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Wear and fixation of the acetabular component

In vivo evaluation of different polyethylenes and modes of fixation in total hip arthroplasty

Thesis by
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Front-page illustrates two RSA radiographs with a cemented (above) and a cementless (below) acetabular component on the left hand edge. The main picture shows a phantom with a metal on polyethylene articulation in a cementless cup design.
The radiograph on the back page shows the measuring lines used to evaluate radiolucent zones and cup position.

Tutors
Professor, Kjell G Nilsson, Umeå, and Adelaide, Australia
Professor Bosse Nivbrant, Perth, Australia

Public defense, Betula hall
Umeå April 29th 2004, 1.00 p.m.
Faculty opponent: Professor Lars Nordsletten
Oslo, Norway

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PRINCIPIIS OBSTA!
SERO MEDICINA PARATUR,
CUM MALA PER LONGAS CONVALUERE MORAS.

WEHRE DEN ANFÄNGEN!
ZU SPÄT WIRD DIE MEDIZIN BEREITET,
WENN DIE KRANKHEIT SICH DURCH LANGEN AUFSCHUB BEREITS VERSCHLIMMERT HAT.

VAR UPPMÄRKSAM FRÅN BÖRJAN!
FÖR SENT GES MEDICINEN,
NÄR SJUKDOMEN GENOM LÅNG FÖRDRÖJNING HAR HUNNIT FÖRSÄMRAS.

BE AWARE AT THE BEGINNING!
TOO LATE THE REMEDY IS ADMINISTERED,
WHEN THE DISEASE HAS AGGRAVATED OVER LONG TIME.

PUBLIUS OVIDIUS NASO

Content

Abstract

Wear and fixation of the acetabular component

In vivo evaluation of different polyethylenes and modes of fixation in total hip arthroplasty

Stephan Maximilian Röhrl

Polyethylene wear and micromotion of the implant play an important role in the multifactorial etiology of osteolysis leading to aseptic loosening of acetabular components. Despite excellent results in primary total hip arthroplasty in a 10-15 year perspective there are still unsolved problems. The weakest link is the longevity of the acetabular component. Young and active patients have a clearly worse outcome than older patients. Consequences of polyethylene wear and ways to reduce wear have therefore been in focus during recent years. *In vivo* measurements of wear and stability of implants require methods with high precision in order to detect early significant differences. Radiostereometry (RSA) has high precision and accuracy and is, therefore, the golden standard in such measurements.
RSA was used to record the efficacy of fixation of cemented and uncemented cups. The amount of wear of old and newly designed polyethylenes (PE) was related to cup stability and radiological and clinical measures of outcome.

Study 1: 201 acetabular components with different means of sterilization were analyzed for wear in a multi-center study. Highest wear was found in cups sterilized with ethyleneoxid (EtO) with uncemented cups showing higher wear than cemented. Cups sterilized by γ-irrdiation in air or in inert atmosphere displayed lower wear with no differences between cemented and uncemented fixation.
Study 2: Wear of three different polyethylenes was studied in fifty consecutive cups up to three years. Group one received conventional PE γ-sterilized in air; Group two received moderately cross-linked heat stabilized PE; and Group three received highly cross-linked PE. There was no difference in wear between conventional and moderately cross-linked PE. Highly cross-linked PE displayed 85% reduction in wear compared to the other groups. No negative effects radiographically or clinically could be found between the different PE:s.
Study 3: Eighty seven uncemented cups were randomized to four modes of fixation: press-fit only, or press-fit augmented with screws, pegs, or HA-coating. At five years equally stable groups indicate that augmentation is not needed for primary stability of press-fit cups. However, sealed and HA coated cups displayed a better interface, with HA cups having a tendency of increased stability. Cups with screws and pegs had more radiolucent lines and osteolytic lesions. The annual wear rate of the EtO sterilized polyethylene liners was high (0.2 mm) but did not differ between the groups
Study 4: Fourty five cementless porous-coated Harris Galante cups type I and eighteen type II were consecutively inserted with line-to-line technique in young patients. After a mean of twelve years four PE liners together with the femoral stem had been revised because of osteolysis. RSA measurements revealed stable metal sockets but instability of the PE inserts within the metal shell. Fifty-five percent of the cups showed osteolytic lesions. Radiolucent lines were visible in twenty-five cups but only tvelve percent of the interface. Annual wear was low (0.09 mm) despite the use of thirty-two mm femoral heads.

This study showed that cementless cups inserted with pressfit technique do not need additional augmentation. Screws and pegs increase the risk for radiolucencies and osteolytic lesions but are helpful tools in cases where primary stability is jeopardized. In the second decade clinically silent osteolysis is common for the porous coated Harris Galante cup with unsealed screw holes. The locking mechanism of the PE liner in this cup is unsatisfactory and an increase of liner dissociations is expected.
EtO sterilized PE displayed high *in vivo* wear and we do not recommend its continued use but close monitoring of patients with earlier inserted EtO sterilized implants. The substantially reduced wear in cemented highly cross-linked PE cups without any negative *in vivo* trade-offs might have a substantial impact on choice of material and operating technique in the near future. However, we still recommend its restrained use in controlled series until longer follow up data is available. Nevertheless, the short term *in vivo* results of modern highly cross-linked PE look promising and might improve the outcome of cemented and uncemented hip arthroplasties by reducing complications and revisions.

Keywords: Total hip arthroplasty, acetabular component, wear, fixation, osteolysis, RSA

Abbreviations and definitions

BMD	Bone Mineral Density
CISM	Cold Irradiated Subsequent Melt
CIAN	Cold Irradiated Annealed Non-Melt
CMM	Coordinate Measuring Machine
CoCr	Cobalt Chrome
CTFE	Chloro-triflouro Ethylene
DEXA	Dual-Energy X-ray Absorptiometry
EtO	Ethylene Oxide
HA	Hydroxyapatite
HCLPE	Highly Cross-Linked Polyethylene
HHS	Harris Hip Score
HDE	High Density Polyethylene
PE	Polyethylene
PMMA	Poly-Methylmethacrylate
PTFE	Polytetrafluoroethylene
Rigid body	In RSA number of markers forming a segment corresponding to either part of the body or the object of interest
RLL	Radiolucent Line
RSA	Radiostereometric Analysis
RCT	Randomized Controlled Trial
THR	Total Hip Replacement
TKR	Total Knee Replacement
UCLPE	Ultra Cross Linked Polyethylene
UHMWPE	Ultra High Molecular Weight Polyethylene
WIAM	Warm Irradiated Adiabatic Melting
WISM	Warm Irradiated Subsequent Melt
ZrO	Zirkonium Oxide

Original papers

1
Digas G, Thanner J, Nivbrant B, Röhrl S M, Ström H, Kärrholm J
Increased early femoral head penetration using ethylene oxide sterilized polyethylene
Acta Orthop Scand, 74, Vol 5/2003, 531-41

2
Röhrl S M, Nivbrant B, Hewitt B, Li M
***In vivo* wear and migration of highly cross-linked polyethylene cups. A RSA study of 50 hips**
Journal of Arthroplasty, October 2003, in press

3
Röhrl S M, Nivbrant B, Ström H, Nilsson KG
Effect of cup augmentation on stability, wear and osteolysis – a 5 year follow-up study with RSA,
Submitted, Journal of Arthroplasty, November 2003

4
Röhrl S M, Nivbrant B, Nilsson KG, Snorrason F, Kärrholm J
Porous coated cups fixed with screws.
55 hips with clinical and 23 with radiostereometric 12 years follow-up
Submitted, Acta Orthopaedica Scandinavica, April 2004

Thesis at a glance

The general purpose of this investigation was to examine the effect of different means of fixation (papers 2, 3 and 4) and different means of polyethylene treatment (papers 1, 2, 3 and 4) of the acetabular component in THA on the stability, wear and biological bone reaction.

Paper 1

Question: Does ethylene oxide sterilized PE decrease wear in cemented and cementless cups?

Material & Methods: Thirty-seven cemented and 69 cementless cups were operated with ethylene sterilized PE. Each group had a control group of similar size with conventional PE γ-sterilized with 2,5 Mrad in either air or nitrogen. The patients were followed clinically, with conventional radiography and with RSA up to 2 years. The study is a meta analysis comprising 5 prospective studies in Gothenburg, Uppsala, and Umeå.

Results & Conclusions: At 2 years cups with PE sterilized in EtO and young patients showed increased proximal and 3D penetration. This raises concerns about long term problems especially in younger patients.

Paper 2

Question: How does highly cross-linked PE perform clinically with regard to wear and stability?

Material & Methods: Fifty consecutive cemented cups were separated into three groups. Group 1 received all-poly cups sterilized with γ-irradiation in air (control), group 2 heat stabilized low cross-linked PE and group 3 highly cross-linked PE with 7.5 Mrad and submelt stabilization. Group one and two were followed to 2 years and group 3 up to 3 years clinically and with RSA. Conventional radiography was done at the 2-year follow up.

Results & Conclusions: Highly cross-linked PE had significantly less wear. No adverse clinical or radiological signs could be detected up to three years. This corroborates the results of earlier hip simulator studies and might be a big step towards solving the problem with particle associated osteolysis.

Paper 3:

Question: How do screws, pegs or hydroxyapatite coating effect the stabiliy, wear and development of osteolysis in cementless pressfit cups?

Material & Methods: Eighty-seven cups were randomized to either screws, pegs, hydroxyapatite coating, or insertion by pressfit technique only. All cups received an EtO sterilized PE liner. The patients were followed with RSA, conventional radiography and clinically.

Results & Conclusions: The augmentation of the cups did not influence the stability, but HA showed a tendency to decreased proximal migration and displayed the best interface. Cups with screws or pegs had more radiolucent lines and osteolytic lesions than the other groups. The wear rate of the EtO PE liner was high but did not differ significantly between the groups. Two cups with a peri-operative fracture of the acetabular rim showed large initial migration but stabilized thereafter.

Paper 4

Question: What is the long term survival of cementless cups with conventional (γ-irradiation in air) sterilized PE? Is there development of osteolysis and is the PE liner stable? Are the cups migrating and how much does the PE wear against a ceramic head?

Material & Methods: Sixty-three cups of a cementless hemispherical design with two different liner locking mechanisms were followed for a mean of 12 years with RSA, conventional radiography and clinically.

Results & Conclusions: Osteolysis was a common finding in this cementless acetabular cup. All cups showed high rotations of the liner in the shell although the sockets were stable. The wear was low. We expect an increase of failures by clinical liner dissociation. Patients with detected osteolysis should be closely monitored in order to avoid cup protrusion and gross acetabular defects.

Conclusions

Highly cross-linked PE substantially reduced wear up to 3 years. This looks promising but longer follow up data is necessary before general use is recommended. In contrast, we are concerned about the use of EtO sterilized PE. This material displayed double the wear rate compared with conventional PE. We reject the continued use in cementless implants with thin liner for young patients.

Augmentation by screws or pegs is not necessary for cementless cups inserted in pressfit technique. Both augmentations increase the risk for osteolysis but are a reliable salvage procedure in patients with compromised bone stock. Porous coated sockets show excellent stability but the PE liners are unstable with the metallic shell. They increase the risk for implant failure by liner dissociation and wear. We recommend a close follow up for those patients in the second decade after surgery.

Introduction

Hip arthroplasty is one of the most successful surgical interventions of today. After over a century of intensive research and clinical experience the benefits of hip arthroplasty are impressive. It restores function to almost normal, relieves pain over a long time period and corrects deformity immediately. Worldwide, millions of people suffering from hip diseases, mainly osteoarthrosis, have been helped so far. The increasing life expectancy and activity in the population will propel even further the need and expectations today's surgeons will have to face and live up to.

Still, positive results over the years have not been granted for all designs. Some designs have vanished from the market after a few years of uncontrolled surgical practice. As a consequence the number of patients to present with loose implants has increased because the time interval expanded between early revisions and late failures, leaving many patients with unprecedented and unsolved problems and even more severe - with a loose implant.

Nevertheless, lasting therapy for hip osteoarthrosis is feasible and predictable for patients over 70 years of age as surgery can achieve a survival rate of almost 100 % at 10 years, with satisfying results up to 20 years or more (for some designs). This changed the primary focus from where a hip replacement was regarded to be a solution only for the less active elderly patient. Now, the challenge lies in providing remedy for active young patients with hip disease.

Nowadays, two basically different approaches exist to implant fixation: To insert the implant with or without bone cement. On the basis of historical reasons, cemented implants are still unsurpassed because of longer follow-up and good reproducible results. Cementless implants, striving towards biological fixation, are still to prove their lasting success, as early solutions have ended in failures and revisions. Lack of implant stability and wear have emerged as the main factors threatening a long implant survival for the modern hip arthroplasty. Both factors interact and may finally lead to clinical loosening of the implant, with the acetabular component more prone to loosening than the femoral stem. Therefore, the main interest today is to address the acetabular component.

The aim of this study is to investigate the stability, wear and biological bone reaction of conventional and newly developed acetabular components in THA using high-resolution methods.

History and late facts about hip prostheses

The beginning

Revolutionary advances in medicine during the nineteenth century enabled the treatment of patients on a reproducible basis. The development of anesthesia during surgery by William Morton 1846 at the Boston Medical Center, USA, and antiseptic by Joseph Lister 1860 in Glasgow, Scotland, were prerequisites for surgeons to start treatment of destroyed joints, mainly by infections such as tuberculosis. Another important step for the understanding of the function of the skeletal system was the discovery of x-rays by Wilhelm Konrad Röntgen 1895 in Würzburg, Germany. It was during the same time

period that Themistocles Gluck, 1891, experimented with prostheses of ivory in animals and humans in Berlin, Germany. Although the results were not satisfying and most prostheses had to be revised shortly after implantation because of difficulties in eradicating infection, the idea of the artificial joint was tempting to many surgeons.

Besides arthrodesis, the idea of interpositioning either animal tissue such as bladder from pigs or parts of the human fascia lata as a sliding membrane between rounded bones became popular in the early twentieth century. It was not before 1939, however, that Smith-Pedersen partly succeeded with his "mold-arthroplasy" made of Vitallium. A molded cup was interpositioned between the femoral head and acetabulum, the surfaces of which had been smoothed by hand-reaming. However, despite good early results the long-term survival was discouraging (Law 1962). At about the same time the Judet brothers developed a prosthesis made of polymethylmethacrylate, similar to the bone cement of today and that was inserted with a stem into the femoral neck (Judet and Judet, 1952) whereas the acetabulum was untouched. In 1938, Philipp Whiles was the first to implant a matching femoral and acetabular component made of stainless steel (Wiles, 1958) in London, England. The cup was screwed into the acetabulum and the stem secured in the femur with bolts. McKee and Watson-Farrar picked up this idea and started using a metal on metal articulation in a ball and socket type prosthesis (McKee and Watson-Farrar, 1966). Fixation was achieved by screws but the use of the implant was discontinued because of loosening rates similar to former designs. Another metal prosthesis was used by Austin Moore who developed the first intramedullary stem with a metal head (Moore, 1957). The stem achieved good results and was popular for a long time, used mainly for patients with femoral neck fractures (Jadhav et al., 1996). In the early fifties Haboush (Haboush, 1953) experimented with dental cement to improve fixation of implants but did not succeed in a lasting success. All these prostheses had in common the aim to imitate anatomical structures in size and shape resulting in large diameters of the implants and bearing surfaces (38-44 mm). Hence, after the risk of infection had decreased, the main problems encountered in these designs were fixation and wear.

The start of modern total hip arthroplasty

It was John Charnley who changed the odds in total hip arthroplasty. His outstanding intellectual achievement was to reduce the size of the articulating surfaces causing less wear and reducing the frictional torques at the implant interface. He introduced the "low friction arthroplasty" – a cemented metal stem prosthesis with a cemented polyethylene acetabular cup (Charnley, 1960, Figure 1). A few years later, as infection still jeopardized his surgical results, he developed a sterile air operating theater enclosure (Charnley, 1964). Although his technique spread fast in the western countries, he emphasized the importance of his surgical technique requiring every surgeon to be trained by himself.

"The total hip prosthesis which I call 'low friction arthroplasty,' in which a plastic socket is an integral part of the design, is being released (November 1966) under pressure from surgical colleagues to a restricted number of surgeons (in particular those who have worked with me over six months) prior to considering a general release in January 1968."

- John Charnley, November 1966

The achievements in applying new materials, surgical technique, and ambitious teaching might have had a synergistic effect for the excellent results with his design that are still unsurpassed (Callaghan et al., 1998, D'Lima et al., 1998, Eftekhar, 1987, Older, 2002, Halley and Glassman, 2003, Callaghan et al., 2000, Berry et al., 2002). The Swedish hip register (Malchau et al., 2003) indicates an 80% survival rate after 15 years for cemented implants with revision as the failure end point. Taking into consideration the improvement of cementing technique in the beginning of the 1990s even better results are to be expected with current implants. This is clearly shown by an increased survival rate (95 %) after 10 years of implants operated with the new cementing techniques (Malchau et al., 2003).

Are there still challenges? The problem of choosing the right primay fixation seems to be solved; however, the longer the components are in situ the more important becomes the endurance of the material and the biological reaction. The predictable good results of hip replacement have widened the indications. If Charnley still saw his procedure as a solution exclusively for the elderly, it has now become a feasible option for younger patients suffering from hip disorders. These patients have evolved to become the main challenge as they have markedly worse outcome (Berry et al., 2002, Malchau et al., 2003). In stem fixation, cement has remained the golden standard although the latest national register data reports excellent results for some cementless femoral designs as well. For the acetabular component the situation is different because the survival of cemented cup seems to be less promising. Mainly young and active patients appear to be the crucial group for achieving lasting cup survival (Ballard et al., 1994, Garcia-Cimbrelo et al., 2000, Sullivan et al., 1994, Mulroy et al., 1995).

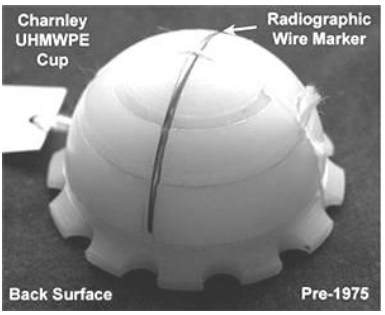

Figure 1: Early Charnley cup. Photo from the Thackray museum in Leeds (from www.uhmwpe.org).

Series of young patients revealed unsatisfactory results for the acetabular component (Chandler et al., 1981). Adverse effects of methyl methacrylate particles (Willert et al., 1974) were deemed responsible. The negative effects of these particles became widely accepted as "cement disease" (Jones and Hungerford, 1987) providing grounds for the interest to search for alternative fixation in the early 1980s (Dorr et al., 1983).

To overcome this drawback, cementless implants were introduced in the 1980s aiming for a "biological" fixation. The first cementless cups had large threads on the outer surface and were screwed into the bone to secure primary stability. The pressure on the edges of the threads was too high causing bone necrosis (Huiskes, 1987) with high migration of the cups as a consequence (Snorrason and Kärrholm, 1990, Gouin et al., 1993, HernandezVaquero et al., 1996b, Fink et al., 2004). However, some of the threaded cups performed better than others (Effenberger et al., 2003). Therefore, third generation threaded cups are still on the market in Europe with some new series showing promising

results up to 10 years (Epinette et al., 2003, Delaunay and Kapandji, 1998) but their use is restricted to specialized centers (Müller et al., 2003).

The first generation of modular porous coated cups experienced unsatisfactory results related to large femoral heads, poor liner socket congruity and locking mechanisms, and thin polyethylene (Astion et al., 1996, Bojescul et al., 2003, Thanner et al., 1999). Many of these problems have been addressed and reduced in the second generation. Locking mechanisms have been changed, the backside of the polyethylene improved, the porous coating changed to pure titanium, and additional augmentation with screws, pegs or HA has been introduced. These cups demonstrate improved fixation, but their modes of failure are osteolysis (Harris, 1995) and liner dislodgement (Berry et al., 1994). As catastrophic failures of the liners are expected to diminish because of modifications of the locking mechanism, osteolysis has emerged to be the single most imminent problem. Implant wear, lack of implant stability and pressure waves of the joint fluid are considered the main causes for osteolysis (Harris, 2001, Aspenberg and van, V, 1998, Mjöberg, 1997). The etiology of osteolysis is probably a combination of all three factors. As socket stability has improved the main strategies to reduce osteolysis are to reduce wear of the bearing and non-bearing surfaces and to reduce access to bone of joint fluid carrying wear particles.

This is aimed for by using cups without holes and additional augmentation, but it is not known whether those cups are as stable as previous designs and Schmalzried hypothesized that the wear particles would gain access to the bone via the periphery of the cups, implying that cups with no holes may still develop osteolysis (Schmalzried et al., 1994). HA coating has been postulated to create a sealing effect around the cup but early studies have shown the HA coating to delaminate from smooth surfaces and the risk for increased wear has halted their general acceptance.

Newer implants and designs, however, show promising short and midterm results (Malchau et al., 2002). These reflections led to the introduction and widespread use of hybrid implants (Harris, 1996) — a combination of a cemented and a cementless component. Cemented femoral stems and cementless cups give excellent mid and long term results (Callaghan et al., 1996, Clohisy and Harris, 1999a, Goldberg et al., 1996, Berger et al., 1996).

Rationale of cup fixation

Cementing techniques evolved from first to currently the third generation cementing technique. Early cementing techniques with reaming of all subchondral bone to a cancellous bed, no bone preparation, and finger-packing of the cement led to an insufficient bone cement interdigitation (Crites et al., 2000,Mulroy, Jr. and Harris, 1990). A fibrous membrane was often formed around the implant. A cause to this finding was thought to be heat developing during the curing of the cement, causing cell damage and thereby implant instability (Toksvig-Larsen et al., 1991, Mjöberg, 1986). The periprosthetic membrane of failed cemented implants resembles histochemically and histologically a synovial membrane with predominantly macrophages and fibroblasts (Goldring et al., 1983, Jiranek et al., 1993, Santavirta et al., 1992). Within these membranes macrophages are

producing proinflammatory cytokines causing bone resorption. Because cement ages, shrinks and becomes brittle with time, this was thought to be unique for cemented implants, but similar membranes have also been found surrounding failed cementless implants.

Advocates for cemented implants emphasize the importance of the quality of cementing technique (Mulroy and Harris, 1997, Smith et al., 1998). Ranawat found that the longevity of the implant is directly related to the depth of the cement penetration into the acetabular bone. This was addressed through improved cementing techniques and has markedly further improved implant survival. A well cemented socket in a patient with osteoarthrosis has a 98% survival at 10 years (Ranawat et al., 1995). Still, the effect of the new cementing techniques has not proven to be as effective for the cups as on the femoral side. Especially in the young, late aseptic loosening after 15 to 20 years is still an unsolved problem and leaves room for innovation.

Cementless cup fixation aims to preserve host bone to allow for ease of revision and, most importantly, to provide lasting fixation and a living interface without cement (Harris and Maloney, 1989). Many different modes of cementless fixation have been clinically tested in patients. Although some designs were associated with good early results, high failure rates were often reported after 5 years, mainly caused by insufficient fixation, progressive socket migration, polyethylene wear and severe bone resorption (Morscher et al., 1982, Wilsonmacdonald et al., 1990). Threaded cups, screwed into the acetabulum, gave high failure rates after the customary primary period of enthusiasm when a new method is introduced (Winter et al., 1992, Mahoney and Dimon, 1990, Snorrason et al., 1989, HernandezVaquero et al., 1996a). Another concept of achieving biological fixation was by bone ingrowth into a rough implant porous surface. Hemispherical cups with a porous surface are now perhaps the most promising cementless cup design (Friedman et al., 1993, Maloney et al., 1999). But we do not yet know the most effective method of primary cup fixation in the young and active patient (Figure 2).

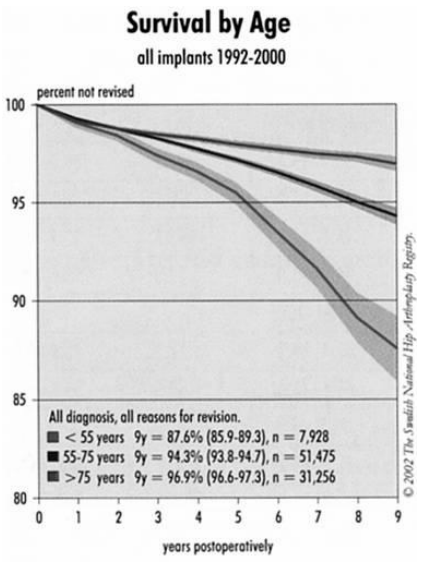

Figure 2: Young patients show decreased survival for hip implants (Swedish hip registry).

One approach is to achieve a line-to-line fit of the implant to the bone by reaming the acetabular bone bed to a diameter as big as the implant. Additional fixation with screws and pegs (spikes) is mandatory to assure primary stability until bone ingrowth has occurred. Additional fixation, however, is not without controversies either. Damage to vessels and nerves by the screws (Keating et al., 1990, Wasielewski et al., 1990, Wasielewski et al., 1992), possible migration of wear particles via screw holes or along pegs and screws

(Schmalzried et al., 1994, Huk et al., 1994), and peripheral opening of the implant bone interface at the edge of the implant predisposing to osteolysis (Lachiewicz et al., 1992) have been documented with these kinds of implants.

Another approach is the press-fit technique. This means the use of 1 - 2 mm oversized implants that are pressed into the prepared acetabular bone. The advantage is a tight rim fit, possibly obtaining a mechanical barrier for wear particles at the entrance of the implant bone interface (sealing effect). It is unclear, however, if press-fit alone will give enough primary stability or whether additional fixation is necessary. Several studies suggest on the basis of cadaveric experiments that sufficient primary stability can be achieved in the absence of additional screws (Kwong et al., 1994, Won et al., 1995). These results are corroborated by good mid term clinical results. A disadvantage with press-fit fixation is the risk of a fracture of the acetabulum at insertion. A cup not more than 2 mm oversized, however, has been considered to be safe (Kim et al., 1995b). Postoperative gaps, often occurring between the apex of the cup and the bottom of the acetabulum, normally disappear after 2 years (Schmalzried et al., 1994). These gaps, however, may be of concern since particles may be pressurized through holes in the cup (Schmalzried et al., 1997). The area that can be reached by joint fluid is called the effective joint space (Schmalzried et al., 1997) and is considered to play a major role in the development of bone resorption (focal osteolysis) around the implant.

To achieve better stability for cementless implants, hydroxyapatite has been sprayed on implants as a coating. Animal studies (Moroni et al., 2001, Øvergaard et al., 1997, Lind et al., 1999, Søballe, 1993, Geesink et al., 1987) have shown a osteoconductive effect of HA, and clinical short and midterm studies have supported the stabilizing effect of the HA coating (Nivbrant et al., 1996, Önsten et al., 1996, Moilanen et al., 1996, Thanner, 1999, Tonino et al., 2001, Capello et al., 1998). It is important to emphasize that HA serves only as a better bed for bone ingrowth (osteoconductive) and not as an inductor for increased growth. Most previous studies have examined the effect of the HA on the stability of the femoral component. However, recently the acetabular component has become the object of numerous studies. Rahbek (Rahbek et al., 2000 and 2001) found a positive sealing effect of the HA-coating at the implant bone interface in an animal study but the risk of third body wear from debonded HA particles has so far somewhat hampered the international enthusiasm for HA (Lai et al., 2002, Reikerås and Gunderson, 2002, Bloebaum et al., 1994, Røkkum et al., 1999, Morscher et al., 1998). These two, seemingly opposing, effects of hydroxyapatite (improved fixation/increased wear) divide surgeons of today into supporters and rejecters. Another important question is whether HA prevents or induces the development of periprosthetic osteolysis. Tonino (Tonino et al., 2001) addressed this question in a retrieval study of 6 implants and found no osteolysis and a high degree of bone ingrowth (20-50 %). Røkkum et al., (1999) on the other hand regarded the HA particles responsible for the osteolysis leading to a high failure rate found in his patients.

These studies are hard to compare. General criticism concerns the incoherence of the quality of the HA coating (cup surface, application technique, HA thickness, crystallinity), different femoral head sizes used, improper study designs (no control group) or unconventional modes of cup fixation (Bauer, 1998, Øvergaard and Søballe, 2000).

Different HA coatings lead to different results and for the time being a plasma sprayed HA layer of 50-100 microns is considered to be optimal. However, randomized studies showing the actual efficiency are still of need.

Osteolysis and cup loosening

Osteolysis (bone resorption) first described in association with cemented implants is meanwhile also recognized as the main problem limiting the survival of uncemented acetabular components (Harris, 2001). It may develop in all implants regardless of design and fixation (Figure 3). The predominant causative agent for osteolysis is polyethylene wear particles (Garcia-Cimbrelo and Munuera, 1992, Barrack et al., 1997, Dumbleton et al., 2002) but new interest also arises in fluctuating pressure waves of the joint fluid. (Mallory et al., 2000, Manley et al., 2002, van der Vis et al., 1999, Walter et al., 2004). Probably both mechanisms and their combination contribute to the development of osteolysis.

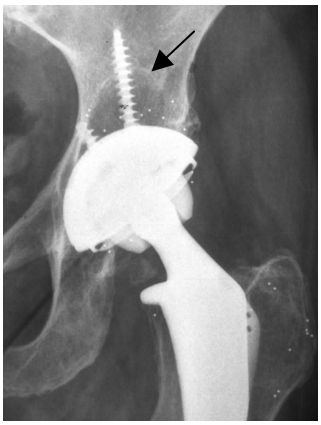

Figure 3: Osteolysis (arrow) in an uncemented design.

Wear particles within the joint fluid are transported within the "effective joint space" (Schmalzried and Callaghan, 1999). The "effective joint space" is defined as all periprosthetic areas accesssible to joint fluid. Within the joint fluid the particles are phagocytized (macrophages, fibroblasts, osteoblasts and osteoclasts) and start an inflammatory process stimulated by increased levels of cytokines such as TNFα, IL-1a, IL-1β, IL-6 and PGE_2 (Bauer, 2002). This stimulates macrophages and fibroblasts to break down bone by enzymes. Osteoclasts seem not to be the main cell type involved in degradation of bone tissue (Bauer, 2002, Eisler, 2003). This complex process of inflammation and bone resorbtion is not yet fully understood. It appears though that differentiation of macrophages to osteoclast-like cells may be activated by either TNFα or by the RANKL-RANK interaction on wear-particle-laden macrophage precursors (Haynes et al., 2001). Besides the inflammatory reaction, joint fluid creates fluctuating pressure waves that can lead to bone resorption (Aspenberg and van, V, 1998, van der Vis et al., 1999, Walter et al., 2004). Both the particles as well as the joint fluid under high pressure alone or in combination play an important role in the development of osteolysis. Which of these factors is the more dominant is not yet quite clear, but a multifactorial genesis with both as a trigger is the most probable.

Stability is another factor that is mandatory for a successful implant. Wear particles may also be generated by scratching between interfaces such as in an unstable implant. Micromotions at the interface may generate particles and at the same time facilitate the spread of these around the implant (Mjöberg, 1989). Therefore, according to this theory, loosening starts due to early insufficient stability or a late loss of fixation caused by daily life activities (Mjöberg, 1997).

Radiographically, osteolysis may appear differently depending on whether the cup has been implanted with or without cement. In cemented implants the radiolucency is linear and usually starts equatorially where cement and bone meet at the interface. This reflects the theory that loosening of cemented implants is of biological nature, triggered by particles in the joint fluid from the implant periphery (Schmalzried et al., 1992). Linear radiolucencies are usually measured in length and width. In most studies radiolucencies are measured if wider than one mm but recent data suggests considering radiolucencies wider than 0.3 mm. (Hultmark et al., 2003). A complete radiolucency on either the AP or lateral view should be regarded as a radiographic failure

In cementless implants radiolucencies have a predominantly expansile pattern starting from the interface and expanding into the cancellous bone. They produce considerably more bone loss than linear radiolucencies but the cups may maintain stability (Zicat et al., 1995). The non ingrown area behind a cup is accessible by joint fluid carrying particles causing bone resorption. It seems obvious that unsealed screw holes would facilitate the spreading of particles, however, this theory was contradicted by Schmalzried who showed a higher number of osteolysis in cups without holes (Schmalzried et al., 1999). The role of unsealed cups in the complex pathogenesis of osteolysis is still controversial. Usually the area of expansile osteolysis is measured on conventional radiographs and the precision increases by the number of projections obtained (Southwell et al., 1999). Because of progress in software programming in recent years it has become possible to evaluate osteolysis by computer tomography. Sophisticated software filter artefacts but their use is still restricted to highly specialized centres and is also a financial question. Stulberg found "silent osteolyses" with a prevalence of 48% for cups evaluated with CT scan (Stulberg et al., 2002). This implies that osteolysis might be more prevalent than is thus being anticipated by conventional radiography.

Osteolytic lesions are miscellaneous in their nature. They may persist unchanged or progress slowly over the years. Few studies exist that have really followed the evolution of osteolysis in a standardized way (Hultmark et al., 2003, Stulberg et al., 2002) and the optimal screening for patients after surgery is still of debate.

Treatment of osteolysis in cemented cups is revision of the acetabular component because the osteolysis is always associated with implant loosening. In cementless cups the situation is more complicated. Patients might have excessive osteolysis but no symptoms. A close follow up is often the first step but in cases with progressive osteolysis and impending wear-through revision is recommended (Claus et al., 2003). Two types of osteolysis are usually encountered in cementless cups: Type I is osteolysis combined with a liner problem and a stable socket. Type II is osteolysis combined with an unstable socket. The latter is a clear indication for a total cup revision, but in Type I appropriate treatment is of debate, leaving it up to the surgeon to decide whether revision of the liner only or the whole acetabular component is to be performed (Terefenko et al., 2002, Maloney et al., 2001, Mallory et al., 2000, Claus et al., 2003).

Wear

Even in the early years of total joint replacement the importance of wear became obvious (Brown et al., 1977, Mittelmeier, 1975, Charnley and Halley, 1975). Wear is defined as the progressive removal of material from the prosthesis in the form of particulate debris and may occur basically anywhere there is motion. In a normally functioning hip prosthesis the most important location of wear is between the femoral head and the polyethylene of the cup. It is estimated that one million submicron polyethylene particles are released with every single step. A cascade of known and as yet unknown factors influences the complex mechanism of wear. Material parameters such as hardness, surface finish, conformity, femoral head size and patient related factors such as joint pressure, lubrication and physical activity are some of them. Orishimo found in patients with bilateral hip implants of the same design that patient and component factors could account for approximately 60 % of the wear rate. He concluded that other factors also play an important role (Orishimo et al., 2003) in determining the amount of wear.

For a better understanding of wear it is important to distinguish between wear mechanisms, damage and wear modes.

Wear mechanisms are: *adhesive*, *abrasive* and *fatigue* (Figure 4). *Adhesive* wear involves debonding and pulling away particles of surfaces (visualized as sticking together of tiny regions) when they move against each other under load (Schmalzried and Callaghan, 1999). *Abrasive* wear is a mechanical mechanism wherein small sharp asperities on the harder surface cut through a softer surface resulting in removal of material, called two-body abrasive wear. In three-body abrasive wear small particles are trapped in-between and scratch the sliding surfaces. Exceeding the fatigue strength of a material creates *fatigue* wear. After a certain number of loading cycles the material releases particles from the surface. This has been especially destructive in polyethylene inserts in knees prostheses and is called *delamination*. In knees shear stresses ca 1 mm below the surface initiate cracks, breaking off large particles when the crack reaches the surface (Pruitt et al., 1995). Conversely, in hip prostheses the stress occurs very close to the surface causing small wear particles (Shanbhag et al., 1994) and a smooth wear surface. *Pitting* is another fatigue phenomenon

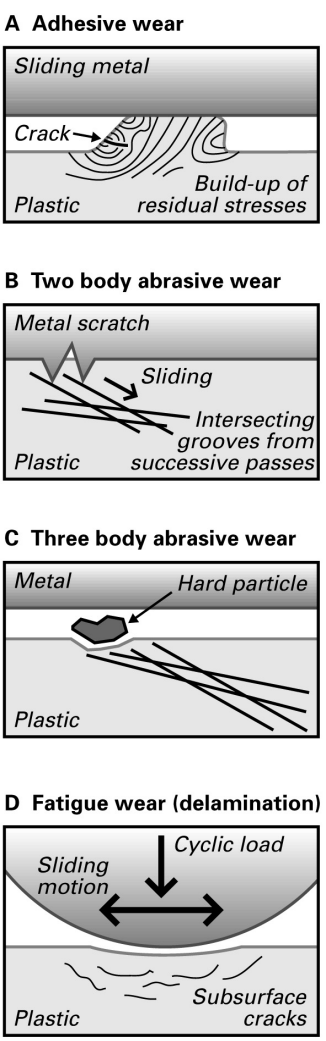

Figure 4: Wear mechanism, adhesive (A), abrasive (B, C) and fatigue (D) (after Chapman, 2001)

which is caused by cracks on the surface and is usually seen locally in older implants. Another cause for wear is called *fretting* which occurs between two surfaces that are intended to be statically fixed together but cause cyclic shear stresses across an interface. Examples are screw heads pressurizing the acetabular shell or the polyethylene insert or the polyethylene insert with the acetabular shell (Huk et al., 1994).

Wear damage is the resultant change in shape or texture of the bearing surfaces, and wear modes are the manner of how the materials are worn against each other. Wear modes are the conditions under which wear occurred. Movement between two materials that are intended for this purpose creates wear that is called *Mode-1* (femoral head and acetabular component). *Mode-2* is the movement of two materials against each other that are not intended to do so, i.e. a femoral head wears against the metal shell in either a dislocated hip or when the polyethylene liner is completely worn. *Mode-3* is the condition of third bodies like cement, bone or wear from other materials (polyethylene, HA, metal) entrapped between two articulating surfaces. The particles scratch the surfaces and can cause extremely high wear rates. *Mode-4* is the motion between two materials that are not intended for motion such as in fretting or impingement of the neck against the socket.

The size of polyethylene particles differs but is predominantly in the submicron range (Campbell et al., 1995). The shape is either fibril-like, rounded submicron granules, beads or longer wider shreds of polymer (McKellop et al., 1995). Size and shape determine the biological reaction. Polyethylene particles induce a significant higher biological reaction than ceramic and metal particles (Warashina et al., 2003).

In the early phase of use, polyethylene takes up loads and deforms. This plastic deformation lasting some months is called creep and does not release particles (Isaac et al., 1996). Charnley (1975) described it as an initial running-in of the bearing, resulting in better conformity, lower contact stresses and a lower wear rate (Bartel et al., 1986, Wroblewski et al., 1996).

All factors contributing to wear are not yet fully understood and especially their *in vivo* interactions are difficult to predict. The multifactorial etiology of wear depends on the properties of the material, characteristics of the surgical procedure and patient factors. Metals and ceramics produce less wear than PE. Even within the group of PE, modifications of the material such as sterilization have been shown to have influence on the wear behaviour (Sychterz et al., 2000). Sakalke found a lateralized implant (i.e. higher offset) to have a beneficial effect on the wear rate whereas Karachalios showed a positive effect of a medialized centre of rotation (Sakalkale et al., 2001, Karachalios et al., 1993). In cementless cups a decrease of polyethylene liner thickness of 1 mm increased wear about 25 % (Jasty et al., 1997) and a thickness of at least 8 mm is nowadays recommended. The amount of wear particles generated by the femoral head is directly proportional to its size (Livermore et al., 1990). The larger the femoral head the more particles generated in spite of the simultaneous decrease in joint area pressure. When moving at a certain angle in the articulation a defined point at the femoral head surface is spinning faster and over a longer distance in cases with a larger head. A 32 mm head creates roughly about 40% more wear particles than a 22 mm head (Callaghan et al., 2003). Implant time in situ is less important.

The more the patient uses his artificial joint the faster it will wear (Schmalzried et al., 2000). Young, active and heavy patients are more prone for wear necessitating revision surgery (Devane et al., 1997).

Assessment of wear and migration

Various methods are available to assess wear in hip implants. Wear can be measured directly in cups such as in retrieval studies (revised or explanted cups of deceased patients), in laboratory experiments, or indirectly on radiographs for *in vivo* assessment.

Retrieved cups or those used in hip simulator studies give the possibility for volumetric wear measurements. This is also called "fluid displacement measurement". The expected amount of fluid displaced is compared to the actual amount of fluid displacement. This measures the 3 dimensional (volumetric) wear of an implant and includes creep. It also enables a visual evaluation of wear damage.

Radiographic methods to measure *in vivo* wear have been developed by many authors. Two of the first more commonly applied methods were developed by Nunn and Livermore. Both methods are simple and use a ruler for measuring of distances. The intra- and interobserver reliability is observer and projection dependent and the methods only detect linear femoral penetration (unidirectional or longitudinal wear). Nunn reports a total error of ± 3 mm mm (Nunn et al., 1989) and Livermore 0.1 mm (Livermore et al., 1990). For higher precision computer assisted methods have been defined. The most commonly used methods are those developed by Devane (Devane and Horne, 1999) and Martell (Martell and Berdia, 1997). The latter has gained more popularity lately and describes an accuracy of 0.08 mm. However, the reported high precision for these methods has been widely debated. In Europe wear measurements according to EBRA are done in some centers and this method has shown superior results compared to other two dimensional methods (Ilchmann et al., 1995). Criticism of those methods is their sensitivity to varying x-ray technique by different personnel and sensitivity to patient positioning (Phillips et al., 2002).

The golden standard for *in vivo* wear measurement is RSA (Ilchmann, 1997). In experimental set-up RSA has an accuracy of 22 µm for proximal femoral head penetration and 55 µm for the resulting 3D vector length (Bragdon et al., 2002). This accuracy cannot be obtained in clinical studies but advances in digital technique and software development yields an accuracy of about 0.1 mm for proximal head penetration and 0.22 mm for the 3D vector length (Digas et al., 2003). All studies included in this paper use radiostereometry as the measuring tool for wear and migration.

Before clinical use, materials for articulation are usually tested for their wear performance in an experimental setting with a hip simulator. Hip simulators use bovine serum as a lubricant and can simulate non-linear motions as they occur in the hip. Non-linear motion generates around 10 – 100 times higher wear rates than linear motion, resulting in a polishing effect.

The polyethylene insert

The modularity of a cementless hemispheric cup includes the easy insertion of the polyethylene liner into the metal shell. A locking mechanism is supposed to secure the liner tightly and safely within the shell, preventing movements between them. Each manufacturer favors its own design of locking mechanism. In the first and second generation modular cups, case reports of liner dissociation and excessive wear in cementless acetabular components pointed out unsatisfactory locking mechanisms (Werle et al., 2002, Gonzalez, V et al., 2001, Louwerse and Heyligers, 1999). It was found that the polyethylene insert could rotate out of the metal shell. Clinically the patient feels a sudden pain followed by a decreased range of motion. Figure 5 shows an example of one of our patients with a dislocated liner. In such cases there is extreme wear at the rim of the polyethylene liner (Figure 8, chapter PE). Some authors discuss extreme wear in combination with material fatigue and a decentralization of the femoral head under load as the cause for overloading and finally breaking the locking mechanism of the liner (Werle et al., 2002, Gonzalez, V et al., 2001). Until the liner dislodges from the shell the patient may be clinically absolutely asymptomatic, therefore not much is known about the prevalence of liner dissociation. Jacobs et al (2002) found a prevalence of around 1 in 1000 in his material but other authors are concerned the number of liner dissociations may be even higher (Neumann and Dorn, 2003).

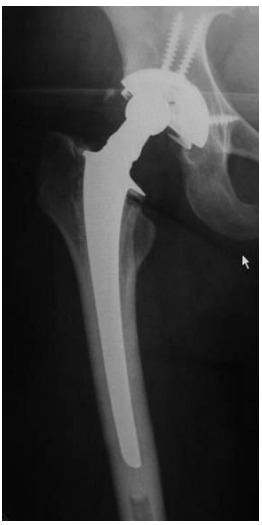

Figure 5: Decentralization of the femoral head suggests either excessive wear or liner dislocation.

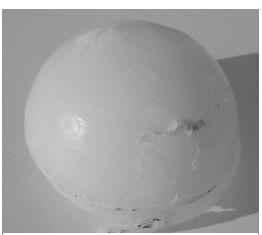

Figure 6: Backside scratch marks on a retrieved PE liner.

Instability of the liner may cause backside wear, classified as Mode-4 (motion between two implants not intended to move). William et al. found clear differences in the performance of different locking mechanisms (Williams et al., 1997). Both the micromotions between the two surfaces in case of instability and the viscoelastic nature of polyethylene may contribute to increased wear in modular acetabular components (Yamaguchi et al., 1999, Scott et al., 2000) (Figure 6). Therefore, and because there will always be wear, the liner should be at least between 8 and 10 mm thick (Callaghan et al. 1999).

Bearing surfaces

The hip joint is a ball and socket joint that moves multidirectionally in all three planes. Charnley's experiences demonstrated that, besides biocompatibility, low friction and wear were essential for long lasting clinical success. This led to intensive investigations searching for the best articulation surfaces for the hip prosthesis. Experimental and clinical data have developed experience with different materials and to date there are three types of bearing

surfaces on the market: metal-on-metal, ceramic-on-ceramic, and a hard surface (metal or ceramic) against polyethylene. So called hard-on-hard bearings such as metal and ceramic articulations have lately gained new attention mainly from recent studies in Europe, but articulation with polyethylene is still regarded the golden standard.

Different properties of materials should be considered for articulating surfaces in THA with respect to friction and wear. These include macro-geometry (head size, clearance), micro-geometry (corrosion resistance, surface roughness), strength and lubrication characteristics.

Larger heads result in higher wear. Volumetric wear can only be measured in retrieved cups. This led to the common use of the cylindrical formula: $\nu = \pi r^2 \omega$ (r = radius of the femoral head; ω = proximal wear) for comparing volumetric wear. Clinical studies have corroborated the correlation of increasing *femoral head size* and increasing volumetric wear (Livermore et al., 1990, Kabo et al., 1993). This was astonishing as it was expected that increasing the head diameter would decrease the contact stresses and therefore result in wear reduction. Although contact stresses are a function of material properties and inversely proportional to contact area, it seems that they are sufficiently low and it seems that it is the increased sliding distance of larger femoral heads that is the more prominent factor causing the wear.

It is understandable that the larger the contact area between the articulating surfaces the larger is the potential for wear. *Clearance* is the size of the gap between the surfaces at the equator of the bearing. If the socket and ball have the same size the clearance is zero with a maximum contact area leading to high frictional torques and wear. Increasing clearance also influences the effect of *lubrication* and different materials have different combinations of clearance, size and lubrication (Kothari et al., 1996, Schey, 1996, Chan et al., 1999). The wettability of materials influences lubrication as well. It is expressed by the angle of the edge of a drop of fluid against the surface of the material. The smaller the wetting angle (the more spreading of the drop) the better the lubrication (Greenwald and Garino, 2001).

Corrosion is only an issue for metal implants. High content of chromium gives good restistance to corrosion and Chrome, Cobalt and Molybdenum alloys are harder than stainless steel. These aspects led to the preferred use of CrCoMo-alloys today.

The surface of an implant is not quite smooth but has peaks and valleys depending on the specific material. Those irregularities are invisible for the human eye but may be measured with a laser that scans the surface and makes an analogue recording resembling the vertical section of a mountain area. The *surface roughness* (R) is specific for materials and referred to in different forms throughout the literature. Widely used is the arithmetic mean Ra of the absolute value of height deviations measured from the graphical centerline. Other measurement parameters are the peak or valley heights that give the distance from the mean plane to either the highest peak Rp or the deepest valley Rv. Elfick could not find conclusive connections between surface finish and the influence on wear in hard surfaces (Elfick et al., 1999). He showed that wear has a multiphasic nature with a wear-in period, steady-state phase until a head-roughening event may cause a rapid wear period in cementless implants (Elfick et al., 2000). The harder the material the less scratching of the

surface. Titanium femoral heads have proven inferior clinical results (Bankston et al., 1993) compared with CoCrMo femoral head implants but ceramic implants are even harder.

All these parameters interfere with each other and influence the performance of an implant. It is therefore so difficult to predict whether one change in design renders a positive or negative outcome.

Metal on metal

Interest in metal-on-metal bearings is becoming in-vogue again as wear is the main problem of modular cementless and cemented arthroplasties with polyethylene. The early metal-on-metal designs were made of stainless steel and were of inferior quality. Problems arose from high friction and bad lubrication (Willert et al., 1996). The later McKee prosthesis showed volumetric wear lower than in cups with polyethylene (Kothari et al., 1996) as long as the bearing components were properly matched by a clearance of not more than 0.15-0.20μm securing a lubricating fluid film (Santavirta et al., 2003). The 2nd generation metal-on-metal implants were introduced by Weber from Switzerland. He improved the material properties and the resulting Metasul THR was approved by the French ministry of health in 1998 and by the FDA in the United Stated in 1999. Meanwhile over 150 00 prostheses have been implanted. The initial *in vivo* wear rate may be high but the scratches diminish by a self polishing effect causing a lower steady-state wear rate. Siebert found a 60-fold wear reduction in retrieved 2nd generation metal implants (Sieber et al., 1999). Metal particles are smaller than polyethylene particles. With less than 100 nanometers in size they do not affect the macrophages and their total amount is low although their total number is high (Green et al., 1998). Concerns are the systemic distribution of the metal ions. Brodner et al. showed a higher Co and Cr concentration in patients with metal-on-metal bearings compared to ceramic-on-ceramic THR implants (Brodner et al., 1997). Hypersensitivty and an increased risk for cancer have been discussed and are of concern, but so far the literature does not give conclusive answers (Jacobs et al., 2003, Antony and Holden, 2003, Lewis and Sunderman, Jr., 1996, Hallab et al., 2001, Clarke et al., 2003).

The recent years have seen a revival of the idea of resurfacing metal-on-metal bearing surfaces in the hip (Buechel, 1996). Supporters claim they are suitable for the young and demanding patients because of low wear rate and high range of motion due to anatomical restoration of the hip joint (Silva et al., 2004), but long term results are scarce and side effects of increased metal ions even with the newer designs are yet unknown (Clarke et al., 2003).

Ceramic on ceramic

Parallel to metal implants, ceramic implants have improved and continue to stand the test of time. Clear advantages of ceramic-on-ceramic articulations are their markedly low wear rate which is proven in tribological (Böhler et al., 2000, Mochida et al., 2001) and clinical studies (Böhler et al., 2000, D'Antonio et al., 2003, Garino, 2000). Ceramic has a high wettability, is extremely hard and has low surface roughness. Böhler found that the wear rate for alumina bearings was 39 μm per year (Böhler et al., 2000). Currently, alumina and

zirconia are available on the market. Late improvements in manufacturing have drastically decreased risk for fracture of the ceramic femoral head, which was a catastrophic complication earlier (Allain et al., 2003, Bierbaum et al., 2002). Newer designs of ceramic acetabular cups are assembled in a so-called sandwich technique to achieve more elasticity. As ceramics are much stiffer than bone, a polyethylene liner is inserted as a spacer between a ceramic bearing surface and a metal shell. However, fractures still occur (Hasegawa et al., 2003) as a consequence of incorrect insertion (Santavirta et al., 2003). Even so, short term results are encouraging (Ravasi and Sansone, 2002). Ceramic-on-ceramic implants require exact positioning as neck socket impingement is a known complication. Inclination angles less than 35 degrees and more than 45 degrees in combination with a high shaft angle (>140 degrees) are prone to impingement, causing a fracture at the rim of the ceramic liner (Santavirta et al., 2003) or increased wear because of stress concentration (Walter, 1992).

Zirconia was thought to be a solution for the problem of fracture. Zirconia is stronger than aluminia and performed better in lab studies (Cales, 2000). However, zirconia is available in 2 forms, stabilized by yttria or by magnesia. Zirconia with yttria can undergo a phase transformation at high temperatures and should therefore not be sterilized in the autoclave. This might be held responsible for increased wear and failure of zirconia in clinical steries (Hernigou and Bahrami, 2003). Phase transformation also seems to occur *in vivo*.

The classic: Hard surface on poly

Charnley's low friction articulation between CoCr and ultra high molecular polyethylene is still the golden standard for older patients in cemented and uncemented implants. However, the excellent results in the elderly caused increased demands and expectations even in younger patients wanting to experience the benefits of a total hip replacement. The main complication nowadays is aseptic loosening triggered by wear. Therefore main efforts address how to reduce particle generation from the polyethylene.

Articulation of polyethylene with ceramic femoral heads is such a successful attempt. The wear rate should not exceed 0.1 mm per year (Dumbleton et al., 2002). Clinical studies demonstrate that articulations with alumina heads are safely below this critical limit (Tanaka et al., 2003, Schuller and Marti, 1990).

During the last decade it became obvious that the method of sterilization has influence on the wear qualities of polyethylene. Intensive tribological and experimental studies followed to elucidate quality changes caused by different sterilization methods. Thus, clinical experience with the new polyehtylenes is only available for some early methods of enhancement.

Polyethylene

Today ultra high moleculare weight polyethylene is the most commonly used bearing surface in hip prostheses. Polyethylene is used in everyday life as for instance cutting boards, as gliding surfaces of skis and in snowmobiles because of low wear and excellent gliding qualities. UHMWPE used in orthopedics is an enhanced form of PE that consists of long polyethylene chains having approximately 10 times the molecular weight of high

molculare PE and its raw material comes in powder form. Two processes of production are used in making implants. Compression molding includes pressing the powder under temperatures over the melting point directly into the final shape. Ram extrusion stands for compressing and heating the powder into cylindrical bars, which are then machined into implants. The particle of the powder determines the so called resin. GUR 1050 is the most commonly used resin in orthopaedic implants today. Most currently available resins are fabricated with ram extrusions and the literature is not concise whether compression molding or ram extrusion is more beneficial for wear behaviour (Bankston et al. 1995). The role of the starting resin on the effect on wear and mechanical properties is still one of the underreported areas needs further research (Lewis 2001).

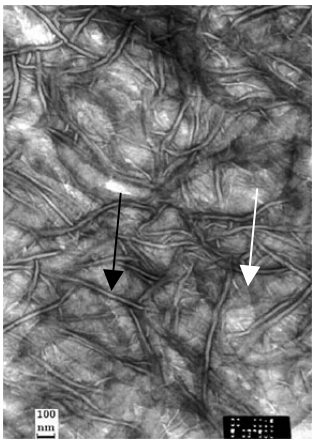

Figure 7: Amorph (white arrow) and crystalline (black arrow) regions in PE (from www.uhmwpe.org)

The quality of the polyethylene has to meet international standards (ASTM and ISO) and is characterized by a variety of laboratory parameters. The structure of PE consists of amorphous and crystalline regions (Figure 7). The relative amount of crystalline material for standard PE is around 55 % and the crystal size is 40-70 nm. Earlier attempts to improve the qualities of UHMWPE have been made. *Carbon fiber reinforcement* showed better strength and a lower wear rate *in vitro* but failed in clinical practice (Wright et al., 1988). The experimental results with the so called *Poly-2* were promising (Fruh and Willmann, 1998) but the *in vivo* results were devastating (Kilgus et al., 1992). It appeared that fatigue strength was lower than in normal UHMWPE resulting in delamination and clinical failures (Korkala and Syrjanen, 1998). *Hylamer* was another attempt to improve UHMWPE. Through high pressure and temperature the crystallinity was increased and material properties were enhanced, confirmed by *in vitro* studies. Thousands of prostheses were implanted worldwide without a randomized clinical study performed verifying the *in vivo* performance. Now Hylamer implants show high failure rates because of increased wear in clinical series (Sychterz et al., 2000, Scott et al., 2000, Chmell et al., 1996, Livingston et al., 1997). Another attempt to improve UHMWPE was heat pressing, but after 4 years the inserts already showed extreme delamination (Bloebaum et al., 1991, Engh et al., 1992, Mintz et al., 1991). The lessons of the past are that the *in vitro* results cannot be applied uncritically to the *in vivo* performance of implants. Small well controlled randomized *in vivo* studies are therefore needed before a new implant, after having passed through the laboratory tests, may be used on a big scale (Malchau, 2000).

UHMWPE is an outstanding material for orthopaedic applications with excellent abrasion resistence, low coefficient of friction, high impact resistance, self lubricating surface, negligible water absorbtion, good chemical resistance, energy absorbtion and sound damping properties. These properties can be maintained in temperatures between -269ºC and 90ºC (Stein 1999). However, modifications of the original polyethylene may change its mechanical properties to either enhanced or deteriorated clinical performance.

Engineers around the world try to simulate biological conditions in laboratory experiments, however, the biological processes are so complex that even excellent experimental data cannot guarantee corresponding clinical results.

Material properties include basic mechanical properties such as *modulus of elasticity* (stiffness), *creep* (cold flow) or *ductility* and mechanical strength properties such as *ultimate strength*, *yield strength*, *fatigue strength* and *elongation to break*. It is important to note that each property relates to the material itself and not to the shape of the object.

The *modulus of elasticity* expresses the ratio between stress per unit area acting to deform a body and the amount of deformation that results from it. Polyethylene exhibits a special behavior that is called strain softening. This means an apparent reduction of the elastic modulus with strain.

Creep or *cold flow* is a term to describe the strain reaction of a material when load is applied. Creep results from the fact that the long polymer chains tend to slide over each other. If a load is suddenly and continuously applied, the material resists it immediately (reacts with an immediate strain), however, the strain decreases with time (asymptoticly) and the material deforms slowly. This process of deformation is reversible when the load is released. Polyethylene is a material that reacts with creep to applied loads. Creep data are difficult to find, but is often expressed in terms of a *creep modulus*.

Polyethylene is *ductile*. This means that there is a region of plastic deformation whereby the material elongates with essentially the same applied load. Releasing the load leaves a permanent deformation.

Ulitmate strength is the maximum stress achieved prior to failure of a component on a single application of the load. *Yield strength* is determined by the amount of stress at which a permanent (plastic) deformation in a component becomes measurable. *Fatigue strength* (fatigue limit) is the stress below which no failure would occur no matter how many cycles of loading occurred.

Elongation to break is the load over the elongated length of polyethylene until it breaks.

PE oxidizes both during storage before operation and *in situ*. The oxidation process deteriorates the mechanical properties of PE and is therefore called oxidative degradation (Figure 8). It results in a stiffer and more brittle material that is less resistant to wear (Ries et al., 1996, Kurtz et al., 2003, Edidin et al., 2000). This degradation is not in the nature of PE itself but is a consequence of γ-irradiation in air, a common sterilization method up to the end of the last millennium. Wang et al. (2003) found in a simulator study that ultimate tensile strength is the key mechanical property for fatigue performance of cross-linked PE.

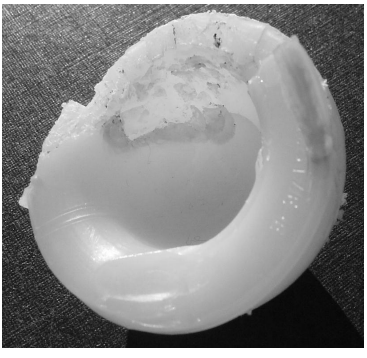

Figure 8: PE liner retrieval showing signs of degradation.

Sterilization methods

Every implant has to be sterilized before clinical use. Effective ways are by moist heat (temperature up to 130º), chemically (gas plasma or EtO) or with irradiation (γ-rays or electron beam). Since the early 1970s γ-irradiation in air has been the industrial standard procedure. Gamma rays have a wave length similar to x-rays and are emitted by Co^{60} resulting from the transition of an excited (unstable) to a ground (stable) state of the atomic nucleus. During the irradiation of PE, the polymer chains are broken and free radicals are generated. The broken chains recombine within the same chain, cross-link with another chain or react with oxygen, if present (Figure 9). In an oxygen containing atmosphere the free radical will predominantly react with oxygen. This oxidation alters the mechanical properties of PE. The average molecular weight increases and the degree of cristallinity decreases. Tensile strength slightly increases up to 10 Mrad followed by a gradual decrease, and the modulus of elasticity, oppositely, decreases first and then increases. Impact strength falls continuously after about 50 Mrad. Embrittlement may occur even as irradiated PE decreases in hardness. (Eyerer and Ke, 1984, Collier et al., 1996a). Clinical evidence has shown inferior performance of oxidized PE (Sutula et al., 1995, Collier et al., 1996a, Collier et al., 1996b).

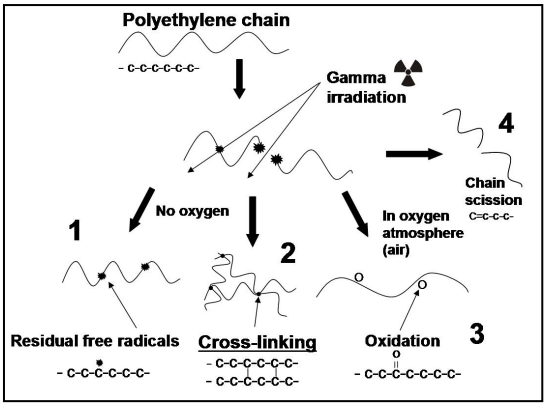

Figure 9: Gamma irradiation causes free radicals in the PE. Those may either remain (1), cross-link (2) or react with oxygen (3). In some cases the PE chain will also be cut in 2 pieces (4).

These findings led to sterilization of products by γ-irradiation in an oxygen free atmosphere, or by chemical agents expecting to reduce the oxidative degradation of PE caused by γ-irradiation in air.

Still, free radicals that were trapped within the crystalline phase after the sterilization could oxidize the implant during storing (shelf life) or, even if the implant was protected during storing, after implantation *in vivo*.

To eliminate the possibility of oxidation by free radicals, surface sterilization with gas plasma and ethylene oxide was thought to be a solution. Gas plasma is a dry ionizing technique at low temperatures that sterilizes by oxidizing microorganisms. Ethylene oxide gas sterilizes by alkylating proteins, enzymes and bacterial DNA (Dempsey 1989). Both methods sterilize only the surface and do not alter the characteristics of the polyethylene. This means the PE chains are not cross-linking at all. Experimental data confirms no oxidation in never implanted cups or substantially lower level of oxidation in retrieved EtO sterilized cups (Williams et al., 1998, Bargmann et al., 1999). Oxidation may still occur

in vivo emphasizing time as an important factor in predicting long term performance. Such results were confirmed by artificially aged implants that were exposed to high temperature over a certain time interval (Edidin et al., 2002). A disadvantage of surface sterilized implants, however, is the lack of cross-linking. In hip simulator studies with non-aged and artificially aged PE sterilized with EtO, the wear rate was higher than in PE sterilized by irradiation (McKellop et al., 2000, Affatato et al., 2002). It is not yet clear whether the decreased level of oxidation influences the clinical performance of non cross-linked polyethylene cups.

Highly cross-linked polyethylene

Parallel to hard-on-hard bearings a new alternative has evolved over the past few years. Researchers started to experiment with even higher loads of irradiation to achieve higher wear resistance and called the new polyethylene: "Highly Cross-linked PE". The aim was to enhance abrasion performance to eliminate wear and reduce osteolysis. Cross-linking of polyethylene can be achieved by either chemical agents such as silane, peroxides or by irradiation in the molten or the solid states. The idea was not new, Atkinson and colleagues cross-linked PE with silane and after *in vitro* testing they stated that "cross-linked PE is an exciting prospect in the field of prosthetic materials" (Atkinson and Cicek, 1984). In South Africa, Grobbelar et al. used acethylene and CTFE as cross-linking agents and a γ-source to irradiate PE (Grobbelaar et al., 1978). His *in vitro* material testings showed superior wear resistance and an eight times higher cross-linking at the surface of the implant. At follow up after 14 - 21 years, Grobbelar found a lack of radiographically measurable wear in 56 of 64 cases. Two implants were revised due to osteolysis (Grobbelar et al, 1999). In Japan about the same time period, Oonishii with coworkers started to irradiate finished PE cups with extremely high doses (100 Mrad). Similar to Grobbelar he found substantially reduced wear compared to standard PE sterilized in air (Oonishi et al., 1998). More recently Wroblewski and his team cross-linked PE chemically with a silane process. After eight years of clinical follow up he found a wear rate of only 22 μm per year. This was far below the wear rate of standard tretaed polyethylene (Wroblewski et al., 1999). These positive clinical experiences with highly cross-linked implants were encouraging, however the methods of crosslinking in those early attempts were substantially different to the ones used today. Through the extreme irradiation and high levels of cross-linking the mechanical properties of PE are changed negatively, none of these early materials were treated thermally to eliminate free radicals and none of these studies investigated for mechanical failures.

Before the turn of the millennium a number of research laboratories were experimenting with highly cross-linked PE with hip simulators and found a 90 % decrease in wear rate with increasing amount of cross-linking (McKellop et al., 1999, Kurtz et al., 1999). These findings created interest to find the best possible way to enable increased cross-linking and at the same time avoid the negative consequences of oxidation.

In principle all current cross-linking manufacturers have 3 important procedures in common: 1. Crosslinking (irradiation), 2. thermal treatment (annealing or remelting) and 3. final sterilization (EtO, gas plasma or irradiation in inert atmosphere) (Figure 10).

In the cross-linking process polyethylene chains are cut which produces free radicals. These free radicals may either recombine with another chain (cross-link) or stay

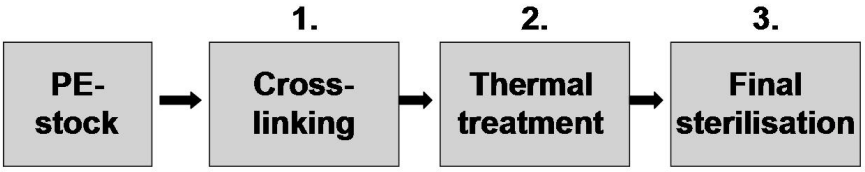

Figure 10: The manufacturing process of cross-linking involves 3 major steps: 1. Crosslinking (irradiation), 2. Thermal treatment (annealing or remelting) and 3. Final sterilisation (EtO, gas plasma or irradiation in inert atmosphere). Each step is performed differently by different manufacturers.

predominantly in the crystal region of the molecule (Figure 7, chapter PE). By adding energy to the molecule the free radicals increase their energy level and their tendency to react. If oxygen is present the free radical has a higher affinity to react with oxygen leading to increased oxidation and over a matter of time, to degradation (Premnath et al., 1996). Therefore the cross-linking is performed in an oxygen free atmosphere and the material is treated thermally. The heat process causes the free radicals to react and form more cross-links. The melting process is a method to get rid of all the free radicals (Muratoglu et al., 2001b, Atkinson and Cicek, 1984). Muratoglu uses an electron beam in a heated PE (submelt temperature 125ºC) and afterwards melts it to eliminate all radicals (WIAM) whereas the WISM process only warms the PE up to 40ºC before it is melted. Once the cross-linking process is finished, with few or no radicals left, the decision about the final method of sterilisation has to be made. All manufacturers have abandoned irradiation in air. The methods of choice are either by surface sterilisation with EtO or gas plasma, or by γ-irradiation in nitrogen.

To date, there are seven products with differing amounts of cross-lining on the market. They are produced in five different ways of cross-linking and combination of thermal treatment and final sterilization. The commercially available product is named in parenthesis (Table 1).

1. **Heat stabilized**. The machined UHMWPE cup is exposed to a low dose (3 Mrad) of γ-irradiation in N_2 environment, creating cross-links and free radicals. The PE is then heat annealed in package (60°C) for 6 days (Duration™). This PE was used in one of the groups in study 2.

2. **Cold Irradiated Subsequent Melt** (CISM). The ram extruded UHMWPE rod is γ-radiated (5 Mrad), heated above melting point (>135°C), machined to final shape, and

finally sterilized with gas plasma (Marathon™) or ethyleneoxide (XLPE 5™ and XLPE 10 ™ crosslinked with 10 Mrad).

3. **Cold Irradiated Annealed Non-melt** (CIAN). The ram extruded UHMWPE rod is γ-irradiated (7.5 Mrad), heat annealed below melting point, machined to final shape and finally γ-irradiated (2,5 Mrad) in N_2 or vacuum (Crossfire™). This PE was used in one of the groups in study 2.

Another CIAN UHMWPE (Aeoniam™) is cross-linked with a lower irradiation rate (3.5 Mrad) but the rest is according to the process of the one above.

4. **Warm Irradiated Adiabatic Melting (WIAM).** The ram extruded UHMWPE rod is warmed to 125°C, radiated with electron beam (9.5 Mrad), thereafter heated above melting (>135°C) for 2 hours, machined into final shape and finally ethylene oxide sterilized (Durasul™).

5. **Warm Irradiated Subsequent Melt (WISM).** The ram extruded UHMWPE rod is warmed to 40°C, radiated with electron beam (10 Mrad), thereafter heated above melt (>135°C) for 6 hours, machined into final shape and finally sterilized with gas plasma (Longevity™).

The first generation heat-stabilized PE (Duration™) is treated with a relatively lower irradiation rate (3 Mrad) and is therefore only moderately cross-linked. Common for all methods is the intention to reduce the wear rate by cross-linking, to maintain or improve the mechanical properties of conventional PE and to protect the finished cup inserts from oxidative degradation. Hence, this new alternative cross-linked PEs fueled intensive mechanical property testing by hip simulators for wear rate and mechanical performance.

Table 1: Available highly cross-linked PE and their Process description

Tradename	Radiation Source & Dose	Thermal Treatment (temp and time)	Sterilization Method
Marathon™	Gamma 5 Mrads	Re-melt (155°C 24h)	Gas Plasma
Longevity™	E-beam 10 Mrads (40°C)	Re-melt (>136°C 6h)	Gas Plasma
Durasul™	E-beam 9.5 Mrads	Re-melted (150 °C 2h)	EtO
XLPE™	Gamma 5 or 10 Mrads	Re-melted (150 °C)	EtO
Duration™	Gamma in N_2 3 Mrads	Heat stabilized (60°C)	
Aeoniam™	Gamma 3 Mrads	Annealed (110 °C 10h)	3-Mrads Gamma in N_2
Crossfire™	Gamma 7.5 Mrads	Annealed (>120°C<136°C)	3-Mrads Gamma in N_2

The amount of cross-linking changes the crystallinity of the original PE and reduces material properties such as toughness and resistance to fatigue crack propagation (Muratoglu et al., 1999). However, all cross-linked materials on the market still meet the requirements of standard institutions (ASTM, ISO). The engineers behind the heat

requirements of standard institutions (ASTM, ISO). The engineers behind the heat stabilized and CIAN methods use annealing rather than melting in their process. Melting has been shown to alter PE properties and they therefore believe to preserve the original properties of PE in the finished product by using annealing rather than melting (Wang, Manley, Serekian 2003). However, some free radicals from the cross-linking process will be left in the material. Melted materials lack free radicals but it is unclear whether the changes in creep and fatigue properties caused by the melting may compromise the clinical performance. Muratoglu quantified the concentration of free radicals in a hip simulator study with artificially aged PE that was melted (WIAM), annealed and γ-irradiated in air as a control. He found a three times higher oxidation level in annealed PE compared to the controls and no radicals in the melted group (Muratoglu et al., 2003b). The melted cross-linked PE was tested for wear in the hip simulator with aluminium and cement as interposed materials (third body wear). They found a substantial lower wear rate (0.5 mg per million cycles) compared to conventional PE (Bragdon et al., 2003). On the other hand annealed PE preserves the original properties better, which have proven effective in over two decades of clinical use. Even so, there are at least 5 different ways to cross-link material and little attention has been given to crack propagation rate, fatigue and fracture toughness in *in vitro* studies (Lewis 2001). Finally, experiences from the past have shown that *in vitro* studies do not always predict correctly the clinical performance of new materials (Thanner et al., 1995, Chmell et al., 1996).

Undoubtedly, cross-linked PE lowers the wear rate in laboratory tests, but little is known whether this will help to reduce osteolysis and enhance clinical survival of acetabular implants. The size of highly cross-linked wear particles is smaller, however the total number of particles similar to conventional PE (Ries et al., 2001, Muratoglu et al., 2003b). Endo et al. found a higher biological reaction of macrophages challenged with (moderately) cross-linked particles compared to non cross-linked particles (Endo et al., 2002).

So far there are two short-term follow-ups with modern highly cross-linked PEs published in the literature. Digas and colleagues followed sixty-one cases randomized to either highly cross-linked PE (WIAM) or conventional PE sterilized in an inert gas atmosphere. The highly cross-linked cups displayed a 50 % reduction of proximal wear compared to the control group when the patients were examined with RSA in the standing position (Digas et al., 2003). Martell and his group followed forty-six patients for a mean of 2.3 years radiographically (Martell et al., 2003). Twenty-four received highly cross-linked PE (CIAN) and twenty-two conventional PE sterilized in nitrogen. He found a 42 % reduction in proximal and a 32 % reduction in 3D wear. These results look promising, but further studies with high resolution measuring methods for all highly cross-linked PEs are necessary. It remains to be seen whether the highly cross-linked PEs will continue their success on the clinical proving ground.

Aims

Late loosening of cups is still a problem in total hip arthroplasty. Biological fixation by cementless implants and particle reduction by material modifications are attempts to improve implant survival.

The general aim was to investigate the effect of different modes of fixation and new materials on migration and wear. Specifically we wanted to:

1. Investigate the effect of different modes of sterilization of polyethylene on wear (**study 1**)

2. Investigate the *in vivo* performance of highly cross-linked polyethylene (**study 2**)

3. Investigate the effect on migration and wear of cementless acetabular cups with different methods of fixation (**study 3**)

4. Investigate the long-term clinical performance, wear and migration of cementless porous coated screw fixed cup (**study 4**)

Material and methods

Patients

Study 1 comprises cemented and uncemented acetabular cups from 5 prospective and randomized studies performed at the orthopedic departments of Umeå, Sahlgrenska, and Uppsala University Hospitals. In total 237 hips were available. 30 of these had to be omitted because too few tantalum markers were visible on the postoperative or 2-year follow-up examinations. Six patients had bilateral operations, but only the first hip that was operated on was included. This left 201 total hip arthroplasties in 201 patients (117 women, 84 men) to be included.

In **study 3** eighty-seven hips in 81 patients (39 women, 42 men) were followed for 5 years. Sixty-eight hips were operated in Umeå and 19 in Uppsala. The hips were stratified for gender and hospital and randomized to four different modes of fixation by opening a sealed envelope at the time of operation (Figure 23, appendix). 69 of the 87 hips were also included in study 1. The remaining 18 hips consisted of the second hip in hips operated on bilaterally (n=6), and 12 hips with insufficient tantalum markers not allowing wear measurements in study 1.

Study 2 included fifty hips in 50 patients (27 women, 23 men) operated in Umeå. The patients consecutively received 1 of three designs of cups made of different polyethylene. Mean follow-up was 2 years for two of the groups, and 3 years for the third group.

Study 4 includes 63 consecutive hips in 58 patients (21 women, 37 men) operated in Umeå between 1987 and 1990. Inclusion criteria were young age, primary hip arthrosis and no metabolic bone diseases. Mean follow up was 12 years (range 10 -14). Eight patients had died before the last follow up.

Implants

The following acetabular components were evaluated. For details about the cup implants and patient study groups see table 2 and for bearing surfaces and femoral prosthesis table 3.

The **Lubinus®** cup (Waldemar Link, Hamburg, Germany) (Study 1) is an eccentric all polyethylene cup intended for cemented fixation. It is manufactured by compression-molding technique using Chirulen 1020 resin, and is sterilized with gamma irradiation (2.5 Mrad) in vacuum. The cups were inserted with Palacos Gentamicin cement and articulated against 28 mm femoral heads made of cobalt-chromium.

Lubinus cup

The **Reflection®** all polyethylene cup (Smith&Nephew, Memphis, Tennessee, USA) (Study 1) is an all polyethylene cup intended for cemented fixation. It is manufactured by ram extrusion technique using GUR 1050 resin, and is sterilized with EtO. The cups were inserted with Palacos Gentamicin cement and articulated against 28 mm femoral heads made of cobalt-chromium.

The **Trilogy®** cup (Zimmer, Warsaw, Indiana, USA) (Study 1) is a hemispherical metal-backed cup intended for uncemented fixation. The liner is manufactured by compression molding technique using GUR 1050 resin, and is sterilized with gamma irradiation (2.5 Mrad) in nitrogen environment. The thickness of the liners ranged between 6.3 and 11.3 mm. The liners articulated against 28 mm femoral heads made of cobalt-chromium. The metal shell of the cup is made of titanium-aluminum-vanadium alloy with a fiber mesh of pure titanium attached to its outer surface. The mesh is plasma sprayed with a 40 μm coating consisting of 70 % hydroxyapatite and 30 % tricalcium phosphate. The cups were inserted with 1 – 2 mm of under reaming. About 30 % of the cups had no holes for additional screws, in the remaining 70 %, 1 – 3 screws were inserted in the 3 screw holes available.

Trilogy

The **Reflection®** metal backed cup (Smith&Nephew, Memphis, Tennessee, USA) (Study 1, 3) is a hemispherical metal-backed cup intended for uncemented fixation. The liner is manufactured by ram extrusion technique using GUR 1050 resin and is sterilized with EtO. The thickness of the liners ranged between 6 and 12 mm. The liners articulated against 28 mm femoral heads made of cobalt-chromium or zirconium-oxide. The metal shell of the cup is made of titanium-aluminum-vanadium alloy with a highly polished inner surface. The outer surface is porous coated with commercially pure titanium beads. The

central hole for the cup inserter was sealed in all cups with a hole cover. In the groups randomized to hydroxyapatite the outer surface was plasma sprayed with a 40 µm hydroxyapatite coating (purity 96 %, crystallinity 66 %, shear strength 44.6 MPa, and tensile bond strength 73.8 MPa). In the groups randomized to 3 pegs or screws the shells had additional 6 holes. The unused holes were not sealed. The cups were inserted with 1 – 2 mm of under reaming.

The **Exeter®** cup (Stryker, Orthopaedics, Mahwah, NJ, USA) (Study 2) is an all polyethylene cup intended for cemented fixation. It is manufactured using GUR 1050 resin and is gamma sterilized (2.5 Mrad) in air. The cups were inserted with Palacos Gentamicin cement and articulated against 28 mm femoral heads made of cobalt-chromium.

The **Rozing®** cup (Stryker, Orthopaedics, Mahwah, NJ, USA) (Study 2) is an all polyethylene cup, almost identical in design to the Exeter cup, and intended for cemented fixation. The polyethylene (Duration®) is manufactured by ram extrusion using GUR 1050 resin which is gamma irradiated (3 Mrad) and thereafter heat stabilized at 50 degrees for 6 days. The cups were inserted with Palacos Gentamicin cement and articulated against 28 mm femoral heads made of zirconium oxide.

The **Osteonics®** cup (Stryker, Orthopaedics, Mahwah, NJ, USA) (Study 2) is an all polyethylene cup, almost identical in design to the Exeter cup, ram extruded and intended for cemented fixation. The highly cross-linked polyethylene (Crossfire®) is made of GUR 1050 resin. The cup is gamma irradiated (7.5 Mrad), heat annealed below melt temperature and finally gamma sterilized (2.5 Mrad), all in inert atmosphere. The cups were inserted with Palacos Gentamicin cement and articulated against 28 mm femoral heads made of cobalt-chromium.

The **Harris Galante®** cup (Zimmer, Warsaw, Indiana, USA) (Study 4) is a hemispherical metal-backed cup intended for uncemented fixation. The liner is manufactured by ram extrusion technique using GUR 1150 resin and is gamma sterilized (2 Mrad) in air. The liners articulated against 32 mm femoral heads made of aluminum oxide. The metal shell of the cup is made of titanium-aluminum-vanadium alloy with a fiber mesh of pure titanium attached to its outer surface. The cup design was introduced in 1984 (HG I) and was improved 1988 (HG II). The liner locking mechanism in HG I consists of 4 pairs of tines at the periphery of the shell. The HG II had more tines, and the thickness of the shell was increased from 3.7/4.7 mm to 5.6 mm. The cups were inserted with line to line fit. The cups had several holes, in 3 of them screws were inserted and the remainder were left unsealed.

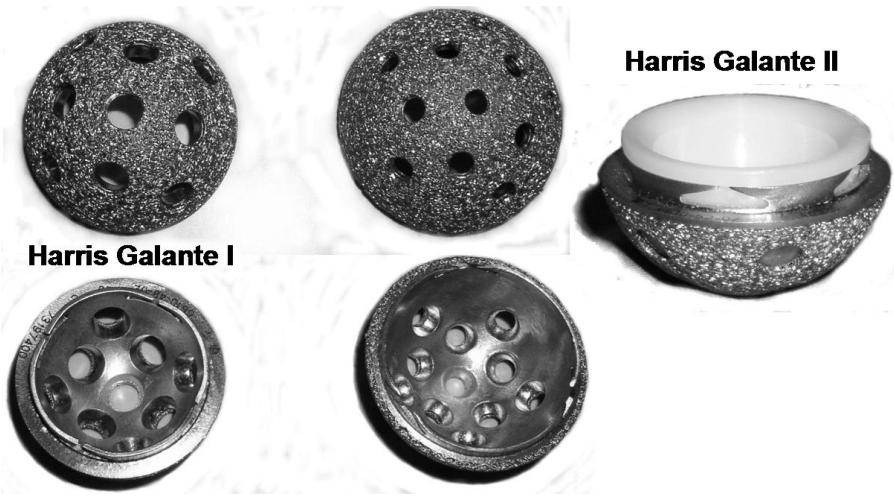

Table 2: Overview of all cups, their method of sterilisaton, manufacturing and material properties and patient parameters of all study groups.

	Lubinus n = 30	Trilogy n = 65	Reflection n = 37	Reflection PF n_1 = 18 n_3 = 20	Reflection PF + HA n_1 = 17 n_3 = 20	Reflection PF + pegs n_1 = 18 n_3 = 21	Reflection PF + scews n_1 =16 n_3 = 20	Exeter n = 20	Rozing n = 20	Osteonics n = 10	Harris Galante I n = 45	Harris Galante II n = 18
Study	1	1	1	1 and 3	1 and 3	1 and 3	1 and 3	2	2	2	4	4
Fixation	cemented	uncemented	cemented	uncemented	uncemented	uncemented	uncemented	cemented	cemented	cemented	uncemented	uncemented
Resin type	Chirulen 1020	GUR 1050	GUR 1050	GUR 1050	GUR 1050	GUR 1050	GUR 1050	GUR 1050	GUR 1050	GUR 1050	GUR 1150	GUR 1150
Method of manufacturer	Compression molded	Compression molded	Ram extruded	Ram extruded	Ram extruded	Ram extruded	Ram extruded	Compression molded	Ram extruded	Ram Extruded	Ram extruded	Ram extruded
Sterilisation	γ-irrad. in vac. 2.5 Mrad	γ-irrad. in N_2. 2.5 Mrad	EtO	EtO	EtO	EtO	EtO	g- irrad. in air 2.5 Mrad	γ-irrad. in N_2. 3 Mrad	γ-irrad. in N_2. 2.5 Mrad	γ-irrad. in air. 2.5 Mrad	γ-irrad. in air. 2.5 Mrad
Cross-linking	low	low	no	no	No	no	no	low	Moderate (Heat-stabilized)	high (7,5 Mrad)	low	low
Male/female	13 / 17	25 / 40	10/27	8 / 10_1 9 / 11_3	10 / 8_1 12 / 8_3	11 / 8_1 12 / 9_3	8 / 7_1 9 / 11_3	12 / 8	5 / 15	6 /4	31/14	10 / 8
Age (years)	68 (53 – 78)	60 (32 – 81)	72 (31 – 78)	53 (34 – 65)$_1$ 54 (34 – 65)$_3$	58 (47 – 66)$_1$ 56 (36 – 66)$_3$	56 (40 – 64)$_1$ 56 (40 – 64)$_3$	56 (40 – 65)$_1$ 56 (40 – 65)$_3$	70 (61 – 81)	67 (48 – 73)	58 (49 – 79)	55 (38 – 69)	56 (46 – 69)
Weight (kg)	77 (53 – 100)	75 (38 – 111)	70 (49 – 115)	73 (54 – 100)$_1$ 76 (54 – 100)$_3$	80 (55 – 106)$_1$ 80 (55 – 106)$_3$	80 (57 – 100)$_1$ 79 (57 – 100)$_3$	77 (58 – 105)$_1$ 73 (51 – 110)$_3$	75 (45 – 98)	70 (57 – 90)	72 (60 – 87)	80 (51 -125)	67 (54 – 84)
Primary/sec arthosis	29 / 1	44 / 21	26 / 11	14 / 3_1 17 / 4_3	13 / 5_1 17 / 5_3	14 / 5_1 16 / 6_3	12 / 3_1 15 / 7_3	17 / 3	19 / 1	7 / 3	33 / 12	12 / 6
Cup size (mm)	52 (46 – 56)	52 (48 – 62)	52 (46 61)	55 (52 – 58)$_1$ 55 (52 – 60)$_3$	57 (50 – 62)$_1$ 57 (50 – 62)$_3$	57 (50 – 60)$_1$ 56 (50 – 60)$_3$	57 (50 – 60)$_1$ 56 (50 – 60)$_3$	52 (48 – 56)	48 (48 – 56)	52 (48 – 56)	55 (48 – 64)	56 (52 – 62)
Inclination (°)	49 (26 – 67)	40 (27 – 56)	44 (33 – 55)	50 (30 – 64)$_1$ 49 (30 – 64) $_3$	53 (41 – 66)$_1$ 53 (41 – 66) $_3$	48 (39 – 60)$_1$ 48 (39 – 60) $_3$	50 (35 – 61)$_1$ 49 (35 – 61) $_3$	50 (34 – 67)	48 (40 – 80)	51 (28 – 64)	41 (29 – 57)	43 (28 – 55)

Study 1_1 and study 3_3

Table 3: Distribution of the acetabular and femoral components and the type of bearing surface for all studies.

Stem design	Cup design													
	Lubinus		Trilogy			Reflection				Exeter	Rozing	Osteonics	Harris Galante I	Harris Galante II
	+ flange	-	+ screws	-	Cemented	PF	PF+HA	PF+pegs	PF+scews					
Study	1	1	1	1	1	1 and 3	1 and 3	1 and 3	1 and 3	2	2	2	4	4
Cemented														
Lubinus SP II	17[a]	13[a]												
Lubinus Titan													12[c]	1[c]
Spektron			25[a]	0	37[a]	15_1[b] 17_3[b]	14_1[b] 17_3[b]	14_1[b] 17_3[b]	12_1[b] 17_3[b]					
Exeter										20[a]		10[a]		
Anatomic-option			9[a]	8[a]										
Definition											20[a]			
Lubinus SP														
Rippen													8[c]	
Tifit													17[c]	3[c]
Uncemented														
Epoch			3[a]	3[a]										
Anatomic			7[a]	10[a]										
Cone							1_{1+3}[a]	1_{1+3}[a]	1_{1+3}[a]					
Bimetric						2_1[a] 4_3[a]	3_1[a] 4_3[a]	4_1[a] 4_3[a]	2_1[a] 4_3[a]					
Tifit porous													2[c]	9[c]
Tifit HA													6[c]	5[c]
Total	17	13	44	21	37	21[d]	22[d]	22[d]	22[d]	20	20	10	45	18

Study 1_1, study 3_3

[a]CoCr (Cobalt chromium) and 28 mm head diameter

[b]Zr (Zirconium) and 28 mm head diameter

[c]Al (Aluminium) and 32 mm head diameter

[d]Stems in study 1 are only counted once

Radiostereometric analysis

All studies are based on the RSA principles described by Selvik (Selvik, 1989). Modifications by Nyström (1990) and Söderkvist (1990) developed radiophotogrammetry further and Kärrholm applied it in various orthopaedic fields (Kärrholm, 1989). RSA is today the most sophisticated and accurate method to measure micromotion *in vivo*. Besides dynamic studies (Nilsson, 1992) its use is strongly recommended for small controlled trials as a first step in introducing new implants (Kärrholm et al., 1997).

The possibilities of RSA are widespread. The whole process of RSA measurements consist of 4 consecutive steps. Depending on location and type of examination the technique differs slightly. Because the main topic of the current research in this book is the acetabular component all steps will be explained by means of acetabular implants but the method may be applied to basically any implant or part of the body The complete process of RSA requires meticulous control of quality parameters in each single step.

1. Insertion of markers

All patients from study 1 – 4 were marked with tantalum markers (diameter 0.8 mm) intraoperatively. Nine markers were inserted into the aectabulum and another 9 markers into the periphery of the polyethylene liner. Tantalum is an inert radio-opaque metal and has been implanted in thousands of patients over 3 decades without any known side effects. These markers serve to identify landmarks and form rigid bodies. Markers in the polyethylene are visible in the phantom picture and the radiographs on the cover.

2. Radiography

Within two weeks after surgery the patients were x-rayed for the first time (reference examination) with 2 simultaneously exposing tubes. The standard exposure was about 110 kV and 10-15 mAs. The x-ray tubes are mounted mobile on the ceiling at an angle of about 40º between each other. The x-ray beams are directed to cross each other at the level of the prosthesis (region of interest). The patients were in the supine position and a calibration cage containing the film cassettes was placed beneath the measuring table (Figure 11). The subsequent examinations in each study were performed as shown in table 4.

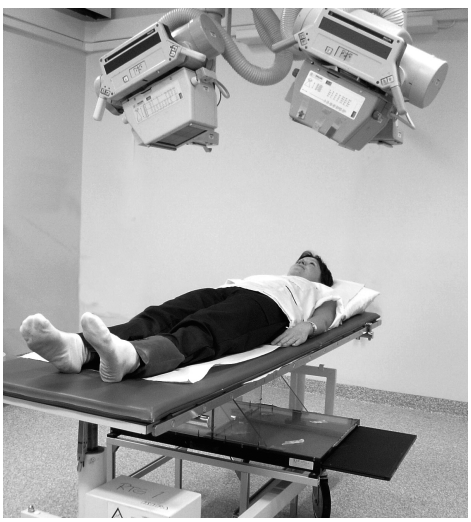

Figure 11: Patient on the examining table with xray tubes and cage.

Table 4: Time intervals of follow-ups for each study (m = months, y = years).

Study	postop	2 m	6 m	1y	2 y	3 y	5 y	12 y
I.	–	–	–	–	–			
II.	–	–		–	–	–		
III.	–	–		–	–		–	
IV.	–	–		–	–		–	–

3. Marking and measuring of radiographs

This step implies to identify and pair each marker on the radiographs. Up until 1999 all radiostereographs were analyzed by analogue technique. This means that the patients were x-rayed with analogue radiographs, which were then measured on an analogue measuring table. From 1999 a semi digital RSA technique became standard. This includes conventional x-rays, scanning of the films, editing the scanned x-rays, and finally measuring the scanned pictures on the computer. Due to pictures being of sometimes poor quality during the period when analogue technique was used, some patients had to be excluded from the follow-up. The digital technique however enables the original postoperative radiographs to be re-measured and edited and thereby allowing several previously excluded patients to be analyzed. In study 4 this technique was used to re-measure all postoperative radiographs in order to evaluate the performance of the uncemented cups inserted at a mean 12 years previously. Since 2002 the complete process is fully digital and by implementation of new image detection software more precise (Börlin et al., 2002).

After measuring the 2 dimensional coordinates of all implanted markers, the soft-ware calculates their 3 D coordinates.

4. Calculation of motion

All markers (at least three) within a segment (either acetabulum or cup) form a rigid body. Each rigid body has to be checked for contained quality in consecutive RSA examinations. The quality is determined by the number of markers, the condition number and the mean error of rigid body fitting (Kärrholm et al., 1997). These have to be checked for each individual segment and each examination. Strict quality limits such as 100 in condition number and 0.3 for mean error of rigid body fitting are the reason for the high number of drop outs in study 4. In some patients we accepted single parameters slightly above the limits when the other parameters were indicating excellent or good quality.

The movement of the cup segment at different follow up occasions was then calculated (cup migration) by means of UmRSA software (UmRSA, Biomedical, Umeå, Sweden). This is done by the program mathematically "repositioning" the reference segment in the postoperative position. The other segments follow and enable calculations of the relative motions of a segment between two examinations. In all studies migration of the cup over time was measured as rotations about the 3 cardinal axes. Thus X-rotation corresponds to anterior-posterior tilt, Y-rotation corresponds to anteversion/retroversion, and Z-rotation

corresponds to changing inclination of the cup. Translation of the cup along the 3 cardinal axes was measured at the gravimetric center of the inserted cup markers (Figure 12).

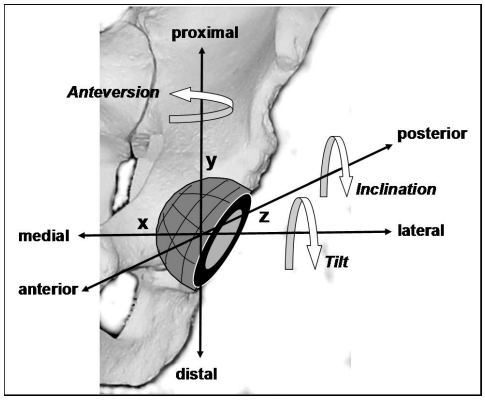

Figure 12: Nomenctalure of translations and *rotations* along the three cardinal axes.

In **study 4** we faced the problem of possible liner rotations within the shell. Therefore we determined the center of the cup in the reference examination (after surgery) as the femoral head centre. This point was then relocalized in relation to the other liner markers on the following RSA pictures. This enabled us to measure the translation of the center of the cup without influences (noise) of liner rotations because all rotations would meet in this point.

To facilitate interpretation of rotations we also combined RSA information about liner motions with information based on conventional radiography. Cups in which the rotations exceeded the detection level for our measurements for only one direction corresponding to significant rotation about only one of the cardinal axis were regarded to have a stable liner. In these cases the rotations were small and were presumed to have occurred within the first postoperative months. If there were interface radiolucencies (zones or osteolysis) less than 50 % of the interface and at least 2 rotations of the 3 cardinal axes exceeded the detection level for our measurements they were classified as possible liner rotations. Significant rotations about all 3 cardinal axes in cups with RLL < 50 % were classified as probable liner rotations. If the radiolucencies exceeded 50% these rotations were classified as liner and/or shell rotations.

Measurement of polyethylene wear was determined both as proximal as well as 3-dimensional penetration of the femoral head into the polyethylene liner using the markers in the polyethylene liner as a reference. This simplification has become standard in most wear measuring methods.

5. Precision of measurements

The precision of the RSA measurements was calculated by repeating the radiostereometric examination in after an interval of 5-10 minutes (double examination). The absolute mean value of all the recorded differences between two double examinations with a standard deviation of 1.96 represented the total error of the determinations at the 95 per cent level of significance based on a normal distribution for each type of movements (Kärrholm et al., 1997, Bragdon et al., 2002). In study 4 we only had 18 valuable RSA examinations therefore we adjusted to 2.1 standard deviations (Table 5).

Table 5: Precision in each study based on double examinations (95 % confidence limits for significant motions).

(detection Limit)	**Study 1** (99%)	**Study 2** (95%)	**Study 3** (95%)	**Study 4** (95%)
n (mig/wear)		116/99	156	18/19
Translation				
Medio - lateral		0.23	0.24	0.18
Proximal - distal		0.28	0.17	0.10
Anterior - posterior		0.19	0.32	0.18
Rotation				
Tilt		0.81	0.80	0.61
Ante- retroversion		0.55	0.80	0.62
Inclination		0.38	0.45	0.37
Wear				
Medio - lateral		0.14	0.22	0.51
Proximal - distal	0.05-0.20	0.10	0.15	0.79
Anterior - posterior		0.23	0.70	1.13
3D	0.15-0.4	0.27	0.5	1.34

Inducible displacements

To study possible inducible displacement of the cup during provocation (study 3), stress examinations were performed both at 1 week after operation and at 2 months. First, a RSA exposure was taken at rest in the supine position. A second exposure was then obtained with the patient lifting his foot of the operated leg 10 cm above the table. At two months the stress test was performed similarly, but with an additional 2 kg weight attached to the ankle of the leg (Figure 13).

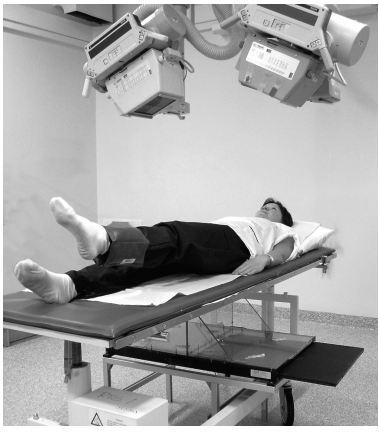

Figure 13: Straight leg rise with a 2kg weight on the ankle.

Surgeons judgement of cup stability

In study 3 the surgeon intraoperatively subjectively graded the achieved quality of the cup fixation as *doubtful*, *good*, or *optimal*.

Clinical evaluation

In studies 1 and 2 Harris hip score was determined before operation and at 2 years (Harris, 1969). In study 3 we evaluated HHS also at 5 years and in study 4 all patients were examined and interviewed at the 12 year follow up.

Conventional radiography

To evaluate postoperative alignment of the hip arthroplasty, and the development of radiolucent lines and osteolysis, antero-posterior (AP), lateral, and pelvic radiographs were taken preoperatively and postoperatively at 1 week. The pelvic views were centered on the symphysis. In study 1 and 2 radiographs were obtained at the final 2 year and in study 3 at the 5 year follow up. In study 4 not all postoperative pictures were available. We compared the pictures from the final follow up in 17 cases with the postoperative radiographs, in seven with the one-year follow up radiographs, in 11 patients with the two-year and in 7 more patients with radiographs from the 5 year follow up. At 2, 5 and 12 years, AP and lateral radiographs were obtained. Up to 2 years the radiographs in study 1,2 and 3 were measured with a digitizing table (Orthographics Inc, Salt Lake City, Utah) connected to a personal computer with suitable software (Researchmetrics, Orthographics Inc, Salt Lake City, Utah). The five-year measurements in study 3 and all measurements in study 4 were performed on digital x-rays using Mdesk software (RSA Biomedical Innovations, Umeå).

A small dark line > 0.5 mm between the implant and the bone characterizes radiolucent lines, which may represent bone resorption. To determine the extent of these lines, the cup/bone interface was divided in three equal 60º areas. This differs from the widely used practice of Delee and Charnley who divided the interface in three parts but the middle sector having a 90º angle (DeLee and Charnley, 1976). The amount of radiolucent lines was graded into four groups: Grade 1 equaled a 0% lucency, grade 2 1-50%, grade 3 50-99% and grade 4 a 100% lucency in the zone. We also calculated the percentage of the total interface covered by a radiolucent line. The frequency and magnitude of postoperative gaps between the cup and bone were determined, as well as possible osteolytic lesions.

The presence of osteolysis was noted in study 1 and 2 and in study 3 and 4 the size of the osteolysis was measured digitally as the area on the radiograph on the AP and lateral view. In all studies we measured the inclination of the cup in relation to the connecting line between the tuber ischii, the height of the rotational center above the greater trochanter (T-value), off set, the distance from the line of Köhler (mediolateral position ratio only study 1, 2 and 3) and proximodistal position above the tuberline. The radiological parameters are outlined in figure 14.

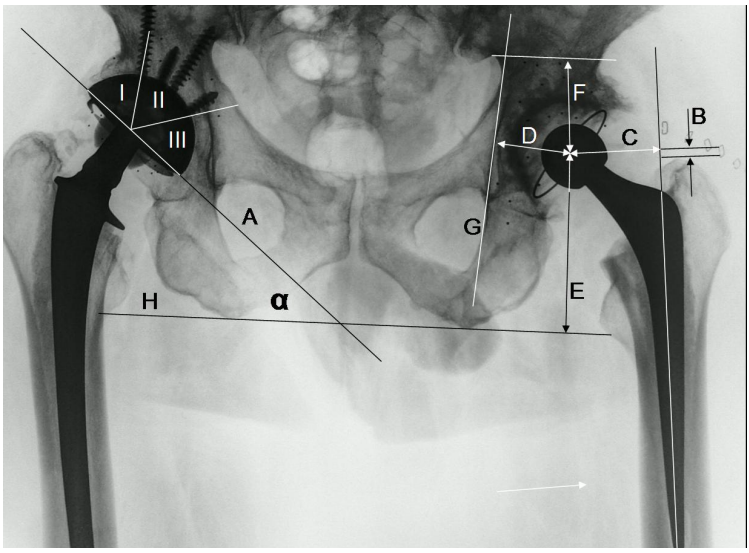

Figure 14: Standard x-ray of a hip with landmarks and help lines for measurement of cup alignment. A = inclination of the cup, B = height of the rotational center above the greater trochanter (T-value), C = off set, distance from the line of Köhler G (mediolateral position ratio D/C), proximodistal position (Ratio F/E of the distance of the center of rotation to the sacroiliacal joint and the connecting line H between the tuber ischii) total radiolucency and radiolucent zones within the sectors according to Charnley and DeLee (right hip in picture).

Evaluation of activity

In study 1 the activity level of the patients was evaluated by a questionnaire, which was sent to the patients at the 2 years follow-up. The questionnaire included 10 questions (appendix). Each question tried to collect information about magnitude and frequency of different types of activities performed by the patients. Types of activities included weight- and non-weight bearing activities, dynamic and non-dynamic activities, static and repetitive movements, and amount of impact at the joint of more than the body weight. The last question on the questionnaire asked the patients to subjectively grade their activity level from 1 – 5 (very low activity, less active, normal, active or very active). We used this question as an overall estimation of the patients' activity in study 2. For each question the patient rated the time and frequency spent with that particular activity during the previous week on a nominal scale from 0 to 3 or 5 depending on question. More time and/or higher frequency spent on the activity yielded a higher value. A patient could achieve a minimum of 9 and a maximum of 39 points. We studied the repeatability in a total of 20 patients (13 patients from Umeå) who answered the questionnaire a second time 2 weeks after the first time.

Statistics

We performed a Kolmogorov-Smirnov test for normality in some RSA results, which were mainly non parametricly distributed. For parametric data we used students T-test and for non parametric data Kruskal Wallis test to evaluate group differences in RSA results, length and distribution of radiolucent lines (Study 1, 2 and 3). For non quantitative data we used chi2 test between 2 and more groups (study 3). In the case of significant differences we applied a Mann-Whitney U test with Holm's corrected Bonferroni post hoc test for multiple testing. Changes over time were analyzed with Wilcoxon signed-rank test. Influence of patient (sex, age, weight, side, diagnose), implant (cupsize, type of cup and stem) and radiological factors (offset, inclination, osteolysis, size of osteolysis) on cup migration, wear and development of osteolysis was examined with stepwise linear regression.

In study 3 we performed a pre study power calculation. Based on an estimated clinically significant difference of 0.6 degrees or 0.6 mm between groups (Snorrason and Kärrholm, 1990, Önsten et al., 1998) a sample size of 20 in each group was required to achieve 80% power at the 0.05 significance level.

Ethics

The studies were approved by the ethics committee at the medical faculty at the University of Umeå and all patients gave an informed consent.

Results and conclusions

Study 1

Increased early femoral head penetration using ethylene oxide sterilized polyethylene

Objective

Sterilization by EtO minimizes the risk of oxidation but does not induce crosslinks in the PE. We therefore studied the penetration of the femoral head of conventionally sterilized PE (γ-irradiation) and EtO in cemented all poly cups and cementless sockets with PE liners.

Results

Femoral head penetration: The mean proximal penetration at two years was below 0.2 mm for the γ-sterilized cups, but more than 0.3 and 0.4 mm for the 2 groups that were EtO sterilized (p = 0,0005, Kruskal-Wallis test). The mean medial/lateral and anterior/posterior penetration was less than 0.1 mm in all 4 designs (p = 0.25 and 0.18). The mean total and three-dimensional penetration at two years was almost equal in the 2 γ-sterilized designs (0.27 / 0.29 mm) and higher (0.40 / 0.57 mm) in the 2 EtO designs (p = 0.0005). Uncemented cups with EtO sterilized PE displayed the highest penetration rate. In the uncemented EtO sterilized group 4 different fixation principles (press-fit with or without HA, pegs or screws) were used. HA coated cups had the highest proximal and three dimensional penetration rate (0.55 and 0.76 mm), whereas screw fixed cups had the lowest rate (0.40 and 0.47 mm; p= 0.07 and p = 0.007 Kruskal Wallis test) (table 6, appendix).

The early penetration of the uncemented group with EtO PE differs from graph in the original paper. The follow up was down at 2 and not at 6 months (Figure 15).

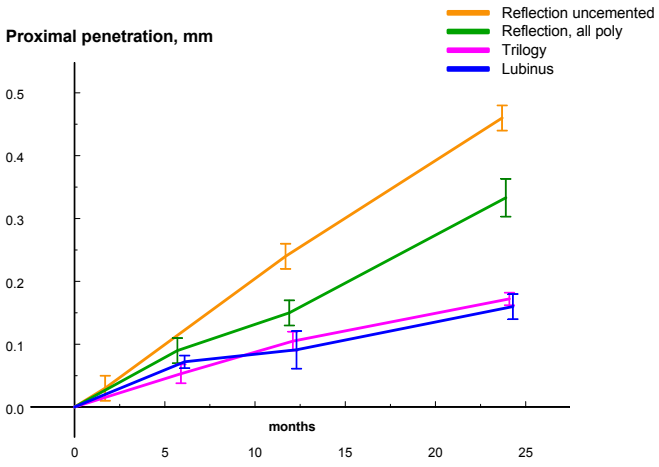

Figure 15: Proximal penetration of the femoral head. Mean (SE).

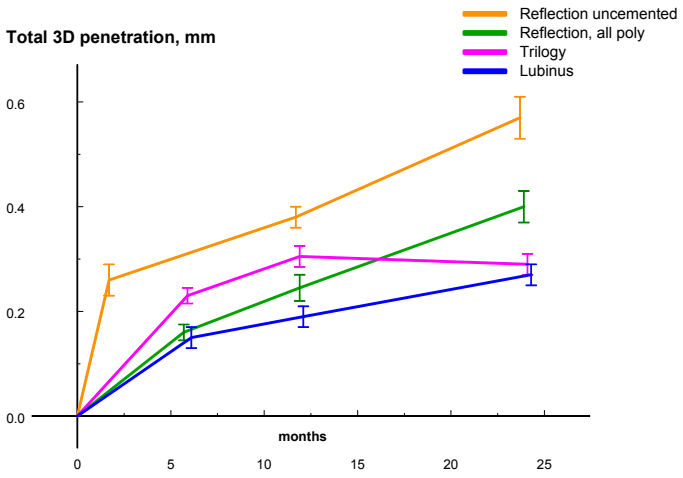

Figure 16: The total or three-dimensional vector length of femoral head penetration. Mean (SE).

The **three dimensional (3D) penetration**, but not the proximal penetration differed between uncemented EtO sterilized cups articulating against zirconium vs. chromium-cobalt (0.62 vs. 0.50 mm, p = 0.02; and 0.54 vs. 0.41 mm, p = 0.17). 3D penetration, but not proximal penetration differed between uncemented γ-sterilized cups fixed with screws vs. when no screws were used (0.26 vs. 0.33 mm, p = 0.04; 0.17 vs. 0.19 mm, p = 0.28) (Figure 16).

Stepwise linear regression analysis revealed that the proximal penetration increased with use of EtO sterilized cups (p=0.0005, adjusted $r^2 = 0.37$), decreasing age at operation (p = 0.0005, increase of r^2 to 0.46), male gender (p = 0.003, increase of r^2 to 0.49), increasing activity score (p=0.007, increase of r^2 to 0.51), and proximal migration of the cup (p = 0.046, increase of r^2 to 0.52). The total or three-dimensional penetration increased with use of EtO sterilized polyethylene (p=0.0005, adjusted $r^2 = 0.17$), increasing body weight (p=0.0005, increase of r^2 to 0.25) and decreasing age (p = 0.004, increase of r^2 to 0.28). The remaining variables (diagnosis, socket size, cement-no cement, inclination of the cup, side, medial/lateral, anterior/posterior and three dimensional migration of the cup) had no influence on penetration rate. There was weak correlation between activity score and age (r = 0.18, p = 0.05, Pearson correlation).

The repeatability for the questionnaire of the activity level varied between fairly well to full agreement between first time answering and second time (Kendall's tau = 0.7-1.0, table 7 appendix).

Conclusion

Method of sterilization affected the femoral head pentration rate of PE. EtO sterilized PE displayed higher wear than γ-irradited PE.

Study 2

In vivo wear and migration of highly cross-linked polyethylene cups. A RSA study of 50 hips

Objective

Modern cross-linked PE has in hip simulator studies proven superior resistance to wear compared to conventional PE, however data about *in vivo* performance was not available at the start of this study. Therefore, we investigated *in vivo* wear, migration and performance for the first released cross-linked polyethylene cups.

Results

Femoral head penetration: Proximal femoral head penetration over the whole time of follow up was 0.2 mm for conventional PE, 0.23 mm for heat stabilized and 0.08 mm for highly cross-linked PE corresponding to a 60 % wear reduction between study and control group (Figure 17). During the first two months the mean proximal penetration was for Groups 1 to 3: 45 μm, 86 μm, and 51 μm. This initial penetration was regarded as being mainly due to creep or plastic deformation. From 2 to 24 months the penetration (wear) was 156 μm (group 1), 138 μm (group 2), and 23 μm (group 3) (Kruskal Wallis test $p < 0.001$). There was no difference between sexes for either proximal or 3D wear ($p=0.3$ and 0.3).

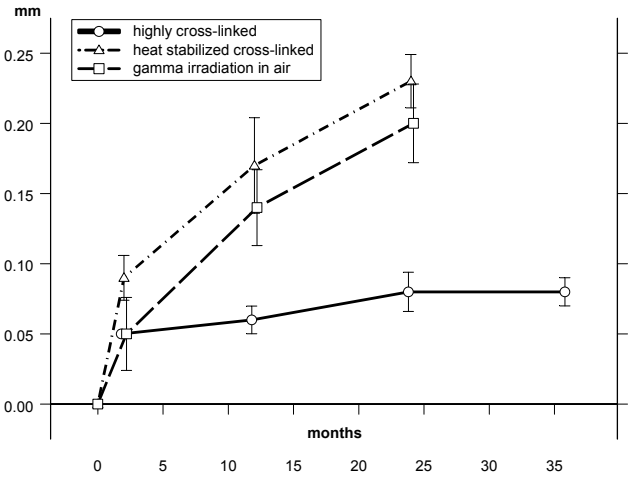

Figure 17: Creep and wear of the three groups. Highly cross-linked polyethylene had significant less proximal wear up to three years. Mean (SE).

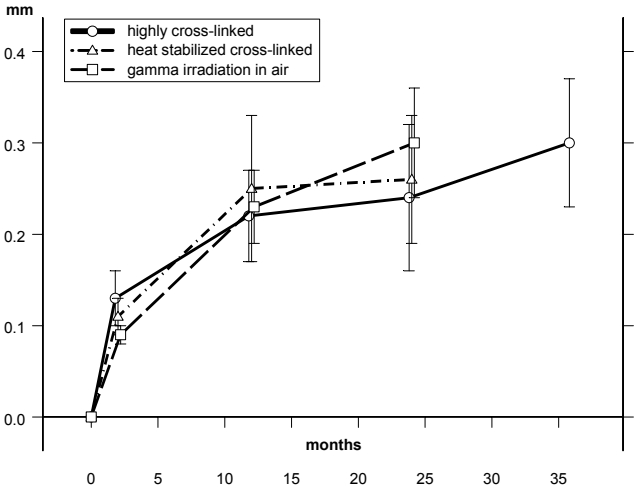

Figure 18: The total or three-dimensional vector length of femoral head penetration. Mean (SE).

Migration of the cups in the 3 groups was small with no significant differences between the groups (Figure 18)

Radiographic evaluation: Radiolucent lines > 1 mm were found in a mean of 3% of the interfaces post op and in 4% at 2 years. The change in RLL:s up to 2 years did not differ between the groups (p=0.8). There were no signs of early osteolysis in any of the groups. The inclination of the cups did not differ between the groups (p=0.3).

Clinical evaluation: The cups performed well with no differences between the 3 groups. Mean Harris Hip score for pain and total HHS improved from 17 preoperatively to 41 at two years respectively from 45 to 93, also without any group differences (p= 0.9 respectively 0.08, table 8 appendix).

Regression analysis revealed that neither age, weight, sex, cup size, inclination nor activity level did influence the magnitude of penetration. The personal estimation of activity displayed a 48 % correlation with proximal wear.

Conclusion

Highly cross-linked PE displayed lower *in vivo* wear without any negative effects on radiographic or clinical performance.

Study 3

Effect of cup augmentation on stability, wear and osteolysis – a 5 year follow up study with RSA

Objective

Augmentation by screws, pegs or HA coating is common in cups inserted by pressfit technique. The benefits and risks, however, are still controversial. We therefore studied the effects of augmentation in pressfit cups with focus on stability, development of osteolysis and wear.

Results

Migration of the cups: At five years the mean (SD) translation for all cups was 0.13 (0.28) mm proximally, 0.002 (0.41) mm medially, and 0.13 (0.42) mm anteriorly. The inclination increased 0.13° (0.84°), anteversion 0.13° (0.84°), and anterior tilt 0.15° (0.92°). There were no differences in migration between the four modes of fixation (Table 9 appendix, Figure 18).

The two cups in which the acetabular rim fractured during insertion had a much higher migration than the others during the initial year, but thereafter stabilized (Figure 19).

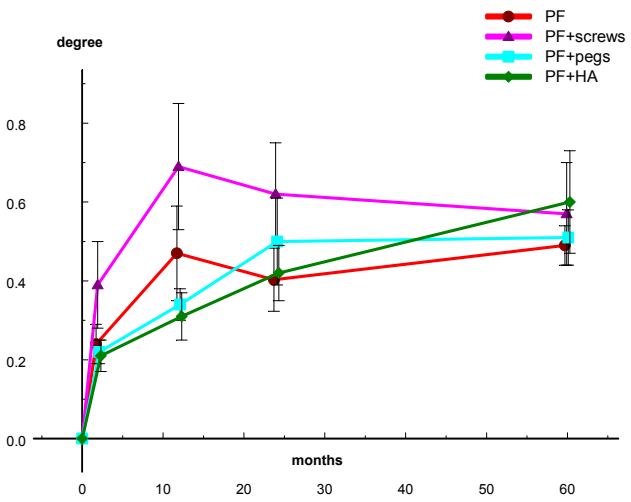

Figure 18: 3D migration of each group. Mean (SE).

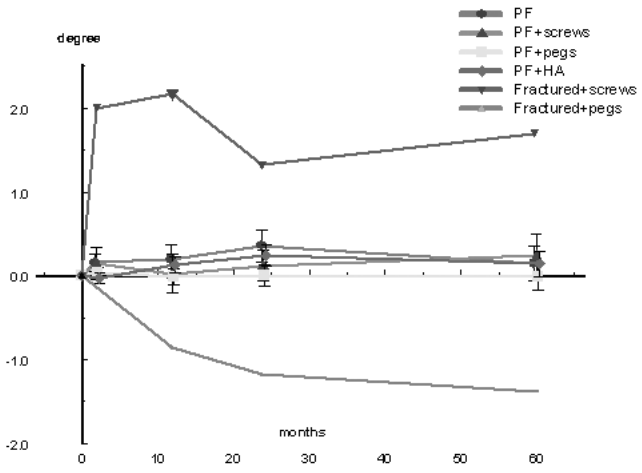

Figure 19: Change in inclination and migration of 2 augmented cups because of a fractured rim at insertion. Mean (SE).

PF = press-fit only, PF+HA = Press-fit plus hydroxyapatite coating, PF+screws = Press-fit + screw augmentation, PF+pegs = Press-fit with peg augmentation.

Inducible displacements: The inducible displacements 1 week and 2 months after operation were small, well below the detection limit of RSA, and did not differ between the groups.

Conventional radiography: The median (min - max) inclination of all cups was 49 (30 - 66) degrees and did not differ between the groups. Also there were no differences between the four groups for the horizontal or vertical cup position. Femoral median off-set was 35 (20 - 50) mm without group differences. Thirty-five of the 87 cups had a minor central gap at the postoperative radiographs (”non bottoming”) but it did not differ between the 4 groups ($p = 0.36$, Chi Square test). All gaps disappeared within the first 2 years. One PF+HA cup had a 3 mm large gap postoperatively but an excellent interface at 5 years anyway. The presence of gaps was not related to the development of radiolucencies at 2 or 5 years.

Quality of cup insertion: Fifty-six percent of the cups were graded to have optimal fixation at the time of operation, whereas 28 % were graded good, and 16 % doubtful. We could not detect any statistically significant correlations between this grading and the measured migration at any time postop.

Radiolucent lines and osteolysis: The HA-coated cups displayed less radiolucent lines (RLLs) ($p = 0.003$) than the other groups, both when measured as zone percentage as well as determined in the DeLee-Charnley zones (Table 10, appendix). The RLL were somewhat more common in women (17% vs 10%). Cups augmented with screws and pegs

developed RLL in 19% of the interfaces whereas cups with no holes (PF and PF+HA) had RLL in only 9% ($p = 0.001$). There were no differences in the development of RLLs between cups with or without a central gap at the postoperative x-ray.

At five years, focal osteolytic lesions around the cup were found in 5 hips with PF+screws, 4 of them were located in association with the screws. One hip with PF+pegs had a lesion close to a peg. Five hips with PF and two hips with PF+HA had osteolysis as well. Most of the lesions progressed slowly up to five years, however, retrospectively, five of nine could already be detected at the 2-year AP radiograph.

Two patients sustained a perioperative rim fracture. One patient received a PF+peg cup and developed RLLs in 70% of the interface, mainly distally. The other patient received a PF+screw cup and displayed no RLLs at the interface but developed an osteolytic lesion around one of the screws.

Wear: The proximal head penetration (wear) was 1.02 mm (SD 0.42), and the 3-D penetration 1.05 mm (0.42) after five years with no differences between the groups (Figure 20 appendix). This data corresponds to an annual wear rate of 0.2 mm. Men displayed more proximal as well as 3D wear than women did ($p = 0.02$-0.03). Wear was not significantly different between ZrO and CoCr heads.

Factors influencing migration and wear: Stepwise linear regression revealed that low proximal migration was significantly associated with hydroxyapatite coating and few radiolucencies ($p = 0.001$, adjusted $r^2 = 0.189$), increased weight ($p = 0.001$, increased adjusted r^2 to 0.208) and male gender ($p = 0.001$, increased r^2 to 0.21).

Polyethylene wear measured as proximal penetration was influenced by Charnley group ($p = 0.014$, $r^2 = 0.093$), male sex ($p = 0.016$, increase of r^2 to 0.126), increased weight ($p = 0.019$, increase of r^2 to 0.149), increased proximal cup migration ($p = 0.03$, increase of r^2 to 0.162) and low age at operation ($p = 0.043$, increase of r^2 to 0.173). The development of RLLs was associated with proximal cup migration, young age at operation, and female sex ($p = 0.002$, $r^2 = 0.205$). Remaining variables (mode of fixation, cup size, diagnosis, and migration in other directions) had no influence on wear or development of RLLs.

Conclusion

The stability of the cups did not differ between the groups, but HA showed a tendency to decrease proximal migration. HA coated cups displayed the best interface with hardly any signs of radiolucent lines indicating a superior sealing effect of the HA coating. Cups with screws or pegs had more radiolucent lines and osteolytic lesions than the other groups.

Study 4

Porous coated cups fixed with screws. 55 hips with clinical and 23 with radiostereometric 12 years follow up

Objective

In retrieval studies increased incidence of liner dissociation and wear are reported for first generation cementless cups in the second decade after surgery. Only with RSA *in vivo* stability of the liner can be measured. We therefore investigated long term survival of a first generation cementless cup. We focused on migration, liner stability, wear and development of osteolysis.

Results

Clinical results: Four patients with HG I cup were reoperated after a median of 11 years (6 - 11). The liner was exchanged in three cases and in one case an all poly cup was cemented into the socket. All metal shells were stable and left in situ. The overall cup survival for HG I cups (45) at 14 years with revision (liner and stem revision) for any reason was 89 % (CI ±14 Kaplan-Meier analysis) (Figure 21, appendix). None of the HG II cups had been revised with 12 years as the longest follow up. In all revision cases the femoral stem was removed. Three for excessive osteolysis and one for pain. Three were cemented Tifit stems and one was an uncemented Rippen stem. The median pain and Harris hip score increased up to 2 years ($p=0.0001$) but did not change significantly up to 12 years ($p=1.0$ and 0.4) (Table 11, appendix).

Osteolysis and radiolucencies: At the last follow up 30 cups out of 55 had developed acetabular osteolysis without difference between the HG I and HG II designs regarding numbers or size ($p=0.4$). Most osteolyses were located superolaterally often with a partial extension into the central region (Table 12). All osteolyses seemed to be in contact with screws and could in all cases be seen on the AP view and in 19 of 44 hips on the lateral view. There was no difference between male and female gender regarding size or number of osteolyses ($p=0.9$ and 0.1). The 3 revised Tifit stems tended to show more pronounced osteolyses than the remaining cases ($p=0.05$).

Table 12: Osteolysis and radiolucencies for Harris Galante cup type I (n=38) and type II (n=17). Distribution (0% / 1-49% / 50-99% / 100%) of radiolucent lines in each DeLee and Charnley region on the AP radiograph in the four groups of fixation. Length of radiolucent lines > 1 mm in percent of the total interface length at 12 years (antero-posterior view only).

Osteolysis (expansile)	**HG I**	**HG II**	**total**	***p-value****
Number with osteolysis	19	11	30	*0.4*
Size (mm^2)				
Mean (SD)	346 (174)	327 (160)	339 (166)	*0.8*
Min - max	19 - 715	66 - 545	19 - 715	
Contact to screws	Yes	Yes	All	
Localization				
(proximolateral/central/mediodistal)	11 / 2 / 1	8 / 2 / 0	19 / 4 / 1	
Radiographic views with osteolysis	17 AP and pelvicviews, 2 lateral	10 AP and pelvicviews, 1 lateral	27 AP and pelvicviews, 3 lateral	
Radiolucencies (linear)				
Number with RLL	17	10	27	
Median (Min – max)	16 (5 – 100)	21 (7 -60)	17 (5 – 100)	*0.3*
Charnley Delee				
I (proximal)	30 / 5 / 1 / 1	12 / 4 / 1 / 0	42 / 9 / 2 / 1	
II (central)	35 / 1 / 0 / 1	15 / 1 / 0 / 1	50 / 2 / 0 / 2	
III (distal)	26 / 5 / 4 / 2	10 / 4 / 1 / 2	36 / 9 / 5 / 4	

* HGI *vs*. HGII, Mann-Whitney U test

Radiolucent lines (RLL) were visible in 25 cups without any significant difference between the 2 designs of HG shells (p=0.21). Twelve radiolucencies were located in region I, 4 expanded into region II and 19 were visible in region III. There was no gender related difference (p=0.6). One cup displayed a circumferential osteolysis/radiolucency. The mean length of RLL of the total interface was 25 % (range 5-100).

Radiostereometry: *Translation*: The mean (SD) medial and proximal migration for the center of the cups was 0.14 (0.91) mm and 0.07 (0.75) mm respectively (Table 13, appendix). The cups translation did not increase over time (Figure 22).

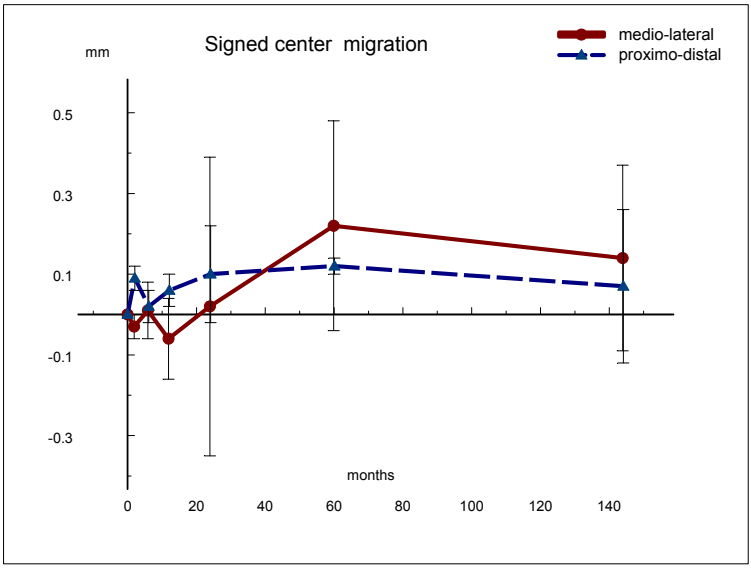

Figure 22: The mean signed translations (SEM) of the center of the cups (after point transfer). The cups were stable after 5 years.

Rotations

The absolute mean (SD) change in anterior-posterior tilt was 1.7 (0.99) degrees, the angle of anteversion changed 1.3 (1.7) degrees and inclination 1.8 (2.16) degrees.

All 16 cups displayed at least one rotation over the detection limit. Three cups rotated significantly in all 3 and 9 cups in 2 directions. These were classified as probable respectively possible liner rotations. One cup displayed RLL slightly over 50 % and was therefore classified as liner and/or shell rotation. This cup had migrated 1.48 mm medially, 1.74 proximally and 1.80 posteriorly. The remaining three cups were stable (Table 13, appendix).

Wear: The mean proximal and three-dimensional femoral head penetrations were 1.09 (SD 1.6) and 1.93 (2.46) mm, respectively (n = 15, table 14 appendix). The corresponding annual penetration rates were 0.09 mm and 0.16 without any differences between HG I and II (p = 0.6 and 0.8).

Conclusion

Survival including revision for any reason is comparable to cups cemented with first generation cementing technique. The PE liner displayed a high number of probable rotations within the shell. The metal shell was stable despite osteolytic lesions in over 50%. Most of these changes were clinically silent. We therefore recommend regular follow up of patients with HG cups to avoid sudden loosenings and complicated revisions.

Discussion study 1 - 4

Study 1

A statistically significant relationship between patient age and excessive wear has been reported by several authors (Nashed et al., 1995, Shih et al., 1997, Sychterz et al., 1997). In a review of the literature, Goldsmith et al. (2001) found that implant and patient related factors partly could explain the different amount of wear reported in the literature. Patient activity varied 25-fold when measured with a pedometer. Our finding that both age and activity have to be considered in the regression analysis probably mirrors the weakness of the correlation between these two variables. This implies contrary to common belief, that activity is unlikely to be the most important factor affecting the wide range of clinically measured wear. Other age dependent factors such as step length and walking speed or choice of physical activities might also influence the wear.

Our study was not randomized and could therefore not be controlled for several confounding factors. We are aware of this, but we believe that this problem do not jeopardize the overall conclusions.

One of the factors that could not be completely evaluated in our study is the use of zirconium heads in the uncemented Reflection group. Zirconium ceramics have been developed as an alternative to aluminum ceramics, because it is stronger and provides a greater margin of safety. The hardness and wettability of zirconium is superior to cobalt-chromium (Piconi and Maccauro, 1999). Experimentally the wear of zirconium against polyethylene was initially 2 to 3 times lower than that of cobalt-chromium on polyethylene bearings (McKellop and Luh, 1992, Derbyshire et al., 1994). The use of zirconium head in the majority of the cases with porous coated Reflection cups slightly reduced the early penetration rate. If all these cases had had heads of cobalt chromium, the wear rate would probably have been even higher. Meanwhile some reports have shown negative wear behaviour with Zirconium heads (Haraguchi et al., 2001; Allain et al., 1999; Kim et al., 2001) but the penetration rate did not increase substantially in our groups up to 5 years.

Another factor is the type of resin, since all Lubinus cups are made of Chirulen 1020 compared to GUR 1050 in the other 3 groups. Early penetration rate was similar between both PE suggesting that this factor was of minor importance.

The tendency to increased penetration at two years in the cups with pure hydroxyapatite coating is an interesting observation. Thanner et al. (Thanner, 1999) found no such effect in a case-control study of Harris-Galante cups with and without ceramic coating. The ceramic coating in these cups was a mixture of hydroxyapatite and tricalcium phosphate (HA/TCP). This coating resorbs faster than the pure hydroxyapatite coating used in the present study. It might be that HA/TCP particles may dissolve faster than pure hydroxyapatite particles and therefore with reduced tendency to induce wear. A number of studies have raised concerns about wear and osteolysis related to the disintegration of HA coatings (Lintner et al., 1994, Bloebaum et al., 1994, Røkkum and Reigstad, 1998). It is, however not clear if these observations can be related to the use of pure hydroxyapatite per se or other problems related to implant design such as thin polyethylene or insufficient

liner lockings. Criticism towards earlier studies is that they lack control group, have unconventional cup design (screw cup) and femoral head size predisposing for high wear (32 mm), and disadvantageous quality of the HA coating. The subgroups within the cementless Reflection group were randomized and used contemporary hemispherical press-fit cups with 28 mm femoral heads and HA-coating. Although most shortcomings of previous studies seem to have been eliminated it is not clear whether the temporary increase in wear is caused by the HA coating. The third body wear of hydroxyapatite particles before being completely resorbed, as found by Bloebaum (1994), could be the first hand explanation. Any influence of hydroxyapatite on long-term fixation, wear and osteolysis is probably dependant on the quality of the coating used and the underlying surface. In our study an EtO sterilized PE was used. It might be that EtO sterilized PE is more sensitive to wear caused by abraded HA particles, especially when zirconium femoral heads are used. Zirconium heads are harder than CrCo heads scratching the PE faster, at least temporary, in the presence of intercalated particles.

Our observations suggest that the use of a more resorbable coating could be beneficial, but this presumption needs to be further substantiated in controlled studies.

Men had more wear than women. This is in accordance with other authors (Schmalzried and Callaghan, 1999).

The effect of creep (cold flow) is most visible within the early postoperative phase and becomes negligible by 12 – 18 months. In our material we did not find a clear decelerating pattern for proximal penetration. The early phase in our 3D wear patterns could be interpreted as "wear in period". However, 3D corresponds to the length of a vector and cannot have a negative value. This is especially important when measuring the first recording, because the smallest change may be expected. If the mean error of this parameter is 0.1 the first penetration will be 0.1mm even if the true penetration is 0. In signed values the corresponding error will be positive and negative leaving the mean unaffected. Therefore the early 3D data should be interpreted with caution and strictly speaking does not represent a "wear in " period without reservations. Both uncemented designs show a more prominent decelerating pattern than the cemented cups. This might be an effect of more difficult conditions for measuring wear in uncemented cups caused by the "noise" of the metal socket.

A factor determining the ultimate effect of polyethylene wear is the biological response to these particles. Experimental studies (Scott and Widding K, 2001) have shown that particle diameter, surface area and volume are higher for ethylene oxide sterilized components. The biological response of macrophages to polyethylene particles varies depending on these factors. It has also been shown that oxidized polyethylene particles are more efficiently phagocytized than non-oxidized polyethylene resulting in higher release of IL-1 (Kamikawa K et al., 1998). The biologic response to wear particles is therefore difficult to predict.

Study 2

At 2 years highly cross-linked PE cups (made in the CIAN process) had 85% reduced wear *in vivo* compared to conventional PE γ-sterilized in air. This result is similar to that predicted by hip simulator studies.

This study was not randomized but consecutive. However, the groups studied were well matched in all variables except age, with the group with CIAN polyethylene being slightly younger. Younger patients generally display more wear and so this was not considered an advantage for the group with CIAN PE (Goldsmith et al., 2001). In addition, linear regression analysis did not indicate any influence of age or other patient variables on wear. Also, the surgical technique and follow-up methods were identical and the wear measurement done with RSA was not subject to measurement bias. Therefore, we believe the groups to be comparable enough for this study to be valid without being randomized.

The number of cups in each group was too small in order to detect significant differences concerning migration. The question now arises as to whether we can extrapolate these excellent wear results at 3 years to the longer term. Dowd (Dowd et al., 2000) has demonstrated that in the majority of cases, wear rate of cups is linear, which is also in accordance with previous RSA studies. Therefore, we believe extrapolation of these data to be a reasonable assumption. One reason this would not be the case is if the highly cross-linked PE oxidizes over time in situ. The CIAN PE used in this study is γ-sterilized after annealing. This seems a contradiction since this will again lead to generation of free radicals able to oxidize the PE *in vivo* (Jahan et al., 1991). However, based on *in vitro* tests and clinical experience so far, it seems that γ-sterilization in N_2 of cross linked PE after heat annealing is not detrimental.

Clinically, what we are most interested in is not the wear itself but its results, i.e. polyethylene debris and subsequent periprosthetic osteolysis. Wear rates below 0.1 mm/y are associated with a low probability of osteolysis and wear rates below 0.05 mm/y is considered to be a "safe" level, (Sochart, 1999, Dumbleton et al., 2002). The 0.01 mm/y wear rate found in this study is far below this threshold. What is not clear is whether these wear results will improve the longevity in the long run. The relationship between wear and osteolysis is complex and involves patient-dependant response to wear debris. *In vitro* studies have shown that the cellular response to wear particles is dependant on their size, shape, resin of origin, and concentration, with particle surface area possibly being the most important factor (Ren et al., 2002, Tipper et al., 2002). Ten Mrad cross-linked PE seems to produce particles somewhat smaller than conventional PE, but the total amount of the smaller particles is still much less than what is found for conventional PE (Ries et al., 2001). Comparisons of bioactivity between debris of different PE's are important however, if we are to extrapolate wear rates and osteolytic response of conventional PE to different cross-linked PE's.

Recently there has been an increasing interest in the relationship between hip joint pressure, cup instability, and osteolysis (Aspenberg and van, V, 1998) suggesting that new

wear resistant polyethylenes, even if they work fine clinically, may not totally abolish the problem of osteolysis all by themselves. Even if the wear problem itself is not close to being solved completely by the new cross-linked PE's, they might however have other positive effects on arthroplasty, such as allowing the reintroduction of large femoral heads with their better range of motion and stability (Muratoglu et al., 2001a).

Other highly cross-linked PE's such as those of the WIAM process appear to change the crystallinity and the physical properties more than the CIAN process (Muratoglu, 2001). It is important to realize that the different techniques to highly cross-link PE might yield PE's with different properties. Therefore it is important that all new highly cross-linked PE's are rigorously tested clinically for safety before being used on a world-wide scale.

In a recently presented report of retrieved cups made of highly cross-linked PE by the CIAN method, alarming high amount of oxidation *in vivo* and increased wear rate was found (Bhattacharyya et al., 2004). We will therefore re-examine our patients from study 2 with Crossfire PE as soon as possible.

Study 3

Our results corroborate that good primary stability of uncemented press-fit cups can be achieved up to 2 years irrespective of mode of augmentation. This is in accordance with Takedani (1991) who found in an acetabular cadaver study that all commonly available means of fixation are roughly equivalent as long as low torsion loads are applied. This might be the case in everyday life. Although many authors report superior fixation of cups augmented with screws (Takedami 1991, Lewallen 1996, Goldberg 1996) we did not find this in our patients.

Postoperative gaps i.e., distance between the bottom of the cup and bone, were seen with equal distribution in all 4 groups. Press-fit cups have been found to have such gaps, especially with under reaming of 2 mm (Kim et al., 1995a, Kwong et al., 1994). Postoperative gaps in press-fit cups are generally interpreted as inferior operating technique and disadvantageous for cup survival. However a tight rim fit preferably in combination with cups sealed with HA coating might even have a positive effect by inhibiting particle dissemination (Rahbek et al., 2001). Søballe (1993) found clear bridging of the initial 1 mm gap already after 4 weeks in a dog model and the stability was superior to plain titanium press-fit implants. The postoperative existence of gaps might therefore be acceptable because they (a): disappear within a short time when using HA coating; (b): have superior fixation by bone ingrowth (Geesink et al., 1987); and (c): provide a good rim-sealing effect.

The HA cups had the best radiographic interface between metal shell and bone. Reikerås and Gunderson (2002) also found in their patients an excellent radiological interface. However some implants were revised because of pain. Intraoperatively they found the cup was loose in spite of a lack of osteolysis. Their results are, however, not quite comparable to the present study because of differences in HA coating and in cup surface structure. Reikerås' cups had a three times thicker HA layer sprayed on grit blasted

cups. Their finding of HA delamination from the grit blasted surface might, therefore, not necessarily apply to HA coated cups used in our study.

The interface of the HA coated cups was more able to withhold the development of osteolysis compared to the other groups. As suggested by Rahbek et al. (2000) this might be due to a sealing effect of the HA coating on the space behind the cup preventing spreading of wear particles. It will be interesting to see how long the bone interface will remain pristine and how well the cups will perform in the long run when higher amounts of particles are disseminated.

Screw augmented cups had significantly more volumetric osteolysis than peg augmented cups – mainly located around the screws. This might be caused by cup micromotions, unsealing screw wholes. A difference between screws and pegs is that the screws are inserted into the bone holding the cup through tension forces in place. By micromotions and bone remodeling the cup might subside, opening small gaps between the cup and the screw head, letting particles pass through. Since we found less osteolysis in the group augmented with pegs we interpret the results as a rational for an improved sealing effect of the cup holes by the pegs. Reason might be a tighter contact between the pegs and the cup, actually holding the cup in place through rigorous fixation between each other rather than tension forces pressing the cup against the bone.

Two acetabular rims fractured during cup insertion. Ries et al. (1997) found that when a constant millimeter increment in cup oversizing is used, there may be a greater risk of rim fracture in small acetabulae and a greater risk of inadequate press fit stability in large acetabulae. To achieve the same amount of acetabular deformation and magnitude of strain, more oversizing is needed in a large acetabulum and less oversizing is needed in a small acetabulum. Kim et al. (1995) reported a 60% frequency of fractures during insertion of 2 to 4 mm oversized cups, and not all fractures were apparent on normal AP and lateral radiographs. With around 2% fracture rate detected intraoperatively,the real fracture rate might be higher. The increased migration of the cups with broken rim shows that additional fixation is mandatory for cups with defects in the rim as advocated by Adler (1992). We suggest screws or pegs as save salvage procedures to achieve stability in compromised bone stock.

Study 4

Our study is the first long-term follow up of a cementless porous coated acetabular component with radiostereometry. In this study we did, however, meet with a number of technical problems not foreseen when these studies were initiated in 1987. Use of thin liners, a large femoral head and change of the stereoradiographic set-up implied that liner markers easily became hidden behind the radiopaque parts of the prostheses. In addition, liner rotations obviously occurred, further jeopardizing visualisation of the same markers over time. In the future, marking of the metallic shell or current development of stereoradiographic techniques (Börlin 2004, personal communcation) enabling accurate determination of cup position will reduce the need to visualise implant markers.

In this study we wanted to ascertain good technical quality and therefore discarded all examinations with poor marker configuration or signs of marker instability.

Despite these technical problems, the remaining cases provided us with some important information. The small early micromotions observed with this cup design (Kärrholm and Snorrason, 1992) indicated stable fixation at least in the 12 year perspective. Osteolysis occurred at a high frequency despite absence of migration. In cases where the osteolysis progresses the process will subsequently result in loosening and even fracture of the remaining anchorage. In such cases late commencing migration may occur (unpublished observation).

Our RSA data also suggested that liner rotations, incidental or continuous, are comparatively common with this cup design. Small rotations above the detection limit may also be caused by early migration of the shell. A definite limit between migration and instability of the liner is difficult to determine. It is reasonable to believe that more pronounced liner rotations in combination with minimum translations and absence of complete radiolucencies after 12 years represent anything but instability of the liner. Small Liner instability will increase backside and probably also articular wear. It also indicates inferior liner fixation and a predisposition to dissociation.

In our study cup migration was calculated as the motion between two rigid bodies i.e. acetabular and the cup markers. This means that the translation of the cup is represented by the gravitational center of all markers visible at the postoperative examination. In most cases this center could be supposed to be situated close to the center of the cup. If eccentrically placed, any rotation of the liner will change the point of measurement and suggest a translation of the shell, which never took place. To overcome this problem a so-called fictive or real point (eg. the femoral head center position at the postoperative examination) may be used. This position can be found on the subsequent examination by the use of the liner markers as utilized in our evaluation. This procedure will eliminate or at least reduce the influence of liner rotations on the measured translations. As indicated above future studies may use new and alternative techniques to overcome this problem.

Thanner found a proximal wear rate of 0.12 mm /year in 21 cementless cups (Trilogy®, Zimmer) with a liner sterilized by γ-irradiated in nitrogen after 2 years (Thanner et al. 2000). This wear rate is somewhat higher than in our study but their observations might be due to relatively more creep because of shorter observation time. Comparison of wear data obtained with use of alternative measuring techniques is often less valid as wear rates vary depending on the precision of the measuring method used (Schmalzried 1998).

Our patients had low wear rate despite their young age (Maloney et al., 1999). Schmalzried pointed out that wear is not a function of time but of use (Schmalzried et al., 2000). We do not think that our patients were less active than the average and especially because most of them lived in a forest environment or rural area, where physical activity is usually a part of daily living.

Nivbrant (Nivbrant et al., 2001) studied cemented all poly cups up articulating against aluminium ceramic heads up to five years. In these cups the 3D wear was substantially lower (0.07 mm). This could suggest that all-polyethylene sockets wear less, but these

patients were at least ten years older and different base resins were used indicating that no conclusive comparison can be done due to confounders.

More than half of all patients developed osteolysis in our series. To our knowledge this is the highest number of osteolysis reported for this cup. In a midterm perspective around 25% osteolysis are a reported complication (Soto et al., 2000, Clohisy and Harris, 1999b). Manley explains the development of osteolysis as a "disease for which access is required" (Manley et al., 2002). The Harris Galante cup has multiple holes for versatile screw fixation. Easy access of joint fluid carrying particles through these holes or the fluctuating pressure as such might be of importance (Aspenberg and Van, V, 1998).

Schmalzried questioned the influence of holes. They examined cups with and without holes (Schmalzried et al., 1999) and found more osteolysis in the later group. The patients were followed 40 - 108 months and within that period there was a correlation between osteolysis and length of follow up. We followed our patients for a longer mean time than the upper limit in this study, which could be an explanation for the high frequency of osteolysis in our series. Osteolysis occurred in young light patients with a cemented stem. Young age and low weight characterize an active patient group and the material of the stem was titanium. Our findings confirm the correlation of activity and osteolysis (McClung et al., 2000) with low survival of a cemented titanium stem (Malchau et al., 2002).

Survival: We found 89% survival rate including all revisions for any cause up to 12 years. A more aggressive surgical attitude in the treatment of osteolysis would certainly decrease the survival rate even more. Although the metal socket was found to be stable ingrown we anticipate that the high prevalence of liner rotations and osteolysis will result in more revisions in the future.

General discussion and future implications

Wear of the acetabular component

The search for more resistant materials has been the focus of the last decade. Particles created by material abrasion were the defined enemy to be eliminated. Up till now, three alternative bearing surfaces are the choices next to the classic and still most widespread metal on poly articulation in hip arthroplasty. This includes the two hard on hard articulations metal on metal and ceramic on ceramic and the new generation of metal on soft articulation with highly cross-linked PE. The minimal requirement for each solution is to perform better than the common standards. This is not an easy task as long term follow up data confirm a 25 year survival of about 80 % for the Charnley prosthesis cemented with first generation technique (Malchau et al., 2003, Berry et al., 2002). During the last 25 years many new designs have tried to beat this record but vanished after unsatisfying short or mid term results leaving many patients abandoned for revision surgery as the only solution.

One of the reasons is oxidative degradation over time of conventional PE resulting in substantial decrease of wear resistance (Kurtz et al. 2003). Free radicals produced by γ-irradiation in air are responsible for this process which may start even already before implantation during the implant's shelf life. Engineers, researchers and manufacturers took advantage of surface sterilization by gas plasma or EtO to avoid free radicals at the expense of lacking cross-linking of the material. The other development was to increase cross-linking and perform final sterilization in an inert atmosphere (Nitrogen) or with EtO.

We tested both materials in clinical *in vivo* trials. EtO had twice the wear rate of conventional polyethylene whereras highly cross-linked displayed an 80% reduction (**study 1 and 2**). The strength of study 1 is that it embraces a relatively large group of patients and both studies were initiated early and use a high resolution measuring method (RSA). A weakness is the non-randomized design with study 1, being a meta analysis and study 2 a consecutive one. But the results of both studies have been confirmed by others (Oroshino et al., 2003b, Martell et al. 2003, Digas et al. 2003). **Study 1** is at least partly responsible for the stop in manufacturing EtO sterilized PE after a short time of production.

Decisive, however, is not the reduction of wear per se but the effect of wear particles on human metabolism causing bone resorption and implant loosening. Particle analysis has revealed that EtO particles are larger but not necessarily more abundant. This also effects the biological activity of these particles. Ingham (2000) showed that it is not the wear volume itself that determines the biological response but rather the volume that is within the range of critical particle size. Hence, it is not yet clear whether these particles will have a deleterious effect leading to osteolysis or not. We found osteolysis in 13 cups (15 %) after 5 years which is similar to other modular designs (HG, PCA). However, we used different fixation methods that could be possible confounders. Still, most osteolysis was detected even already after 2 years and progressed up to 5 years (**study 3**) which does not favour positive long-term results for EtO sterilized implants. Additionally, if the wear were continuous, complete wear through of the PE might lead to mode 2 wear, such as the

femoral head scratching against the metal shell. Non cross-linked PE might be free of radicals but this will not show a positive effect if the cup fails because of wear through and osteolysis in the first decade.

On the contrary, recently published *in vivo* data seems to confirm high wear resistance for highly cross-linked PE, at least in the short term. In a RSA study Digas and colleagues found a 50 % reduction of proximal wear for highly cross-linked PE (WIAM method) compared to conventional PE (sterilized with γ-irradiation in nitrogen). Interestingly the difference reached significance only when the patients were studied standing but not in the supine position. However, Digas et al. relates this to the fact that the standing evaluation was not started until 3 months after the operation and therefore presumably does not include creep. Another reason could be the reduced strength and elasticity modulus leading to a measurable plastic deformation when loaded. Martell and his team followed 46 hips randomized to either highly cross-linked PE (CIAN) of the same type as used in this thesis or a control group with conventional PE γ-irradiated in nitrogen. He used a computer assisted edge detection method on plane radiographs and measured a 42 % reduction in proximal wear after 2 years. Surprisingly, the reduction in wear rate was not as large as the the wear rate reduction of more than 90 % found in *in vitro* tests (McKellop et al., 1999). Similarly to the Digas group, Martell claims the initial bedding in effect of the femoral head is responsible for the difference between predicted and observed wear rate. We found a 60 % reduction in wear including and an 85 % reduction excluding the first 2 months, which is slightly higher than Digas' results. In our measurements from the second month after surgery, bedding in of the femoral head and creep might certainly still be a considerable factor and therefore result in a higher wear reduction. Yet, all three *in vivo* studies confirm a wear reduction of 40 – 60 % up to 2 years for highly cross-linked PE compared to conventional polyethylene which is analogous to that suggested in simulator studies.

In our study moderately cross-linked PE did not reduce wear substantially up to 2 years compared to conventional PE sterilized in air. Hopper and colleagues studied the *in vivo* wear of another moderately cross-linked PE and found a substantial reduction compared to the gas plasma sterilized control (Hopper, Jr. et al., 2003). The mean annual wear rate for moderately cross-linked PE was 0.08 mm and for the controls 0.18 mm. The control group was not cross-linked which could be an explanation for the higher wear rate. The annual wear rate in our material was 0.11 mm. Follow up in both studies is short and the cross-linking might show effect compared with conventional PE first in a longer follow up period.

In accordance to our results, none of the *in vivo* studies so far reported have shown any negative effects on radiographical appearance and stability, neither in cemented (Digas et al., 2003) nor in cementless cups (Hopper, Jr. et al., 2003, Martell et al., 2003). Digas and colleagues measured bone mineral density (BMD) in three regions of interest (ROI) in the acetabulum and found a significant increase in BMD proximally and a tendency to decreased values medially for highly cross-linked cups. However, despite these findings, there were no differences between the study and the control group at 2 years. They concluded that it might be that the different mechanical properties of the PE influence

BMD, but if so, the differences were too small or the follow-up not long enough to be detected by DEXA.

The so far promising *in vivo* results of highly cross-linked PE do not, however, allow their use without restrictions. Costa et al. studied PE retrievals and found a high amount of synovial fats (cholesterols and esters of cholesterols) embedded 1-2 mm into the subsurface area (Costa et al., 2001). These fats make the surface softer and their effects on mechanical properties and performance changes are not known yet. These findings should be taken into account when interpreting hip simulator data, as they use non-human lubricants. Rieker and colleagues found micro-cracks at the surface of retrieved highly cross-linked PE liners (Rieker et al., 2001). Such cracks have also been described earlier in conventional PEs as well, and the maximum depth was not exceeding 5 μm. The authors therefore believe that there is no risk for further crack propagation leading to material damage. Muratoglu examined optically the damage on retrieved tibial component inserts and found less damage on highly cross-linked implants (Muratoglu et al., 2004). They found restoration of machining marks and disappearance of surface scuffing after melting the implant to activate its shape memory. They concluded that the visible changes on the surface were due to plastic deformation and not to abrasion. Endo found a higher amount of smaller particles in cross-linked wear debris (Endo et al., 2002). Smaller particles from cross-linked PE did not display a smaller functional biological reaction than particles from conventional PE. This leaves the question open as to whether the highly cross-linked particles in fact over time actually will cause less bone resorption.

Another important aspect to consider is that cross-linking may be achieved by several methods and that the current manufacturing processes differ substantially. As described earlier, melting is a question of debate because it changes the PE microstructure. Bhattacharyya et al. (2004a) studied retrieved cups made of annealed (non remelt) highly cross-linked PE wit γ-irradiated as final sterilization (CIAN, see highly cross-linked PE). He found severe oxidation and a high amount of free radicals in these cups. The hip simulator tests showed extremely high wear rates. These results are alarming and emphasize the importance for small controlled trials with regular follow-ups and high resolution measuring methods. Data on mechanical testing of different highly cross-linked PEs are not equally available for all materials and new developments in this field are extremely fast. For example, now, mechanical compressing is suggested as a possible means to eliminate free radicals and the negative effects of remelting the PE, to thereby sustain the good mechanical properties of UHMWPE (Bhattacharyya et al. 2004b, Turell et al. 2003). The first *in vitro* results were encouraging. We do not know what will be the best solution for the acetabular component. This might partly depend on economical dynamics of the open market but the final user should know that substantial differences exist. Not all highly cross-linked materials will stand the test of time. Therefore, it is even more important to critically review results in this fast evolving area.

In addition, highly cross-linked PE might be a future solution for wear management in acetabular components, but these accomplishments should not uncritically be transferred to other implants and locations. Shanbhag and Endo found larger particles of varying

shapes around retrieved knee implants compared to what was found in hip implants (Endo et al., 2002, Shanbhag et al., 2000). Reasons might be higher local compressive forces and a more unidirectional loading pattern compared to the hip joint (Lewis 2001). Delamination caused by oxidation is the predominant failure mode in knees. Muratoglu studied tibial inserts *in vitro* and found better delamination resistance even in aged highly cross-linked inserts compared to the conventional control group (Muratoglu et al., 2003a). This sounds promising, but *in vitro* measurements of wear and delamination is yet not possible and, therefore, only time will tell whether laboratory results are valid also in clinical practice of knee implants.

Still, if further *in vivo* data confirms improved wear resistance without any clinical side effects, it will strengthen the debate concerning increasing the size of the femoral head (Callaghan 2003 and Maloney 2003). *In vitro* studies claim that wear of highly cross-linked PE is independent of variations in femoral head size ranging from 22 to 44 mm (Muratoglu et al., 2003). This certainly might be helpful to decrease the dislocation rate and offer a larger range of motion to the patients, but as yet it is difficult to predict whether this leaves cup performance unaffected. History has proven that small design changes can have enormous effects on implant survival. But for now, *in vivo* data is not available yet to answer these questions and leaves interesting issues for future clinical investigations.

Fixation of the acetabular component

The optimal fixation of the acetabular component is still a topic of discussion. In 1998 a meta analysis of 234 published articles found no clear advantage for either uncemented or cemented fixation in the short to medium time frame. But the rate of acetabular revision in cemented implants remained problematic (Faulkner 1998). Clohisy found, in a matched pair analysis of 45 cemented and 45 cementless implants, that 97 % of the patients in each group were satisfied with the surgery after 9 - 12 years. Clinically the results in both groups were excellent but the cemented design displayed significantly higher number of radiographically loose implants (Clohisy 2001). Although cemented cups had more RLLs they were clinically without symptoms. Currently, the powerful outcome tools of national hip registers favour the cemented design (Malchau et al., 2003, Norwegian hip arthroplasty register 2002). Considering the length of follow-up and the number of patients included the record to aim for are the long-term results of cemented cups, in particular those of the Charnley's low friction cup with first generation cementing technique. The success of promising cementless designs in the mid term perspective has recently been hampered by decreasing survival rates in the second decade when revision for any cause was considered (Havelin et al., 2003). Fixation with modern cementless cups, however, is not the main concern. Metal porous coated sockets are stable. In cementless acetabular components liner associated problems such as wear and dissociation and osteolysis are the main reasons for revisions. Our long term results confirm this (**study 4**). Thanner et al. found that satisfactory stability can be achieved using uncemented hemispheric cups with a titanium surface and that modifications will improve the modular design of uncemented cups (Thanner 1999). His group studied designs inserted with the line to line technique in which

the fixation was augmented by screws. Our results indicate that a reliable stability in cementless press-fit cups may be achieved without additional augmentation up to 5 years (**study 3**). Reduction of intraoperative complications such as damage of vital structures by the screws (Wasielewski 1992) and reduction of costs (material and operating time) might further effect the survival of the cementless implants.

Study 4 suggests that an increase in liner associated complications in the second decade after implantation of the Harris Galante cup are to be expected. According to the manufacturer, there were around 300,000 Harris Galante cups implanted world wide (personal communication). We expect that a high number of these patients are still alive because this cementless design was intended for young patients. Liner instability in those patients increases the risk for backside wear and osteolysis, and also puts the patients at risk for liner dislodgement in extreme situations.

Other cup designs, such as the modern theaded cups and the extreme macroporous cups with and without coating, are in use in single centers, but their results are hard to compare because unbiased data from controlled randomized trials or comparable registers are often lacking. Müller et al. (2003) collected data from 17,951 cases over 33 years. They found a 97% survival after 10 years for threaded titanium cups compared to 76% for cemented PE cups. This differs dramatically from the data from the Scandinavian hip registers. Müller explains the difference by the fact that they started to collect data 10 years earlier than the Swedish register and that they do not differ between stem and cup loosening. The main reason, however, might, be that Müller did not define revision, but rather radiological loosening as the end point. And the reporting of data was optional, which, despite motivation of the doctors, always is a possibility for bias. Each design might be a potent solution for current problems, but before they may gain general acceptance they need to be evaluated with modern measuring tools against reliable and documented solutions considering the complete scope of today's health systems.

Still, the main problem of osteolysis for stable cemented and uncemented acetabular components remains. The etiology of osteolysis might be more complex than the bare elimination of particles. Stress shielding behind the stiff metal socket or fluctuating pressure waves of the joint fluid are other models that might gain more attention in future research. We found a tightly sealed interface and no RLL in the HA coated cups in **study 3**. HA did not affect proximal wear negatively up to 5 years. Other designs and materials such as mono-block prostheses to reduce interfaces in cementless designs, new metals with more physiologic elasticitic modulus to reduce stress shielding, or new coatings and compounds are already on the market and challenge new and old implants. Since highly cross-linked PE was approved by the FDA in the United States, it has already gained substantial shares of the American market, however predominantly in cementless designs. Criticism against the cemented designs is the risk for late aseptic loosening by a biological reaction starting at the periphery of the implant by particles infiltrating the interface (Schmalzried et al., 1992). Hence, the reduction of wear by highly cross-linked PE will even dampen the biological reaction at the interface in cemented implants. This implies maybe an even larger benefit for cemented implants than for cementless.

Every improvement offers new possibilities for groups at risk. Young, male and active patients are the clearly defined group of concern. We could confirm these risk factors partly for migration and for wear. This makes clear that every patient offers and demands individual factors to be considered before surgery. Cementless hip arthroplasty is in general faster because time for meticulous preparing of the bone bed and cement hardening is not necessary. Further, fat embolization, a reported complication when cementing implants, is diminished (Sharrock et al., 1995). Both aspects favour cementless fixation in patients with riskfactors because of less traumatic surgery.

The surgeon is in the position to choose the right implant at surgery with the right technique. Primary surgery is the golden chance to do it right already from the beginning and determines the patient's fate in his life with a hip prosthesis (Eisler 2003). The *right surgeon* should decide on the *right implant* for the *right patient*. Therefore, the question about the best fixation method can not be answered without considering the triangular complexity of the question and its interactions.

This system will only be as strong as the weakest part and consists always of a combination of all three factors: *Surgeon*, *patient* and *material!* Each one is influenced by external factors such as tradition, quality assessment or health systems and individual circumstances. Therefore, the optimal solution with regards to fixation and bearing surfaces will be different for different constellations of these three factors.

But within each one of these factors there always exists a need for improvement and reflection. For surgeons, in decision making and surgical technique; for patients in understanding how to live with the prosthesis; and for manufacturers of materials to offer the best non-organic solution in a biological environment.

Conclusion

Study 1: Polyethylene sterilized by ethylene oxide has twice the penetration rate (0.2 mm/year) as compared with conventional PE. The long term effects are yet unknown, but we are strongly concerned about the continued use of this less wear resistant polyethylene in young patients in combination with cementless implants and thin polyethylene.

Study 2: Highly cross-linked PE has substantially less wear (0.01 mm/year) compared to conventional PE during the first 3 years. Heat stabilized, moderately cross-linked PE was not better than conventional PE up to 2 years. So far, the reduced wear is not at the expense of increased migration, early radiolucencies or known clinical disadvantage. Short term results are promising but longer follow-up data is necessary to rule out late clinical shortcomings.

Study 3: Screws or pegs did not improve the excellent fixation of press-fit hemispherical cups. Sealed cups (i.e. no screw holes) and HA coating resulted in less radiolucencies and better interface without any trade offs. Since the main problem with press-fit cups is osteolysis rather than stability, a fully sealed HA coated cup seems a logic alternative. Augmentation by screws or pegs is not necessary in primary cementless cup fixation but is a reliable salvage procedure when primary stability is compromised, for instance if intraoperative rim fractures occur.

Study 4: The survival of the first generation cementless cups is comparable to cups cemented with first generation cementing technique up to 10 years. The main problem seems to be liner instability due to poor locking mechanism with a high number of probable liner rotations within the shell. The metal shell was stable despite osteolytic lesions in over 50%. Most of these changes were clinically silent. We therefore recommend regular follow-up of patients with HG cups to avoid sudden loosenings and complicated revisions.

The factors surgeon, implant and patient determine the best suitable solution. Osteolysis is still the main problem. In the second decade expansile osteolysis may necessitate revision in cementless cups and linear osteolysis jepeardize stability in cemented cups. The survival of both designs may improve if highly cross-linked PE continues to prove increased wear resistance without any negative clinical consequences.

Summary - Populärvetenskaplig sammanfattning

Swedish - Svenska

Betydelsen av slitage och förankring av ledskålen hos höftproteser -In vivo analys av olika plaster och fixationsmetoder

I slutet av 1960-talet lanserade Sir John Charnley den moderna höftprotesen—ett ledhuvud och stam av metall samt en ledskål i bäckenet av polyetylen (plast), alltsammans fixerat till ben med bencement (polymetylmetakrylat, ”plexiglas”) — en design som än idag används i olika varianter. De enskilda komponenterna i den totala höftartroplastiken har sedan dess genomgått en kontinuerlig utveckling för att bättre leva upp till de krav som en successivt ökad protesanvändning resulterat i. Således har olika material och design för de olika komponenterna lanserats, liksom har alternativa förankringssätt introducerats. Resultaten har dock varit varierande.

De tidigaste höftproteserna lossnade ofta, av vad som man tolkade vara infektionsutlöst bennedbrytning av det protesnära benet. Detta visade sig också i många fall vara riktigt, men numer ökar antalet lossningar utan association till infektion, något som kallas aseptiskt lossning. Man kommit fram till tre huvudorsaker 1) materialslitage (ffa av polyetylen); 2) instabilitet, och 3) skada på det protesnära benet genom ökat ledvätsketryck. Alla dessa faktorer samverkar troligen. De mikrometerstora slitagepartiklarna från polyetylenet transporteras med hjälp av ledvätskan till det protesnära benet och stimulerar kroppens celler till att bryta ner detta.. Om protesen är lös initialt har ledvätskan lättare att finna väg till benet och därmed underlättas bennedbrytningen. Olika typer av mer slitagetålig polyetylen har på senare år konstruerats, men litet är känt om deras kliniska prestanda. Dessa nya plaster har, förutom bättre slitagetålighet, dock förändrade elasticitetsegenskaper, vilket teoretiskt kan påverka protesfixationen negativt. Detta gäller framförallt för yngre och aktiva patienter som utsätter plasten för större krav.

För att kunna studera protesers fixation och slitage krävs sofistikerade röntgenmätningar med hög precision. Vi använder radiostereometrisk analys (RSA), vilket är den gyllene standarden för att mäta mikrorörelser mellan protes och ben samt slitage *in vivo*. Dessutom användes konventionell röntgen och kliniska mätmetoder.

Studie 1: Vi undersökte slitage och stabilitet av 201 ledskålar (cup) med olika sorters polyetylen, vilka skilde sig åt genom olika steriliseringsmetod, en faktor känd för att kunna påverka plastens materialegenskaper. Största slitaget hade cementfria proteser med etylenoxid (EtO) steriliserad polyetylen. Polyetylen som var γ–steriliserad i luft eller i inert atmosfär hade mindre slitage, men det fanns ingen skillnad mellan cementerade och cementfria proteser.

Studie 2: Två nyutvecklade, förmodat slitagetåligare, polyetylener jämfördes med konventionell polyetylen (γ–steriliserad i luft) hos 50 patienter i upp till tre år. Den ena av de nya plasterna var enbart värmebehandlad — en behandling som i måttlig grad ökar tvärbindningarna mellan plastens polyetylengrupper (”måttlig tvärbindning”). Den andra plasten var behandlad med en hög dos γ–strålning — en metod som i hög grad ökar

tvärbindningarna (”kraftig tvärbindning”). Efter två år uppvisade plasten med moderat tvärbindning lika stort slitage som konventionell plast. Plasten med kraftig tvärbindning, däremot, visade 85% lägre slitage utan att uppvisa tecken på sämre förankringsförmåga eller andra negativa röntgenologiska eller kliniska fynd.

Studie 3: 87 ocementerade ledskålar randomiserades till fyra olika förankringsmetoder; 1) enbart pressinfattning, eller pressinfattning kombinerad med 2) skruv, 3) stift, eller 4) hydroxyapatit (HA) beläggning och följdes under 5 år. Resultaten visar att varken skruv eller stift förbättrar förankringen jämfört med enbart pressinfattning, men att de leder till mer uttalad bennedbrytning (osteolys). HA förbättrar inte heller förankringen, men förhindrar utveckling av osteolys, troligen beroende på högre grad av beninväxt. Slutsatsen blir att en HA belagd cup insatt med enbart pressinfattning ger bäst förankring och minst risk för osteolys.

Studie 4: 58 patienter (median 55 år) (63 höfter) höftprotesopererades med två olika typer av cementfri skruvfixerad ledskål, vilka skiljer sig åt främst vad gäller tjockleken på plast och metallskal. Uppföljningstiden var 12 (10-14) år. Alla ledskålar var stabila enligt RSA, och slitaget var klart mindre än 0,2 mm per år, vilket är i enlighet med andra studier av samma protes. I mer än hälften av fallen förekom mer eller mindre uttalad bennedbrytning i bäckenbenet runt protesen. Så gott som samtliga plastinsatser föreföll ha lossnat från sin infästning i metallskalet och kunde mer eller mindre rotera fritt. Detta pekar på att problemet med en över tiden alltmer försvagad låsmekanism för plastinsatsen är betydligt större än hittills uppskattats.

Moderna cementfria ledskålar med pressinfattning är således stabila även utan tilläggsförstärkning. Skruvar och stift ökar risken för bennedbrytning, men kan vara tillförlitiga hjälpmedel om man inte kan åstadkomma tillräcklig stabilitet initialt. Bennedbrytning är en allvarlig senkomplikation till skruvfixerade ocementerade ledskålar, och kan vara en följd av bristfällig förankring av plastinsatsen till metallskalet. På grund av högt slitage av EtO steriliserad plast bör fortsatt användning av sådana upphöra, och redan opererade patienter bör kontrolleras regelbundet för att tidigt kunna åtgärda komplikationer. Plast konstruerad med ökad halt tvärbindningar uppvisar extrem slitagereduktion *in vivo* i jämförelse med konventionell plast. Detta kan ha betydelse för framtida val av material och operationsmetod. Man bör dock fortsätta att använda dessa material enbart i kontrollerade studier tills resultaten från längre tids uppföljning finns tillgängliga. Korttidsresultaten är dock lovande och kan ge längre livslängd för cementerade såväl som för ocementerade proteser och minska antalet komplikationer och revisioner.

German - Deutsch

Verschleiß und Verankerung der Pfanne von Hüftendoprothesen -In vivo Beurteilung von unterschiedlichen Polyethylenen und Fixationsarten

Ende der sechziger Jahre entwickelte Sir John Charnley die moderne Hüftprothese – einen Gelenkkopf und einen Stiel aus Metall sowie eine Gelenkpfanne aus Polyethylen. Beide Komponenten wurden mit Zement (Polymethylmetacrylat, „Plexiglas") im Knochen befestigt, ein Design, das noch heute in verschiedenen Variationen angewandt wird. Die jeweiligen Komponenten haben im Laufe der Zeit eine ständige Weiterentwicklung erlebt, um den Erwartungen und der gesteigerten Anwendung gerecht zu werden. So wurden eine Vielzahl verschiedener Prothesen und Verankerungsmethoden entwickelt, doch war deren Erfolg unterschiedlich.

Die frühen Kunstgelenke lockerten sich meist durch infektionsbedingten Knochenverlust nahe des Implantates, doch haben in den letzten Jahren Lockerungen ohne Infektionen zugenommen. Diese werden aseptische Lockerungen genannt. Man diskutiert derzeit 3 Ursachen für derartige Lockerungen mit prothesennahem Knochenverlust: 1) Materialabrieb (Verschleiß von Polyethylen); 2) Instabilität und 3) Gelenkflüssigkeitsdruck. Dies gilt vor allem für junge aktive Patienten, welche die Kunstgelenke stärker beanspruchen.

Alle Faktoren spielen einzeln eine Rolle und wirken wahrscheinlich auch gegenseitig aufeinander ein. Die Verschleißpartikel (Abrieb) des Polyethylens werden durch die Gelenkflüssigkeit zum Knochen transportiert und stimulieren dort knochenabbauende Zellen. Eine instabile Prothese erleichtert und beschleunigt diesen Vorgang. Deshalb wurden neue widerstandsfähigere Arten von Polyethylen entwickelt. Doch ist nicht sicher, ob diese experimentell geprüften Materialien den hohen Erwartungen auch in der klinischen Anwendung gerecht werden. Die neuen Herstellungsverfahren ändern auch die mechanischen Eigenschaften und könnten theoretisch die Stabilität negativ beeinflussen.

Um die Stabilität und den Verschleiß von Prothesen zu untersuchen, benötigt man Messmethoden mit hoher Genauigkeit. Radiostereometrie (RSA) ist durch eine hohe Präzision der goldene Standard für die Erfassung von *in vivo* Mikrobewegungen. Neben RSA verwenden wir konventionelles Röntgen und klinische Meßmethoden zur Datenerhebung.

Studie I: Wir untersuchten 2 unterschiedliche Polyethylene bezüglich Verschleiß und Stabilität in 201 Hüftpfannen. Das Polyethylen unterschied sich durch die Sterilisationsart, welche die Eigenschaften des Materials entscheidend verändert. Nach 2 Jahren zeigten die unzementierten Pfannen, die mit Ethylenoxid (EtO) sterilisiert wurden, den größten Verschleiß. Deutlich geringeren Abrieb und zudem keinen Unterschied zwischen zementierten oder zementfreien Implantaten hatten Pfannen mit Polyethylen, das mit γ-Strahlung in Luft oder in einer inerten Atmosphäre sterilisiert wurde.

Studie II: Zwei im Laborversuch widerstandsfähige neuartige Polyethylene wurden in 50 Patienten bis zu drei Jahren untersucht. Die eine Gruppe erhielt Pfannen aus Hitze stabilisiertem und damit mittelmäßig vernetztes Polyethylen (cross-linked) und die andere Gruppe erhielt hochvernetztes Polyethylen (highly cross-linked). Die Kontrollgruppe bestand aus Pfannen mit herkömmlichem Polyethylen sterilisiert mit γ-Strahlung in Luft. Zwischen herkömmlichem und gemäßigt vernetztem Polyethylen bestand nach zwei Jahren kein Unterschied, doch zeigte das hoch-

vernetzte Polyethylen 85% weniger Verschleiß gegenüber den beiden anderen Gruppen. Die Stabilität war nicht beeinträchtigt und auch röntgenologisch sowie klinisch konnten keine negativen Nebenwirkungen oder Folgeerscheinungen festgestellt werden.

Studie III: Wir randomisierten 87 zementfreie Hüftpfannen in vier Gruppen mit jeweils unterschiedlicher Verankerungsart. Press-fit (Stabilisation durch Druck- und Scheerkräfte) und Press-fit mit zusätzlicher Verstärkung durch Schrauben, Nieten oder Hydroxyapatit (HA) Beschichtung. Nach fünf Jahren waren alle Gruppen vergleichbar stabil. Dies bedeutet, dass eine zusätzliche Verstärkung von press-fit Pfannen zur Gewährleistung der primären Stabilität zum Knocheneinwuchs nicht notwendig ist. Jedoch zeigten geschlossene Pfannen (ohne Schraubenlöcher) und solche mit HA-Beschichtung röntgenologisch eine bessere knöcherne Grenzschicht und letztere auch eine Tendenz zu besserer Stabilität. Hüftpfannen mit Schrauben- oder Nietenverstärkung entwickelten größere Knochenresorption. Wie schon in Studie 1 beschrieben, war auch nach 5 Jahren der jährliche Verschleiß des EtO sterilisierten Polyethylens hoch (0.2 mm), unterschied sich jedoch nicht zwischen den einzelnen Verankerungsarten.

Studie IV: 58 Patienten (Durchschnittsalter 55 Jahre) (63 Hüften) erhielten 2 unterschiedliche zementfreie Gelenkpfannen, die sich in Dicke des Polyethylens und der Metallschale unterschieden. Der Nachuntersuchungszeitraum war durchschnittlich 12 (10-14) Jahre. Die RSA Messungen zeigten stabile Metallschalen und der jährliche lineare Verschleiß war 0,09 mm, was mit Ergebnissen aus anderen Studien übereinstimmt. Mehr als die Hälfte der Patienten zeigte zystischen Knochenabbau im Beckenknochen nahe der Pfanne und der Schrauben. Fast alle Polyethylen-Einsätze waren in der Metallschale instabil. Dies deutet auf ein größeres Problem mit dem Verschlussmechanismus hin als bisher angenommen.

Diese Studien zeigen, dass moderne zementfreie press-fit Pfannen keine zusätzliche Verstärkung (Augmentation) benötigen. Schrauben oder Nieten erhöhen das Risiko für Knochenresorption, sind aber zuverlässige Hilfsmittel in Fällen mit mangelnder intraoperativer Primärstabilität. Knochenresorption ist eine häufige Komplikation bei der Harris-Galante Pfanne. Dies könnte auf einen erhöhten Verschleiß des Polyethyleneinsatzes und einem unzureichenden Verschlussmechanismus zurückzuführen sein. Wir erwarten eine zunehmende Anzahl von Patienten mit Lockerungen des Polyethleneinsatzes nach einer Laufzeit von mehr als 10 Jahren.

Aufgrund des hohen *in vivo* Verschleißes von EtO sterilisiertem Polyethylen raten wir von dessen weiterer Nutzung als Pfannenmaterial ab. Wir empfehlen vielmehr Nachuntersuchungen von Patienten mit bereits implantierten EtO Polyethylen, um möglichen Komplikationen vorzubeugen. Der erheblich verminderte Verschleiß von hochvernetztem Polyethylen hat sich auch *in vivo* bis zu drei Jahren bestätigt. Dies kann große Bedeutung für zukünftige Materialwahl und Operationstechnik haben. Jedoch empfehlen wir derzeit noch Zurückhaltung und die Anwendung von hochvernetztem Polyethylen ausschließlich für Patienten mit geplant kontrollierten Nachuntersuchungen, solange noch keine Daten über längere Zeiträume vorliegen. Die Kurzzeitergebnisse mit hochvernetztem Polyethylen sind vielversprechend und können die Überlebensdauer von zementierten sowie unzementierten Hüftprothesen durch eine Verminderung der Komplikationen verlängern und deren Anzahl an Revisionen vermindern.

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Appendix

Study 1

Table 6: Proximal and total penetration 2 years postoperatively in uncemented cups using different fixation techniques (signed values, mm)

	n	*mean*	95% confidence limit of the mean	Range	p-value
Trilogy					
Proximal					
Pressfit [d]	21	0,20	0,12–0,26	*-0,18–0,44*	0,2 [b]
Pressfit and screws	44	0,17	0,13–0,21	*-0,09–0,67*	
Total					0,03 [b]
Pressfit [d]	21	0,34	0,27?0,41	*0,06–0,75*	
Pressfit and screws	44	0,26	0,21?0,31	*0,05–0,95*	
Reflection uncemented					
Proximal					
Pressfit without HA [d]	17	0,42	0,35–0,50	*0,19–0,71*	
Pressfit with pegs	19	0,47	0,41–0,54	*0,24–0,78*	0,07 [a]
Pressfit with screws	15	0,40	0,33–0,48	*0,26–0,74*	
Pressfit with HA	18	0,55	0,46–0,63	*0,28–0,95*	
Total					
Pressfit without HA [d]	17	0,51	0,43–0,58	*0,32–0,78*	
Pressfit with pegs	19	0,54	0,50–0,59	*0,34–0,78*	0,007 [a]
Pressfit with screws	15	0,47	0,38–0,56	*0,30–0,88*	
Pressfit with HA	18	0,76	0,48–1,04	*0,37–2,97*	

[a] Kruskal Wallis test
[b] Mann-Whitney test
[d] no additional fixation

Table 7: Repeatability of the questionnaire

Activity related item	Levels	Difference occasion 1-2[1]	Kendall´s tau	Numbers who changed their reply
Walking	5	0 -1–1	0,84	3
Less demanding physical activity	5	0 -2–0	0,87	3
Biking/swimming	5	0 -1–1	0,68	4
Running/dancing	5	0 -1–2	0,76	4
Demanding physical activity	4	0 0–1	0,72	1
Very hard work	4	0 0–0	1,0	0
Use of cane or crotch	3	0 0–2	0,75	2
Walking stairs	3	0 -1–1	0,71	3
Self estimated degree of activity	5	0 -1–0	0,81	4

[1]Time between occasion 1 and 2: 2 weeks. Median difference, *range*

Study 2

Table 8: Harris Hip score and radiographical data for the 3 different polyethylenes

Groups	γ-irradiation in air median (min-max)	Heat stabilized + cross-linked median (min-max)	Highly cross-linked median (min-max)
Pain score	42 (30 – 44)	41 (20 – 44)	43 (40 – 44)
HHS	92 (76 – 100)	93 (57 – 100)	97 (90 – 100)
Inclination (º)	50 (34 – 67)	49 (39 – 80)	50 (28 – 64)
Off set (mm)	37 (34 – 67)	32 (17 – 40)	33 (24 – 42)
t-value (mm)	5 (-6 – 17)	7 (0.2 – 33)	6 (-10 – 28)
Osteolysis (%)	6 (0-50)	0 (0 – 2)	3 (0- 30)

Study 3

Table 9: Cup migration in the different groups of fixation at five years. PF = press-fit only, PF+HA = Press-fit plus hydroxyapatite coating, PF+screws = Press-fit + screw augmentation, PF+pegs = Press-fit with peg augmentation.

	mean	95 % CI	median	range	p-value*
Medial / lateral translation					0.598
PF	0.06	-0.06-0.20	-0.01	-0.31-0,50	
PF + HA	-0.05	-0,27-0.17	-0.7	-0.63-1.06	
PF + screws	0.02	-0.28-0.33	-0.05	-1.23-1.33	
PF + pegs	-0.05	-0.26-0.15	-0.09	-0.84-0.60	
Proximal / distal translation					0.053
PF	0.27	0.14-0.40	0.26	-0.08-0.78	
PF + HA	-0.01	-0.18-0.16	0.02	-0.91-0.48	
PF + screws	0.13	0.06-0.21	0.11	-0.10-0.47	
PF + pegs	0.11	-0.07-0.29	0	-0.24-0.85	
Anterior/ posterior translation					0.679
PF	0.03	-0.11-0.16	0.06	-0.38-0.46	
PF + HA	0.26	-0.02-0.55	0.11	-0.40-2.17	
PF + screws	0.10	-0.19-0.38	0.8	-0.90-1.26	
PF + pegs	0.11	-0.04-0.26	0.08	-0.35-0.61	
Anterior / posterior tilt					0.396
PF	0.06	-0.32-0.45	0.08	-1.08-1.64	
PF + HA	-0.11	-0.52-0.31	0.04	-2.76-0.95	
PF + screws	0.33	0.04-0.62	0.36	-0.32-1.24	
PF + pegs	0.22	-0.20-0.63	0.09	-1.05-1.83	
Anteversion / retroversion					0.923
PF	0.01	-0.36-0.35	0.12	-1.31-1.25	
PF + HA	0.05	-0.26-0.36	0.13	-1.25-1.14	
PF + screws	0.48	-0.30-1.26	0.06	-1.32-4.64	
PF + pegs	0.10	-0.38-0.36	-0.0	-1.64-1.84	
Increased (-) /decreased (+) inclination					0.903
PF	0.15	-0.29-0.59	0.03	-1.33-1.69	
PF + HA	0.25	-0.02-0.51	0.8	-0.63-1.55	
PF + screws	0.24	-0.30-0.79	0.06	-1.34-3.24	
PF + pegs	-0.01	-0.37-0.36	-0.13	-1.06-1.36	

*Kruskal-Wallis test

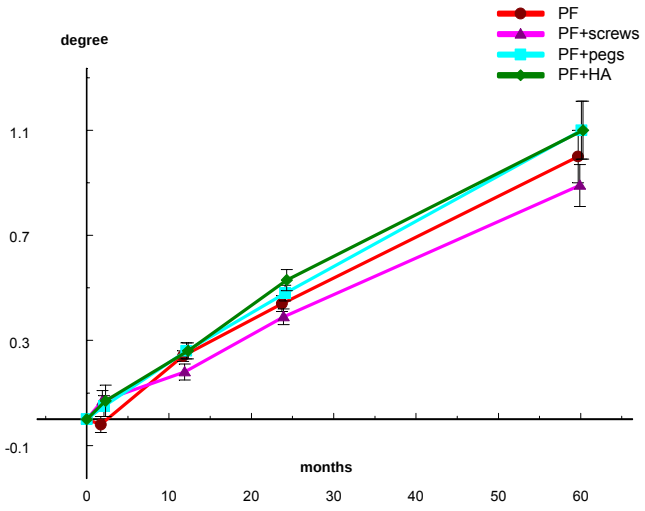

Figure 20 : Proximal wear did not differ between the groups. Mean (SE).

Table 10: Distribution (0% / 1-49% / 50-99% / 100%) of radiolucent lines in each DeLee and Charnley region on the AP radiograph in the four groups of fixation. Length of radiolucent lines > 1 mm in percent of the total interface length at five years (antero-posterior view only).

		PF n = 20	PF+HA n = 21	PF+screws n = 21	PF+pegs n = 21
Charnley Delee					
I	(proximal-lateral)	13/4/2/1	21/0/0/0	17/2/1/1	14/6/1/0
II	(central)	18/1/0/1	21/0/0/0	17/0/3/1	14/6/1/0
III	(medial-distal)	14/3/2/1	19/2/0/0	12/5/1/3	12/2/4/3
Length (median)		0	0	11	18
Q 25-50-75		0-0-27	0-0-0	0-11-35	0-18-29
range		0-87	0-14	0-78	0-54
p-value			0,003*		

*Kruskal Wallis test, see table 1 for abbreviations.

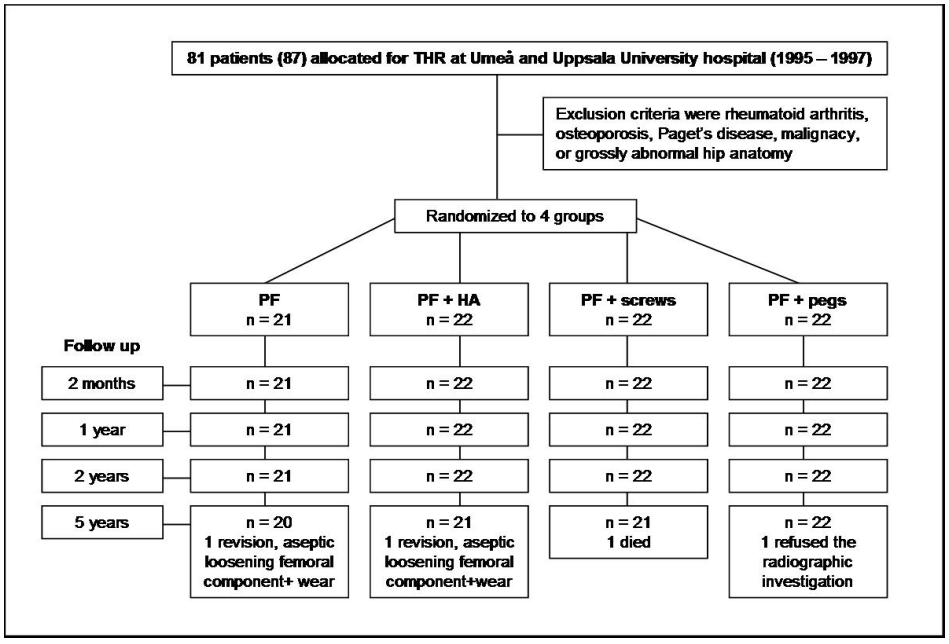

Figure 23: Flow chart of the study design showing all follow up examinations, the number of patients and reasons for drop outs (PF = Press-fit only, PF+HA = Press-fit with Hydroxyapatite, PF + screws= Press-fit with screws; PF + pegs = Press-fit with pegs

Study 4

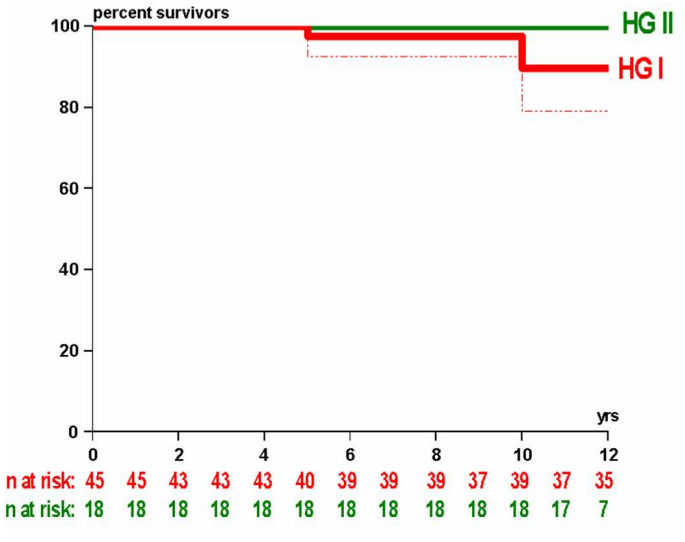

Figure 21: Survival of Harris Galante cup I and II.

Table 11: Harris hip score and pain score.

	pre			2 y			5 y			12 y			2-12y
	n	median	range	n	median	range	n	median	range	n	median	range	*
Pain	39	10	0-30	63	40	20-40	38	44	20-40	55	44	0-44	1
HHS	39	43	14-62	63	94	3-100	37	96	69-100	55	96	20-100	0,4

*Wilkoxon signed rank test p-value

Table 14: Proximal head penetration and 3D penetration of the femoral head after 12 years.

Penetration	n	Mean	95% confidence limit of the mean	Range	HG I *vs.* II *p-value**
Proximal					
HG I	12	1,25	0.12 – 2.37	-0.55 – 6.53	*0.6*
HG II	3	0,45	-1.28 – 2.17	-0.35 – 0.93	
3D					
HG I	12	2,17	0.44 – 3.90	0.48 – 9.46	*0.8*
HG II	3	0.98	0.39 – 1.56	0.75 – 1.22	

*Mann-Whitney U test

Table 13: Data in 63 patients. (Study 4)

n	HG	Stem[1]	Diagnos[2]	Time[3] F.up (rev) months	Liner[4]	osteolysis size mm³	osteolysis location	RSA[5] Translation mlc	Translation pdc	Translation apc	Rotation ts	Rotation ars	Rotation is	Wear prox	Wear 3D
1.	1	A	prim	162											
2.	1	A	prim	†											
3.	1	B	prim	161 (133)	rev										
4.	1	A	prim	161		227	central								
5.	1	B	prim	153											
6.	1	B	prim	162											
7.	1	A	prim	160		201	central								
8.	1	A	prim	159	prob			1,23	0,01	1,72	-3,05	2,41	-3,01	0,41	0,49
9.	2	A	sec	†											
10.	1	A	prim	158		212	central							6.53	9.49
11.	1	A	prim	158											
12.	1	B	sec	158	prob			0,17	0,12	1,64	-2,15	1,25	,70	0,40	0,48
13.	1	A	prim	157	poss	19	central	2,10	0,41	0,85	-1,80	0,45	3,86		
14.	1	A	prim	†											
15.	1	A	prim	174		498	distal								
16.	1	A	prim	157										1,74	1,99
17.	1	B	sec	155		406	proximal								
18.	1	B	sec	153											
19.	1	B	sec	153											
20.	1	A	prim	155	stable			-0,25	0,26	-0,23	0,49	-0,23	-0,74	0,69	0,74
21.	1	B	prim	160											
22.	1	C	prim	†											
23.	1	C	sec	145 (133)	rev	542	dorsal								
24.	1	C	sec	161	poss	552	proximal	0,07	0,34	0,11	1,11	0,07	-1,25	1,25	1,34
25.	1	C	prim	179											
26.	1	C	prim	145		290	proximal							0.34	0.73
27.	2	D	prim	137		66	central								
28.	1	C	prim	144 (72)	rev	407	proximal								
29.	1	C	sec	144		106	proximal								
30.	1	C	sec	156 (144)	rev	294	proximal								
31.	1	C	prim	†											
32.	1	C	prim	144	poss			-0,87	-0,18	-0,05	1,72	,32	-1,49	0,92	0,97

33.	1	C	prim	†											
34.	1	C	prim	†											
35.	1	C	prim	142	poss			0,03	-0,17	-0,74	2,13	1,15	-0,08		
36.	1	C	prim	†											
37.	1	C	prim	142											
38.	1	E	prim	143	pla/sh	285	proximal	1,48	1,74	-1,80	1,02	-5,28	1,30		
39.	1	C	sec	144		376	proximal							1,30	1,52
40.	1	E	sec	144		184	proximal								
41.	1	C	sec	137		715	dorsal							0,51	0,53
42.	1	E	prim	146											
43.	1	E	sec	139		372	proximal								
44.	1	E	prim	138	stable			-0,04	0,24	0,97	-2,16	0,49	0,05	-0,55	1,95
45.	1	E	prim	137		562	proximal								
46.	1	D	prim	137										1,40	5,80
47.	2	D	prim	133		545	,								
48.	1	D	prim	141	prob	331	proximal	0,11	0,12	-0,35	3,64	3,94	-2,49		
49.	2	C	prim	138		522	proximal								
50.	2	C	prim	111											
51.	2	D	prim	138										0,93	0,96
52.	2	D	prim	138	poss	393	proximal	-0,46	0,32	1,12	-1,76	-0,44	-0,81	-0,35	,75
53.	2	E	prim	135	poss	302	proximal	-1,22	0,40	0,02	-0,20	1,17	-3.32		
54.	2	E	lux	135											
55.	2	D	lux	124											
56.	2	D	sec	136	poss			-1,03	-2,12	0,49	1,83	-0,01	-8,68		
57.	2	E	sec	136		168	proximal								
58.	2	E	prim	131		392	proximal								
59.	2	E	prim	126	poss	205	central	1,00	-0,33	-0,31	-3,19	-4,39	-0,73		
60.	2	D	prim	131	stable	224	proximal	-0,17	-0,21	0,54	-0,32	0,39	0,45		
61.	2	D	sec	132	poss			0,02	0,22	0,08	1,39	0,12	-0,61	,76	1,22
62.	2	D	prim	132		264	proximal								
63.	2	C	prim	116		515	proximal								

[1]Stem: **A = Sp I® titan cement; B = Rippen® cementless; C = Tifit®+cement; D = Tifit®+porous; E = Tifit®+hydroxyapatite;**
[2]Diagnosis: **prim = primary arthrosis; sec = secundary arthrosis;**
[3]Time: **Period between index operation and follow up or revision, † = died, f.up= follow up, rev = revision;**
[4]Liner: **rev = revision, prob = probable liner rotations; poss = possible liner rotations, pla/sh = liner and/or shell rotation;**
[5]RSA: **Translation of center: mlc = mediolateral; pdc = proximodistal; apc = anteroposterior;**
Rotation of segment: ts = tilt; ars = ante/retroversion; is = inclination, 3D = three dimensional;

Activity score (in swedish)

Bäste Patient Med Höftprotes

Proteslossning verkar till viss del bero på förslitning av protesdelarna. Då vi har räknat ut protesslitage och lossningstendens på din höftprotes med RSA teknik vore det mycket intressant att veta hur mycket du har använt den sedan operationen. Vi vore därför mycket tacksamma om du vill fylla i dessa frågor. Ditt svar kommer naturligtvis att vara sekretess skyddat. Svaren får ju bli lite ungefärliga och som ett medelvärde under året för **aktiviteten både på arbetstid och på fritid**. Du behöver inte sitta och räkna eller tänka alltför mycket. Kryssa sedan i lämpligt alternativ. Var så snäll och ta med formuläret när du kommer till oss. Tack för hjälpen i förhand.

Namn: _____ man kvinna vikt _____ kg

1. Hur många timmar per vecka promenerar du eller åker spark, spelar golf etc?
   inga | mindre än 5 | 5-10 | 10 – 20 | mer än 20

2. Hur många timmar per vecka gör du lättare kroppsarbete som att jobba i trädgård, hugga ved, lätt snöskottning eller liknande?
   inga | mindre än 1 | 1-3 | 3 – 7 | mer än 7

3. Hur många timmar per vecka cyklar eller simmar du?
   inga | mindre än 1 | 1-3 | 3 – 7 | mer än 7

4. Hur många timmar åker du längdskidor eller joggar/dansar/gympar/per vecka?
   inga | mindre än 1 | 1-3 | 3 – 7 | mer än 7

5. Hur många timmar tränar du hårdare aktiviteter (idrott) som tennis/badminton eller liknande?
   aldrig | mindre än 1 | 1 – 3 | mer än 3

6. Utövar du tungt arbete som skogsarbete, tung snöskottning, tunga lyft eller liknande?
   aldrig | 1 gång/år | 2-5 ggr/år | mer än 5 ggr/år

7. Utövar du ibland extra aktiviteter någon vecka som fjällvandring, slalom eller liknande?
   aldrig | 1 vecka/år | 2-3 veckor/år | mer än 4 vecko/år

8. Använder du käpp? aldrig | 1 käpp | 2 käppar/rollator

9. Går du mycket i trappor? aldrig | normalt | ofta

10. Hur uppskattar du själv din aktivitetsnivå?
    mycket låg | låg | normal | hög | mycket hög