, a register study usually reflects the performance of many surgeons and it has been proposed that register studies often reflect the average surgeon [35]. With rare and highly specialized procedures the lack of surgical skill may alter the results and not necessarily reflect the performance of the implants themselves. A RCT can present results of radiographic findings (e.g. wear, osteolysis, implant micro movement and patient clinical score), while register studies often cannot present such data. A potential failure in a clinical trial could be discovered with an x-ray. But it might not be revised because the patient might have other medical risk factors making surgery inadvisable. Such a failure in a clinical trial should be identified, while in a register study this situation might be classified as a success. Some of these differences between clinical trials and register studies have been discussed by Garellick et al. [28]. This is why we think that a randomized trial and a register study are good complements when performing THR research.

When using data from the NAR it is always uncertain how well and accurate primary and revision surgeries are reported. However there have been several studies proving a high degree of completeness in the NAR [15, 137, 138].

In 3 of 4 papers we have used two highly accurate and precise methods, namely RSA and DXA. The RSA method measures implant movement and wear very precisely, and a strength of our laboratory is that this method has been validated in a cadaver model measuring sacroiliac movement [141]. A weakness is that we should have also done this in a phantom

model of a THR. In study 4 we used the markerless RSA method with a different shell than Børlin et al. used [134]. It would have been interesting, and also strengthend our study, if this method was validated in our laboratory with the same type of shell we used in the clinical trial.

A weakness regarding RSA in paper 2 was that all patients were mobilized before the x-rays were taken. This might influence the early migration, especially of the cementless stem, measured with RSA. One can imagine that the stem could subside when the patient was mobilized, weight bearing as tolerated. The pattern of micro migration is described, but a possible confounding factor is that early migration might have been somewhat higher. In a study by Thien et al.[155] they found no adverse effects of immediate full weight bearing, compared to partial weight bearing, using a cementless stem. The study was performed using RSA. In our study, postoperative RSA scans were taken at a mean of 7 days (range 4-31). Therefore some patients had their initial scans taken beyond one week. In paper 4 the standardization of follow-up was better. RSA was performed after a mean of 4 days (range 1-7) postoperatively. In paper 4 we had established RSA in our department and it was therefore easier to obtain the scans at desired times. In paper 2 patients had to be transported to Ullevål University Hospital to perform the RSA scans, and prior appointments had to be made.

Since we did not have a true lateral radiographic view it was difficult to estimate the anteversion of the cup. Lucency on this projection was therefore not obtained in paper 2 and 4.

Paper 1

The pros and cons of register studies have been discussed. In this particular study the results are confined to the specific prosthesis combinations and the time of follow-up. The finding of fewer periprosthetic femoral fractures for the cemented group is in accordance with findings from the Swedish Hip Registry [32]. We found no difference in survival with deep infection as endpoint, and a register study has confirmed lower rates of infection using cements with antibiotics, compared to cements without antibiotics [156]. It is not clear if antibiotic loaded cemented cups can protect against infection, but it is a factor to consider. Dale et al. found increased risk of revision of cementless THR compared to cemented THR due to infection.

However the cause was unclear, but a hypothesis is that antibiotics in the cement may protect against deep infection [157].

Concern about HA on cementless stems has been raised [47, 158]. With 97 % of the stems having HA, but with different thicknesses, we found no difference in survival between study groups. We could not measure polyethylene wear in this register study. Therefore we could not conclude if HA causes more wear. Wear related complications might appear with longer follow-up.

We performed survival analysis and, as discussed in the paper we are aware that the Kaplan Meier method may overestimate the risk of revision. Marianne Gillam et al. [159] have proved that the Kaplan-Meier method may overestimate the risk of revision compared to the cumulative incidence function method, as both death and emigration are competing risks to revision. The cumulative incidence function uses competing risk methods in the analysis [159]. In the register study we concluded that the Kaplan Meier method was appropriate due to the relatively short follow-up and low incidence of death.

The proportion of males was higher and the mean age was lower in the reverse hybrid group than in the cemented group regarding all ages. In this register study there was no scoring for activity. Due to this skewness in the demographic data, there could be a bias in comparing young men to a group with elderly women. In both groups the median follow-up for total material, and for cases below 60 years, differed significantly. These could also be biases as they could mask differences between the 2 groups, with such differences in follow-up.

Paper 2

This RCT and its results are limited to the prosthesis used and by the follow-up period. We know that the quality of the HA may influence its properties. A thicker HA coating may probably have a greater risk of de-bonding [47]. Both stems subsided and rotated slightly into retroversion, and thereafter stabilized. This migration pattern has been shown earlier and confirms early stabilization of the stems, as expected [40, 57, 160]. It has been questioned if the Spectron EF femoral stem, with a proximal grit blasted area, is inferior to other cemented prostheses. Hypotheses about this stem and its performance have been discussed in earlier studies and also discussed in this thesis. Short time follow-up in other studies with RSA have shown acceptable results [161, 162]. To follow this cohort in the long-term it will be of interest to

see if migration of the stem increases. Kärrholm et al. [160] studied the cemented Lubinus femoral stem with RSA and found that continuous migration during the first two years was associated with increased probability of revision [160]. With respect to the Lubinus stem, cut off values for the probability of revision regarding 2 year RSA data were presented. Kärrholm et al. found a revision probability greater than 50 % if the stem had subsided more than 1.2 mm at 2 years. The Exeter, another well-documented femoral stem with a different design, behaves differently as this stem is found to have a continuous migration during the first decade after implantation [163]. In the same study this stem also subsides and migrates into retroversion more than the Lubinus stem during the first two years. The Spectron EF femoral stem has also been documented with RSA with two years follow-up and is found to subside and migrate into retroversion, within the limits proposed by Kärrholm regarding the Lubinus stem. In a randomized study, the Spectron stem at 2 years follow-up had less retroversion than the Charnley stem [161]. Therefore RSA documentation indicates that early migration of cemented femoral stems may be design dependent. However, RSA is proposed to be an early indicator regarding late revision [164]. As we did not have tantalum markers in the cement, migration of the stem in relation to the cement could not be measured. Three different RSA studies with 3 different cemented stems have shown that migration mainly occurs relative to the stem-cement interface [144, 165, 166].

Kadar et al. have discussed if destabilization of the Spectron EF stem from the cement may have been a contributing factor leading to stem failure, but they point out that the high wear rate of the Reflection all poly cup may also have influenced the NAR results [161]. Debonding of this stem from the cement mantle has been discussed by Digas et al.[167] also. Confirmation of the high wear rate of the Reflection all poly cup was found in our study. RSA has also been used to examine late failures of cemented acetabular cups. In a RSA study of revised cemented cups early migration was a good predictor of later aseptic loosening [168]. A recently published meta-analysis review has found an association between early migration of acetabular cups and late revision due to loosening [169]. A proximal migration up to 0.2 mm was found to be acceptable during a 2-year period. The authors suggested that certain thresholds regarding migration of acetabular cups could be used in the early phase of new cup introduction. Even if the 2-year migration of the cups in our study could be classified as acceptable [169], the high wear rate may be responsible regarding the decreased survival in the earlier register study [24]. Therefore even if primary fixation is classified as acceptable, other properties regarding the implant may influence long-term survival. Monitoring wear for new

implants may be an important factor in this respect. Perhaps early RSA is not a good tool to predict late loosening of the Spectron EF stem, and other considerations may affect long-term durability. In register studies a large number of cases are followed. Therefore we do not know if some of these cases initially had increased migration exceeding the limits proposed by Kärrholm regarding the Lubinus stem, and thereby were at risk [160].

The lack of data for some patients, especially RSA, and the reduced sample size due to early termination including the patients and exclusion of some patients, may have reduced the power of the study. Given the reduced sample size we did prove, using the effect size, that the upper limit of the CI of the mean difference during a 2 year follow-up did not exceed the proposed annual wear rate of 0.1 mm/y. Therefore we did not prove any clinically important differences in wear between the cementless HA coated stem and the cemented stem at 2 years follow-up. Our findings regarding wear of the polyethylene have been confirmed in earlier studies [62, 88, 89]. This finding must be taken in consideration when comparing results for reverse hybrid THR in the future. High wear rates may lead to increased revision rates. A method like reverse hybrid may not perform well if a polyethylene with poor wear-properties is used.

When using DXA to compare BMD around a cemented and a cementless implant, the cement may bias the results. Including the cement may improve precision regarding DXA measurements [144, 147]. However including the cement may lead to a high bone mineral density on the initial scan [144] . A loss of BMD might be underestimated because of the constant cement with a false high BMD value masking the real BMD in the defined ROI.

With an increase in BMD the same methodological error may persist. In an analysis showing an increase in BMD, the true increase would probably have been greater if the cement was not included.

We noted a positive change in Gruen zone I for the cemented stem, and a negative change for the cementless stem. We think that there is a real difference in bone remodeling in this zone. Digas et al. [144] also found an increase in bone remodeling in Gruen zone 1 with the same

prosthesis, and in the other Gruen zones they also found a decrease compared to the postoperative scan. This is in accordance with our findings [144].

A weakness of this study regarding the DXA measurements may be that we have not corrected for medications taken by the patient. Ideally we should have corrected for these possible confounding factors, or had stricter inclusion criteria. All patients were tested using the same DXA machine and the 2 groups were compared to each other. The accuracy of a DXA machine was calculated as below 1 % in another study [170].

A weakness of this study is the lack of activity measure for the two groups. Activity has been found to be a major factor regarding wear in THR[151]. If this cohort of patients is followed up further with RSA it is important to include an activity score for both groups.

Only one observer, without a calculation of intra observer reliability, performed the radiographic evaluations. Ideally this should have been done, but the radiographic measurements were not the main goal, and were performed to see if there were discrepancies between groups. We know that poor intra observer reliability could be a bias.

Paper 3

This study relied on RSA results and radiographic measurements from paper 2. We found a statistically significant difference with an overestimation of wear when using markers in the periacetabular bone, compared to markers in the polyethylene. The cemented all poly cup migrated in both the total 3D and the y-axis. This migration pattern could at least partly explain differences between the two methods. Proximal migration of cemented cups during the first 1–2 years have been previously reported [61, 171]. In the published paper we have discussed the possibility to use wear measurements using periacetabular bone markers when comparing 2 groups with the same e.g. cup material. The results may though be weakend by the assumption of stable cups or the same migration pattern of the cups in the study groups.

In this study we used a paired sample to estimate wear using 2 different methods. Each patient was therefore measured according to both methods using the same RSA scans taken at the same time. Using this paired sample we also used the non-parametric Wilcoxon signed rank test to look for differences between study groups. Strength of this study is the paired sample

with the use of two different methods on the same patient, at the same time and using the same RSA scans.

Paper 4

In this paper we performed a sample size calculation and allowed for possible dropouts. We based our sample size calculation on the precision of a markerless RSA study [134] . Since we did not know the actual wear threshold regarding highly cross-linked polyethylene, we assumed a clinically important wear difference of 0.1 mm based on studies on UHMWPE [154]. The precision of 0.17 mm measured in the y-axis may have reduced the power of our study. Röhrl et al. had a precision of 0.15 mm using tantalum markers in the liner [62], while Börlin et al. had a precision of 0.1 mm using the markerless method [134]. Precision of 0.09 mm has been achieved in a study by Röhrl et al. [92]. In that study they used tantalum markers in the polyethylene. We performed a block randomization of 10 cases into the 2 different study groups. We randomized after reaming the acetabulum. If a 36 mm head was used a shell size of 54 mm or more had to be implanted. 32 mm heads could be used with both 50 and 52 mm shells. Therefore we had to exclude 3 patients who were randomized to a head size of 36 mm in conjunction with a shell size of 50 or 52. In retrospect, we are aware the possible bias in that the two smallest shell sizes could only accommodate 32 mm heads. The reason for choosing this randomization was that we wanted to use the cementless shells in different sizes, and the surgeon should not remove more bone than necessary to prepare for the study prosthesis. Using the markerless method we did not have any exclusions due to poor marker placement, but we experienced one missed RSA analysis due to a poor post-operative RSA scan. Using the markerless method, that has been previously validated [128, 134], we performed wear measurements. A weakness is that the markerless method was documented with another cup [134]. In our study we used a hemispherical cup and this cup had a rim flare and pegs to secure the rotation of the liner. These pegs and the rim flare were prominent on the RSA scan. The rim flare and the pegs made it somewhat difficult to mark up the back of the shell together with the cup opening. We think this could explain the poorer precision compared to Børlin et al. [134]. In retrospect it would have been interesting if we had tantalum markers in the polyethylene liner. Then we could have compared the markerless method with the standard RSA method with this type of shell, although placing markers in the liner would have been more demanding. Then placement of the markers and analyses would have demanded more resources. Bragdon et al. have validated the markerless method using both 28 and 36 mm

heads, and they found comparable results using the standard RSA and the markerless method [128]. We should remember the ethical considerations in using tantalum markers in the components. If wear measurements can be taken without markers, I think this is preferable for our patients.

The outline of a ceramic head of Biolox delta was easy to locate on the scans, but we do not know if a 32 mm head is more difficult to mark with RSA than a 36 mm head. All these factors could influence precision. The small, yet statistically significant difference in wear at 2 years in the total 3D direction between study groups is difficult to explain, but could be influenced by the factors aforementioned. In addition we found no statistical difference in wear estimates for the total material from 3 months to 2 years. We assume that the bedding-in period (plastic deformation, seating of the liner, interposition of blood or tissue) takes place during the first 3 months postoperatively. In this period the bedding-in seemed to be less for 36 mm heads (Figure 14 and 15). This may be an explanation for why there is a small difference between 32 and 36 mm heads at 2 years follow-up. The mean difference was also below the level of accuracy for markerless RSA [134], and included also zero within the 95% CI. The finding with less wear for 36 mm heads is also contradictory to an in vitro study [77]. Bragdon et al. [128] found no difference in wear comparing 28 mm with 36 mm heads using highly cross-linked polyethylene. In that paper, no information on sample size calculation prior to the study start was given, and the sample used may have been too small. This could have led to difficulties in revealing differences between study groups, with the possibility of type 2 errors.

In this study we used the UCLA activity score. It is important to measure activity because it affects wear [151]. A limitation to activity measurement is that we used the English version on a Norwegian cohort of patients. Ideally we should have translated and validated this version prior to the activity measurements. In addition the UCLA score was used at 2 years follow-up. We could also have used this activity score preoperatively, but the activity then could have been biased by the painful hip, and not necessarily reflect the activity of the patients after THR.

We also used radiographic measurements according to study 2, with the limitations described above of not having a true lateral view.

We have presented 2-year follow-up data in the present study. This time period is perhaps short comparing wear using 2 different heads in conjunction with highly cross-linked polyethylene. Is it likely there will be a difference between these head sizes at this time of follow-up? We have not seen any studies with 2 years follow-up for this polyethylene and we found it necessary to present data on the total material, and for the different head sizes used at this time. Later follow-up will be presented, and of course long-term data is most interesting. Analysis of the total material (47 hips), with a low wear rate after the period of bedding-in has been proved with this 2-year follow-up. Bragdon presented preliminary data using RSA with the E-Poly [172]. 19 patients were available in one year for RSA, and proximal median penetration was estimated to be 0.03 mm. Bragdon et al. also investigated 28 mm and 36 mm heads with RSA using Longevity liners. They found no difference between 28 mm and 36 mm heads, and the median proximal penetration at 3 years was 0.062 mm for 28 mm heads [128]. In a prospective series at 2 years, Campell et al. measured the proximal penetration at 0.024 mm using X3 liners with 32 mm heads [173]. Kadar et al. investigated the XLPE at 2 years follow-up. They used 28 mm heads with either oxinium or cobalt chrome. No difference was found regarding head material, and the wear in proximal direction was 0.08 and 0.09 mm respectively [89]. Digas et al. found that wear of Longevity liners was 0.08 mm in proximal direction at 2-year follow-up using RSA [174]. Röhrl et al. found a proximal penetration of 0.08 mm at 6 years follow-up using 28 mm heads and Crossfire liners [175]. The proximal mean wear at 2 years follow-up in our study, including bedding-in, for the total material (both 32 and 36 mm heads) was 0.04 mm. Comparing to other studies this is a very low wear. As the wear of both 32 mm and 36 mm heads are very low it may be difficult to reveal differences between these 2 head sizes. Without knowing the wear threshold regarding highly cross-linked polyethylene, it is difficult to conclude if small differences may be of clinical importance. Long-term follow-up is needed to study if there will be a difference in wear between these 2 head sizes and if this difference will be of clinical importance.

2 long-term RSA studies have been presented. Röhrl et al. have 8 cases with 10 years follow-up. No adverse effects for this cemented highly cross-linked polyethylene were found, and at 10 year follow-up the wear was estimated to be 0.07 mm and 0.2 mm in proximal and 3D direction respectively [92]. Johanson et al. have recently published 10 years results for a Durasul highly cross-linked polyethylene. The proximal penetration rate from 2 to 10 years was estimated to be 0.005 mm/y compared to 0.055 mm/y for conventional polyethylene [91]. Our data confirms low wear for this E-vitamin infused highly cross-linked polyethylene, and good

wear data has been found comparing with other RSA studies using highly cross-linked polyethylene. Long-term follow-up of this E-vitamin infused highly cross-linked polyethylene is needed to document wear properties and investigate if the anti-oxidative effects of vitamin E will be beneficial.

Conclusion

Paper 1

The reverse hybrid group and the cemented group performed satisfactory and similarily in a national observational registry study with up to 10 years of follow-up.

We found a higher risk ratio concerning periprosthetic fractures for the RH group, but no difference regarding deep infection.

Therefore the reverse hybrid method using UHMWPE with a short to medium term follow-up seems to be an alternative to all-cemented THR, but long-term follow-up will be required to finally evaluate whether the concept has any advantage over all-cemented THR.

Paper 2

The cementless femoral stem had more bone loss in Gruen zone 1 compared to the cemented stem. No difference in bone remodeling around the cup during the study period between the reverse hybrid THR and the cemented THR was found. Wear of the cemented all polyethylene Reflection cup was high and comparable with other studies, but the partially HA coated stem did not cause more wear than the cemented stem with up to 2 years follow-up. A minor difference regarding cup migration around the x-axis was found, but no difference regarding stem migration was detected between study groups.

Paper 3

We found that using tantalum markers in the periacetabular bone as a reference segment will overestimate wear compared to tantalum markers in the polyethylene. Migration of the cup may partly be responsible for this difference.
Therefore our conclusion is to use the traditional RSA method with markers in the polyethylene to measure wear.

Paper 4

Low wear of an E-vitamin infused highly cross-linked polyethylene, with up to two years of follow-up, was found. We could not detect differences in wear comparing 32 with 36 mm ceramic heads in the vertical direction. In the total 3D direction we found a statistically significant difference with less wear for the 36 mm group ($p=0.045$). The mean difference was very small (0.037 mm) and difficult to explain, and included zero within the 95% CI leading to uncertainty when interpreting the statistical difference using the non-parametric Mann-Whitney U test. We found no statistically significant difference in wear for total material from 3 months to 2 years. This may indicate that most of the wear measured is the effect of bedding-in. The bedding-in appeared to be less for 36 mm heads, and this may be another explanation why there is a small difference between 32 and 36 mm heads in that direction at 2 years follow-up.

Summary

The main aim of this thesis was to evaluate the reverse hybrid THR.

Overall, we found good results for certain reverse hybrid THRs in the Norwegian Arthroplasty Register compared to cemented THR with up to 10 years of follow-up. For these combinations using conventional UHMWPE, the results were generally satisfactory. It is not possible to extrapolate these findings to other combinations of THR, or using other polyethylenes. A higher RR because of periprosthetic femoral fractures, with cementless stems in the RH group compared to the cemented group, has been documented also in other studies. This complication is of some concern, but generally this complication is not a frequent cause of revision looking at the survival at 5 years follow-up. The not statistically significant difference in deep infection between study groups was interesting and could be attributed to antibiotics used in the cement of the acetabular component. In the randomized study comparing a reverse hybrid and a cemented THR, we found minor differences between the two groups. Total material wear was high for the non cross-linked cemented Reflection all poly cup, but there were no differences between study groups. We found increased bone loss for the cementless stem in Gruen zone 1. Given the good long-term survival of the Taperloc stem this finding might not be a limiting factor regarding survival of the implant, but might reflect differences in stress shielding between the cementless and the cemented stem. Both stems subsided and rotated slightly into retroversion before stabilizing. Given the acceptable migration pattern with the Spectron EF stem, it might be interesting to follow this cohort in the future. An earlier register study found inferior results for this stem compared to some other cemented stems in the long-term. Therefore, it would be interesting to see if our cohort will show a significant increase in migration over time. Using the same cup in both groups did not influence stem migration. Using two different stems also did not influence bone remodeling around the cemented all polyethylene cup, and only a minor difference in cup migration was found. We speculated that the initial position of the cup or stem could contribute to this small difference. In paper 3 we recommended markers in the polyethylene to estimate head penetration into the polyethylene when measuring wear with RSA. With respect to the point motion of the head, if markers in the periacetabular bone are used, wear in the vertical and total 3D directions will be overestimated if the cup migrates.

In paper 4 we found that an E-vitamin infused highly cross-linked polyethylene exhibits low wear rates with up to two years follow-up, and most of the wear measured may be the effect of bedding-in. During the study period we found no adverse reaction to this polyethylene. We found no difference between 32 and 36 mm heads regarding wear in the vertical direction, but in the total 3D direction we found reduced wear for 36 mm heads. The mean difference is below the level of the accuracy of markerless RSA, and the mean difference also included zero within the 95% CI. Therefore this finding is uncertain, and with respect to the clinical importance, we do not know the wear threshold regarding this polyethylene. Finally, we recommended long-term follow-up of this polyethylene to substantiate the promising early results.

The future

For further research, I suggest a register study from the NARA (Nordic Arthroplasty Register Association) on the reverse hybrid THR. With increasing numbers of prostheses it might be possible to perform subgroup analyses on different reasons for revisions, for different prosthesis combinations as discussed in paper 1.

Digas et al. [174] published results from two randomized studies with the use of conventional and highly cross-linked polyethylene. They used both cemented and cementless sockets in combination with cemented stems. I think it would have been interesting to perform a randomized study on the reverse hybrid method and to compare this method against a cementless THR using the same highly cross-linked polyethylene. As the trend turns towards cementless THR it would be of interest to compare these methods. Hopefully, one would be able to conclude if cemented or cementless fixation of the acetabulum is preferable regarding micro motion, wear and bone remodeling in the long-term using highly cross-linked polyethylene.

Good results for THR have been documented. How many resources should be used to improve this already successful procedure? In 2010 there were 7230 primary THRs implanted, and 1250 (14,7 %) revisions were performed in Norway, with the percentage of revisions being approximately the same since 1999 [176]. An increasing number of primary THRs will therefore lead to an increasing number of revisions if the percentage stays at the same level. In Australia 25100 THR have been implanted in 2010 [20]. Revision surgery ratio is

around 11 % in this register. Kurtz et al. have estimated that there will be an increase in primary THRs from 2005-2030 by 174% to 572 000 procedures annually, and they also estimate that the demand for hip revisions may double by 2026 in the USA [177].

The development of different types of THR, and the use of materials with different tribological properties is continuing. New prostheses are released on the market and often heavily advertised by the manufacturer. In research we have a responsibility to compare new types with established ones to see if they perform better, equally or worse. Even if short-term follow-up shows good results we know that long-term follow-up is necessary to compare different types of THR. Therefore it is important to perform clinical studies with new implants and to present early results to see if the expected results measure up to well documented implants. Small differences in survival may have a great impact on the number of revision surgeries as the number of primary surgeries is increasing.
Improving long-term durability is extremely important, especially for young patients undergoing THR, and research is needed to achieve this. Research regarding the fixation of components and how to avoid loosening, in conjunction with the development of good bearings will be necessary to improve the long-term durability for this patient group.

Also for the elderly it is important to perform research to prevent complications and especially early complications. A reduction in the dislocation rate, periprosthetic fractures and infection could reduce the number of revision surgeries globally in a group of patients that is especially vulnerable to these complications and the subsequent revisions. In the future it is important to clarify which fixation is preferred, and perhaps to differentiate fixations between age groups. The BMD and the configuration of the bony anatomy may be important factors when considering different implant fixation. How large heads should be used to avoid problems with the trunion and also to preserve low wear rates should also be studied. To predict the future is difficult, but inevitably research on THR must focus on avoiding unnecessary complications with the release of new products, restoring maximal function, increasing long-term durability and reducing early complications related to this procedure.

Summary in Norwegian

Hovedmålet med dette doktorgradsarbeidet var å evaluere omvendt hybrid totalprotese i hofteledd. Omvendt hybrid totalprotese består av en usementert lårben stamme i kombinasjon med en sementert plastkopp. I Norge har det vært en økning i bruk av denne metoden i de siste 10-12 årene og klinisk dokumentasjon av denne metoden har vært sparsom.

I det norske leddregisteret fant vi gjennomgående gode resultater for ulike kombinasjoner av omvendt hybride totalproteser. Overlevelse av disse implantatene var sammenlignbare med de 10 vanligste sementerte totalproteser fra det samme registeret med en oppfølgingstid på 10 år. For disse kombinasjonene ved bruk av konvensjonell plast var resultatene samlet tilfredsstillende. Vi kan ikke overføre disse resultatene til andre kombinasjoner av omvendt hybride totalproteser eller til bruk av andre plasttyper. Relativ risiko for brudd rundt den usementerte lårbensstammen var høyere enn for den sementerte og dette har også blitt funnet for usementerte stammer i en studie fra Sverige. Denne tidlige komplikasjonen er av en viss bekymring, men når vi ser på overlevelse etter 5 år synes denne komplikasjonen totalt sett til å være en sjelden årsak til reoperasjon. Det var ikke økt risiko for dyp infeksjon hos den omvendt hybride gruppen. Dette funnet er interessant og kan være et resultat av antibiotika i sementen rundt den sementerte plastkoppen. I en annen studie er det funnet økt risiko for dyp infeksjon hos usementerte proteser sammenlignet med sementerte proteser.

I artikkel 2, som var en randomisert studie, har vi sammenlignet omvendt hybrid totalprotese med sementert totalprotese og vi fant kun minimale forskjeller. Den samme sementerte plastkoppen ble brukt i begge grupper. I gruppen omvendt hybrid brukte vi en Taperloc usementert og delvis hydroxyapatitt bekledd stamme. I den sementerte gruppen ble en Spectron EF stamme brukt. Vi målte slitasje av plasten og mikrobevegelse av protesekomponentene med Radiostereometrisk analyse (RSA). Benremodellering rundt protesekomponentene ble målt med Dual Energy X-ray Absorptiometry (DXA). Slitasje av den sementerte Reflection plast koppen var høy for totalmaterialet, og i tidligere RSA studier har man også funnet høy slitasje for denne plast koppen. Vi fant imidlertid ingen forskjell i plastslitasje mellom de to studiegruppene Vi fant at den usementerte stammen hadde et beintap i Gruen sone 1 som var signifikant øket i forhold til den sementerte stammen. Den sementerte stammen hadde en økning i bentetthet i samme sone, mens det i de andre sonene ikke var forskjell i bentap mellom de to stammene. Den usementerte Taperloc stammen er godt dokumentert med god langtids overlevelse. Beintap i Gruen sone 1 for denne stammen er derfor ikke nødvendigvis en begrensende faktor for langtidsoverlevelse, men kan være uttrykk for ulik benremodellering rundt den usementerte og sementerte stammen. Begge stammene sank noe og roterte i retroversjon for deretter å stabilisere seg. Dette mønsteret av mikrobevegelse er påvist i tidligere studier, og

bevegelsene var innenfor det som er akseptert. Den sementerte Spectron EF stammen har vist noe dårligere resultater i en studie fra det norske leddregisteret sammenlignet med andre sementerte stammer. Det vil derfor være interessant å se om våre RSA data vil vise endring etter lengre oppfølgingstid. Ved bruk av den samme sementerte plastkoppen kunne vi ikke påvise forskjeller i mikromigrasjon av de to stammene. De to stammene påvirket heller ikke benremodelleringen rundt koppen. En svært liten forskjell i mikromigrasjon av koppen rundt x–aksen mellom studiegruppene ble påvist. Vi har spekulert på om stammenes utgangsposisjon kan ha bidratt til denne forskjellen. Samlet sett har derfor omvendt hybrid totalprotese vist gode resultater i både en registerstudie og i en klinisk randomisert studie.

I tilegg til å evaluere den omvendt hybride metoden gjennomførte vi en studie der vi sammenlignet to metoder for å måle slitasje av plasten i en sementert kopp. I artikkel 3 fant vi at slitasjemålinger med RSA hvor markører i plasten ble brukt er å anbefale. Denne metoden er tidligere godt dokumentert. Tantalum markører i beinet rundt acetabulum medførte en overestimering av slitasjen grunnet migrasjon av koppen, i både vertikal og i 3 dimensjonal retning.

Studie 4 var en klinisk prospektiv randomisert studie der vi målte slitasje av en ny plast som var kryssbundet og tilsatt vitamin E. Pasientene ble randomisert og fikk operert inn 32 eller 36 mm hode av keramikk og en identisk usementert totalprotese. Plasten syntes å være godt tolerert av pasientene i studieperioden og vi kunne ikke påvise noen bivirkninger. Vi fant ingen forskjell i slitasje mellom 32 og 36 mm hoder av keramikk i vertikal retning, men i total 3D fant vi en uventet statistisk mindre slitasje for 36 mm hoder. Plasten som var tilsatt vitamin E har lav slitasje etter 2 år og det meste av slitasjen skyldes deformasjon (”bedding in” eller ”creep”). Gjennomsnittlig forskjell mellom de to hodestørrelsene var under nivået til RSA-metodens nøyaktighet. Klinisk viktig terskel for slitasje av kryssbundet plast er heller ikke kjent grunnet begrenset langtidsoppfølging av denne plasttypen. Forskjellen statistisk sett mellom 32 og 36 mm hode i denne retningen er derfor usikker i relasjon til klinisk viktig slitasje. Vi anbefaler derfor lang tids oppfølging av denne plasten for å evaluere slitasjen og for å se om det er forskjell mellom hodestørrelsene på lang sikt.

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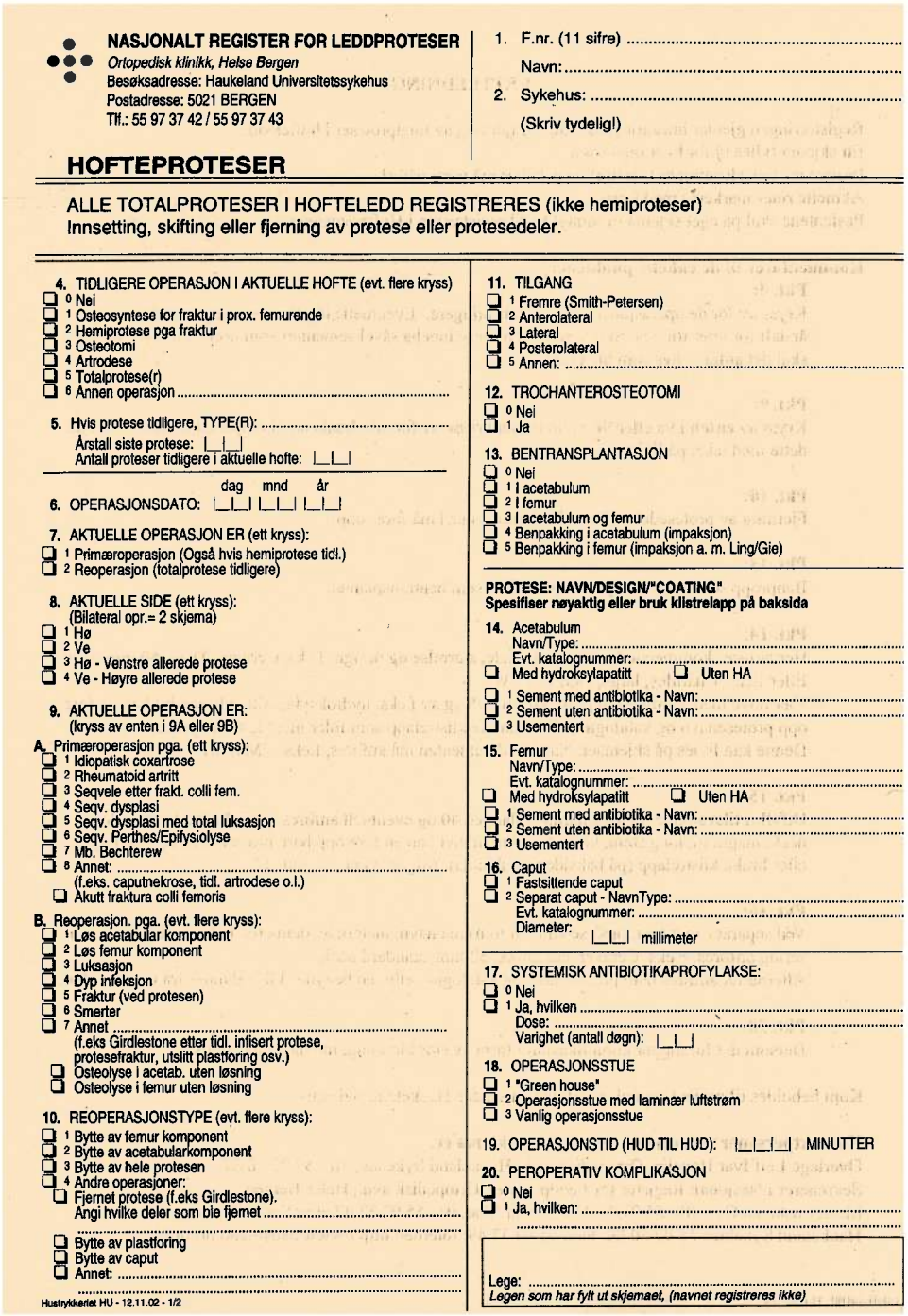
Appendix

Forms from the Norwegian Arthroplasty Register



NASJONALT REGISTER FOR LEDDPROTESER
Ortopedisk klinikk, Helse Bergen
Besøksadresse: Haukeland Universitetssykehus
Postadresse: 5021 BERGEN
Tlf.: 55 97 37 42 / 55 97 37 43

1. F.nr. (11 sifre) .....
Navn: .....
2. Sykehus: .....
(Skriv tydelig!)

HOFTEPROTESER

ALLE TOTALPROTESER I HOFTELEDD REGISTRERES (ikke hemiproteser)
Innsetting, skifting eller fjerning av protese eller protesedeler.

4. TIDLIGERE OPERASJON I AKTUELLE HOFTE (evt. flere kryss)
❑ 0 Nei
❑ 1 Osteosyntese for fraktur i prox. femurende
❑ 2 Hemiprotese pga fraktur
❑ 3 Osteotomi
❑ 4 Artrodese
❑ 5 Totalprotese(r)
❑ 6 Annen operasjon .....

5. Hvis protese tidligere, TYPE(R): .....
Årstall siste protese: |_|_|
Antall proteser tidligere i aktuelle hofte: |_|_|

dag mnd år
6. OPERASJONSDATO: |_|_| |_|_| |_|_|

7. AKTUELLE OPERASJON ER (ett kryss):
❑ 1 Primæroperasjon (Også hvis hemiprotese tidl.)
❑ 2 Reoperasjon (totalprotese tidligere)

8. AKTUELLE SIDE (ett kryss):
(Bilateral opr.= 2 skjema)
❑ 1 Hø
❑ 2 Ve
❑ 3 Hø - Venstre allerede protese
❑ 4 Ve - Høyre allerede protese

9. AKTUELLE OPERASJON ER:
(kryss av enten i 9A eller 9B)
A. Primæroperasjon pga. (ett kryss):
❑ 1 Idiopatisk coxartrose
❑ 2 Rheumatoid artritt
❑ 3 Seqvele etter frakt. colli fem.
❑ 4 Seqv. dysplasi
❑ 5 Seqv. dysplasi med total luksasjon
❑ 6 Seqv. Perthes/Epifysiolyse
❑ 7 Mb. Bechterew
❑ 8 Annet: .....
(f.eks. caputnekrose, tidl. artrodese o.l.)
❑ Akutt fraktura colli femoris

B. Reoperasjon. pga. (evt. flere kryss):
❑ 1 Løs acetabular komponent
❑ 2 Løs femur komponent
❑ 3 Luksasjon
❑ 4 Dyp infeksjon
❑ 5 Fraktur (ved protesen)
❑ 6 Smerter
❑ 7 Annet .....
(f.eks Girdlestone etter tidl. infisert protese, protesefraktur, utslitt plastforing osv.)
❑ Osteolyse i acetab. uten løsning
❑ Osteolyse i femur uten løsning

10. REOPERASJONSTYPE (evt. flere kryss):
❑ 1 Bytte av femur komponent
❑ 2 Bytte av acetabularkomponent
❑ 3 Bytte av hele protesen
❑ 4 Andre operasjoner:
❑ Fjernet protese (f.eks Girdlestone).
Angi hvilke deler som ble fjernet .....
.....
❑ Bytte av plastforing
❑ Bytte av caput
❑ Annet: .....
.....

Hustrykkeriet HU - 12.11.02 - 1/2

11. TILGANG
❑ 1 Fremre (Smith-Petersen)
❑ 2 Anterolateral
❑ 3 Lateral
❑ 4 Posterolateral
❑ 5 Annen: .....

12. TROCHANTEROSTEOTOMI
❑ 0 Nei
❑ 1 Ja

13. BENTRANSPLANTASJON
❑ 0 Nei
❑ 1 I acetabulum
❑ 2 I femur
❑ 3 I acetabulum og femur
❑ 4 Benpakking i acetabulum (impaksjon)
❑ 5 Benpakking i femur (impaksjon a. m. Ling/Gie)

PROTESE: NAVN/DESIGN/"COATING"
Spesifiser nøyaktig eller bruk klistrelapp på baksida

14. Acetabulum
Navn/Type: .....
Evt. katalognummer: .....
❑ Med hydroksylapatitt ❑ Uten HA
❑ 1 Sement med antibiotika - Navn: .....
❑ 2 Sement uten antibiotika - Navn: .....
❑ 3 Usementert

15. Femur
Navn/Type: .....
Evt. katalognummer: .....
❑ Med hydroksylapatitt ❑ Uten HA
❑ 1 Sement med antibiotika - Navn: .....
❑ 2 Sement uten antibiotika - Navn: .....
❑ 3 Usementert

16. Caput
❑ 1 Fastsittende caput
❑ 2 Separat caput - NavnType: .....
Evt. katalognummer: .....
Diameter: |_|_| millimeter

17. SYSTEMISK ANTIBIOTIKAPROFYLAKSE:
❑ 0 Nei
❑ 1 Ja, hvilken .....
Dose: .....
Varighet (antall døgn): |_|_|

18. OPERASJONSSTUE
❑ 1 "Green house"
❑ 2 Operasjonsstue med laminær luftstrøm
❑ 3 Vanlig operasjonsstue

19. OPERASJONSTID (HUD TIL HUD): |_|_|_| MINUTTER

20. PEROPERATIV KOMPLIKASJON
❑ 0 Nei
❑ 1 Ja, hvilken: .....
.....

Lege: .....
Legen som har fylt ut skjemaet, (navnet registreres ikke)

The Norwegian Arthroplasty Register 2000-2005

Nasjonalt Register for Leddproteser
Ortopedisk klinikk, Helse Bergen HF
Haukeland Universitetssykehus
Møllendalsbakken 11
5021 BERGEN
tlf 55973742/55973743

F.nr. (11 sifre).....

Navn:.....

(Skriv tydelig ev. pasient klistrelapp – **spesifiser sykehus**.)

Sykehus:.....

HOFTEPROTESER

ALLE TOTALPROTESER I HOFTELEDD REGISTRERES (ved hemiproteser etter hoftebrudd sendes skjema til hoftebruddregisteret). Innsetting, skifting eller fjerning av protese eller protesedeler.

TIDLIGERE OPERASJON I AKTUELLE HOFTE (ev. flere kryss)
☐0 Nei
☐1 Osteosyntese for fraktur i prox. femurende
☐2 Hemiprotese pga. fraktur
☐3 Osteotomi
☐4 Artrodese
☐5 Totalprotese(r)
☐6 Annen operasjon ……

OPERASJONSDATO (dd.mm.åå) |__|__| |__|__| |__|__|

AKTUELLE OPERASJON (ett kryss)
☐1 Primæroperasjon (også hvis hemiprotese tidligere)
☐ 2 Reoperasjon (totalprotese tidligere)

AKTUELLE SIDE (ett kryss) (Bilateral opr.= 2 skjema)
☐1 Høyre ☐2 Venstre

AKTUELLE OPERASJON (KRYSS AV ENTEN I A ELLER B)

A . Primæroperasjon pga. (ev. flere kryss)
☐1 Idiopatisk coxartrose
☐2 Rheumatoid artritt
☐3 Sekvele etter frakt. colli. fem.
☐4 Sekv. dysplasi
☐5 Sekv. dysplasi med total luksasjon
☐6 Sekv. Perthes/Epifysiolyse
☐7 Mb. Bechterew
☐8 Akutt fraktura colli femoris
☐ Annet ……
(f.eks caputnekrose, tidl. artrodese o.l)

B . Reoperasjon pga. (ev. flere kryss)
☐1 Løs acetabularkomponent
☐2 Løs femurkomponent
☐3 Luksasjon
☐4 Dyp infeksjon
☐5 Fraktur (ved protesen)
☐6 Smerter
☐7 Osteolyse i acetab. uten løsning
☐8 Osteolyse i femur uten løsning
☐ Annet ……..
(f.eks Girdlestone etter tidl. infisert protese)

REOPERASJONSTYPE (ev. flere kryss)
☐1 Bytte av femurkomponent
☐2 Bytte av acetabularkomponent
☐3 Bytte av hele protesen
☐4 Fjernet protese (f.eks Girdlestone)
Angi hvilke deler som ble fjernet ……
☐5 Bytte av plastforing
☐6 Bytte av caput
☐ Andre operasjoner ……

TILGANG (ett kryss)
☐1 Fremre (Smith-Petersen) ☐3 Lateral
☐2 Anterolateral ☐4 Posterolateral
☐5 Annen ……

LEIE ☐0 Sideleie ☐1 Rygg

TROCHANTEROSTEOTOMI ☐0 Nei ☐1 Ja

BENTRANSPLANTASJON (ev. flere kryss)
Femur ☐0 Nei ☐1 Ja ☐2 Benpakking a.m. Ling/Gie
Acetabulum ☐0 Nei ☐1 Ja ☐2 Benpakking

BENTAP VED REVISJON (Paprosky's klassifikasjon se baksiden)

Acetabulum		**Femur**	
☐1 Type I	☐4 Type II C	☐1 Type I	☐4 Type III B
☐2 Type II A	☐5 Type III A	☐2 Type II	☐5 Type IV
☐3 Type II B	☐6 Type III B	☐3 Type III A	

PROTESE NAVN / DESIGN / "COATING"
(spesifiser nøyaktig eller bruk klistrelapp på baksiden)

Acetabulum
Navn/Type ……
ev. katalognummer ……
☐ Med hydroksylapatitt ☐ Uten hydroksylapatitt
☐1 Sement med antibiotika – Navn ……
☐2 Sement uten antibiotika – Navn ……
☐3 Usementert

Femur
Navn/Type ……
ev. katalognummer ……
☐ Med hydroksylapatitt ☐ Uten hydroksylapatitt
☐1 Sement med antibiotika – Navn ……
☐2 Sement uten antibiotika – Navn ……
☐3 Usementert

Caput
☐1 Fastsittende caput
☐2 Separat caput - Navn/Type ……
ev. katalognummer ……
Diameter ……

MINI INVASIV KIRURGI (MIS) ☐0 Nei ☐1 Ja

COMPUTERNAVIGERING (CAOS) ☐0 Nei ☐1 Ja
Type navigering ……

TROMBOSEPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken type……
Dosering opr.dag……Første dose gitt preopr ☐0 Nei ☐1 Ja
Senere dosering……Antatt varighet……døgn
Ev. i kombinasjon med ……
Dosering…… Antatt varighet……døgn
Strømpe ☐0 Nei ☐1 Legg ☐2 Legg + Lår Antatt varighet ……døgn
Mekanisk pumpe ☐0 Nei ☐1 Fot ☐2 Legg Antatt varighet……døgn

SYSTEMISK ANTIBIOTIKAPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken (A).....
Dose (A)..... Totalt antall doser ..... Varighet .....timer
Ev. i kombinasjon med (B).....
Dose (B).....Totalt antall doser..... Varighet .....timer

OPERASJONSSTUE
☐1 "Green house"
☐2 Operasjonsstue med laminær luftstrøm
☐3 Vanlig operasjonsstue

OPERASJONSTID (hud til hud) ……min

PEROPERATIV KOMPLIKASJON
☐0 Nei
☐1 Ja,hvilke(n) .....

ASA KLASSE (se baksiden for definisjon)
☐1 Frisk
☐2 Asymptomatisk tilstand som gir økt risiko
☐3 Symptomatisk sykdom
☐4 Livstruende sykdom
☐5 Moribund

Lege .....
Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

15.06.2005

H

Nasjonalt Register for Leddproteser
Ortopedisk klinikk, Helse Bergen HF
Haukeland universitetssjukehus
Møllendalsbakken 11, 5021 BERGEN
Tlf 55973742/55973743

F.nr. (11 sifre).....

Navn:.....

(Skriv tydelig ev. pasient klistrelapp – **spesifiser sykehus**.)

Sykehus:.....

HOFTEPROTESER

ALLE TOTALPROTESER I HOFTELEDD REGISTRERES (ved hemiproteser etter hoftebrudd sendes hoftebruddskjema til Hoftebruddregisteret). Innsetting, skifting eller fjerning av protese eller protesedeler.

TIDLIGERE OPERASJON I AKTUELLE HOFTE (ev. flere kryss)
- ☐0 Nei
- ☐1 Osteosyntese for fraktur i prox. femurende
- ☐2 Hemiprotese pga. fraktur
- ☐3 Osteotomi
- ☐4 Artrodese
- ☐5 Totalprotese(r)
- ☐6 Annen operasjon .....

OPERASJONSDATO (dd.mm.åå) |__|__| |__|__| |__|__|

AKTUELLE OPERASJON (ett kryss)
- ☐1 Primæroperasjon (også hvis hemiprotese tidligere)
- ☐ 2 Reoperasjon (totalprotese tidligere)

AKTUELLE SIDE (ett kryss) (Bilateral opr.= 2 skjema)
☐1 Høyre ☐2 Venstre

AKTUELLE OPERASJON (KRYSS AV ENTEN I A ELLER B)

A . Primæroperasjon pga. (ev. flere kryss)
- ☐1 Idiopatisk coxartrose
- ☐2 Rheumatoid artritt
- ☐3 Sekvele etter frakt. colli. fem.
- ☐4 Sekv. dysplasi
- ☐5 Sekv. dysplasi med total luksasjon
- ☐6 Sekv. Perthes/Epifysiolyse
- ☐7 Mb. Bechterew
- ☐8 Akutt fraktura colli femoris
- ☐ Annet .....
  (f.eks caputnekrose, tidl. artrodese o.l)

B . Reoperasjon pga. (ev. flere kryss)
- ☐1 Løs acetabularkomponent
- ☐2 Løs femurkomponent
- ☐3 Luksasjon
- ☐4 Dyp infeksjon
- ☐5 Fraktur (ved protesen)
- ☐6 Smerter
- ☐7 Osteolyse i acetab. uten løsning
- ☐8 Osteolyse i femur uten løsning
- ☐ Annet .....
  (f.eks Girdlestone etter tidl. infisert protese)

REOPERASJONSTYPE (ev. flere kryss)
- ☐1 Bytte av femurkomponent
- ☐2 Bytte av acetabularkomponent
- ☐3 Bytte av hele protesen
- ☐4 Fjernet protese (f.eks Girdlestone)
  Angi hvilke deler som ble fjernet .....
- ☐5 Bytte av plastforing
- ☐6 Bytte av caput
- ☐ Andre operasjoner .....

TILGANG (ett kryss)
- ☐1 Fremre (Smith-Petersen)
- ☐2 Anterolateral
- ☐3 Lateral
- ☐4 Posterolateral
- ☐5 Annen .....

LEIE ☐0 Sideleie ☐1 Rygg

TROCHANTEROSTEOTOMI ☐0 Nei ☐1 Ja

BENTRANSPLANTASJON (ev. flere kryss)

Acetabulum	☐0 Nei	☐1 Ja	☐2 Benpakking
Femur	☐0 Nei	☐1 Ja	☐2 Benpakking a.m. Ling/Gie

BENTAP VED REVISJON (Paprosky's klassifikasjon se baksiden)

Acetabulum		**Femur**	
☐1 Type I	☐4 Type II C	☐1 Type I	☐4 Type III B
☐2 Type II A	☐5 Type III A	☐2 Type II	☐5 Type IV
☐3 Type II B	☐6 Type III B	☐3 Type III A	

PROTESE NAVN / DESIGN / "COATING"
(spesifiser nøyaktig eller bruk klistrelapp på baksiden)

Acetabulum
Navn/Type .....
ev. katalognummer .....
☐ Med hydroksylapatitt ☐ Uten hydroksylapatitt
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

Femur
Navn/Type .....
ev. katalognummer .....
☐ Med hydroksylapatitt ☐ Uten hydroksylapatitt
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

Caput
☐1 Fastsittende caput
☐2 Separat caput - Navn/Type .....
ev. katalognummer .....
Diameter .....

MINI INVASIV KIRURGI (MIS) ☐0 Nei ☐1 Ja

COMPUTERNAVIGERING (CAOS) ☐0 Nei ☐1 Ja
Type navigering .....

TROMBOSEPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken type.....

Dosering opr.dag.....Første dose gitt preopr ☐0 Nei ☐1 Ja

Senere dosering.....Antatt varighet.....døgn

Ev. i kombinasjon med .....

Dosering..... Antatt varighet.....døgn

Strømpe ☐0 Nei ☐1 Legg ☐2 Legg + Lår Antatt varighet .....døgn
Mekanisk pumpe ☐0 Nei ☐1 Fot ☐2 Legg Antatt varighet.....døgn

SYSTEMISK ANTIBIOTIKAPROFYLAKSE
☐0 Nei ☐1 Ja, hvilken (A).....

Dose (A)..... Totalt antall doser ..... Varighet .....timer

Ev. i kombinasjon med (B).....

Dose (B).....Totalt antall doser..... Varighet .....timer

OPERASJONSSTUE
- ☐1 "Green house"
- ☐2 Operasjonsstue med laminær luftstrøm
- ☐3 Vanlig operasjonsstue

OPERASJONSTID (hud til hud) .....min

PEROPERATIV KOMPLIKASJON
- ☐0 Nei
- ☐1 Ja,hvilke(n) .....

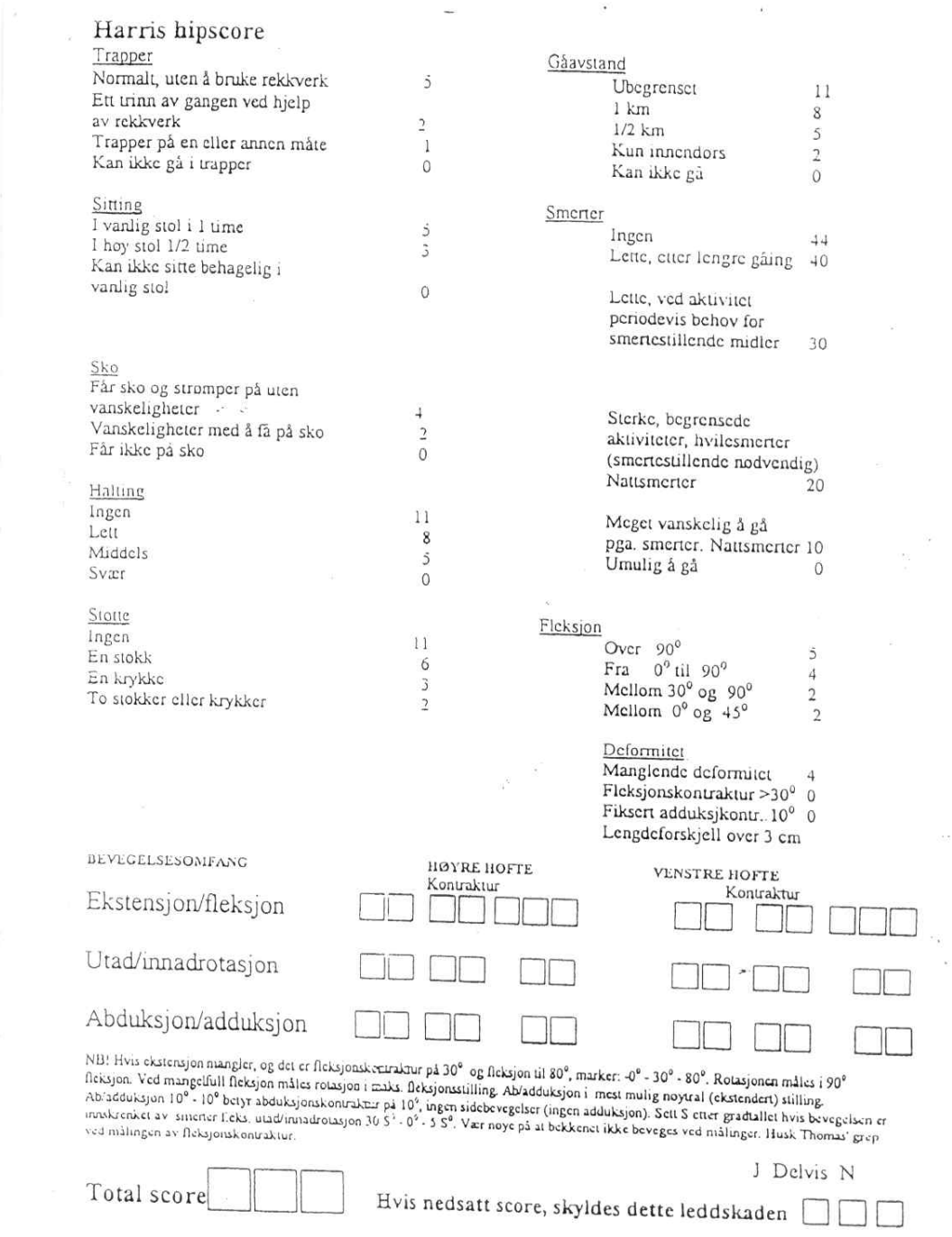
ASA KLASSE (se baksiden for definisjon)
- ☐1 Frisk
- ☐2 Asymptomatisk tilstand som gir økt risiko
- ☐3 Symptomatisk sykdom
- ☐4 Livstruende sykdom
- ☐5 Moribund

Lege .....
Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

17.07.2007

Harris hip score, Oxford hip score and UCLA activity score

Harris hip score



Harris hipscore

Trapper
- Normalt, uten å bruke rekkverk 5
- Ett trinn av gangen ved hjelp av rekkverk 2
- Trapper på en eller annen måte 1
- Kan ikke gå i trapper 0

Sitting
- I vanlig stol i 1 time 5
- I høy stol 1/2 time 3
- Kan ikke sitte behagelig i vanlig stol 0

Sko
- Får sko og strømper på uten vanskeligheter 4
- Vanskeligheter med å få på sko 2
- Får ikke på sko 0

Halting
- Ingen 11
- Lett 8
- Middels 5
- Svær 0

Stotte
- Ingen 11
- En stokk 6
- En krykke 3
- To stokker eller krykker 2

Gåavstand
- Ubegrenset 11
- 1 km 8
- 1/2 km 5
- Kun innendørs 2
- Kan ikke gå 0

Smerter
- Ingen 44
- Lette, etter lengre gåing 40
- Lette, ved aktivitet periodevis behov for smertestillende midler 30
- Sterke, begrensede aktiviteter, hvilesmerter (smertestillende nødvendig) Nattsmerter 20
- Meget vanskelig å gå pga. smerter. Nattsmerter 10
- Umulig å gå 0

Fleksjon
- Over 90° 5
- Fra 0° til 90° 4
- Mellom 30° og 90° 2
- Mellom 0° og 45° 2

Deformitet
- Manglende deformitet 4
- Fleksjonskontraktur >30° 0
- Fiksert adduksjkontr.. 10° 0
- Lengdeforskjell over 3 cm

BEVEGELSESOMFANG

	HØYRE HOFTE Kontraktur	VENSTRE HOFTE Kontraktur
Ekstensjon/fleksjon	☐☐ ☐☐ ☐☐☐	☐☐ ☐☐ ☐☐☐
Utad/innadrotasjon	☐☐ ☐☐ ☐☐	☐☐ ☐☐ ☐☐
Abduksjon/adduksjon	☐☐ ☐☐ ☐☐	☐☐ ☐☐ ☐☐

NB! Hvis ekstensjon mangler, og det er fleksjonskontraktur på 30° og fleksjon til 80°, marker: -0° - 30° - 80°. Rotasjonen måles i 90° fleksjon. Ved mangelfull fleksjon måles rotasjon i maks. fleksjonsstilling. Ab/adduksjon i mest mulig noytral (ekstendert) stilling. Ab/adduksjon 10° - 10° betyr abduksjonskontraktur på 10°, ingen sidebevegelser (ingen adduksjon). Sett S etter gradtallet hvis bevegelsen er innskrenket av smerter f.eks. utad/innadrotasjon 30 S° - 0° - 5 S°. Vær noye på at bekkenet ikke beveges ved målinger. Husk Thomas' grep ved målingen av fleksjonskontraktur.

J Delvis N

Total score ☐☐☐ Hvis nedsatt score, skyldes dette leddskaden ☐☐☐

O Roise, juni 00

Oxford hip score

Oxford hip score

Initialer | F.nr.

Hofte/side | ☐ Venstre ☐ Høyre

OXFORD-EVALUERING AV HOFTEFUNKSJON – SIDE 1

Evalueringsdato: _____/_____/_____(dd/mm/åååå)

√ merk av en boks for hvert spørsmål

1. **I løpet av de siste 4 ukene,** hvordan vil du beskrive smertene du vanligvis hadde i hoften?
☐ Ingen
☐ Meget svake
☐ Svake
☐ Moderate
☐ Alvorlige

2. **I løpet av de 4 siste ukene,** har du hatt problemer med å vaske deg og tørke deg (over hele kroppen) på grunn av hoften?
☐ Ingen problemer i det hele tatt
☐ Meget få problemer
☐ Moderate problemer
☐ Svært vanskelige
☐ Umulig å gjennomføre

3. **I løpet av de 4 siste ukene,** har du hatt problemer med å komme deg inn og ut av bilen, eller bruke offentlige transportmidler på grunn av hoften (alt etter hva du vanligvis bruker)
☐ Ingen problemer i det hele tatt
☐ Meget få problemer
☐ Moderate problemer
☐ Svært vanskelig
☐ Umulig å gjennomføre

4. **I løpet av de 4 siste ukene,** har du vært i stand til å ta på deg sokker, strømper eller strømpebukser?
☐ Ja, med letthet
☐ Med litt besvær
☐ Med moderat besvær
☐ Med stort besvær
☐ Nei, umulig

5. **I løpet av de 4 siste ukene,** kunne du gjøre innkjøp av dagligvarer på egen hånd?
☐ Ja, med letthet
☐ Med litt besvær
☐ Med moderat besvær
☐ Med stort besvær
☐ Nei, umulig

Oxford hip score

Initialer	F.nr.

Hofte/side	☐ Venstre ☐ Høyre

OXFORD-EVALUERING AV HOFTEFUNKSJON – SIDE 2

Evalueringsdato: ____/____/_____(dd/mm/åååå)

√ merk av en boks for hvert spørsmål

6. **I løpet av de siste 4 ukene,** hvor lenge har du kunnet gå før smertene i hoften blir alvorlige (med eller uten stokk/krykker?
- ☐ Ingen smerter/mer enn 30 minutter
- ☐ 16 til 30 minutter
- ☐ 5 til 15 minutter
- ☐ Kun rundt om i huset
- ☐ Ikke i det hele tatt – alvorlige smerter når jeg går

7. **I løpet av de 4 siste ukene,** har du vært i stand til å gå opp trapper?
- ☐ Ja, med letthet
- ☐ Med litt besvær
- ☐ Med moderat besvær
- ☐ Med stort besvær
- ☐ Nei, umulig

8. **I løpet av de 4 siste ukene,** etter å ha spist (etter å ha sittet ved et bord,), hvor smertefullt har det vært å reise seg fra stolen på grunn av hoften?
- ☐ Ikke smertefullt i det hele tatt
- ☐ Litt smertefullt
- ☐ Moderat smertefullt
- ☐ Meget smertefullt
- ☐ Uutholdelig

9. **I løpet av de 4 siste ukene,** har du haltet når du går på grunn av hoften?
- ☐ Sjelden/aldri
- ☐ Av og til, eller bare i begynnelsen
- ☐ Ofte, ikke bare i begynnelsen
- ☐ Nesten alltid
- ☐ Alltid

10. **I løpet av de 4 siste ukene,** har du fått plutselig alvorlige smerter – "jagende", stikkende" eller "kramper" – fra den gjeldende hoften?
- ☐ Ingen dager
- ☐ Kun 1 eller 2 dager
- ☐ Noen dager
- ☐ De fleste dager
- ☐ Hver dag

Oxford hip score

Initialer	F.nr.

Hofte/side	☐ Venstre	☐ Høyre

OXFORD-EVALUERING AV HOFTEFUNKSJON – SIDE 3

Evalueringsdato: ____/____/_____(dd/mm/åååå)

√ merk av en boks for hvert spørsmål

11. **I løpet av de siste 4 ukene,** hvor mye har smerter i hoften forstyrret ditt vanlige arbeid (inkludert husarbeid)?

☐ Ikke i det hele tatt
☐ Litt
☐ Moderat
☐ I stor grad
☐ Fullstendig

12. **I løpet av de 4 siste ukene,** har du hatt problemer med smerter i hoften når du ligger i sengen om natten?

☐ Ingen netter
☐ Kun 1 eller 2 netter
☐ Noen netter
☐ De fleste netter
☐ Hver natt

UCLA activity score

Table 1. UCLA Activity-Level Rating

Level	Activity
10	Regularly participate in *impact sports* such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking
9	Sometimes participate in *impact sports*
8	Regularly participate in *very active* events, such as bowling or golf
7	Regularly participate in *active* events, such as bicycling
6	Regularly participate in *moderate activities*, such as swimming and unlimited housework or shopping
5	Sometimes participate in *moderate activities*
4	Regularly participate in *mild activities*, such as walking, limited housework, and limited shopping
3	Sometimes participate in *mild activities*
2	Mostly *inactive:* restricted to minimal activities of daily living
1	Wholly *inactive:* dependent on others; cannot leave residence

Paper 1-4

Is reverse hybrid hip replacement the solution?

3,963 primary hip replacements with cemented cup and uncemented stem, from the Norwegian Arthroplasty Register

Einar Lindalen[1], Leif I Havelin[2,3], Lars Nordsletten[4], Eva Dybvik[2], Anne M Fenstad[2], Geir Hallan[2], Ove Furnes[2,3], Øystein Høvik[1], and Stephan M Röhrl[4]

[1]Department of Orthopaedic Surgery, Lovisenberg Deaconal Hospital, Oslo; [2]Department of Orthopaedic Surgery, Norwegian Arthroplasty Register, Haukeland University Hospital, Bergen; [3]Section of Orthopaedic Surgery, Department of Surgical Sciences, University of Bergen; [4]Orthopaedic Department, Oslo University Hospital, University of Oslo, Oslo, Norway
Correspondence EL: eli@lds.no
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Background and purpose Reverse hybrid hip replacement uses a cemented all-polyethylene cup and an uncemented stem. Despite increasing use of this method in Scandinavia, there has been very little documentation of results. We have therefore analyzed the results from the Norwegian Arthroplasty Register (NAR), with up to 10 years of follow-up.

Patients and methods The NAR has been collecting data on total hip replacement (THR) since 1987. Reverse hybrid hip replacements were used mainly from 2000. We extracted data on reverse hybrid THR from this year onward until December 31, 2009, and compared the results with those from cemented implants over the same period. Specific cup/stem combinations involving 100 cases or more were selected. In addition, only combinations that were taken into use in 2005 or earlier were included. 3,963 operations in 3,630 patients were included. We used the Kaplan-Meier method and Cox regression analysis for estimation of prosthesis survival and relative risk of revision. The main endpoint was revision for any cause, but we also performed specific analyses on different reasons for revision.

Results We found equal survival to that from cemented THR at 5 years (cemented: 97.0% (95% CI: 96.8–97.2); reverse hybrid: 96.7% (96.0–97.4)) and at 7 years (cemented: 96.0% (95.7–96.2); reverse hybrid: 95.6% (94.4–96.7)). Adjusted relative risk of revision of the reverse hybrids was 1.1 (0.9–1.4). In patients under 60 years of age, we found similar survival of the 2 groups at 5 and 7 years, with an adjusted relative risk of revision of reverse hybrids of 0.9 (0.6–1.3) compared to cemented implants.

Interpretation With a follow-up of up to 10 years, reverse hybrid THRs performed well, and similarly to all-cemented THRs from the same time period. The reverse hybrid method might therefore be an alternative to all-cemented THR. Longer follow-up time is needed to evaluate whether reverse hybrid hip replacement has any advantages over all-cemented THR.

The reverse hybrid method (also known as "inverse hybrid") uses a cemented all-polyethylene cup in combination with an uncemented stem. This method is partly based on good clinical results of cemented cups and of some uncemented stems in the Norwegian Arthroplasty Register (NAR) (Havelin et al. 2000a,b, Hallan et al. 2007). The register has also shown that some uncemented femoral stems may have better long–term results (> 10 years) than cemented stems in patients 60 years of age or younger. Based on these findings, the NAR suggested 10 years ago that the use of cemented cups in combination with uncemented stems might be justified in young patients (Havelin et al. 2000a). In the Swedish Hip Arthroplasty Register, the performance of uncemented THR was found to be inferior to that of cemented THR (Hailer et al. 2010). The authors of that study found that cemented cups performed better than uncemented cups and that uncemented femoral stems had better survival than cemented stems, with aseptic loosening as endpoint. In the Finnish Arthroplasty Registry, Mäkelä et al. (2010) found better long-term survival regarding aseptic loosening for the best performing types of cementless stems compared to the cemented reference group, in the age group 55–74 years.

McNally et al. (2000) studied survival of the Furlong HA coated femoral stem in combination with a cemented ultra-high-density polyethylene cup at 10–11 years, and found values of 99% for the stem and 95% for the cup. Alho et al. (2000) reported results with cemented Lubinus cups and uncemented Furlong stems, and they also pointed out the possibility of using the principle of reverse hybrid arthroplasty. We are not aware of any other reports on the reverse hybrid method.

In a reverse hybrid THR, an uncemented stem and a modular head are most often combined with a cemented cup of another name or from another company. Combining implants that are not designed to fit each other might theoretically lead

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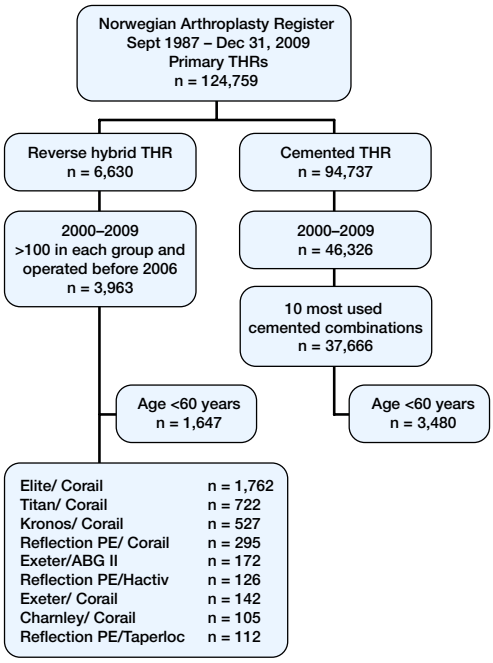

Figure 1. Flowchart of the study.

to unexpected complications such as increased wear, loosening, or dislocation. This concern was raised by the NAR already in their report from 2005 (Norwegian Arthroplasty Register 2005). As the use of reverse hybrids is increasing, we decided to evaluate the short- to medium-term results with this concept and to compare them with those from all-cemented THRs, using data from the NAR.

Patients and methods

The NAR was established in September 1987 (Havelin et al. 1993). Data on primary and revision THR surgery are collected, and the patients are followed prospectively until revision, death, or emigration. The unique identification number assigned to each resident of Norway makes it possible to link the primary operation to revision surgery and to the National Population Register, which provides information on death or emigration. Completeness of registration is high for total hip replacement, for both primary and revision surgery (Arthursson et al. 2005, Espehaug et al. 2006, Hulleberg et al. 2008).

From September 1, 1987 through December 31, 2009, 124,759 primary THRs were registered. Of these, 6,630 cases involved reverse hybrid THR. 15 different cups and 13 different femoral stems had been used for these reverse hybrids. Since reverse hybrid THR has mainly been used during the last decade, we included only operations performed after December 31, 1999. This gave 6,485 primary operations. We included only the combinations of cup and stem for which there had been more than 100 procedures since 2005. Thus, 3,963 operations in 3,630 patients were included (Figure 1) for survival estimation at 5 and 7 years, involving 9 implant combinations (cup/stem) (Tables 1 and 2). In these implant combinations, all cups were made from conventional ultra-high-molecular-weight polyethylene (UHMWPE).

From the register, we extracted information on the brand(s) of the components, the diameter and the material of the femoral heads, the diagnosis, the name of the hospital, the surgical approach to the hip, and reasons for revision surgery. We estimated survival at 3, 5, and 7 years for the total material with any revision as the endpoint. Further subgroup analyses included survival at 3, 5, and 7 years in patients less than 60 years of age, with any revision as endpoint. Furthermore, we compared reverse hybrid THR to cemented THR for the total material, with deep infection, dislocation, aseptically loos-

Table 1. Breakdown of numbers of different combinations of prosthesis components in the reverse hybrid group during the study period

	Combination of cup and stem (reverse hybrid)									
Year	Elite/ Corail	Titan/ Corail	Kronos/ Corail	Reflection PE[a]/Corail	Exeter/ Corail	Charnley/ Corail	Exeter/ ABG II	Reflection PE[a]/Hactiv	Reflection PE[a]/Taperloc	Total
2000	38	3	3	6	1	6	0	0	0	57
2001	43	22	14	13	2	4	0	0	0	98
2002	45	46	6	37	3	7	0	0	0	144
2003	61	50	9	55	8	2	61	0	0	246
2004	83	72	14	63	16	9	50	12	0	319
2005	178	79	39	69	10	5	61	37	34	512
2006	269	82	66	18	11	14	0	29	49	538
2007	365	75	98	26	18	34	0	18	29	663
2008	362	113	157	5	28	13	0	16	0	694
2009	318	180	121	3	45	11	0	14	0	692
Total	1762	722	527	295	142	105	172	126	112	3963

[a] Full brand name: Reflection Cemented All-Poly.

Table 2. Comparison of different combinations of prosthesis components in the reverse hybrid group

Brand name cup/stem	Manufacturer cup/stem	N	Revisions	Median follow-up (range)	Mean age (min–max)	% < 60 year	% male	No. of hospitals (max % at hospital)
Elite/Corail	Landos Depuy/Depuy	1762	40	2.6 (0–10)	60 (21–92)	48	40	15 (34%)
Titan/Corail	Landos Depuy/Depuy	722	21	3.0 (0–9.8)	63 (27–91)	36	36	11 (34%)
Kronos/Corail	Landos Depuy/Depuy	527	12	1.8 (0–9.7)	63 (20–92)	33	32	4 (83%)
RPE [a]/Corail	Smith & Nephew/Depuy	295	17	5.6 (0–9.9)	58 (18–90)	58	37	11 (35%)
Exeter/ ABG II	Stryker [b]/Stryker	172	6	5.4 (1.4–7.0)	73 (50–88)	2	37	2 (82%)
RPE [a]/Hactiv	Smith & Nephew/Scanos [c]	126	5	3.6 (0–5.6)	64 (19–91)	38	37	2 (97%)
Exeter/Corail	Stryker [b]/Depuy	142	2	1.9 (0–9.9)	64 (19–87)	35	18	5 (67%)
Charnley/Corail	Depuy/Depuy	105	2	2.8 (0.4–9.9)	58 (21–86)	61	21	14 (46%)
RPE [a]/Taperloc	Smith & Nephew/Biomet	112	3	3.8 (2.5–4.7)	61 (40–82)	36	33	1 (100%)

[a] Full brand name: Reflection Cemented All-Poly.
[b] Full brand name: Stryker, Osteonics, Howmedica
[c] Full brand name: Scanos Evolutis

Table 3. Cup/stem combinations in the cemented group. These have been thoroughly described by Espehaug et al. (2009)

	Manufacturer	Number of prostheses
Charnley/Charnley	Depuy	12,192
Exeter/Exeter	Stryker, Osteonics, Howmedica	6,419
Reflection PE/Spectron	Smith & Nephew	8,618
Titan/Titan	Landos, Depuy	2,736
Spectron/ITH	Smith & Nephew	162
Link IP/Lubinus SP(I,II)	Waldemar Link	2,203
Contemporary/Exeter	Stryker, Osteonics, Howmedica	2,707
Kronos/Titan	Landos, Depuy	1,073
Elite/Titan	Depuy/Landos Depuy	1,139
Reflection/ITH	Smith & Nephew	417

ened stem, and aseptically loosened cup as endpoint in the same period.

We compared the results to the 10 most commonly used cemented cup/stem combinations in the study period. These cemented implants and the cups in the reverse hybrid group have been described by Espehaug et al. (2009) (Table 3). Details of the stems in the present study are given in Table 4. We excluded patients operated with CMW cement, due to the poor results described by others after use of this cement (Havelin et al.1995, Espehaug et al. 2002).

Statistics

Risk Ratio (RR) with 95% confidence interval (CI) was estimated using Cox regression analyses, with adjustments for age (< 50, 50–59, 60–69, 70–79 and > 80), sex, and diagnosis (osteoarthritis (OA), inflammatory arthritis, and others). We used plots with scaled Schoenfeld residuals for each covariate to test that the Cox proportional hazard model was fulfilled. The Kaplan-Meier method was used for estimation of survival probabilities for the prostheses, with 95% confidence interval (CI). Ranstam and Robertsson (2010) have discussed statistical analysis regarding arthroplasty register data and found a negligible effect on survival estimates including bilateral hips. We therefore included bilateral hips. When less than 20 hips remained at risk, survival probabilities were not calculated. Median follow-up was calculated using the reverse Kaplan-Meier method. We used chi-squared test to test for binary outcomes between study groups, and the non-parametric Mann-Whitney test was used to determine whether the distribution of medians was different between study groups. All p-values less than 0.05 were considered to be statistically significant. We used the statistical software packages SPSS (SPSS 17.0 for Windows) and R (version 2.8.1; http://www.R-project.org).

Table 4. Details of the characteristics of the uncemented femoral stems used in the reverse hybrid group. 97% had HA coating

Stem	Material	Shape	Surface	Thickness of HA	Company
Corail	Ti6A14V	Straight, tapered	Fully HA-coated	155 µm	DePuy
ABG II	Ti alloy	Anatomic	HA-coated proximal, polished distally	50 µm	Stryker
Hactiv	Ti6A14V	Straight, tapered	Fully HA-coated	155 µm	Evolutis
Taperloc	Ti6A14V	Straight, tapered	Without HA in this study, proximal plasma spray coating		Biomet

Table 5. Comparison of demographic data for cemented and reverse hybrid THRs, both for total material and for patients aged < 60 years. Comparison of survival (in %) and relative risk (RR) of revision for cemented and reverse hybrid THRs, with all revisions as endpoint, for total material and for patients aged < 60 years

	Total material			Age < 60 years		
	Cemented	Reverse hybrid	p-value	Cemented	Reverse hybrid	p-value
n	37,666	3,963		3,480	1,647	
Revisions	1,140	108		135	41	
Median follow-up (range)	4.7 (0–10)	2.9 (0–10)	< 0.001 [b]	5.2 (0–10)	3.4 (0–10)	< 0.001 [b]
Mean age (min–max)	73 (16–98)	61 (18–92)	< 0.001 [b]	54 (16–60)	52 (18–60)	< 0.001 [b]
% < 60 years	9	42	< 0.001 [a]	100	100	
% male	29	36	< 0.001 [a]	36	39	0.06 [a]
Deceased	5,928 (15.7%)	104 (2.6%)		229 (6.6%)	25 (1.5%)	
Emigrated	58 (0.2%)	8 (0.2%)		21 (0.6%)	4 (0.4%)	
Missing	2	0		0	0	
Alive	31,678 (84.1%)	3,851 (97.2%)		3,230 (92.8%)	1,618 (98.2%)	
Diagnosis			< 0.001 [a]			< 0.001 [a]
Osteoarthritis	78.6%	70.9%		56.6%	55.9%	
RA/Inflammatory	3.3%	4.2%		8.0%	6.0%	
Sequelae hip fracture	8.9%	5.2%		7.1%	4.8%	
Dysplasia	4.3%	11.6%		16.5%	20.4%	
Perthes'	0.6%	2.2%		3.1%	4.5%	
Other	4.4%	5.9%		8.7%	8.4%	
3-year survival (95%CI)	97.9 (97.7–98.0)	97.7 (97.2–98.2)		98.0 (97.5–98.5)	98.3 (97.7–99.0)	
5-year survival (95%CI)	97.0 (96.8–97.2)	96.7 (96.0–97.4)		96.7 (96.0–97.3)	97.5 (96.6–98.5)	
7-year survival (95%CI)	96.0 (95.7–96.2)	95.6 (94.4–96.7)		94.9 (94.0–95.9)	96.2 (94.6–97.8)	
RR [c] (95%CI)	1 (Reference)	1.1 (0.9–1.4)	0.3	1 (Reference)	0.9 (0.6–1.3)	0.5

[a] Chi-squared test.
[b] Non-parametric Mann-Whitney.
[c] RR adjusted for age, sex, and diagnosis.

Results

The mean age was lower in the reverse hybrid group than in the cemented group: 61 (18–92) years as opposed to 73 (16–98) years. The proportion of males was higher in the reverse hybrid group than in the cemented group (36% vs. 29%). In addition, 9% of patients were below 60 years of age in the cemented group and the corresponding proportion in the reverse hybrid group was 42%. Furthermore, there were significant differences regarding diagnosis, age, and sex (Table 5). In the total material, median follow-up was 2.9 (0–10) years in the reverse hybrid group and 4.7 (0–10) years in the cemented group. For patients aged less than 60 years, the median follow-up was 3.4 (0–10) years for reverse hybrid and 5.2 (0–10) years for cemented (Table 5).

There was no statistically significant difference in implant survival between cemented and reverse hybrid THRs when the endpoint was any revision. This was also found in analyses of cases less than 60 years of age (Figures 2 and 3, Table 5). In subanalyses of the total material using the endpoints revision due to deep infection, dislocation, aseptically loosened stem, and aseptically loosened cup, no statistically significant differences between cemented and reverse hybrid THRs were found.

The reverse hybrids had a 3.6 times higher risk of revision for periprosthetic femoral fracture compared to the cemented implants (CI: 1.9–6.9; $p < 0.001$). The survival was 99.85% (99.8–99.9) and 99.6% (99.3–99.9), respectively, at 5 years using this endpoint.

We performed analyses of the different cup/stem combinations in the reverse hybrid group with all revisions as the endpoint at 3 and 5 years. No statistically significant differences were found. Reflection PE/Hactiv and Reflection PE/Taperloc had less than 20 hips left at risk at 5 years; thus, 5-year survival of these combinations could not be estimated.

In the reverse hybrid group, 3,832 of the 3,963 prostheses had a femoral head with a diameter of 28 mm. 2,467 heads were made of alumina and 1,286 heads were made of cobalt chromium. In these 2 groups, all head sizes were included.

Among the different groups of reverse hybrid combinations, we noted differences in age, in median follow–up time, and in the male/female ratio. The ReflectionPE/Taperloc combination has been used since 2005, but maximum follow-up for this group only reached 4.7 years. All the other groups of reverse hybrid combinations had a maximum follow-up of more than 5 years (Table 2).

Discussion

The use of reverse hybrids has increased in Norway and Sweden during the last decade. Before 2000, few reverse hybrid operations were performed each year, and with many

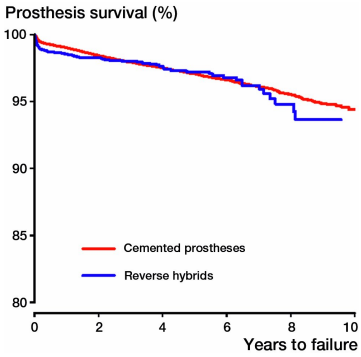

Figure 2. Cox survival curves. Endpoint was any revision of the implant for the total material. Adjusted for age, sex, and diagnosis. Age: < 50, 50–59, 60–69, 70–79 and > 80. Diagnosis: OA, RA/inflammatory, or other.

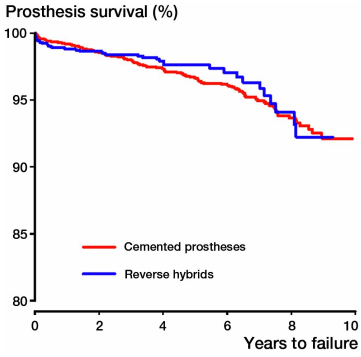

Figure 3. Cox survival curves. Endpoint was any revision of the implant. Age < 60 years. Adjustment for age, sex, and diagnosis. Age: <50, 50–60. Diagnosis: OA, RA/inflammatory, or other.

different combinations of components. In this pre-2000 period, we believe that in some instances failure to achieve solid fixation of an uncemented cup made the surgeon convert to a cemented cup. Since the year 2000, the reverse hybrid concept has been used more systematically in Norway and the number of implanted primary reverse hybrids has increased from 90 in the year 2000 to 1,735 in 2009. In Sweden, the number of hybrid THRs has declined and the total number of reverse hybrids has increased (Swedish Hip Arthroplasty Register 2007). This increase in popularity called for the evaluation of medium-term results using this method.

Comparing the reverse hybrid group with the 10 most used cemented THRs, we found similar implant survival with 0–10 years of follow-up. The only differences found were for subanalyses on femoral fractures, but the difference in survival at 5 years with this endpoint was only 0.25% and 5-year survival exceeded 99% for both groups. This indicates that periprosthetic femoral fractures are an infrequent complication leading to revision surgery.

For the total material, the proportion of males was higher and the mean age was lower in the reverse hybrid group than in the cemented group. We had no scoring for activity level, and there could be a bias in comparing high-demand young men to a group with low-demand elderly women. However, when we limited analyses to patients less than 60 years of age, the groups were much more similar to each other. The median follow-up for total material and for cases below 60 years differed significantly between study groups, and with short follow-up it may therefore be difficult to uncover differences between these 2 concepts.

We found similar risk of deep infection with reverse hybrid and cemented THR. Only revisions that included removal or exchange of parts or the whole implant were reported to the register. Thus, soft tissue revisions without the exchange of prosthetic parts were not reported to the NAR. For the period 2003–2007 and using data from the NAR, Dale et al. (2009) found a statistically significant difference in numbers of revisions due to deep infection with inferior results for uncemented THR compared to cemented THR. One explanation for our finding is that antibiotic in the cement in reverse hybrids may protect against deep infection (Engesaeter et al. 2003).

In the present study, 97% of the stems had HA coating and in the medium term we found results comparable to those for cemented THR (Table 4). In 2002, the NAR reported inferior results for 2 types of HA-coated cups as compared to cemented Charnley cups (Havelin et al. 2002). In 2010, Lazarinis et al. reported increased risk of revision of acetabular cups coated with HA, and in 2009 Stilling et al. reported inferior results for an HA-coated cup compared to those for a non HA-coated cup at 15 years. Concerns have been raised about third body wear induced by HA from HA-coated implants. Røkkum et al. (2002) discussed whether thick HA coatings may delaminate, and suggested that thick HA coatings may be a reservoir for HA particles. Wear and wear-related problems may appear several years after the primary procedure. Studies with large numbers and long follow-up are thus necessary in order to be able to conclude whether the performance of cup implants is influenced by the stem having an HA coating. Regarding this problem, randomized controlled trials measuring wear with precise methods are important, but registry studies collecting a large amount of data on prostheses may also reveal differences between HA-coated implants and those without any HA coating.

In the NAR, femoral fractures are reported if they require revision surgery. We found a higher risk of revision for periprosthetic femoral fracture in the reverse hybrids than in the all-cemented THRs. Although it was more common with uncemented stems, periprosthetic femoral fracture was uncommon in both groups. Hailer et al. (2010) found in a study from the

Swedish Arthroplasty Register that uncemented stems were more frequently revised due to periprosthetic fracture than cemented stems during the first 2 postoperative years.

We used the Kaplan-Meier method to estimate prosthesis survival, censoring death and emigration. Both death and emigration are competing risks regarding revision. In a study from the Australian Orthopaedic Association National Joint Replacement Registry, Gillam et al. (2010) found that the Kaplan-Meier method overestimated the risk of revision compared to a method called the cumulative incidence function. The latter method uses competing risk methods in the analyses. With a short- to medium-term follow-up and a rather low incidence of death, we assumed that the Kaplan-Meier method would be appropriate to use in this study.

Regarding revision due to deep infection, dislocation, aseptically loosened stem, and aseptically loosened cup, we did not find any statistically significant difference between cemented and reverse hybrid THRs. In planning the study, we aimed to do subanalyses with the endpoints revision due to deep infection, dislocation, aseptically loosened stem, and aseptically loosened cup for the different combinations of cup/stem (different brands) in the reverse hybrid group. We found that the number of revisions and the number of procedures in some groups were quite small (Table 2). Thus, 1 single revision would have a large effect on the survival calculations for certain implant combinations. Although our register has a high completeness of data, we do not know for certain that all revisions of the primary THRs included were reported to the register. 1 or 2 missing revisions in 1 study group may offset the results quite dramatically when the groups are small. Furthermore, the accuracy of registry results is not known; the surgeon may type the data into the wrong box on the form, or the register may enter wrong data into the database. It is therefore difficult to make conclusions about the performance of the different components used in the reverse hybrid group. Subtle differences between study groups, if found, should be interpreted with caution—even if they are statistically significant. Factors other than the implant itself, such as surgical technique, revision policy, incorrect registration, or unknown patient factors may bias the results.

In summary, we found no statistically significant differences in survival between reverse hybrid and all-cemented THRs in this population-based registry study. Both groups performed well, with 95–96% survival after up to 7 years of follow-up. Thus, there were no early signs of warning against the reverse hybrid method according to our findings. Due to the small number of revisions in the present study, we cannot make any conclusions regarding the results for the different cup/stem combinations of reverse hybrid THR. With a short- to medium-term follow–up, it appears that the reverse hybrid method might be a promising alternative in THR surgery using UHMWPE. We emphasize that long-term follow-up will be required to evaluate whether the concept has any advantage over all-cemented THR.

EL: conception of study, planning, interpretation of data, and writing of the manuscript. All the others contributed to planning, interpretation of data, and critical review of the manuscript. ED and AMF: statistical analysis.

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No competing interests declared.

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Reverse hybrid and cemented hip replacement compared using radiostereometry and dual-energy X-ray absorptiometry

43 hips followed for 2 years in a prospective trial

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Background and purpose **Total hip replacement (THR) with a reverse hybrid (RH), a combination of a cemented polyethylene cup and a cementless femoral stem, has been increasingly used in Scandinavia. In a randomized trial, we compared an RH THR with a proximal hydroxyapatite- (HA-) coated stem to a conventional cemented THR. Both groups received the same polyethylene cup.**

Patients and methods **51 patients (52 hips) were included. Radiostereometry (RSA) and dual-energy X-ray absorptiometry (DEXA) were performed postoperatively and after 6, 12, and 24 months. 42 patients (43 hips) were followed for 2 years.**

Results **Mean cup rotation around the x-axis was 0.13° for the cemented group and –0.24° for the RH group (p = 0.03). Cup migration in the other axes, and stem migration and wear were similar between the 2 study groups. Bone remodeling around the cup was also similar between the groups. Bone loss in Gruen zone 1 was 18% for the cementless stems, as compared to an increase of 1.4% for the cemented ones (p < 0.001). Bone loss was similar in the other Gruen zones. Harris hip score and Oxford hip score were similar pre- and postoperatively in the 2 groups.**

Interpretation **In the present study, RH THR with a cementless hydroxyapatite-coated stem and conventional cemented THR did not show any major differences regarding stem migration and bone loss after 2 years of follow-up.**

A reverse hybrid (RH) in total hip replacement (THR) is a cemented polyethylene cup with a cementless femoral stem. In the past decade, the use of this method has increased in Norway and Sweden (Swedish Hip Arthroplasty Register 2007, Norwegian Arthroplasty Register 2010). In the Norwegian Arthroplasty Register (NAR), some cementless stems have better survival than cemented ones in patients who are 60 years old or younger, and it has been suggested that the RH method could be an option in young patients due to the good results with cemented cups and with some cementless stems (Havelin et al. 2000). In the Swedish Hip Arthroplasty Register, cemented cups have performed better than cementless cups, and cementless femoral stems have had better survival than cemented stems with aseptic loosening as endpoint (Hailer et al. 2010). A medium-term report from the NAR has shown promising results for certain RH combinations (Lindalen et al. 2011). Some authors have pointed out that hydroxyapatite (HA) particles released from HA-coated implants may increase polyethylene wear (Bloebaum et al. 1994, Røkkum et al. 2002). We have not found any record of randomized trials that have shown that the RH method is superior to conventional cemented THR. In the present study, we compared a RH THR with a proximally HA-coated stem to a cemented THR in a randomized trial. Our null hypothesis was that there would be no differences in clinical results, wear, remodeling of bone, or migration of the components between the study groups.

Patients and methods

51 patients (52 hips) with osteoarthritis were randomized by a nurse before surgery to either a conventional cemented THR or an RH THR. We used sealed envelopes. The patients were operated on from April 2006 through June 2007. The study was terminated in June 2007 due to delay in delivery of study prostheses. 9 patients (9 hips) were excluded for various reasons (Figure 1).

The operations were performed using the posterolateral approach. All patients received a Reflection cemented all-polyethylene cup (Smith and Nephew, Memphis, TN). The

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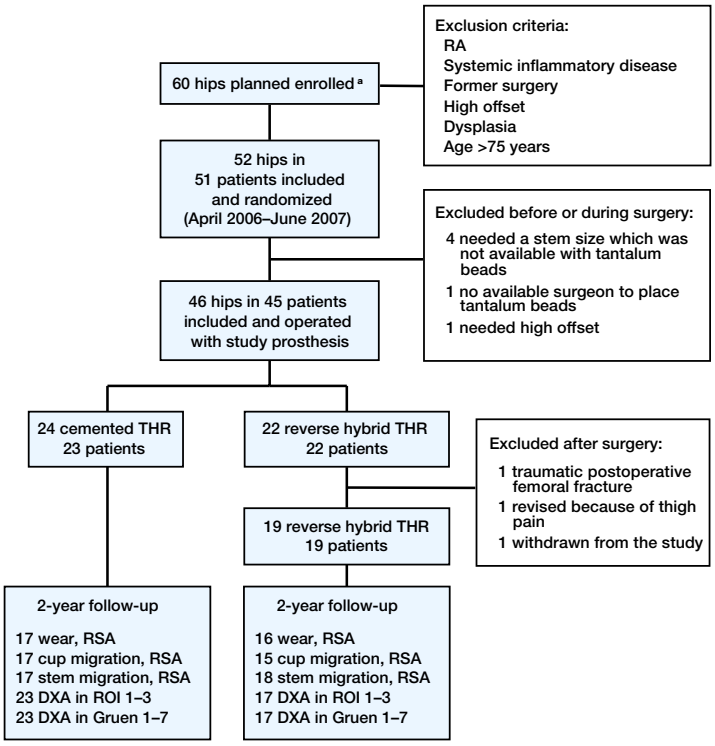

Figure 1. Flow chart illustrating the randomized controlled trial. [a] Due to delay in delivery of study prosthesis inclusion of participants was stopped in some periods and numbers of eligibility are not present

cup was made of UHMWPE, ram-extruded from GUR 1050 and sterilized with ethylene oxide. The cup was inserted by third-generation cementing technique with Palacos R+G (Heraeus, Hanau, Germany). No systematic templating of the hips was performed preoperatively.

All patients received thromboprophylaxis with Fragmin (dalteparin). Pre- and postoperative prophylaxis with cefalotin was administered intravenously. 2 patients received clindamycin due to penicllin allergy. 8 surgeons participated in the study.

Cemented stem

The femur was reamed to adequate size and a Spectron EF stem (Smith and Nephew) of the same size was cemented with Palacos R+G (Heraeus). 3 patients received a stem one size larger than the reamed size. The stem had tantalum balls attached to the tip and to the calcar region. To the neck, a metal piece with a cone and a tantalum marker was attached during surgery. A distal cement restrictor of polyethylene was used and pressurization of the cement was performed before insertion of the prostheses. A 28-mm head of cobalt chrome (Smith and Nephew) was used in all cases. In this group, we had all sizes (1–5) of the femoral stem in standard offset.

Cementless stem

In the RH group, a Taperloc (Biomet, Warsaw, IN) cementless femoral stem made of Ti6A14V was used. The stem had a proximal plasma-sprayed HA coating on top of the porous metal coating. The HA coating was 55 ± 15 µm thick and had a crystallinity of 50–70%. The Taperloc had tantalum balls attached to the tip, at the calcar region and at the neck. We used a femoral stem of the same size as the last reamer. In this group, we had sizes 7.5, 10, 12.5, 15, and 17.5 in standard offset. A 28-mm head of cobalt chrome (Biomet) was used in all cases.

During the operation the cup, the periacetabular bone, the greater trochanter, and the lesser trochanter were marked with 1-mm tantalum balls. The implants used in the study were selected since we used the Reflection cemented all-polyethylene cup in combination with either the cemented Spectron EF stem or the cementless Taperloc stem without HA in our department. The patients were mobilized on the first postoperative day, with weight bearing as tolerated. All patients were scored preoperatively and after 2 years using the Harris hip score and Oxford hip score.

The study was conducted in accordance with the Helsinki Declaration and approved by the regional ethics committee (REK) Sør-Øst in Norway. (Clinical Trials.gov Identifier: NCT00526539). All patients were recruited, operated on, and followed according to study protocol at Lovisenberg Diaconal Hospital. RSA and DEXA scans and analysis were performed at Oslo University Hospital. All patients gave informed consent to participate in the study.

RSA

RSA was performed postoperatively and at 6 months, and at 1 and 2 years. We used a uniplanar calibration cage number 43 (RSA Biomedical, Umeå, Sweden). Radiographs were taken

Table 1. Precision for point motion (wear) and movement (translation and rotation for cup and stem) in x-, y-, and z-axes. n = 108 double examinations for wear, n = 113 double examinations for cup migration, and n = 140 double examinations for stem migration. RSA was performed at a mean of 7 (4–31) days postoperatively

	Wear	Cup		Stem	
		translation	rotation	translation	rotation
	(mm)	(mm)	(°) [a]	(mm)	(°) [a]
x-axis	0.11	0.11	0.58	0.15	0.39
y-axis	0.10	0.11	0.43	0.09	0.59
z-axis	0.19	0.29	0.26	0.31	0.20

[a] degrees around axis

using 2 fixed X-ray tubes with the patient in the supine position. Analysis was done with UmRSA Digital Measure 6.0 (RSA Biomedical, Umeå, Sweden). At least 3 tantalum markers had to be identified in order to calculate wear or migration. In addition to the markers attached to the femoral component, the center of the head was used as a reference point. The cut-off for mean error (ME) was set at 0.30 and condition numbers lower than 150 were accepted (Valstar et al. 2005). The precision of the measurements was calculated by double examinations and expressed as an absolute mean plus 2 times the standard deviation (SD) to cover the 95% confidence interval (CI) (Röhrl et al. 2004) (Table 1). 3-dimensional (3D) wear was measured as the vectorial resultant of all 3 (x-, y-, z-) axes.

Bone mineral density (BMD)

BMD was measured by dual-energy X-ray absorptiometry (DEXA) on a Prodigy scanner (Lunar), with baseline defined by the scan taken postoperatively. Bone remodeling was measured as change in BMD at 6 months, and at 1 and 2 years. During scanning, the patient was placed in a supine position and a foot brace was used to standardize the position. An area from the lower border of the distal sacroiliac joint to an area distal to the tip of the femoral stem was included in the scan. The paint facility was used to exclude non-bony structures.

BMD around the cup was measured according to 3 regions of interest (ROIs) as modified DeLee and Charnley zones, described by Field et al. (2006). When all ROIs had been positioned in 1 patient, they were copied and placed in the same manner in all other scans of the same individual. In the femur, we used Gruen zones 1–7 (Figure 2). We regarded the cement as a constant factor and did not try to exclude it. Double examinations were performed and the patients were asked to stand up; they were then repositioned between the scans to estimate the coefficient of variation (CV) (Table 2). To calculate the CV, we used the formula: CV % = 100 [(δ/√2)/μ], where δ is the SD of the difference in BMD between the double examinations in each individual. μ is the mean of all BMD measurements for each ROI (Wilkinson et al. 2001, Digas et al. 2006).

Table 2. Coefficient of variation (CV) for different ROIs. n = 126 double examinations in ROIs 1–3. CV for Gruen zones 1–7. n = 136 double examinations in zones 1–3 and zones 5–7. n = 130 double examinations in zone 4. DEXA scans were performed at a mean of 7 (4–31) days postoperatively

	ROI			Gruen zone						
	1	2	3	1	2	3	4	5	6	7
CV (%)	2.2	2.7	4.1	1.6	1.4	1.6	1.2	1.6	2.1	2.1

Radiography

Anteroposterior pelvic radiographs and lateral views of the femur were taken postoperatively and at 2 years. These radiographs were studied to see if any of the components were loose and to evaluate lucency. Radiolucency was defined as a lucent line between the cement and bone interface. A radiographically loose cup was defined as complete lucency in the cement/bone interface. M-desk version 3.0 (UmRSA Biomedical) was used by one observer (EL) to calculate the implant position and radiolucency.

Statistics

All data were analyzed using SPSS software version 18. Binary outcomes were analyzed using chi-square test and Fisher's exact test. The Mann-Whitney U test was used to test for differences between the 2 groups. We used the non-parametric Wilcoxon signed-rank test for related samples to test for differences in migration in one group at different times. Based on previous RSA studies (Kärrholm et al. 1997), we chose the sample size as 60 hips, covering for possible drop-outs. Bøe et al. (2011) have calculated that to reveal a difference between 2 groups regarding stem translation of 0.5 mm (SD 0.5), rotation of 0.7° (SD 0.7), and a difference in BMD of 10% (SD 10) with a power of 80% and a significance level of 0.05, a sample size of 17 cases in each group would be appropriate. 95% CIs were calculated. Values of $p < 0.05$ were regarded as statistically significant.

Results

Clinical outcome

Mean pre- and postoperative Harris hip and Oxford hip scores were similar in the 2 groups (Table 3). No infections, dislocations, or nerve injuries were registered. 1 patient with a cementless stem was revised 1 year after the index procedure, due to thigh pain. We had no peroperative femoral fracture in either group. Operating time was 8 min shorter for the RH group ($p = 0.05$) (Table 3).

Wear measurements

Wear for the total material was 0.33 mm (CI: 0.28–0.37) in

Table 3. Descriptive statistics. Values are mean (95% CI of mean). N = 46 hips for those initially operated. Regarding stem sizes, the cemented Spectron stem had sizes 1–5 available whereas the Taperloc stem was used in sizes 7.5, 10, 12.5, 15, and 17.5

	n	Cemented	n	Reverse hybrid	p-value
Age, years	24	68 (65–70)	22	66 (64–68)	
Sex, male/female	24	2/22	22	6/16	
Side operated, right/left	24	11/13	22	12/10	
Cup size, mm	24	52 (51–53)	22	54 (53–55)	
Body mass index	24	26 (25–28)	22	27 (25–29)	
Harris hip score preop.	24	56 (52–60)	19	54 (50–59)	
Harris hip score 2-year	24	97 (96–99)	19	96 (92–99)	
Oxford hip score preop.	24	40 (37–43)	19	39 (35–42)	
Oxford hip score 2-year	24	17 (14–19)	19	19 (14–23)	
Inclination cup, degrees	24	48 (45–51)	19	46 (43–49)	
Offset, mm	24	40 (38–43)	19	38 (36–40)	
T value distance, mm	24	4.3(2.7–5.9)	19	6.4(4.6–8.3)	
Smoker, yes/no	24	5/19	22	4/18	
Operation time, min	24	85 (80–90)	22	77 (72–82)	0.05 [a]
Peroperative bleeding, mL	24	339 (301–376)	22	311 (261–362)	0.3 [a]
Postoperative bleeding, mL	24	336 (268–403)	22	429 (352–506)	0.1 [a]
Total bleeding, mL	24	674 (586–763)	22	740 (662–819)	0.3 [a]
Stem position, varus/neutral/valgus	24	9/14/1	19	4/15/0	0.3 [b]
Stem size (numbers)		1/2/3/4/5 (4/9/8/2/1)		7.5/10/12.5/15/17.5 (1/5/7/8/1)	
Surgeons A–H:					
A	3		6		
B	11		9		
C	1		1		
D	2		0		
E	3		3		
F	1		1		
G	3		1		
H	0		1		

[a] Non-parametric Independent samples Mann Whitney U-test.
[b] Chi-squared

the proximal direction and 0.39 mm (CI: 0.34–0.44) in the 3D direction. The wear in the proximal direction was 0.32 mm (CI: 0.28–0.36) for the cemented group and 0.33 mm (CI: 0.24–0.42) for the RH group. The 3D wear was 0.37 mm (CI: 0.31–0.43) for the cemented group and 0.40 mm (CI: 0.31–0.50) for the RH group (Table 4).

Stability of the cup

Mean rotation of the cup around the x-axis was 0.13° (CI: –0.08 to 0.34) for the cemented group and –0.24° (CI: –0.55 to 0.07) for the RH group (p = 0.03). In the other axes, cup migration was similar in both groups (Table 4).

Stability of the stem

Mean subsidence for the cemented stem was 0.15 mm (CI: 0.04–0.25) and for the cementless stem it was 0.49 mm (CI: 0.08–0.90). Mean retroversion for the cemented stem was 0.55° (CI: 0.25–0.85) and for the cementless stem it was 1.05° (CI: 0.38–1.73) (Table 4, and Figure 2). Comparing the subsidence of the cementless stem from 6 and 12 months up to 2 years we found no statistically significant differences (p = 0.7 and p = 0.2, respectively). In the cemented group, the cone containing a tantalum marker was not stable in 4 cases and it was therefore removed. The resulting high condition numbers were the main reason for excluding these cemented stems.

BMD

Bone remodeling around the cup between baseline (postoperatively) and 2 years was similar in the 2 groups. In Gruen zone 1, we found a bone loss of 18% (CI: 11–24) for the cementless stem as compared to an increase of 1.4% (CI: –3.2 to 5.9) for the cemented stem (p < 0.001). There were no statistically significant differences in the other Gruen zones (Figure 3).

Radiography

There were no radiographically loose cups. Comparing inclination, stem alignment, and radiolucency around the cup and stem, there were no statistically significant differences between the 2 study groups.

Table 4. Wear in mm, including creep. Cup and stem translation in mm and rotation in degrees for the 2 study groups at the 2-year follow-up. The p-values are from the independent samples Mann-Whitney U-test

	Cemented mean (SD)	Reverse hybrid mean (SD)	p-value	Mean difference (95% CI)
Wear, n	17	16		
x	0.00 (0.07)	–0.04 (0.17)	0.9	0.04 (–0.06 to 0.13)
y	0.32 (0.08)	0.33 (0.17)	0.9	–0.00 (–0.10 to 0.09)
z	–0.03 (0.18)	–0.08 (0.15)	0.08	0.05 (–0.07 to 0.16)
3D	0.37 (0.11)	0.40 (0.17)	0.7	–0.04 (–0.14 to 0.07)
Cup translation, n	17	15		
x	–0.05 (0.21)	–0.09 (0.32)	0.9	0.04 (–0.15 to 0.24)
y	0.16 (0.39)	0.11 (0.24)	0.8	0.04 (–0.19 to 0.28)
z	–0.03 (0.21)	0.02 (0.29)	0.4	–0.05 (–0.23 to 0.13)
3D	0.34 (0.38)	0.37 (0.35)	0.9	–0.02 (–0.29 to 0.24)
Cup rotation				
x	0.13 (0.40)	–0.24 (0.56)	0.03	0.37 (0.02 to 0.72)
y	–0.12 (0.27)	–0.03 (0.24)	0.2	–0.09 (–0.28 to 0.09)
z	–0.38 (0.98)	–0.33 (0.80)	0.3	–0.06 (–0.71 to 0.60)
Stem translation, n	17	18		
x	0.05 (0.11)	0.09 (0.18)	0.3	–0.04 (–0.14 to 0.06)
y	–0.15 (0.21)	–0.49 (0.82)	0.6	0.34 (–0.07 to 0.76)
z	–0.24 (0.26)	–0.32 (0.29)	0.5	0.08 (–0.11 to 0.27)
Stem rotation				
x	–0.22 (0.33)	–0.12 (0.35)	0.3	–0.10 (–0.33 to 0.13)
y	0.55 (0.59)	1.05 (1.35)	0.5	–0.51 (–1.23 to 0.22)
z	0.09 (0.24)	–0.08 (0.32)	0.1	0.17 (–0.03 to 0.36)

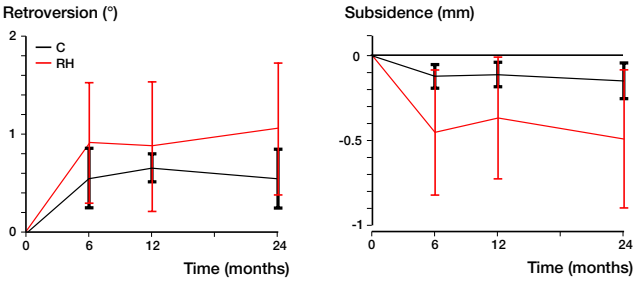

Figure 2. Graphic representation of stem micromovement, retroversion (left panel) and subsidence (right panel), from baseline (postoperatively) to the 2-year follow-up. Mean with 95% CI. n = 18/20, 17/18, and 17/18 for cemented and uncemented stems, respectively, at 6, 12, and 24 months of follow-up. C: cemented; RH: reverse hybrid.

Discussion

We found only minor differences between a reverse hybrid and a cemented THR regarding clinical outcome, wear, prosthesis migration, and change in BMD around the prosthesis. The mean operating time in the RH group was 8 min shorter than for the cemented THR group. In the greater trochanter, the cementless stem gave BMD loss of 18%, as compared to an increase of 1% for the cemented stem.

One strength of this randomized study was the use of high-precision measuring methods. RSA is well established and DEXA has been used in several studies for measuring BMD around hip implants (Wilkinson et al. 2001, Digas et al. 2005, 2006, Field et al. 2006). A weakness of the present study was the missing data for some patients, with a consequent reduction in sample size (Figure 1). Reduction in sample size may have reduced the statistical power, and this could have affected our ability to reveal any differences between the study groups. However, we had enough power to detect a difference in bone remodeling of 10% between the 2 study groups, and in migration of the stems. Other possible confounding factors were the relatively high number of surgeons participating in the study and the fact that there was no systematic templating. The patients were mobilized with weight bearing as tolerated, and RSA was performed after mobilization. There could also be a possible bias in measuring the migration of the uncemented femoral component with the index RSA scan taken after mobilization.

A threshold for clinically important linear wear using UHMWPE has been proposed to be 0.1 mm/year (Dumbleton et al. 2002). We measured the mean difference between study groups regarding wear in the vertical direction (Table 4). A wear difference of 0.1 mm is therefore not within the upper part of the 95% CI, indicating that there was no clinically important differences in wear between the 2 study groups.

All the Reflection cups were made of UHMWPE and sterilized with ethylene oxide. The mean wear, including creep, at the 2-year follow-up was high—both in the proximal direction and in total 3D direction. This finding is in accordance with earlier reports (Digas et al. 2003, Röhrl et al. 2004). Although acceptable according to international standards, the NAR found inferior results for the Reflection cemented all-poly cup in combination with the Spectron EF stem compared to some other prostheses (Espehaug et al. 2009). High wear rates for the Reflection all-poly cemented cup might hypothetically contribute to osteolysis and increased revision rates for the Spectron stem. With longer-term follow-up, one can anticipate the same problem with this cup in RHs as reported for all-cemented THRs.

We found a difference in rotation of the cup around the x-axis (tilt) between the 2 groups. The reason for this finding is uncertain, but the initial position of the stems and cups would probably influence the change around this axis over time.

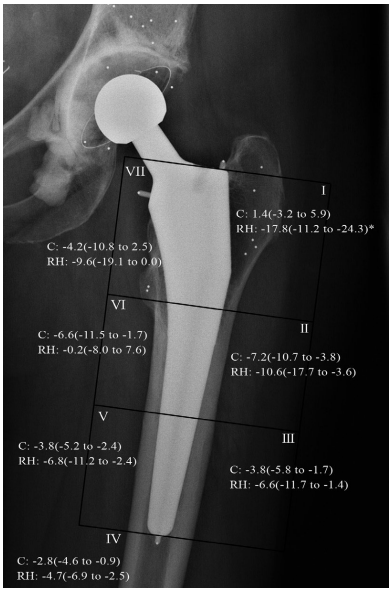

Figure 3. Mean percentage changes in BMD relative to postoperatively in Gruen zones 1–7 at 2 years, with 95% CI of mean. * Statistically significant difference in zone I ($p < 0.001$, independent-samples Mann-Whitney U test). RH: reverse hybrid; C: cemented.

Excellent long-term survival has been documented for HA-coated femoral stems (Hallan et al. 2007). In an editorial, Morscher (1991) raised concerns about HA-coated implants. HA particles may separate from the prosthesis and lead to third body wear (Bloebaum et al. 1994, Morscher et al. 1998). Røkkum et al. (2002) suggested that thick HA coatings may delaminate and that HA coatings may be a reservoir for HA particles. In our study with 2-year follow-up, the magnitude of wear was similar between a proximal HA-coated stem and a cemented stem using the same cup. This finding is in accordance with the work of Önsten et al (1998), who found no difference in wear in a cementless HA-coated cup and a cemented all-polyethylene cup, but the cups used were from two different companies.

Both stems were initially designed as monoblock types and later modified with different offsets and modularity. The Taperloc stem with and without HA has documented good long-term survival (Parvizi et al. 2004, Hallan et al. 2007, McLaughlin and Lee 2010). The monoblock Spectron stem has shown good long-term survival in a randomized study (Garellick et al. 1999). In the present study, we used the modular version with standard offset for both stems. The Spectron EF stem has a grit-blasted proximal area. Concern has been raised about this prosthesis because of early loosening and severe metallosis (Gonzalez et al. 2006). Thien and Kärrholm (2010) investigated this prosthesis with data from the Swedish Arthroplasty Register and found increased revision rates for the smallest Spectron stem, and also with increasing offset. In our study, using standard offset we found that both stems were well fixed up to 2 years. There were no statistically significant differences in migration between the 2 stems, but the cementless stem rotated slightly more in retroversion and migrated more distally than in a previous study (Bøe et al. 2011). In the present study, we used a posterolateral approach while Bøe et al. (2011) used a direct lateral approach. In an RSA study of a cemented stem, Glyn-Jones et al. (2006) found increased rotation in retroversion with the posterolateral approach, compared to the direct lateral approach.

We did not find any continuous subsidence for the cementless stem after 6 months and up to 2 years. An initial subsidence and migration into retroversion, which stabilized later, has been described using RSA for a clinically well-proven cementless stem (Hallan et al. 2007, Campbell et al. 2011). Continuous migration has been associated with inferior results for cemented stems (Kärrholm et al. 1994). The cemented Spectron stem subsided and migrated into retroversion, with comparable results to that described by Kadar et al. (2011). The subsidence did not exceed the limits described by Kärrholm et al. (1994) for cemented stems.

Using the same cup and demonstrating similar wear between the 2 stem designs, our study is ideal for comparison of changes in BMD around the 2 stems. We found higher bone loss in Gruen zone 1 for the Taperloc stem during the 2-year follow-up. The magnitude of this bone loss in Gruen zone 1 is comparable to that found by Bøe et al. (2011) when they investigated the same prosthesis. Comparison of bone remodeling around a cementless stem and a cemented stem might be biased to some degree by the cement. Exclusion of the stem from the cement may be difficult, and regarding the cement as a constant factor may result in higher initial BMD in the different Gruen zones compared to a stem without cement. This would probably influence the percent change in BMD over time. Considering the good long-term survival for the Taperloc stem reported in the literature, it is unlikely that the reduction in BMD is an important clinical finding.

Bone remodeling around the cup was similar between the 2 study groups. We found that we had good precision in each ROI. Many factors can influence precision, and regarding the cement as a constant factor—and not excluding it by using the paint facility—may improve precision. This is supported by studies that have investigated this for the femoral component (Wilkinson et al. 2001, Digas et al. 2005).

The study groups were similar regarding age, sex, and BMI, and all patients operated had primary arthritis. Activity was not measured and this could have led to bias. High activity levels may lead to higher wear rates (Schmalzried et al. 2000).

In summary, we found that a partially HA-coated stem does not cause more wear than a cemented stem, with up to 2 years

of follow-up. The cementless femoral stem had more bone loss in Gruen zone 1 than the cemented stem. Wear of the cemented all-polyethylene Reflection cup was high and comparable to that found in other studies. We did not find major differences between the 2 study groups, but long-term follow-up of the RH concept is necessary.

EL: planning, RSA analysis, DEXA analysis, interpretation of data, statistics, and writing of manuscript. J.D: study idea and study design, planning, interpretation of data, and revision of the manuscript with final approval. SMR: planning, supervision/performance of RSA analysis together with EL, interpretation of data, and revision of manuscript with final approval. LN, FS, ØH: planning, interpretation of data, and revision of manuscript with final approval.

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No competing interests declared.

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Segment choice and cup stability influence wear measurements using radiostereometric analysis
A radiostereometric study comparing wear measured by markers in the polyethylene with markers in the periacetabular bone

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ABSTRACT

Background: Radiostereometry is a well documented method to measure the polyethylene wear after total hip replacements. Wear is measured according to the point motion of the head center in relation to the polyethylene as the reference segment. Increasing head sizes and new cup materials may diminish visibility of markers deteriorating the segment and leading to study drop outs. Alternatively markers in the periacetabular bone may be easier to detect rendering this segment more stable. Our aim was to compare wear measurements against the cup, the acetabuluar bone and a calculated wear estimation including cup migration.
Methods: A prospective randomized controlled trial comparing reverse hybrid with cemented total hip replacement was conducted. 31 patients had tantalum markers in the polyethylene and in the periacetabular bone making it possible to measure wear using both as reference segments. We used a uniplanar radiostereometric technique.
Findings: Wear in the y-axis was overestimated by 53% when markers in the periacetabular bone were used ($P<0.001$). Proximal wear was 0.34 mm (95% CI of mean: 0.29–0.38) when using the polyethylene as the reference and 0.52 mm (95% CI of mean: 0.38–0.65) using the acetabular bone. Migration of the cup seemed to influence the wear calculations, overestimating wear when markers in the periacetabular bone were used as the reference segment.
Interpretation: Wear measured with periacatebular bone markers is influenced by cup migration, overestimating wear measurements. We therefore recommend not using the acetabular bone as the reference segment.

1. Introduction

Radiostereometric analysis (RSA) is the "gold standard" to measure polyethylene wear in total hip replacement (THR). The RSA method has been extensively used in both clinical studies and in vitro studies (Bragdon et al., 2002, 2006; Kärrholm et al., 1997; Onsten et al., 1998; Röhrl et al., 2004). The center of the head is used to measure the penetration into the polyethylene. In cemented cups the polyethylene has to be marked with tantalum balls, defining a rigid body referred to as the cup segment. Penetration of the center of the head into this segment reflects the wear of the polyethylene after the bedding-in phase. Baldursson et al. (1979) first described wear measurements of the polyethylene. He had only four patients and measured wear against markers in the polyethylene and against markers in the acetabular bone. He also estimated the migration of the cup. We have not seen a RSA study compare wear with markers in the bone to markers in the polyethylene. McCalden et al. (2005) reports varying wear rates because some use the polyethylene as the reference segment and others use the periacetabular bone.

RSA is a highly accurate in vivo measuring method but also time consuming and at times cumbersome. Therefore the sample size is kept as low as possible. However this may lead to low study dependability in case of drop outs by insufficiently marked cups, poor quality of radiographs, tantalum balls hiding behind the prosthetic head or radiopaque cup material such as tantalum. Therefore it is tempting to calculate penetration of the femoral head into the acetabular bone as a substitute in cases where the polyethylene segment is not usable.

In the present study, we compared penetration of the head into the polyethylene (Wear-PE: markers in the polyethylene) with penetration of the head into the periacetabular bone (Wear-PB: markers in the periacetabular bone). Additionally, we measured the wear in the y-axis and the effect of vertical migration of the cup (Wear-MIG: wear with

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markers in the periacetabular bone minus the vertical migration of the cup). Our null hypotheses stated that there was no difference between Wear-PE and Wear-PB, with 2 years follow up.

2. Methods

31 patients from a randomized controlled trial (RCT), comparing a reverse hybrid THR and a total cemented THR were included. All patients received a cemented all poly cup through a posterolateral approach in the lateral decubitus position. After reaming and cement hole preparation, the acetabulum was marked with tantalum balls of 1 mm. The acetabular component was then inserted with Palacos® R+G (Heraeus, Hanau, Germany) cement. We used the Reflection* cemented all poly cup (Smith & Nephew, Memphis, Tennessee, USA) in both groups. The cup was marked with 1 mm tantalum markers during surgery. All heads were 28 mm and made of cobalt chrome. We used heads from Smith and Nephew on the cemented Spectron* stem (Smith & Nephew, Memphis, Tennessee, USA) and heads from Biomet® on the uncemented Taperloc® stem (Biomet®,Warsaw, Indiana, USA) because of the different taper dimensions. (*Trademark of Smith & Nephew)

RSA was performed postoperatively and at 6 months, 1 year and 2 years. We used a uniplanar calibration cage number 43. Digital radiographs were taken, using two fixed X-ray tubes with the patient in the supine position. UmRSA® software from RSA Biomedical™, Umeå, Sweden was used. This software enables accurate 3 dimensional measurements from RSA radiographs. Initially cut-off for mean error (ME) was set at 0.30 and condition number at less than 100. While mean error is used to evaluate the stability of markers in a rigid body (segment), the condition number indicates the distribution of markers in a certain segment (Valstar et al., 2005). In one patient the condition number was 137 in configuration 1 at 2 years. This patient is included in the study. Measurement precision was calculated by double examinations and expressed as an absolute mean plus 2 times standard deviation (SD) to cover the 95% confidence interval (CI) (Digas et al., 2003, Röhrl et al., 2004). RSA was performed after a median of 6 (range: 4–20) days post operatively.

Anteroposterior pelvic radiographs were taken post operatively and at 2 years. These radiographs were studied for radiolucency or acetabular loosening. Radiolucency was defined as a lucent line between the cement and bone interface. A radiological loose cup is defined with a complete lucency in the cement/bone interface.

We measured wear and migration in all patients and expressed proximal head penetration in 3 different ways: 1) Wear-PE: Head penetration into the polyethylene; 2) Wear-PB: Head penetration in reference to the periacetabular bone and 3) Wear-MIG: Head penetration in reference to the periacetabular bone minus the individual vertical migration of the cup. 3D wear was calculated in reference to the polyethylene, referred to as 3DwearPE, and to the periacetabular bone, referred to as 3DwearPB. Comparison of the methods was done at 2 years follow up.

The original RCT was conducted in accordance with the Helsinki Declaration and approved by the Regional Ethics Committee, REK Sør-Øst, in Norway (Clinical Trials .gov Identifier: NCT00526539).

2.1. Statistics

We used the non-parametric Wilcoxon signed rank test for related samples to test for differences between the methods. We defined outliers using boxplot from SPSS. Outliers included those defined as outliers in the boxplot with values from 1.5 to 3 interquartile ranges (IQR) from the median value and extreme values defined as values above 3 IQR from the median. Statistical analysis was done with SPSS version 18.0. Significance level was set at 0.05.

3. Results

Vertical Wear-PB was 0.52 mm (95% CI of mean: 0.38–0.65) compared to 0.34 mm (95% CI of mean: 0.29–0.38) for the traditional method (Wear-PE). At 2 years 3DWearPB was calculated to be 0.67 mm (95% CI of mean: 0.51–0.84) compared to 0.38 mm (95% CI of mean: 0.33–0.43) for 3DWearPE (Table 1). Comparing the two methods, during the 2 year follow up we found no statistically significant differences in wear in the x- and z-axes.

Wear-MIG in the vertical was 0.38 mm (95% CI of mean: 0.31–0.44) and $P=0.021$ compared to Wear-PE (Table 1). The Wilcoxon signed rank test comparing total 3D wear for the same data gave also significant statistical difference ($P=0.004$).

Mean cup migration in the y-axis was 0.14 mm (95% CI of mean: 0.02–0.26) with a median value of 0.10 mm (range: −0.26–1.63). The mean total 3D migration of the cup was 0.36 mm (95% CI of mean: 0.23–0.50) with a median of 0.23 mm (range: 0.04–1.67). The mean cup rotation around the z-axis was −0.37 (95% CI of mean: −0.70 to −0.04). Translation in x- and z-axes and rotation around y- and x-axes were close to zero and below the limit of precision (Tables 1 and 2).

Precision for proximal head penetration was 0.1 mm for markers in the polyethylene compared to 0.11 mm for markers in the periacetabular bone. Precision for cup translation in the vertical plane and cup rotation around the out plane axis (z-axis) was 0.11 mm and 0.26 respectively (Table 2).

We identified with boxplot certain outliers with respect to migration among the cups both in translation and rotation. Removing all outliers (n=11) we were able to perform an analyses between Wear-PE and Wear-PB and between Wear-PE and Wear-MIG (n=20). Still we found statistical significant difference between these methods with $P=0.002$ and $P=0.005$ respectively.

In 19 of 31 cups we found different degrees of radiolucency but no cups were radiographically or clinically loose.

4. Discussion

In the present study we found significant statistical differences in wear measurements using the polyethylene and the acetabular bone as reference segments. Proximal wear was overestimated using markers in the periacetabular bone (Wear-PB) compared to markers in the polyethylene (Wear-PE). Correcting for the vertical movement of the cup (Wear-MIG) wear was still overestimated but only by 0.04 mm compared to Wear-PE (P=0.021). Though statistically significant the difference of 0.04 mm is under the limit of the precision (Table 2). It is clear that the penetration of the femoral head is

Table 1
Translation and rotation of the cup. Wear measurements using Wear-PE, Wear-PB and Wear-MIG at 2 years (mean (95% CI of mean)).

Cup migration	Mean	95% CI	
Translation (mm)			
x	−0.08	−0.17–0.02	
y	0.14	0.02–0.26	
z	−0.01	−0.10–0.08	
Rotation (degrees)			
x	−0.04	−0.23–0.15	
y	−0.07	−0.17–0.02	
z	−0.37	−0.70 to −0.04	
Cup 3D migration (mm)	0.36	0.23–0.50	
Wear method and axis	**Mean wear (mm)**	**95% CI**	***P***
Wear-PE y-axis	0.34	0.29–0.38	
Wear-PB y-axis	0.52	0.38–0.65	<0.001*
Wear-MIG y-axis	0.38	0.31–0.44	0.021*
Wear-PE 3D	0.38	0.33–0.43	
Wear-PB 3D	0.67	0.51–0.84	<0.001*

* Wilcoxon signed rank test for related samples.

Table 2
Precision (mean of absolute difference + 2 × SD) for point motion (wear) and movement (translation and rotation around axes of cup) in x, y and z axes. n = 108 double examinations for wear and n = 113 double examinations for cup migration.

	Wear-PE (mm) markers in poly	Wear-PB (mm) markers in bone	Cup translation (mm)	Cup rotation (degrees around axis)
x-axis	0.11	0.15	0.11	0.58
y-axis	0.10	0.11	0.11	0.43
z-axis	0.19	0.35	0.29	0.26

influenced by an unstable cup when the acetabular bone is used as the reference segment. In cases where the cup is stable the penetration distance is the same as using the polyethylene as the reference, theoretically at least.

The all poly cup migrated in both the total 3D and the y-axis at least partly explaining the differences between the two methods. Rotation of the all poly cup around the z-axis, beyond the limit of precision, was also noted. Proximal migration of cemented cups during the first 1–2 years have been reported previously (Onsten et al., 1998; Palm et al., 2007). Therefore we subtracted the proximal cup migration in each individual, but wear was still slightly overestimated. Removing outliers with increased cup migration we were able to perform subanalyses comparing Wear-PE with Wear-PB and Wear-PE with Wear-MIG. Still we found significant differences between these methods. Therefore migration of the cup seemed to influence the wear estimates when we used markers in the acetabular bone as the reference segment and excluding outliers did not improve the results. The importance of our findings is that we proved that wear estimates using markers in the bone as the reference segment will overestimate actual wear in proximal and in total3D direction compared to the traditional RSA-method.

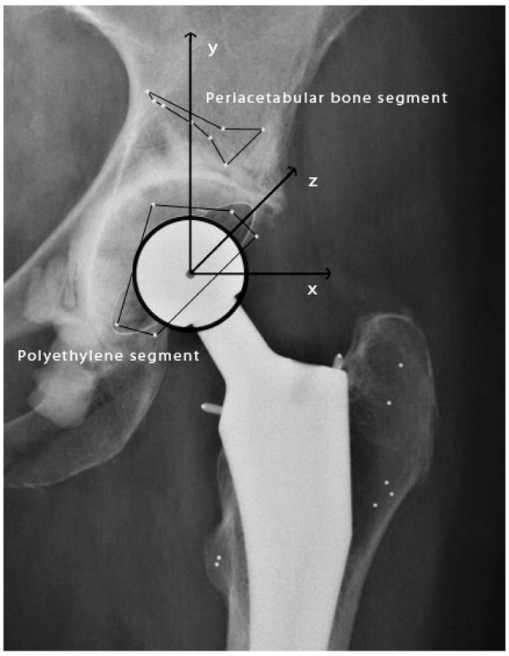

Fig. 1. X-ray of a THR with tantalum markers in the periacetabular bone (periacetabular bone segment) and the cemented cup with tantalum markers (polyethylene segment). In the present study point motion of the center of the head is estimated according to the segments described above.

Edge detection has been used to measure wear in cementless cups. Different software programs have been developed including the Martell Hip Analysis Suite™. With a cementless acetabular cup the Martell method overestimates wear compared to RSA (Bragdon et al., 2006). However, the steady state wear rate between 2 and 5 years indicated comparable results between RSA and Martell in the same study. Our follow up period is only 2 years and therefore we could not calculate the steady state wear rate for longer follow up.

McCalden reports varying wear rates by different research groups using RSA. He explains this by methodological causes such as the use of different reference segments (McCalden et al., 2005). In a case report by Önsten and Mjoberg in 1995 RSA was used to estimate migration of the stem and cup. Although the methodology is not described in detail it seems that they also used RSA to measure wear without marking the all poly cup. It could be that they used the wires in the all poly cup to measure wear (Onsten and Mjöberg, 1995). Baldursson et al. (1979) did wear analysis in 3 cases, relating it to the bone, the all poly socket and migration of the cup. Recently efforts have been made to standardize RSA (Derbyshire et al., 2009; Kärrholm et al., 1997; Valstar et al., 2005). None of these articles discusses using the acetabular bone as the reference segment for wear measurements.

Aspenberg et al. (2008) described the dichotomy of RSA results. They examined vector length and translation along the 3 cardinal axes up to 2 years. When analyzing cup migration individually they found a subgroup of cases with increased migration indicating a possible risk of loosening. We also identified increased migration for some cups. Increased rotation could possibly explain why the center of a rigid body (ie. the cup, which does not necessarily lie in the center of the cup) could change position relative to the center of the head, explaining the difference between the two measuring methods, although correcting for cup migration in the y-axis.

An unstable cup with an asymmetrical center of the rigid body might also hypothetically influence wear measurements using the polyethylene as the reference segment. The center of the cup is not necessarily identical to the center of the segment defined by the markers in the polyethylene. An increase in tilt (rotation around x axis) or inclination (rotation around z axis) of the cup could theoretically move the center of the segment distally and this implies a proximal migration of the femoral head, although in reality there is no proximal penetration into the cup. We believe the RSA software repositions the cup segment, if the cup rotates, to eliminate this false wear. If the cup rotates and the software repositions the cup segment in relation to the calibration cage, this could influence the apparent wear direction. In old conventional UHMWPE this might not be of importance, but in new highly cross-linked polyethylene wear is extremely low. Movement of the cup with a corresponding change of the center of the rigid body in the polyethylene might therefore indirectly affect wear direction measurements. Therefore it is especially important to check for cup stability and relate this to radiological findings on conventional radiographs or use RSA to confirm cup stability.

With its high accuracy and precision RSA is particularly suited for wear studies, exposing very few patients to potential risks from new materials. However, this small sample size is extremely vulnerable to drop outs. Insufficient examinations may be caused by poor marking of the cup, large heads or new cup materials that cover up markers. This may tempt researchers to use the acetabular bone as an alternative reference segment instead of the polyethylene (the traditional method). The present study concludes that wear is overestimated using

periacetabular bone markers. In a clinical setting and performing wear analyses on an individual basis one should be aware of this finding. In a comparative study with the same cup material it might however be possible to use Wear-MIG or Wear-PB to detect differences between groups (for example different head materials or sizes). The overestimation may then be regarded as a methodological error. Of course the results are always weakened by the assumption of a stable cup. We therefore recommend to support the RSA findings with clinical and radiographical evaluation for component loosening. When looking at the absolute value of wear in a single cohort we do not recommend using markers in the periacetabular bone as the reference segment.

5. Conclusion

RSA was used to measure wear with markers in the periacetabular bone as the reference segment. We found statistically significant differences to the traditional method using the polyethylene as the reference segment. Wear was overestimated when using markers in the periacetabular bone. We show that this method is inferior to the traditional method. However, with the assumption of a stable cup and considering the overestimation as a methodological error this alternative method may be used in comparative studies. Our recommendation is to use the traditional RSA method with motion between the head and markers in the polyethylene to measure wear.

EL: Planning, RSA analysis, interpretation of data, statistics, wrote manuscript. S.M.R: Planning, supervised/performed RSA analysis together with E.L, interpretation of data, revising manuscript with final approval. L.N: Planning, interpretation of data, revising manuscript with final approval.

Conflict of interest

None of the authors have any conflict of interest regarding this study.

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Low wear of E-vitamin infused highly cross-linked polyethylene

2 year RSA results from a randomized controlled trial using 32 and 36 mm ceramic heads

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Abstract:

Background: Polyethylene wear has been a major cause of revision of cementless total hip replacements. Highly cross-linked polyethylene has been developed to increase mechanical resistance to wear. However, cross-linking from irradiation of the polyethylene generates free radicals and these can oxidize in vivo and might over time alter the initial mechanical properties. Vitamin-E infused highly cross-linked polyethylene has been developed to reduce the amount of free radicals without compromising the mechanical properties.

Purpose: Measure wear of E vitamin infused highly cross-linked polyethylene and compare wear between two different head sizes.

Methods: In a prospective randomized study between 32 mm and 36 mm alumina heads in 50 hips we analyzed the in vivo wear of the E-poly^{TM} with markerless radiostereometry.

Results: Mean (95% CI) wear for the total material was 0.041 mm (0.015-0.066) in the vertical direction and 0.177 mm (0.155-0.200) in the total 3D direction. After the anticipated period of bedding-in we found no statistically significant differences in wear from three months to two years in vertical and total 3D directions. Although statistical significant differences between 32 and 36 mm heads were found we can not conclude that there are significant clinical important differences in wear comparing these head sizes.

Conclusion: This study shows promising early results with very low wear, also for 36 mm heads, but long term follow-up is necessary to evaluate if this polyethylene will provide low wear and good mechanical properties in the long-term.

Level of evidence: Level II – prospective randomized trial

Introduction

Polyethylene wear has been a major cause of revision of cementless total hip replacements (THR) [15-18]. Therefore, good polyethylene mechanical properties are essential in achieving long-term low revision rates. Cross-linked polyethylene has shown low wear compared with conventional polyethylene with up to 10 years follow-up [11,14,20,27]. Cross-linking from irradiation of the polyethylene generates free radicals and these can react with oxygen in vivo and may over time alter the initial mechanical properties [10]. Reduction of free radicals is therefore desirable. A retrieval study has documented that the liner may be more prone to oxidation in the periphery, than in the central area, and this oxidation has been of some concern regarding rim fractures and potential problems with the locking mechanism of the liner [9]. Heating the polyethylene will reduce the amount of free radicals [21]. Thermal treatment of the polyethylene at or above the melting point is effective in disposing free radicals but may alter its mechanical properties [23], while heating the polyethylene below the melting point may not remove all free radicals [8]**.** A new approach to solve this dilemma is to add an antioxidant in the manufacture of the polyethylene. E-Poly™ (Biomet®) cross-linked polyethylene is irradiated and processed below the melting point. Vitamin-E is added as an antioxidant to reduce the level of free radicals [26]. Finally the polyethylene is sterilized by irradiation. This polyethylene is available for use in THR. Laboratory results have shown promising results, but clinical trials are absent [19,22,24-26]. Dislocation of THR is also a known cause of revision surgery. Large heads address this complication because they allow a theoretically larger range of motion and have a larger jump distance before dislocating [2,6,7]. However, larger heads might lead to increased polyethylene wear [31,32]. Wear resistant polyethylene, even with large heads, may provide a stable hip with good long-term survival. The purpose of this study was to evaluate the wear of E-Poly™ in vivo and to examine whether there is difference in wear between 32 and 36 mm heads. Our null hypothesis stated

that there is no difference between 32 and 36 mm heads regarding the linear wear of the polyethylene.

Patients and methods:

In a prospective randomized study we analyzed the wear of E-Poly™ (Biomet) cross-linked polyethylene high-wall liner with a Biolox® delta ceramic head (Manufactured by Ceramtec for DePuy) with 32 or 36 mm diameters. A cementless Exceed™ ABT (Biomet) shell and a Corail® (DePuy) cementless femoral stem were used in all patients.

50 hips (49 patients aged 50 – 65 years, 35 women) were randomized by a nurse, using sealed envelopes to receive either a 32 or 36 mm head, and included for Radiostereometric analysis (RSA) (Figure 1). Block-randomization of 10 cases was performed during the operation, after reaming the acetabulum. A nurse Inclusion criteria was primary osteoarthritis, without structural abnormality. The operations were performed using the postero-lateral approach. All patients were mobilized the first postoperative day with weight bearing as tolerated. We used Harris and Oxford hip scores preoperatively, and at two years follow-up. The English version of the UCLA (University of California Los Angeles) score was used at 2 years follow-up to compare the two groups regarding activity [33]. All patients filled out the form and were able to ask if something was not understandable.

The Corail® cementless stem is made of Ti6Al4V and is fully coated with an approximately 155 μm thick hydroxyapatite (HA) coating and has a taper dimension of 12/14. We reamed until primary stability, and inserted the prosthesis with the same size as the last reamer. The Exceed™ABT shell used in the study is made of Ti6A14V, had a porous coating with a rim flare and was inserted after under-reaming by 1-2 mm. The porous coating was without HA.

We used the Exceed™ ABT shell with sealed screw holes and the apical hole used to seat the shell into the acetabulum was supplied with a blanking screw. We decided to use a minimum polyethylene thickness of 5 mm. With that minimum thickness of polyethylene, outer diameters of the shell of 50 and 52 mm could only fit liners for 32 mm heads. With an outer diameter of 54 mm or more, the liner could accommodate both 32 and 36 mm heads.

To detect a wear difference of 0.1 mm (SD 0.1) we calculated that 17 patients had to be included to achieve a power of 80 % with alfa 0.05. In case of possible drop outs, we planned to include 50 patients.

All patients were operated on at Lovisenberg Deaconal Hospital in the period from January 2009 to February 2010. The study was conducted in accordance with the Helsinki Declaration and approved by the regional ethics committee (REK) Sør-Øst, in Norway. (Clinical Trials.gov Identifier: NCT00804388). All patients gave Informed Consent to participate in the study.

RSA

Markerless RSA was performed postoperatively (Mean 4 days range: 1-7) and at 3 months, 1 year and 2 years. We used a uniplanar calibration cage number 43 (RSA Biomedical™, Umeå, Sweden). Radiographs were taken using a combination of one fixed and one mobile x-ray tube. Patients were placed in the supine position. The center of the head was used to calculate the migration in relation to the polyethylene with respect to the outer border of the shell [4]. We performed analysis with UmRSA® digital measure 6.0 (RSA Biomedical™, Umeå, Sweden). Cut-off for mean error (ME) was set to 0.30 and condition number should be lower than 100. Measurement precision was calculated by 96 double examinations postoperatively

and at 2 years follow-up, and expressed as an absolute mean plus 2 times standard deviation (SD) [28] (Table 1).

Radiology

Anteroposterior pelvic radiographs and lateral views of the femur were taken at 3 months and at 2 years. Postoperative anteroposterior x-ray of the hip was performed to evaluate the prosthesis and bony structures. These radiographs were studied to see if any of the acetabular components were loose and to evaluate lucency. Radiolucency was defined as a lucent line along the implant and bone interface. A radiologically loose implant was defined by complete lucency in the implant/bone interface. Mdesk™ version 3.0 (UmRSA® Biomedical,Umeå) was used to calculate the implant position and radiolucency on an anteroposterior pelvic radiograph by one observer (EL). We measured the vertical distances from the distal sacroiliac joint, and from the tuber line, to the center of the head. The horizontal distance from the line of Kohler to the center of the head, the rotational centre of the head above trochanter major, offset and alignment of the stem were also calculated. Inclination was estimated with reference to the horizontal tuber line.

Statistical methods

All data were analyzed using the statistical software package SPSS inc. version 18 (SPSS Inc., Chicago,IL,USA). Binary outcomes were analyzed using Fishers Exact test. We used the non parametric Independent samples Mann Whitney U test to test for differences between the two groups. Wilcoxon test for related samples was used to test for wear change between 3 months and 2 years postoperatively for the total material. The effect size was calculated using an independent sample t-test. P-values less than 0.05 were regarded as statistically significant.

Results:

Patient demographic

Regarding age, gender ratio, body mass index, mean preoperative Harris hip score and Oxford hip score, there were no statistical differences between study groups. There was though a tendency towards more females in the 32 mm group (Table 2). During the study period 2 patients died (one of an unrelated cause and one of an unknown cause) and one patient could not be measured due to the quality of the RSA radiographs. 3 patients were randomized to 36 mm heads but got a shell that could not accommodate this size. They were therefore excluded (Figure 1). 1 patient with a 36 mm head experienced 2 traumatic dislocations. During closed reduction the hip was found to be stable. 1 patient had an intraoperative fissure in the calcar region treated with cerclage. 1 patient was initially satisfied with the THR, but approximately 17 months after the operation the hip became painful. After cytotoxic drug treatment and radiotherapy due to a malignant disease (breast cancer) the patient developed local symptoms of periprosthetic joint infection, confirmed by culturing the joint fluid. The hip is scheduled for a two-stage procedure. No other infections or nerve injuries were identified.

Clinical

At 2 years follow-up, Harris hip score had increased to 96 (95% CI: 92-100) and Oxford hip score had decreased to 14 (95%: CI 13-16) for the 32 mm group compared to 99 (95%: CI 98-100) and 14 (95%: CI 12-15) in the 36 mm group (Table 2). The UCLA score at 2 years did not differ between the 2 study groups (Table 2).

RSA

Mean (95% CI) wear including bedding-in for the total material was 0.041 mm (0.015-0.066) in vertical direction and 0.177 mm (0.155-0.200) in total 3D direction (Figure 2). Mean (95% CI) wear for the total material, estimated after 3 months and up to 2 years follow-up, in vertical and total 3D direction was 0.022 mm (-0.004-0.047, p=0.052) and -0.007 mm (-0.043-0.029, p=0.94) respectively. The mean (95% CI) annual total material wear rate in vertical and total 3D directions, from 12 to 24 months, was 0.030 mm (0.002-0.058) and 0.015 mm (-0.018-0.047) respectively. Mean (95% CI) wear including bedding-in in the total 3D direction comparing 32 and 36 mm heads was 0.195 mm (0.166-0.223) and 0.158 mm (0.121-0.195) respectively (p=0.045). In the vertical direction no difference in wear between 32 and 36 mm heads was found. (Figure 3,Table 3).

Radiology

The groups were comparable regarding implant position. Though statistically significant, the mean horizontal distance from the line of Kohler was just 2.3 mm greater for the 36 mm group compared to the 32 mm group. All implants seemed to be osteointegrated and well-fixed radiographically. Mean inclination of the cup was 41 and 42 degrees for the 32 mm and the 36 mm group respectively (Table 2), and we observed that gaps between the shell and bone identified postoperatively, gradually filled out during the study period.

Discussion:

In this study we found a non-detectable wear rate, after the period of bedding-in, in the vertical and total 3D directions at 2 years follow-up. No statistical significant difference in wear for total material from 3 months and up to 2 years was found. This indicates that most of the wear measured is the effect of bedding in during the first 3 months postoperatively. No difference in wear in the vertical direction between 32 and 36 mm Biolox® delta ceramic

heads articulating with E-poly™ liner could be found. Both the stem and the acetabular shell seemed to be well fixed. The concept using E-poly™ liner articulating with delta ceramic heads shows promising early results.

The study was a prospective randomized study using markerless radiostereometry. This measuring method has been found to be accurate [4,5]. The sample size with exclusion of some patients was within the calculated number,

The study has some limitations. The precision of markerless RSA in the present study was somewhat poorer than Børlin et al. [4] found. One reason for this may be the marking of the Exceed™ABT shell. This cup has a rim flare and pegs to secure rotation of the liner. The actual cup opening was in some cases difficult to detect because of the pegs. Børlin et al. [4] used the Reflection shell (Smith & Nephew, Memphis, Tennesee, USA) without a rim flare and pegs. The outline of the delta ceramic head was well defined, but we do not know if this head is more difficult to mark precisely than a head of cobolt chrome. In addition, we do not know if a 32 mm head is more difficult to mark with RSA than a 36 mm head. All these factors could influence precision. Small differences between study groups should be interpreted with caution, and the actual wear values should be compared to the clinical relevance. The small, yet statistically significant difference of wear at 2 years in the total 3D direction between study groups is difficult to explain but could be influenced by the factors aforementioned. In this context it is important to emphasize that the wear measurements were below the estimated threshold of precision in all 3 cardinal axes and our sample size calculation was based on a precision of 0.1 mm in vertical direction. Wear threshold regarding UHMWPE has been proposed to be 0.1 mm/y [13]. Regarding highly cross-linked polyethylene we have not seen any suggestions regarding clinical important wear. Without

knowing the wear threshold for highly cross-linked polyethylene it is difficult to conclude if small differences may be of clinical importance.

We found a slight increase in wear estimates concerning the total 3D direction during the initial 3 months. After 3 months and up to 2 years we did not find any increase in wear in the total 3D direction. This increase could be the effect of the bedding-in (plastic deformation or creep), seating of the liner into the metal shell, or tissue or blood interpositioned between the head and the liner. The bedding in seemed to be less for 36 mm heads (Figure 3). This may be one explanation why there is a small difference between 32 and 36 mm heads at 2 years follow up. The mean difference is also at the level of the accuracy of markerless RSA and included also zero within the 95% CI (Table 3)

The 2 study groups had similar demographic data and activity according to UCLA score (Table 2). Activity has been shown to be an important factor contributing to wear in THRs [29]. To evaluate activity we used the English version of the UCLA score [33]. Using an English form on a Norwegian cohort of patients could be a bias and optimally we would have used a validated form in Norwegian.

Highly cross-linked polyethylene has been used systematically since the late 1990´s [20]. Several studies have documented low wear rates compared with conventional ultra high molecular weight polyethylene (UHMWPE) and clinical results have been good so far [11,14,20,27]. An extensive review published by Kurtz et al. [20] has found less wear and less osteolysis for first generation highly cross-linked polyethylene compared to conventional UHMWPE. Randomized trials with E-vitamin infused highly cross-linked polyethylene have not been reported to date. We found no adverse reactions to the polyethylene. The E-poly™ also showed good resistance to wear. Longer follow-up is necessary to see if the addition of

E-vitamin will protect against oxidation and if the polyethylene will perform equal or better than first generation highly cross-linked polyethylene in the long-term.

Highly cross-linked polyethylene from different manufacturers may have different properties due to different manufacturing processes. In this prospective randomized trial we had no control group to compare the E-poly™ against. The main focus of the study was to measure and compare wear using 32 and 36 mm Biolox® delta ceramic heads. Less long-term wear with ceramic heads, compared to metal heads, articulating with UHMWPE has been reported [12]. Therefore the use of a ceramic head may be beneficial when used in combination with highly cross-linked polyethylene. Long-term follow-up may be needed to reveal possible clinical differences between cobalt chrome heads and ceramic heads articulating with highly cross-linked polyethylene.

Inferior survival of cementless THR compared to cemented THR has been reported [17], and wear and osteolysis have been major problems using conventional UHMWPE [15,16,18]. Highly cross-linked polyethylene with low wear rates and good mechanical properties may increase the longevity of cementless THR. Long-term follow-up is necessary to see if cementless THR will surpass cemented THR using highly cross-linked polyethylene.

Larger heads may reduce dislocation rates with total hip replacements [1,2,6,7]. However, with conventional polyethylene higher revision rates using larger heads have been found [31]. Even with wear resistant polyethylene, we do not know how large heads will affect long-term survival. Therefore caution should be taken in using large heads until proper documentation is available. In the last decade, metal on metal articulations have increased in popularity, both for hip resurfacing and for THR. Increased revision rates for THR with metal on metal articulations have been reported [30]. The same study reported that increased head size

increased the revision rate [30]. Bolland et al. [3] suggested that metal fretting and corrosion in the taper junction may be one factor leading to adverse tissue reactions with the use of large heads on metal on metal articulations in THR. Wear alone is just one factor to regard and caution should be taken in increasing head sizes as this could lead to other problems than wear-related complications.

In summary low wear of an E-vitamin infused highly cross-linked polyethylene, with up to 2 years of follow-up, was found in this randomized controlled trial. No adverse effect of the polyethylene was found. These results look promising and might help to provide stable hips with low wear rates. Long-term data is though needed to substantiate the positive early results with E-vitamin stabilized polyethylene.

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Precision	(mm)
X axis	0.15
Y axis	0.17
Z axis	0.29

Table 1: Precision of n=96 double examinations postoperatively and at 2 years follow-up. During the 2 year examination the patient moved slightly before the second examination was taken.

	n	32 mm	36 mm	p
Age (years)	25/25	62 (60-63)	61 (59-62)	
Male/Female	25/25	4/21	11/14	
Side operated (right/left)	25/25	13/12	14/11	
Body mass index	25/23	28 (26-31)	28 (26-30)	
Harris hip score preop	25/23	56 (51-60)	56 (52-60)	0.72*
Harris hip score 2 year	25/23	96 (92-100)	99 (98-100)	0.53*
Oxford hip score preop	24/24	40 (36-44)	40 (37-43)	0.96*
Oxford hip score 2 year	25/23	14 (13-16)	14 (12-15)	0.72*
Inclination cup (degrees)	25/23	41 (37-46)	42 (40-45)	0.73*
UCLA score at 2 years	25/23	6.6 (6.1-7.1)	6.8 (6.4-7.2)	0.71*

Table 2: Demographic data for the 2 study groups with n=50 for those hips initially operated. Mean (95% CI). Non parametric Mann Whitney U test (p*).

	32 mm heads		36 mm heads			
Wear direction	Mean	SD	Mean	SD	Mean difference (95% CI)	p*
x	-0.007	0.099	-0.029	0.079	0.022 (-0.031-0.075)	0.33
y	0.063	0.089	0.015	0.082	0.047 (-0.003-0.098)	0.06
z	0.075	0.129	0.093	0.101	0.018 (-0.086-0.051)	0.88
Total 3D	0.195	0.069	0.158	0.084	0.037 (-0.008-0.082)	0.045

Table 3: Wear (mm) including bedding in at 2 years follow-up using 32 and 36 mm heads. Non parametric Mann Whitney U test (p*).

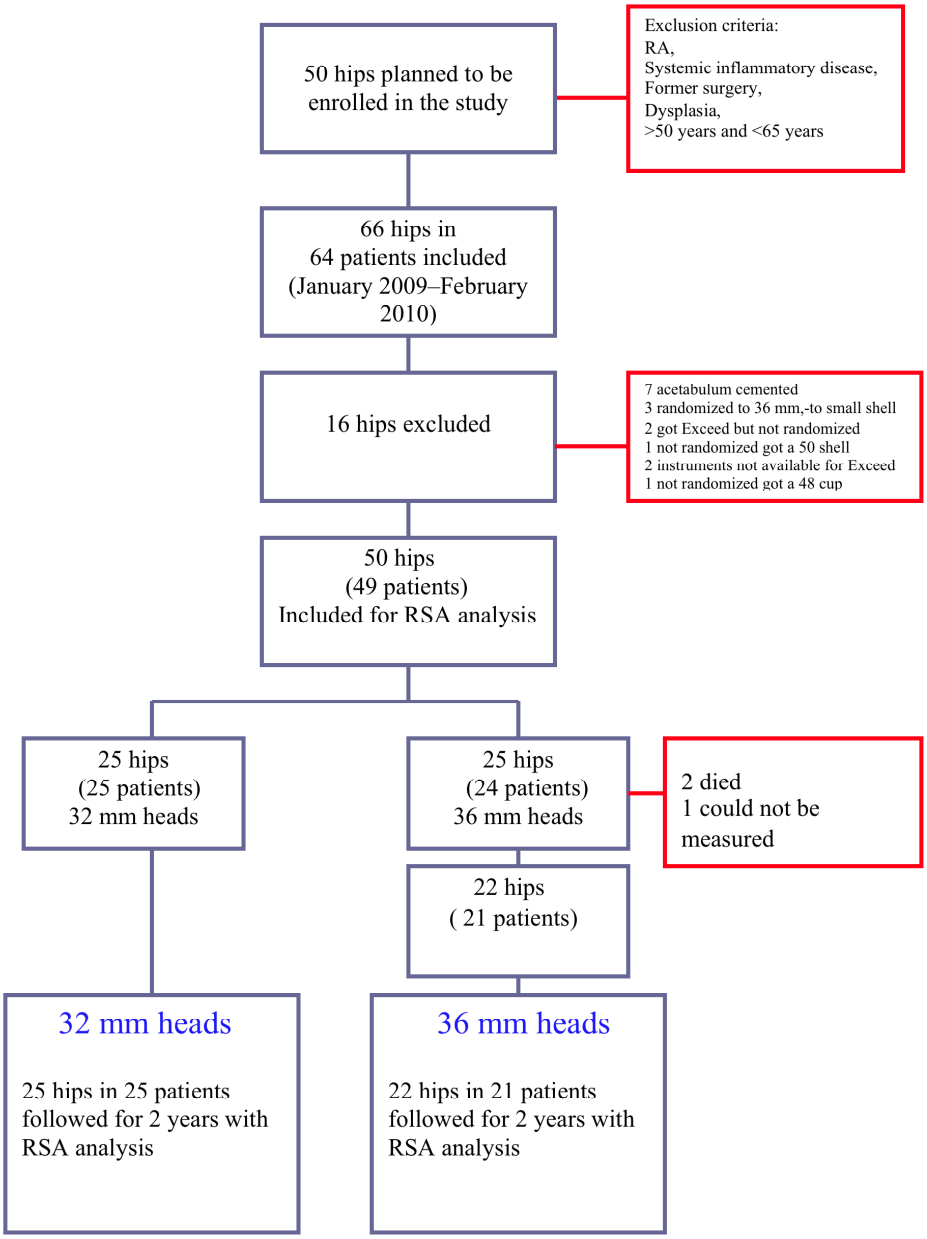

Figure 1: Flow chart of the randomized controlled trial.

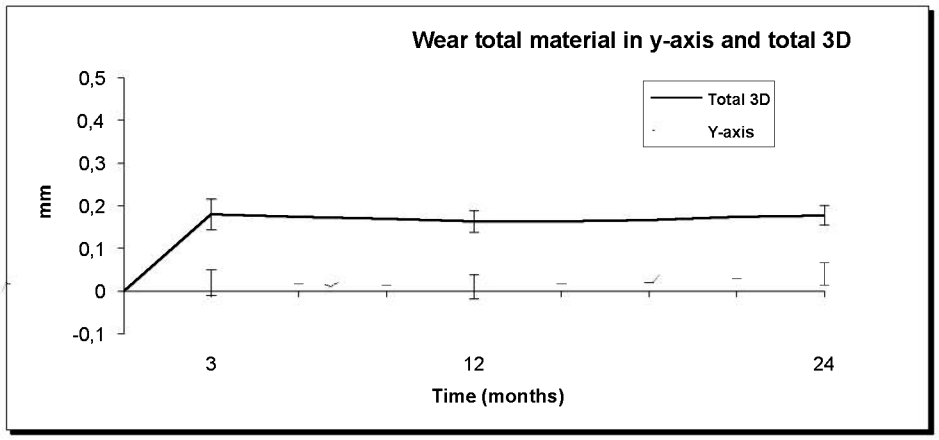

Figure 2 : Graphic presentation of wear for the total material (32 and 36 mm heads) in the vertical (y-axis) and the total 3D direction (Mean (95% CI)). n=48 at 3 months, n=47 at 12 and 24 months.

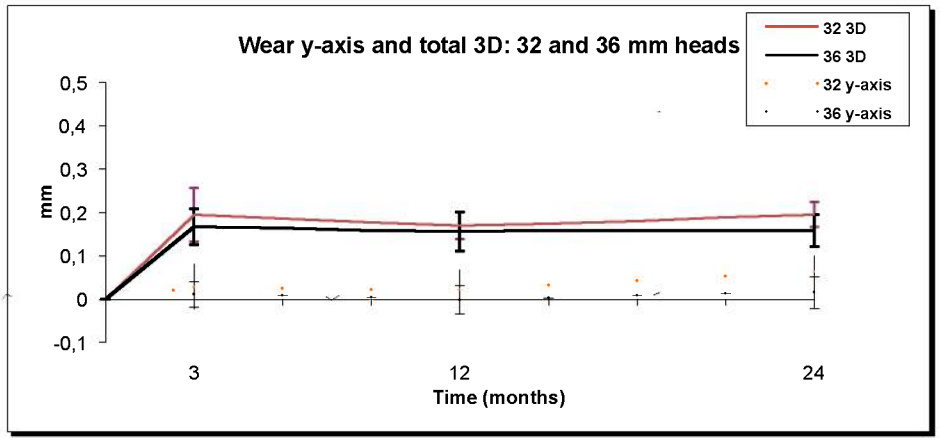

Figure 3: Wear for 32 and 36 mm heads in y-axis and in total 3D (Mean (95% CI)). n=48 at 3 months, n=47 at 12 and 24 months.

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