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WEAR, FIXATION, AND REVISION OF TOTAL HIP PROSTHESES

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Faculty of Medicine
University of Bergen, Norway 2007

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1. ACKNOWLEDGEMENTS

This study was performed at the Department of Orthopaedic Surgery, Haukeland University Hospital, Bergen, Norway.

First I would like to express my gratitude to my friends and colleagues Sven Young and Professor Lasse Engesaeter for luring me into the field of orthopaedic surgery and into the Department of Orthopaedic Surgery at Haukeland University Hospital. The outstanding atmosphere at the department, the enthusiasm in clinical work and research shown by my colleagues has been a source of great inspiration. Sven also deserves acknowledgement for the help he provided as a native English-speaking editor, and Lasse for being a constructive co-author.

Since I entered my position as a resident orthopaedic surgeon in 1998, Professor Leif Havelin has been my supervisor. He immediately introduced me to scientific work and has since then shown great support, initiative and perhaps too much patience. Ove Furnes, now head of the department and leader of the Norwegian Arthroplasty Register, and statistician Stein Atle Lie, have been supervising my work together with Professor Havelin. Their help in the fields of register studies and statistics has been invaluable, and the enthusiasm and light mood they possess has been of great importance. Furthermore, the head of the Section for Joint Replacements and Rheumatoid arthritis-surgery, Arne Skredderstuen certainly deserves credit for his skilful guidance and educative skills in the field of joint replacement surgery, and for making room for my research activities in a busy clinic.

The entire Norwegian orthopaedic community deserves acknowledgement for continuous data reporting to the Norwegian Arthroplasty Register. The surgeons provide the data with patience and accuracy, which of course is the essential basis of the register.

Statisticians Birgitte Espehaug and Eva Dybvik, and the entire staff of the register deserve credit for help with the data and statistics, and for the smooth operating of

the register. I also acknowledge my co-authors Arild Aamodt, Kristin Haugan, and Stein Emil Vollset, and Terje Stokke for providing excellent radiographs for radiostereometric analysis (RSA). Furthermore I acknowledge the help and patience shown by the staff of the operating theatre in the performance of the RSA study.

My thanks are also due to Professors Anders Mølster and Leiv Hove for inspiration and for providing a platform for research in our unit.

Financial support for this study has been received from the local and regional health services, Helse-Bergen and Helse-Vest through financing the Norwegian Arthroplasty Register, and from Biomet Merck company through financing our RSA study.

Thank you also to my parents, Gerd Hallan and Tor Svendsen, and to my brother Paul Hallan Svendsen for relentless support throughout my life.

Finally, I acknowledge the patience and love I receive every day from my fair wife Anne and our masterpieces Ulrik, Aksel and Emil.

2. LIST OF ABBREVIATIONS

ADL	activity of daily living
ANOVA	analysis of variance
AP	antero-posterior
BMI	body mass index
CI	confidence interval
CN	condition number
Co	Cobalt
CoCr	Cobalt Chromium
Cr	Chromium
EBRA	Ein Bild Roentgen Analyse
HA	hydroxy apatite
HG	Harris Galante Porous
HHS	Harris hip score
ISO	International Standards Organisation
ME	mean error
MMA	methyl-metacrylate
n	number(s)
NAR	Norwegian Arthroplasty Register
PC	porous coating
PCA	Porous Coated Anatomic
PhD	philosophiae doctor
PE	polyethylene
PMMA	polymethyl-metacrylate
RCT(s)	randomised controlled trial(s)
RR	relative risk (risk ratio)
RSA	radiostereometric analysis
SCP	Scandinavian Custom Prostheses
THA(s)	total hip arthroplasty(ies)
TNF	tumor necrosis factor
UHMW	ultra high molecular weight
UHMWPE	ultra high molecular weight polyethylene
Ø	diameter

3. LIST OF PAPERS

This thesis is based on the following papers, which will be referred to by their Roman numbers in the text.

- I Hallan G, Lie SA and Havelin LI. **High wear rates and extensive osteolysis in 3 types of uncemented total hip arthroplasty.** A review of the PCA, the Harris Galante and the Profile/Tri-Lock Plus arthroplasties with a minimum of 12 years median follow-up in 96 hips. *Acta Orthop* 2006;77 (4):575-584

- II Hallan G, Aamodt A, Furnes O, Skredderstuen A, Haugan K and Havelin LI. **Palamed G compared with Palacos R with gentamicin in Charnley total hip replacement.** A randomised, radiostereometric study of 60 hips. *J Bone Joint Surg* 2006;88-B (9):1143-1148

- III Hallan G, Lie SA, Havelin LI, Engesaeter LB, Vollset SE, and Furnes O. **Medium and long-term performance of 11 516 uncemented primary femoral stems from the Norwegian Arthroplasty Register.** Submitted.

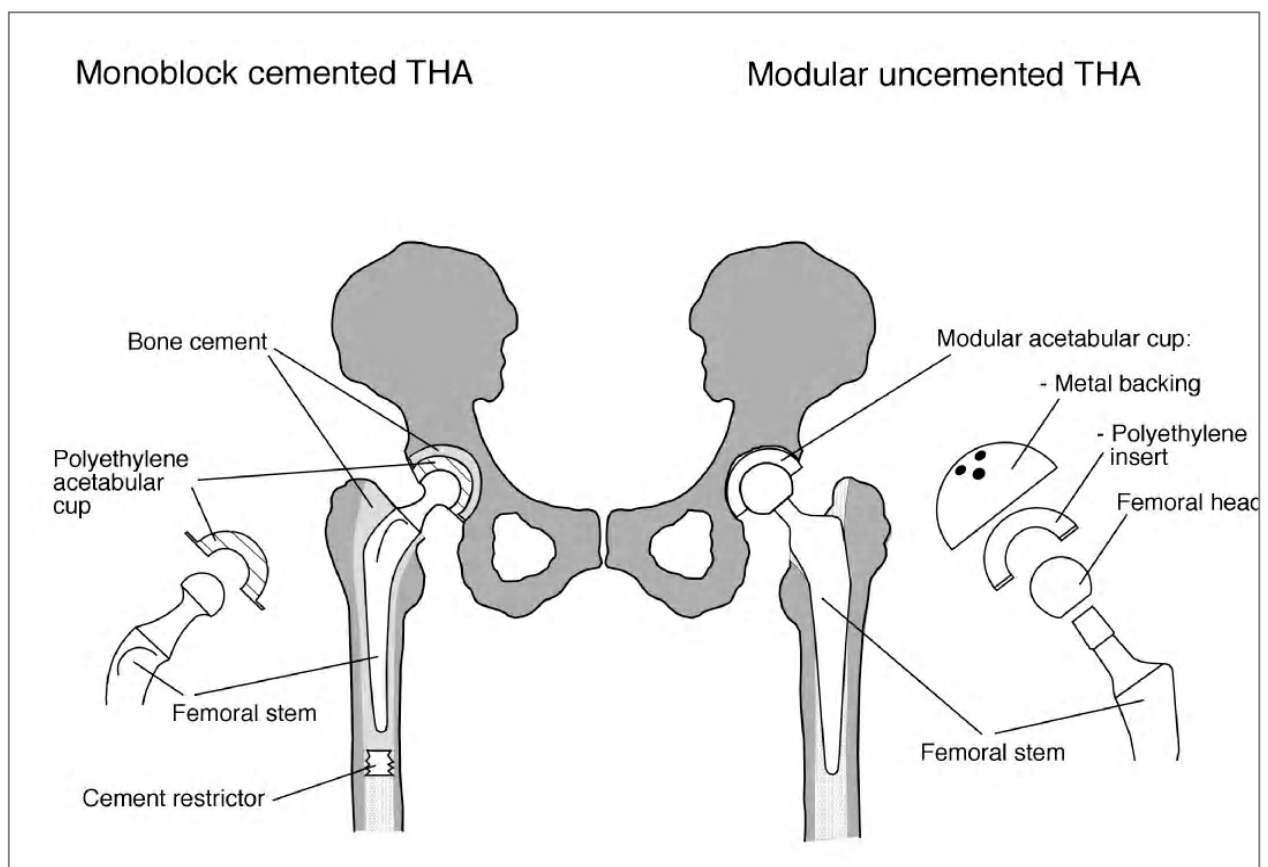
- IV Lie SA, Hallan G, Engesaeter LB, Havelin LI, and Furnes O. **Liner exchange procedures compared to whole cup revisions in revision of uncemented acetabular cups.** A study of 1649 revisions from the Norwegian Arthroplasty Register. Accepted *J Bone Joint Surg (Br)* November 2006.

4. BACKGROUND

4.1 Hip prostheses; Basic concepts

Hip prostheses are used in treatment of disease or injury that leads to painful destruction of the hip joint. A total hip arthroplasty consists of a femoral stem, a femoral head, and an acetabular cup. The femoral stem is either of a modular or a monoblock design. In the former, the femoral head is separate and is attached to the stem through a taper locking mechanism. In the latter, the femoral head and stem comes in one piece. Similarly, the acetabular cup is monoblock or modular; the monoblock cup is a one-piece construct whereas the modular cup consists of a shell that is fixed to the pelvic bone, and an insert (liner), which is fixed inside the shell. The bearing surface of the artificial joint thus is constituted by a metal or ceramic femoral head, and the inner surface of the cup, typically made of polyethylene (plastic), ceramics, or metal.

Figure 1. Illustration of basic concepts in total hip prostheses.



4.2 History of hip prostheses

Hip arthroplasty has a history spanning more than 100 years. Since the early pioneers experimented with prostheses made of ivory (T. Gluck) (1) or platinum (shoulder arthroplasty, J. Pean) (2) in the 1890's, different approaches to hip arthroplasty have been undertaken. In the early twentieth century, resurfacing by the use of organic (fascia, fat) or inorganic (gold foil) materials in the form of membranes were popular. Later, mould arthroplasties dominated (M.N. Smith-Petersen, Boston, 1923 and forward) (3). Hemiprostheses of different designs and materials then prevailed until the advent of low-friction arthroplasty by Sir John Charnley in the early 1960's (4). His ideas of cold-curing polymethyl-metacrylate for fixation, high-density polyethylene in the acetabular component, and a small diameter femoral head improved the outcome of THA quite dramatically. The basic concept of a cemented cup and stem, with a metal-on-polyethylene articulation still is the standard in total hip arthroplasty, a standard to which other arthroplasties are compared. The history of hip replacement surgery is in many aspects a success story. However, during the evolution of total hip arthroplasty, many obstacles have been and still are encountered. The major problems of infection, fixation, biocompatibility and mechanical quality of implant materials in hip replacement surgery are outlined from a historical point of view in the following.

4.3 Material failure and infection

The first known joint arthroplasties were made of ivory or platinum (1;2). Defining success as more than 50% good results, it took some 50 years to get there. The mould hemi-arthroplasties of M. N. Smith-Petersen were made of glass, Pyrex or Bakelite the first fifteen years (3). These failed because of material fragility, high friction, and foreign body reactions. From 1937, Smith-Petersen used Vitallium® (CoCr), and this mould arthroplasty had sufficient mechanical strength to provide long durability. The Judet hemi-prostheses were made of heat-cured acrylic, and the

results were poor due to poor mechanical properties and gross wear of the acrylic leading to deformation and loosening of the prostheses, and also due to osteolysis. The metallic, press-fit stemmed hemiarthroplasties of Moore and Thompson gained popularity in the 1950's. Although the fixation and mechanical properties of these hemi-prostheses were excellent according to contemporary criteria, bone erosions of the acetabulum was a problem. This brought forward the metal-on-metal total hip arthroplasties of McKee-Farrar, Urist, Herbert, Ring and others. These arthroplasties originally had relatively poor results because of high friction and wear leading to pain and loosening. The results after some improvements however, were comparable to the Charnley low friction arthroplasty (5;6).

Ceramics in the bearings were initially subject to failure due to ceramic fractures and fixation problems on the acetabular side. New designs, improved manufacturing processes, and proof testing have improved the mechanical properties of modern ceramic bearings. Nevertheless there have been reports on relatively high rates of fractures also with contemporary materials (7).

The majority of currently used hip implants consist of femoral stems made of stainless steel, titanium alloys, or cobalt-chromium, and acetabular cups made of ultra high molecular weight polyethylene (UHMWPE). Material failure, such as fracture of the metal stem, is currently exceedingly rare unless the implant is loose. The bearing surfaces however, are subject to wear. Failure due to wear and the associated osteolysis has been among the most studied topics in hip arthroplasty during the last two decades.

'Postoperative infection is the saddest of all complications', Sir John Charnley stated in 1982 (8). Deep infection around a joint replacement is a disastrous complication for patients and a costly complication for society (9;10). Treatment usually involves exchange or removal of the prosthesis and great suffering for the patient. In the early sixties, with his Teflon arthroplasty, Charnley found the rate of infection to be about 7%. Efforts have since then been made to lower the frequency of infection, such as strict aseptic discipline before, during, and after the operation, specially designed

operating theatres with laminar airflow and body-exhaust systems, antibiotic prophylaxis, and infection surveillance. The rate of surgical site infection currently is about 1-3% (11), and revision rates with exchange or removal of the prostheses because of infection as low as 0.3% in low-risk patients (9). Infection is not a topic in the publications that constitute this thesis, and is therefore not discussed any further.

4.4 Contemporary problems

4.4.1 Wear, osteolysis and loosening

Wear at the articulating bearing surfaces can be defined as *the removal of particles that occurs as a result of the relative motion between two opposing surfaces under load* (12). From a clinical point of view, wear has the following major implications;

- Mechanical failure of the articulation,
- Osteolysis, and
- Loosening

Mechanical failure of the bearings, such as wear-through of the acetabular liner, failure of the liner locking mechanism with dissociation of the liner, wear-induced instability and dislocation, or fracture of the liner or the femoral head, may lead to revision surgery. Of high importance are also the potential biological effects of the wear-particles that may lead to periprosthetic osteolysis, and eventually to aseptic implant loosening. Aseptic loosening still is by far the most frequent cause of revision of hip prostheses.

The most supported theory on ethiology of progressive osteolysis around hip implants suggests that bone resorption is caused by a foreign-body inflammatory reaction to sub-micron sized wear particles (13;14). The particles activate macrophages, which in turn via pro-inflammatory factors (cytokines, TNF and prostaglandines) trigger osteoclast activity. The macrophages may also transform into osteoclasts themselves. The resulting imbalance in local bone metabolism leads to lesional or linear bone resorption. Generally, osteolysis is progressive, often leading to massive periprosthetic bone loss, loosening, and consequently to more or

less complex revision procedures. The process of osteolysis is probably multifactorial. As described above, a foreign-body reaction to particles of polyethylene, and also to particles of bone cement, metal, or ceramics within a certain size range (sub-micron), is considered essential in the pathophysiology of periprosthetic osteolysis. Probably, mechanical factors also contribute to osteolysis. *Instability*, also in terms of micromotion, have been shown to cause osteolysis by pumping joint fluid into surrounding periprosthetic tissues at high pressures (15-17). Animal studies have indicated that high fluid pressures are capable of inducing osteolysis with or without the presence of particles of PE, PMMA, or metal. Actually, fluid pressure was the most potent of these factors in inducing osteolysis according to these studies (18). Furthermore, the so-called *stress-shielding* of periprosthetic bone may contribute to bone-loss. Stress-shielding is periprosthetic osteopenia most probably caused by altered load transmission in periprosthetic bone. It is believed that stress-shielding may facilitate osteolysis by enlarging the so-called *effective joint-space* (19) and hence allow access of particles and pressurised joint-fluid to wider areas of the bone-prosthetic interfaces. *Host factors* are important in eliciting wear and thereby also osteolysis. Intensity and frequency of use of the prosthesis, which vary with age, gender, body mass index (BMI), and activity, has been shown to affect wear and implant survival (20-22). Furthermore, there is some evidence that individual and perhaps genetic variations in immunological response to particles may affect the patients' osteolytic response (23). Finally, *endotoxins* may contribute by releasing cytokines and eliciting macrophage-induced osteolysis. Endotoxins may be present on implants at the time of implantation (24;25).

High wear rates have been shown to limit the life of a hip replacement (20;26).

Wroblewski et al found that a group of patients with high wear of a cemented socket had an eight-fold increase in revisions for cup loosening when compared to a group of patients with low wear (20). Revision rates of the cemented femoral stem on the other hand, did not significantly differ between the high- and low-wear groups. They concluded that loosening of cemented stems is not a consequence of wear-induced

osteolysis. Schmalzried et al evaluated autopsy studies of well-functioning hip implants. They suggested that cup loosening is a biologic event due to particle-induced osteolysis whereas loosening of the cemented femoral stem is related to mechanical stress (27).

4.4.2 Fixation

The incidence of THA has increased steadily during the last decades. Initially, THA was used primarily in older patients. Nowadays, skeletally mature patients of all ages are subject to this treatment. Young patients have long life expectancies and high demands on their joint replacements. Therefore, secure and long-lasting fixation of implants is imperative. Fixation of total hip arthroplasties is achieved either with or without cement, or one component may be cemented and the other uncemented (hybrid fixation). Uncemented implants generally are more expensive than cemented implants. Both concepts have considerable support in the literature and surgeons have different preferences.

4.4.2.1 Bone cement

Some 45 years after its introduction, acrylic bone cement is still a common mean of implant fixation. The bone cement works as a space-filler allowing mechanical stresses laid upon the prostheses to be transmitted to the surrounding bone. The fixation of cement to bone is purely mechanical, by the means of interdigitation into the surrounding cancellous bone. Bone cement is not a glue, and it does not form chemical bonds to the bone. The basic component of bone cement is methyl methacrylate (MMA), which is a monomer. Polymethyl-methacrylate (PMMA) is formed through polymerisation after mixing the powder and the liquid of the cement. This is done just prior to implantation of the implant. Besides MMA, bone cements usually contain radiopacifiers, other methacrylates, initiators and activators, softeners, emulsifiers, and antibiotics. Characteristics of the bone cements depend on the chemical composition, and on the cementing technique. Although most

commercially available bone cements have a similar basic composition, smaller differences have been shown to result in quite dramatic alterations in mechanical and clinical performance (28-31). The requirements imposed upon bone cements by health authorities are those imposed on medical devices, and include only mechanical testing. Fatigue testing is advocated by several authors as an in vitro method of evaluating bone cements (32), but is not yet required by the health authorities. Mechanical strength proven in laboratory settings is no guarantee of good clinical performance (32). Therefore, all new bone cements should be independently tested both in vitro and clinically according to contemporary methods before widespread clinical use.

4.4.2.2 Cemented total hip arthroplasty

Since the introduction of the Charnley low friction total hip arthroplasty, the changes in cemented hip arthroplasty have been relatively unsubstantive. The metallic stem has been somewhat modified in geometry, surface, and metallic quality during the years. The polyethylene is virtually unchanged and so is the PMMA bone cement. The cementing technique on the other hand has gradually evolved during the last 40 years. The so-called third generation cementing has been shown to substantially improve long-term outcome of cemented total hip arthroplasty (33;34). The methods of sterilisation of the UHMWPE also have changed during the last decades. Sterilisation method influences the mechanical properties of the polyethylene, including the wear characteristics (35). Gamma irradiation in air used to be the preferred sterilisation technique. To reduce the amounts of free radicals causing degradation and oxidation of the polyethylene, sterilisation by gamma irradiation in the absence of air, or chemical surface treatments (Ethylene Dioxide or gas plasma) were introduced. These are the preferred methods of today. Furthermore, operative technique has been adapted making the procedure faster and simpler. The cemented cup is typically all-polyethylene with or without a flange. Cemented femoral stems differ in geometry and in surface characteristics. Some stems are

tapered, and designed to transfer the load evenly at the entire cement-bone interface (e.g. Exeter, CPT, C-stem). Others have features, which serve as more or less local load-transmitters, such as collars, ridges, profiles, or anatomic curvatures (e.g. Charnley, Lubinus, Spectron). The surface of cemented stems is polished or more or less matte. It seems that various stem designs may be capable of providing good long-term performance. However, distinct design modifications may sometimes dramatically alter the clinical performance of the cemented femoral stem as illustrated by the inferior results of the matte Iowa and Exeter stems (36;37) and the Capital hip (38).

If defining 'good results' as more than 90% THA survival at ten years, the results of cemented THA have been overall good. The Charnley total hip arthroplasty is by far the most documented THA system, both in terms of number of publications and length of follow-up (39-42). However, other cemented systems (e.g. Exeter, Lubinus) also have broad documentation of good long-term results (>15 years) in a number of studies (42-44).

4.4.2.3 Uncemented total hip arthroplasty

Uncemented fixation regained popularity in the 1980's in the belief that the uncemented prostheses would provide better durability in the younger patients. This belief was based on reports of poor results of some cemented cups in young patients (45;46), and the belief that the bone cement itself was responsible for these poor results and for the periprosthetic osteolysis (47). Principles of uncemented fixation include primary stability by press-fitting or screwing the components in the bone, and secondary fixation by ongrowth and ingrowth of bone to the implant surfaces. To achieve this, the implant surface is usually roughened by the means of blasting, porous coating, or hydroxy apatite (HA) coating. HA stimulates bone growth adjacent to the implant. The uncemented cup is typically a two-piece construct of a hemispheric metal backing and a polyethylene liner insert fixed to the shell by some kind of locking mechanism. Additional features of some cups include spikes, screws,

fins, or pegs intended to provide additional fixation of the shell. The uncemented femoral stem is typically a titanium modular stem. Various shapes and surfaces are commonly used. Some are fit-to-fill in the proximal femur, some are rectangular cross-section, some are tapered, and some are anatomical. Again, quite dissimilar stem designs have proven good results.

Worldwide, uncemented THA is becoming increasingly popular and is now the preferred choice of many orthopaedic surgeons in most or all patient categories. In Sweden, Norway, and the United Kingdom, cementing is still the most widely used mode of fixation. The results of uncemented total hip arthroplasty are varying. In the Scandinavian registers, the results of uncemented THA have generally been inferior to the well-documented cemented THAs (42;48-52). Generally, the durability in terms of implant fixation is good or excellent (53;54). The problems of wear of the bearings and osteolysis however, suppress long-term implant survival (54-56). Wear and osteolysis, which was blamed on the cement in the 1980's, are problems of even greater magnitude in uncemented hip arthroplasty. In order to address the problem of wear, newer bearings have developed during the last 20 years.

In research on hip replacement surgery, the length of follow-up is generally shorter for uncemented than for cemented implants, but some reports of follow-up of 15 years or longer are now available (57-60). These papers however, usually report on the performance of a cup or a stem only, and most uncemented implants with this length of follow-up are no longer on the market. To my knowledge, no reports on good long-term performance (>15 years) of commercially available uncemented cup and stem combinations exist.

4.5 Revision of hip prostheses

In revision of a hip prosthesis part of or the entire prosthesis is exchanged or removed. Reasons for revision of total hip arthroplasties include aseptic implant loosening, deep infection, instability, wear, osteolysis, pain, and fracture of the prosthesis or of the periprosthetic bone. Clinical outcome after revision surgery is

less predictable and generally inferior to the outcome after primary joint replacements.

Revision of uncemented acetabular cups is most frequently indicated in the case of substantial liner wear, or other PE-related problems such as osteolysis, or aseptic loosening. The choice of revision procedure in each case depends on the extent of bone loss, the patient's activity and co-morbidity, the surgeon's preferences and skills, and the revision instruments and implants available. Exchange of the PE liner only may sometimes be performed, but loose cups always require cup exchange, sometimes combined with reinforcement of the pelvic bone by structural or impacted bone grafts, metal cages -or wedges, or bone cement. In the case of a well-fixed cup with substantial wear or wear-through of the liner, with or without concomitant osteolysis, most authors advocate isolated exchange of the liner insert or cementing a liner into the fixed shell (61;62). The scientific support of different strategies of revision is sparse (63;64), and the available literature consists mainly of moderately sized patient series operated on with a specific technique or implant. Due to the considerable heterogeneity of patients and operative procedures, and the lack of comparative trials, there is little proof to suggest that one procedure is better than the other in a specific patient.

5. THE NORWEGIAN ARTHROPLASTY REGISTER

National registers for surveillance of joint replacement surgery have developed in many countries. The Norwegian Orthopaedic Association founded the Norwegian Arthroplasty Register (NAR) in September 1987, and the register is located at the Department of Orthopaedic Surgery, Haukeland University Hospital in Bergen. Until 1994 only total hip arthroplasties were registered, but since 1994 the register has included individual information on arthroplasty operations in all joints except the jaw. The register is owned by the Norwegian Orthopaedic Association, and it is now funded by the regional and local health authorities, Helse-Vest and Helse-Bergen. The register is primarily intended to function as a quality control system. The main objective is to detect inferior prosthetic implants, bone cements, routines and procedures as early as possible after their introduction. The quality of joint replacement surgery is assessed both nationally and locally since hospital-specific results are reported yearly to all hospitals involved in joint replacement surgery. Data is collected through forms, which are completed by the operating surgeon just after surgery. Information on the diagnosis, operated side, former surgery to that particular joint, operating technique, every detail on the prosthetic components used, use of antibiotics, and prophylactics against trombo-embolism, operating time, complications, etc are received together with the patients unique national identification number (Appendix). The latter allows future revisions in the same hip of the same patient to be linked to the corresponding primary procedure. Thus, the quality of the procedures can be measured in terms of durability. Name or identity of the surgeon is not reported.

A reporting rate close to 100% is essential for the received data to be of value. Validation of the data received to the Norwegian Arthroplasty Register has been done by comparing databases with other nation-wide databases like the former Norwegian Patient Register (65) and the former National Institute for Hospital Research (42;66). Furthermore, the register data have been compared with local

data from reporting hospitals (67;68) and with data obtained from patient cohorts through questionnaires (69). Completeness of data on primary and revision hip- and knee arthroplasties thus has been shown to be 95-100%. In other joints, the reporting has been much more variable ranging from 10 to 90%. These data of course, make analyses less conclusive (65).

Statistical methods used in evaluation of the data typically include Kaplan-Meier survival analysis (70) and Cox regression (71). The end-point in these analyses usually is revision of prosthetic components. The statistical methods are discussed further in Chapter 8.3.

Results obtained from the register data are regularly published in journals and presented at national and international meetings. By January 2006, 46 scientific articles and 5 PhD degrees have been produced. Furthermore, a total number of 276 abstracts, reports and scientific posters have been produced. In printed annual reports, and at www.haukeland.no/nrl/, an overview of national results with comments are given. Hospital-specific results are reported yearly to each participating hospital allowing direct comparison of local and mean national results.

6. AIMS OF THE STUDY

To determine clinical and radiological performance of total hip arthroplasty through evaluation of different implants, bone cements and operative principles.

Paper I. To evaluate the clinical and radiological long-term performances of three different types of uncemented total hip arthroplasties. Reports on inferior results of the PCA were available at the start of the study, and we wished to investigate whether the results of the other, more recent designs were different from the results of the PCA or not.

Paper II. To compare a new, undocumented bone cement (the Palamed G) with a well-documented cement (the Palacos R with gentamicin) by use of radiostereometric analysis. Specifically, we wished to compare the migration of a femoral stem using the two bone cements. Furthermore we wished to determine whether the motion occurred at the implant-cement interface or at the cement-bone interface.

Paper III. To evaluate the medium and long-term survival probabilities of the most commonly used uncemented femoral stems in Norway.

Paper IV. To compare the results of different procedures in revision of uncemented acetabular cups and specifically, to compare the results of liner exchange procedures to whole cup revisions.

7. SUMMARY OF PAPERS I-IV

Paper I

Hallan G, Lie SA and Havelin LI. **High wear rates and extensive osteolysis in 3 types of uncemented total hip arthroplasty.** A review of the PCA, the Harris Galante and the Profile/Tri-Lock Plus arthroplasties with a minimum of 12 years median follow-up in 96 hips. *Acta Orthop* 2006;77 (4):575-584

Background: High wear rates and femoral and acetabular osteolysis have been—and still are—the main problems in uncemented total hip replacement. We reviewed 96 consecutive cementless total hip replacements of 4 different designs.

Patients and methods: 21 PCA, 25 Harris Galante Porous/Harris Galante I (stem/cup), 25 Profile pressfit/Tri-Lock Plus (stem/cup) and 25 Profile HA-coated/Tri-Lock Plus (stem/cup) prostheses were included. The operations were performed in the period 1984–1991. Median follow-up ranged from 12 to 16 years. Wear and osteolysis were measured.

Results: Mean linear wear rates ranged from 0.17 to 0.21 mm/year in the 4 groups, and there were no statistically significant differences between the groups ($p = 0.9$, ANOVA). Moderate or extensive osteolysis was found in 46 of the 96 hips included. The association between high and low wear rates (more or less than 0.20 mm/year) and extent of osteolysis was statistically significant ($p < 0.001$, t-test). We found poor 12-year survival of the primary prostheses in all 4 groups (50–70%), mainly due to revisions because of wear of the polyethylene liner and/or osteolysis. The infrequently documented Profile/Tri-Lock Plus systems did not perform differently from the PCA and the HG.

Interpretation: The poor long-term results with these uncemented total hip arthroplasties, with articulations constituted of metal heads and UHMWPE liners in metal backed cups, illustrate the necessity of regular radiographic evaluation in order to detect osteolysis and liner failure, which are both generally asymptomatic until catastrophic failure appears.

Paper II

Hallan G, Aamodt A, Furnes O, Skredderstuen A, Haugan K and Havelin LI. **Palamed G compared with Palacos R with gentamicin in Charnley total hip replacement.**

A randomised, radiostereometric study of 60 hips. *J Bone Joint Surg* 2006;88-B (9):1143-1148

Background: Bone cements differ in composition, handling properties, and in ability to provide long-term implant survival. The early migration of hip prostheses is associated with the risk of aseptic loosening. We performed a randomised, radiostereometric study comparing two different bone cements, one of which was sparsely clinically documented.

Patients and methods: Randomisation of 60 total hip replacements (57 patients) into two groups of 30 was undertaken. All the patients were operated on using a cemented Charnley total hip replacement, the only difference between groups being the bone cement used to secure the femoral stem. The two bone cements were the Palamed G and the Palacos R with gentamicin. The patients were followed up with repeated clinical and radiostereometric examinations for two years to assess both the micromovement of the femoral component and the clinical outcome.

Results: Subsidence was 0.18 mm and 0.21 mm, and internal rotation was 1.7° and 2.0° at two years for the Palamed G and Palacos R with gentamicin bone cements, respectively. We found no statistically significant differences between the groups. Micromovement occurred between the femoral stem and the cement, while the cement mantle was stable inside the bone. The Harris hip score improved from a mean of 35 points pre-operatively to a mean of 91 points at two years. No differences were found between the groups. Both bone cements provided good initial fixation of the femoral stem and good clinical results at two years.

Interpretation: It is anticipated that the Palamed G bone cement should give equally good long-term fixation of the Charnley femoral stem as the Palacos G with gentamicin bone cement. However, the performance of larger randomised trials with long-term follow-up, and ultimately surveillance in large registers is adviceable to ensure safe practice.

Paper III

Hallan G, Lie SA, Havelin LI, Engesaeter LB, Vollset SE, and Furnes O. **Medium and long-term performance of 11 516 uncemented primary femoral stems from the Norwegian Arthroplasty Register.** Submitted.

Background: In earlier reports from the Norwegian Arthroplasty Register, the results of uncemented total hip arthroplasties were inferior to cemented total hip arthroplasties. High failure rates of uncemented cups were largely responsible for this. In the present study, we focused exclusively on the results of uncemented femoral stems.

Methods: The most commonly used primary uncemented femoral stems reported to the Norwegian Arthroplasty Register in the period 1987-2005, were included in this prospective observational study. The material comprised 11 516 hips in 9 679 patients and 14 different stem designs. Kaplan-Meier estimation and Cox regression were used to analyse the data. Stem revision due to any cause was the primary end-point in the analyses. Subanalyses with cause-specific end-points were also done.

Results: The long-term results of the different stem designs varied from very poor to excellent with 15-year survival ranging from 29% to 97%. The Corail (n= 5456) was the most frequently used uncemented stem, and this design had a survival of 97% at 15 years. The other currently used designs with long-term follow-up, the Taperloc and the Zweymüller, performed inferiorly to the Corail with relative risk of stem revision being 3.4 (95% confidence interval (CI) 2.3-5.2) and 3.1 (95% CI 2.1-4.7), respectively with any stem revision as the end-point. The results for designs with shorter follow-up, the ABG, SCP/Unique and Bicontact, did not differ from that of the Corail. The Filler and the Omnifit HA had an increased risk of revision compared to the Corail with RR 2.1 (95% CI 1.2-3.5) and RR 2.2 (95% CI 1.1-4.5), respectively. With aseptic loosening as end-point, all currently used stem designs performed excellently with survival percentages 96-100 at 10 years. The relative risk of revision of the designs that are no longer in use compared to the Corail, varied from 3 to 41 (all $p < 0.001$). Male gender was associated with a 1.3 times increased risk of stem revision (95% CI 1.05-1.52). Age and diagnosis had no influence on the results.

Conclusions: The best uncemented stem designs had good or excellent survival at medium to long-term follow-up. The results of several of the designs investigated in the current study

however, were unsatisfactory. Follow-up longer than 7 years was needed to identify some of these poorly performing stem designs.

Paper IV

Lie SA, Hallan G, Engesaeter LB, Havelin LI, and Furnes O. **Liner exchange procedures compared to whole cup revisions in revision of uncemented acetabular cups.** A study of 1649 revisions from the Norwegian Arthroplasty Register. Accepted for publication by *J Bone Joint Surg (Br)* November 2006.

Background: We analysed the results of different strategies in revision of primary uncemented acetabular cups reported to the Norwegian Arthroplasty Register. The aim was to compare the risk of further cup revisions after liner exchange procedures and whole cup revisions. Furthermore, we compared the results of exchanging well-fixed cups with those of exchanging loose cups.

Patients and methods: The revisions were reported between September 1987 and April 2005. The following groups were compared: Group 1) Exchange of liner only (n=318), Group 2) Exchange of well-fixed cups (n=398), and Group 3) Exchange of loose cups (n=933).

Results: We found that the risk of a second cup revision was lower after revision of well-fixed cups (RR=0.56, 95 % CI [0.37-0.87]) and loose cups (RR=0.56 [0.39-0.80]), compared to revision of liner only. The most frequent reason for second cup-revisions was dislocation, accounting for 28 % of the re-revisions. Other reasons for second cup revisions included pain (12%), cup loosening (11%) and infection (9%). Re-revisions due to pain were less frequent when whole cups (fixed or loose) were revised compared to liner-revisions (RR=0.20 [0.06-0.65] and RR=0.10 [0.03-0.30], respectively). Risk of second cup revisions due to infection however, did not differ between the groups.

Conclusions: In the present study exchange of the liner only resulted in a higher risk of re-revision compared to revision of the whole cup. Our results suggest that the threshold for revising well-fixed cups in the case of liner wear and osteolysis should be lowered.

8. METHODS

8.1 Radiographic evaluation

Routine radiographs before and after hip replacement surgery include an antero-posterior (AP) pelvic view centred on the pubic symphysis and an AP- and lateral view of the hip. Several methods of wear measurement on plain radiographs are described in the literature (72). In Paper I we used the Livermore method for linear wear measurement (73). This method was originally developed for cemented sockets. Measurements were done on the AP pelvic views. A template with concentric circles was used to find the centre of the femoral head. The shortest distance from the femoral head centre to the outer surface of the cup defined the point of maximum wear, and this point was determined by the use of a compass. In the original method, a calliper is used to measure the thickness of the polyethylene at this point on the postoperative and the latest follow-up radiographs. Linear wear, or rather femoral head penetration, is the difference found between the measurements. In our study (Paper I) we used the method with slight modifications. Instead of measuring the polyethylene thickness directly, we measured the distance from the centre of the femoral head to the outer surface of the metal backing, assuming negligible wear of the metal femoral head. The magnification of the x-rays was determined by dividing the known diameter and the measured diameter of the femoral head. All measurements were corrected accordingly.

8.2 Radiostereometric analysis (RSA)

Radiostereometric analysis is a highly accurate method used in orthopaedic research for in vivo measurement of relative motion in three dimensions. The method as applied to orthopaedics originates from a Swedish research group and dates back to 1974 and Gunnar Selvik (74). Since then, several research groups have further developed the RSA method and there have been improvements in accuracy and in

user friendliness (75;76). RSA has been used in evaluation of motion in a wide range of orthopaedic research fields. However, the most widespread use of RSA has been in evaluation of joint replacements. It has been shown both in RSA studies (77;78) and other studies (79-81) that early motion of implants predicts failure by loosening at mid-term. RSA can determine relative motion in the range of 0.1 mm and 0.05°. High accuracy means that few patients are needed to obtain a high statistical power, and that limited time (1-2 years) is needed for clinical evaluation. RSA is therefore a valuable predictive tool using early migration as a surrogate for long-term clinical failure.

The RSA method used in our work (Paper II) depends on implantation of markers in the host bone, in the bone cement, and on the implants investigated. Alternative methods have been developed that do not necessitate the implantation of markers on the implant (76). In the following, a brief review of the methodology used in Paper II is outlined.

Intraoperatively, spherical tantalum markers (beads) were inserted into the bone surrounding the implant studied, in this case the proximal femur. 5-7 beads ($\varnothing=1.0$ mm) were used in the lesser and greater trochanteric areas. In the cement, 0.8 mm beads were used in order to discriminate bone beads from cement beads. 2 beads were placed in the cement restrictor, 2 in the distal cement mantle during retrograde filling of the femoral canal, and 4 in the proximal cement mantle during and after insertion of the stem. The latter beads were inserted using blunt cannulas with trocars. The manufacturer marked the implant, a Charnley femoral stem, with beads on small towers at the tip and shoulder of the prosthesis. The centre of the femoral head was computed by an edge detection technique and used as the third stem marker enabling accurate three-dimensional evaluation of the stem segment.

Postoperatively, and at regular intervals for 2 years, the RSA examinations were done by two simultaneous exposures with the patient supine and a calibration cage underneath the patient. In the calibration cage, tantalum beads placed in a

systematic fashion make out a co-ordinate system into which the patient markers project on the x-ray images.

The sets of digital x-rays produced were incorporated into an automated system (UmRSA Digital measure version 5.0 software, RSA Biomedical) in which the co-ordinates of the patient markers were determined. The markers in each segment (bone, cement or stem) defined a rigid body, and the relative motions of the three rigid bodies were calculated by comparing sets of examinations. We used the femoral bone segment as a reference, and movement of the femoral stem and cement mantle relative to the bone was calculated at different time intervals up to two years.

The quality of RSA measurements is evaluated in several steps during the process described. First, during the automated measurement of each single marker, markers that are not reliably measured are excluded. The process of measuring the markers is based on mathematical models, and the fit of the model used is again tested. A set cut-off level determines whether the fit is acceptable or not and thereby whether the marker can be used or not. Second, the computed and the known co-ordinates of the cage markers are compared on the x-ray films. Third, the 'condition number' (CN) and the mean error of the rigid body fitting (ME) are determined. The CN describes the three-dimensional 'quality' of the segment. The number and the spread of the markers in all three dimensions determines the CN. A segment defined by few markers or by markers that are close to each other, or on a straight line, will have a high CN. CN 150 is suggested as an upper limit (82). The ME describes the stability of the markers that define each rigid body when comparing different examinations, and should be lower than 0.35 mm (82). Finally, the precision (repeatability) of the measurements is evaluated by double examinations. In practice, two separate examinations on the same hip with a 15 minutes interval in-between are taken. Since the expected migration of the implant between these examinations is zero, the measured migration represents inaccuracy. Limits for significant translations and rotations are calculated as the 99% confidence intervals of the absolute mean values from analyses of the double examinations.

Our RSA study was a cooperation between two centres. The study was conducted from the Department of Orthopaedic Surgery at Haukeland University Hospital, Bergen. The patient inclusion, the surgery, the RSA examinations, and the follow-up was done in Bergen. The x-rays then were sent to the RSA-lab at the department of Orthopaedic Surgery at Trondheim University Hospital for analysis.

8.3 Statistics

Survival analyses describe the distribution of life times till a defined event. In survival analyses of joint replacements time starts with one operation (e.g. the primary procedure) and stops with a defined event (e.g. the first revision procedure). Observations with no event when last seen, are censored observations. Prostheses lost to observation because of patient death or emigration are censored at the time of death or emigration. The methods used for analyses of survival data in the present papers, were the Kaplan-Meier method (70) and the Cox proportional hazards model for regression analyses (71). Time was measured from the date of the primary joint replacement procedure to revision (Papers I and III), or from the first to the second revision (Paper IV). Median follow-up was calculated by the reversed Kaplan-Meier method (83). Statistical significance in survival probabilities was evaluated using the log-rank test (84). Cox regression analyses were used to study relative risks among the study groups and allowed for adjustments for possible confounding factors such as age, gender and diagnoses. Adjusted survival curves at mean of covariates based on the Cox estimates were constructed (Papers III and IV). Analyses with different cause-specific end-points (events) were done.

In Paper II, the effects of the type of bone cement and time on RSA migration data and on clinical outcome data were investigated in a *mixed-effects model* (85). This model allows analysis of repeated and interdependent measures on the same patients.

The S-Plus (Statistical Sciences Inc 1995) and SPSS (SPSS Inc 1999) statistical software packages were used.

8.4 Clinical evaluation

In Paper II, repeated clinical evaluation was undertaken with use of the Harris hip score (86). A maximum of 100 points is given according to pain (44), function (47), range of motion (5), and absence of deformity (4). The Harris hip score system is validated (87) and extensively used in clinical practice and in the literature. The doctor fills in the score by interview and physical examination. The score does not include visual analogue scales for pain or evaluation of patient-satisfaction.

9. DISCUSSION

9.1 Methods

9.1.1 Register studies and randomised controlled trials

National and large regional medical registers are increasingly used to survey medical diseases and treatment modalities. Most studies originating from the Norwegian Arthroplasty Register (NAR) are prospective observational studies in which patients enter with a primary joint replacement and are followed until revision (see also 7.3). The NAR is population-based, the numbers studied are generally high, and the completeness of data has been shown to be very high, at least in primary and revision procedures of the hip and the knee (65;66;68). Furthermore, all hospitals and all surgeons participate in data collection. Therefore, highly specialised centres and surgeons do not generally dominate the results from the register. The results as presented should be achievable for the average orthopaedic surgeon (88). However, the end-point of revision is certainly a crude end-point. The register has no information on radiographic or clinical measures on patients that have not been revised. Probably only about half the patients with clinical and radiographic failure are revised (89). Survival analyses with end-points such as clinical and radiographic failure are of course of great value, but are not readily achievable, are difficult to define, and are less reliable in a register setting (90). Furthermore, although the numbers studied in registers generally are quite high, some implants are used only in a few centres, and by few surgeons. In these cases, factors such as surgical skills, revision policy etc will have a strong influence on the results.

Register observational studies are well suited to identify poor results. Shortcomings due to the reasons listed above, indicate that smaller differences between well-performing implants should be interpreted with caution.

Randomised controlled trials (RCTs) are comparative, prospective studies in which patients are randomly assigned to the treatment groups. RCTs allow the investigators to control factors of known or possible influence on the measures that are studied.

RCTs are generally considered to have the strongest level of evidence for comparison of treatment modalities. However, for comparison of the performance of different implants or techniques in total hip arthroplasty, RCTs are impractical for several reasons. The follow-up time needed is usually at least 10-15 years because differences generally develop from 5-7 years and onwards. Furthermore, since the differences between the study groups are generally quite small, the number of patients required in comparative studies is high. Faulkner et al 1998 calculated the number of patients that was needed to show a difference of 4% implant survival between two implants with an expected survival of 90% at 20 years at 5% level of significance and with a power of 80%. About 3600 patients in each group were needed if the patients had a mean age of 65 years, and dropouts caused by patient death were taken into account. In the same setting, but with expected implant survivorship of 80% and 10% difference between the groups, 500 patients would still be needed in each group (43). Trials of this size and follow-up time would represent a massive workload to the investigators, and they would demand a substantial amount of funding and patience. For these reasons, it may be impractical, or even impossible to use RCTs for comparing long-term performances in total hip arthroplasty (91). To my knowledge, no such large-scale RCT exists for long-term comparative study of hip implants. Very few comparative randomised trials of hip implants are available, and the numbers investigated and length of follow-up are generally insufficient (44). Exceptions are studies with high accuracy methods, such as RSA, in which migration is used as a surrogate end-point for clinical failure. In these studies, few patients and short time is needed thus making RCTs amenable. A RSA study is not however, an alternative to a RCT that evaluates clinical outcome, but rather a supplementary tool in the early phase of the investigation of new implants.

Another problem with randomised controlled trials, is their inability to detect infrequent side effects of treatment. Total hip arthroplasty is overall a successful treatment, and side effects generally are infrequent. Randomised controlled trials of joint implants are usually designed to evaluate outcome measures. As described

above, few or no RCTs are powered to detect differences between implants, unless very large differences are suspected. In order to detect differences in side effects between the study groups, the numbers investigated need to be immense, and far beyond what is realistic. Furthermore, the patients most likely to have adverse effects of treatment, are often not included in the study. Even in large-scale RCTs for assessing post-marketing drug safety, important side effects may not be discovered (92). Population-based, prospective observational studies, such as register studies, may provide insights in assessment of safety not readily offered by RCTs. Therefore, in the search of evidence also studies of designs others than the randomised trials must be considered.

Observational studies have generally been thought to overestimate the effect of treatment, and have therefore been rendered non-suitable in comparative clinical studies by some authors (25;93;94). Others have challenged this statement (95;96). They have shown that in a comparison of observational studies and randomised, controlled trials, the estimates of treatment effects were similar. They also pointed at some advantages of observational studies over RCTs, such as lower costs, a broader range of patients and surgeons, and greater timeliness (96). They concluded that observational studies usually provide valid information.

Observational studies (patient series, register studies) dominate clinical orthopaedic research. Despite the scientific drawbacks of observational studies, they must be included when seeking evidence in clinical questions.

9.1.2 Wear measurements

Methods for measuring migration on plain radiographs have limited accuracy. Intra- and interobserver variability ranging from 0.5 to 5 mm has been reported. Malchau et al concluded that cup migration is detectable when it exceeds 3-4 mm, and stem migration at even higher detection limits (97). All methods used for in vivo wear measurement measure penetration of the femoral head into the acetabular cup. They do not distinguish between the initial deformation of the liner ('bedding in' or 'creep')

and true wear as defined by loss of bearing surface mass. Compared to some computerized methods, and to RSA and Ein Bild Roentgen Analyse (EBRA), the accuracy of all the manual methods is limited. However, their simplicity makes them useful in both research and clinical practice. In our study (Paper I) the metal backing tended to obscure the outline of the femoral head. This was especially a problem with the PCA-cup, which was the most radiodense. Furthermore, the peg of the PCA-cup made the exact definition of the outer surface of the metal shell somewhat uncertain in some cases. Livermore found the accuracy of wear measurements to be 0.075 mm (range 0-0.4 mm) when comparing measurements on x-rays with direct measurements on retrieved cups (73). Other investigators found the precision to be lower, from 0.3 to as high as 0.6 mm (98;99). The Livermore method has been frequently used in the literature to measure linear wear, but the accuracy (99) is limited, and in the present study (Paper I) there were additional factors that possibly made the method even less accurate. Nevertheless, in the presence of relatively high rates of linear wear, like the ones in our study, and long follow-up time the measurements seem reasonable. Our results are consistent with the results of others (100-103). For routine clinical assessment of wear, this simple manual method provides sufficient accuracy. In prospective studies of wear however, more accurate and precise methods, like RSA should be considered.

9.1.3 Radiostereometric analysis

Radiostereometric analysis (RSA) is currently the most accurate and precise method of evaluating motion of implants in vivo. The association between initial micro-instability and later aseptic loosening of implants is documented in three papers (77;78;104). Hence, the predictive value of RSA is great using early micro-motion as a surrogate for later clinical failure. The fact that few patients and short time is needed, make RSA studies attractive as an alternative, or ideally as precursors of larger scale RCTs (105).

The relationship between early migration and late aseptic loosening has been established. It has been shown that stem retroversion or posterior head migration, and subsidence higher than certain critical levels predict aseptic loosening (77;104). The acceptable magnitude of motion however, is related to implant design (104;106). The direct comparison of different implants in terms of magnitude of motion is not in all cases appropriate. Different implant designs have different patterns of early migration, and the one that migrate most is not necessarily inferior to the other in terms of long-term survival. For instance, it has been shown that the polished Exeter femoral stem and the matte Charnley Elite Plus stem have different tolerances to initial micromotion (107). Strictly speaking therefore, the relationship between early migration and later loosening, and the critical magnitude of migration should be evaluated for the design in question to justify the supposed predictive value of early migration.

RSA is still time consuming and demands trained personnel, special equipment and software, and economic resources. During the last two decades, advances in RSA software and automation have certainly made the method more user-friendly and less time consuming. Still, RSA is not practical for routine clinical use, but remains a research tool.

To my knowledge there have been no reports on side effects of the method on patients although RSA with markers has been used on thousands of patients for more than 30 years. In theory however, implantation of markers in bone, cements and on implants is a potential hazard to the patients. Loose markers in the articulation could lead to third body wear. Implant markers could lead to voids in the cement mantle. The somewhat prolonged operation time, and the slightly increased tissue trauma could increase the risk of peri- and postoperative complications (108). Marker-less RSA of course reduces these potential hazards by eliminating implant markers.

In our RSA study (Paper II), the stem and cup used were identical in the two groups thus allowing a direct comparison of the two investigated bone cements.

In measurements of wear, or rather penetration of the femoral head into the acetabular bearing, RSA is the method of choice. Especially when evaluating hard bearings such as metal-on metal, ceramics and highly cross-linked polyethylene, a very accurate and precise method is needed in order to detect small differences in wear properties.

9.2 Results

9.2.1 Wear and osteolysis

We found high wear rates and extensive osteolysis with three different uncemented total hip arthroplasties used in the late 1980's and early 1990's. The PCA THA demonstrated inferior results after 4-5 years. High prevalence of thigh pain was uncovered (109;110), and poor polyethylene characteristics and suboptimal cup fixation were thought to be the reasons for the inferior results of the PCA. These results were known at the time of introduction of the Profile / Triloc Plus and Harris Galante systems investigated in Paper I. The latter two systems were supposedly superior to the PCA system. We did not however find that the other systems proved statistically significant better results than the PCA at long-term follow-up.

Most studies suggest that the wear rates are generally higher in modular metal-backed acetabular cups than in cemented cups with similar conventional UHMW polyethylene (111-115). The reasons for this have been debated. Wear at the backside of the polyethylene insert due to micromotion between the insert and the metal backing is thought partly responsible (116). Furthermore, the higher stiffness of the metal-backed implants gives rise to increased stresses on the articulating PE and hence higher wear rates. The thinner polyethylene also contributes to higher stress on the liner in modular uncemented cups. Some authors also have proposed that particles of hydroxy-apatite originating from the proximal stem or the cup give rise to third-body wear when free in the articulation (117). In our study we found a statistically significant association between wear rates and the occurrence and extent of osteolysis. Other authors have found the same (101;118-120). This finding

however does not prove a causal relationship between the two, but simply shows a co-existence. The ethiology of osteolysis is probably multifactorial (see Chapter 4.5), and is not yet fully understood.

Inferior results of uncemented cups in the Scandinavian registers (42;51;121) and in other reports imply that modular uncemented cups with a stiff metal-backing and a standard UHMWPE should not be routinely used in primary total hip replacement, at least not in younger patients. Promising results have been obtained with modular uncemented cups and alternative bearing surfaces. These new articulations address the problems of wear and osteolysis (see Chapter 10.2).

9.2.2 Bone cement

The bone cement used in fixation of implants may play as important a role as the implant itself in determining its long-term performance. Some cements have been found inferior to others in randomised RSA- or register studies (28-31;122). The cements studied in our trial were very much alike in chemical composition, their properties in laboratory studies regarding mechanical strength and elusion of antibiotics were similar. However, the relationship between results of laboratory tests and clinical results is not fully known (32). Therefore, in vitro evidence of mechanical strength according to ISO-testing is no guarantee of good clinical performance. The Palamed G bone cement fulfilled the standards according to ISO 5833. Pre-chilling of this cement is not necessary to achieve a homogenous cement with reduced porosity (123). The setting time is slightly shorter than that for the reference cement (Palacos R with gentamicin). These characteristics were assumed to be advantageous. Both cements studied contained antibiotics. Laboratory studies have shown conflicting results regarding the strength of antibiotic loaded bone cements compared to plain cements (124;125). The clinical performance of the antibiotic-containing cements have not been proven inferior to their plain counterparts in register studies (30). Also when revisions because of aseptic loosening was the end-

point, the antibiotic-containing cements performed as well or better than the plain cements (30;126).

In our study of bone cements (Paper II), we found no differences in migration or clinical outcome after two years with the two different cements. It is therefore anticipated that the Palamed G bone cement should provide equally good clinical results as the Palacos bone cement at long-term. However, the cement should be implemented in a systematic prospective evaluation before widespread clinical use (see Chapter 11.2).

The stability of the cement mantle depends on stable interlocking between the cement and the cancellous periprosthetic bone. This cement-bone interlocking again depends on the cementing technique, especially pressurisation and cleaning of the bone bed, and on properties of the cement, such as the viscosity. We found that the migration of the femoral stem occurred inside the cement mantle whilst the cement mantle was stable within the femur. This finding corresponds well with other reports (127;128). Some studies however, have shown slight migration also of the cement mantle relative to the bone (129;130). Whether this finding is related to the bone cement, the cementing technique, or implant features is not known.

9.2.3 Implant survival

Currently used uncemented stems generally performed very well in our long-term follow-up study of 11 000 hips (Paper III). Stems with different shapes and surfaces provided excellent fixation. The rate of failure because of aseptic stem loosening at 10 years follow-up, was below 4% for all the stems that were still used at the end of our study. The overall 10 years survival of the same uncemented stems combined with uncemented cups however, was relatively poor (43-91%). The end-point in these analyses was revision of any cause and of any component, including isolated exchange of the acetabular liner. Fixation of both components was generally good. Revisions due to liner wear and osteolysis constituted the main reasons for the poor and mediocre results. In Paper I, we found poor results of three different uncemented

THA systems, and again the reasons were primarily liner wear and osteolysis. When inferior results of implants are reported in journals, surgeons will probably lower the threshold for revision of these implants. This negative feedback effect probably further worsens the results of the implants in question.

In reports from the NAR, the main analyses use the end-point 'revision of any part of the prostheses for any reason'. Aseptic loosening has for decades been the most frequent cause of revision, and in many studies the survival of implants are reported with the end-point aseptic loosening only. However, we believe other reasons for revision should not be omitted when reporting implant survival. It seems that liner revisions are not considered proper revisions by some authors. In Paper I we argue that these operations should be considered revision procedures and should be reported when evaluating survival of hip implants. Although being technically relatively simple, the procedure is of significant cost, has potentially serious complications and may not provide long-term success (Paper IV).

9.2.4 Revision of uncemented acetabular cups

Loose uncemented modular cups generally require cup exchange and, depending on the extent of bone loss, supplementary reconstruction of the acetabulum by the means of bone grafts, metal cages, reinforcement rings, or bulk metal wedges. Failures caused by liner wear or liner dislocation are often treated with isolated liner exchange and bone grafting of osteolytic lesions, if present. In Paper IV we evaluated the results of whole cup revisions compared to exchange of liner and head only. Three groups of revision procedures were compared, namely isolated liner exchange, exchange of well-fixed cups, and exchange of loose cups. Isolated liner exchanges are usually the least complicated of the three, and the concomitant bone-loss supposedly less pronounced in these hips compared to the hips operated on with cup exchange. However, in our study the survival of liner exchanges was statistically significantly inferior to the revisions of the whole cup, regardless if the revised cup was considered fixed or loose. Re-revisions due to dislocation and pain were largely

responsible for these results. Some investigators have reported high dislocation rates after liner exchange procedures (131;132) whereas others found favourable results of these limited revisions (133-135). Studies on results of liner exchange procedures include relatively low numbers of hips. In our study, the total number of hips was 1649. The hips were divided into 3 groups according to the undertaken revision procedure. However, many variables were not taken into consideration in our study. For instance, a wide range of uncemented primary implants, and a wide range of revision implants, both cemented and uncemented, with or without acetabular reconstruction, were included. Furthermore, the amount of bone-loss was not taken into consideration. Therefore, we do not know the influence of these factors on the results. An attempt to subdivide groups according to various variables would create a large number of small sized groups thus making comparison of revision strategies difficult. However, there are reasons to believe that the presence of osteolysis and instability was higher in the groups that were treated with cup exchange than in the group that was treated with liner exchange only. This assumption further strengthens our results.

New techniques for removal of ingrown uncemented shells enable swift cup revision with minimal amounts of bone loss (136). Results with both cemented and uncemented cup revisions are fairly good (63;137;138). Our results suggest that the threshold for revision of the whole cup in the case of liner wear and osteolysis should be lowered.

10. CONCLUSIONS

Paper I:

- We found high wear rates and extensive osteolysis in three different uncemented total hip systems.
- There was an association between the wear rates and the extent of osteolysis.
- Prostheses survival was poor in all groups, the Profile / Tri-Lock Plus and Harris Galante systems did not perform better than the PCA system.

Paper II:

- The Palamed G and Palacos R with gentamicin bone cements provided equally good initial stability of a Charnley femoral stem.
- The stem subsided and internally rotated in both groups.
- The migration occurred at the implant-cement interface whereas the cement mantle was stable inside the femur.
- This RSA study claims that the poorly documented Palamed G bone cement should be safe for clinical use, but propose larger scale trials and surveillance in population based implant registers to ensure safe practice.

Paper III:

- Currently used uncemented femoral stems performed well or excellent in a long-term prospective observational study of 11 000 hips.
- Survival at 10 and 15 years ranged from 90 to 98% with end-point being stem revision of any cause and even better with aseptic loosening as the end-point.
- We found differences between the stems, but these differences were modest. The impact of these differences should not be overestimated due to limitations in the study model.
- Older designs of uncemented femoral stems performed inferiorly or very poorly.
- More than 7 years of follow-up was needed to identify some of the poorly performing stems.

Paper IV:

- Results after liner exchange procedures were inferior to those after whole cup revisions of primary uncemented acetabular cups. The latter had a 0.6 times relative risk of a second cup revision compared to liner exchange regardless if the revised cup was well fixed or loose.
- Reasons for re-revision were dislocation, pain, infection and aseptic cup loosening.
- The results propose that the threshold for revising the whole cup as opposed to isolated liner exchange should be lowered.

11. FUTURE RESEARCH

11.1 New bearings

As outlined throughout this text and in three of the papers that constitute this thesis, wear and osteolysis are the most important issues that need to be investigated in order to further improve the clinical outcome of total hip arthroplasty. New bearings have been developed in order to address these problems. These bearings are currently used throughout the world in younger patients in the belief that they will provide better long-term survival of hip implants. The principal implication of these wear-resistant bearings is the potential reduction in periprosthetic osteolysis. Furthermore, because of low wear larger femoral heads can be used. This means greater range of movement, less femoral neck impingement on the liner, reduced incidence of dislocation, and an increased margin of safety in respect to placement of the components.

Highly cross-linked polyethylene. Some reports on the long-term clinical performance of highly cross-linked polyethylene exist (139;140). However, currently available highly cross-linked polyethylenes differ from the ones in these studies, and they differ from each other. Enhanced wear properties, meaning less femoral head penetration, and less volumetric wear, have been found in numerous laboratory and short term clinical studies (141-145). There is some concern however, that despite the reduction of particle volumes generated with cross-linking, the amount of particles in the size that have a osteolytic potential, remains quite high (146). Thus, the potential for development of osteolysis could possibly be higher than expected from the low wear rates. Furthermore, free residual radicals remaining in the polyethylene after cross-linking may cause oxidation and subsequent embrittlement of polyethylene. In a retrieval study, Bradford et al found surface damage in explanted highly cross-linked liners after an average of 10 months in vivo service. These findings were not predicted by long-term simulator studies (147).

Ceramics. Ceramics have been used in bearing surfaces for more than 20 years (148). Wear characteristics of ceramic femoral heads have generally been superior to standard UHMWPE, but chipping and fracturing of the ceramics limited its popularity. Until recently, ceramic femoral heads were mainly coupled with polyethylene acetabular bearings. Early ceramic acetabular components were not subject to widespread use due to fixation problems. Contemporary alumina ceramics are supposedly of higher quality due to progress in design, manufacturing, and proof testing. Ceramics on both the acetabular and femoral bearing surfaces are becoming increasingly popular. Wear characteristics are favourable in short term clinical follow-up and in vitro studies (149;150). In most reports mechanical failure of the ceramics is exceedingly rare with these modern ceramics, but some authors found relatively high rates of fractures and chipping (7;151). Ceramic-on-ceramic articulations with ceramic femoral heads and ceramic acetabular bearings rely on precise orientation of the components in order to avoid impingement of the ceramics. Modularity in terms of femoral neck length is somewhat restricted. Fractured ceramic bearings usually dictate revisions with new ceramic bearings due to ceramic remnants in the articulation that would give rise to third-body wear with softer bearings. Some have been concerned that the stiff implant will be subject to migration and loosening. Recently however, the stability of cups with ceramic-on-ceramic bearings was found to be no different from the stability of the same cups with polyethylene-on-metal bearings (152).

Metal-on-metal articulations. These articulations have a history spanning 40 years (McKee-Farrar, Ring, Urist). The early designs were abandoned partly because of reported high rates of aseptic loosening and partly because of the increasing popularity of Charnleys low friction arthroplasty. The contemporary metal-on-metal total arthroplasties have been used since 1989 (153). They have very low rates of femoral head penetration both in laboratory studies and in clinical studies (150;154;155). The wear of metal-on-metal bearings is dependent upon the design and the carbon content of the alloy, the head diameter, perfection of sphericity, and

the radial clearance between head and cup. Reports on grossly elevated levels of Co and Cr in serum and erythrocytes have raised concerns about toxicity, renal failure, hypersensitivity, and mutagenesis. There is however no evidence to suggest that the risk of carcinogenesis is of clinical importance (156). Some investigators have found some evidence of hypersensitivity as expressed by osteolysis and inflammatory pain (157;158).

These modern bearings all have improved wear characteristics in laboratory studies and have proved successful in short-term clinical studies. The osteolytic potential, the alteration of mechanical properties during ageing of the implants (highly cross-linked polyethylene, ceramics) and the host tolerance to increased systemic levels of metal ions (metal-on-metal) are questions not yet fully answered. The results of the first generation of highly cross-linked polyethylene, metal-on-metal and ceramic-on-ceramic articulations cannot be superimposed on the more recent bearings because of significant differences in the materials used and in the manufacturing process. Hopefully, the currently used modern bearings will prove efficient in prolonging the life of hip implants. However, longer-term follow-up, surveillance, and more studies on the biomechanical characteristics of these bearings are needed before widespread use is advisable.

Uncemented tantalum, monoblock acetabular cups with higher elasticity, higher friction and enhanced ingrowth of bone have been used clinically since 1998. This cup has a rather thin metal backing made of porous tantalum (159). The polyethylene is direct compression molded into the tantalum backing, and the cup is therefore a one-piece construct. Possible advantages of this cup compared to standard, modular titanium cups include enhanced primary fixation due to the high friction, faster and more solid bone in-growth, less stress-shielding due to more physiological load transmission to periprosthetic acetabular bone, less polyethylene wear as a consequence of a more elastic construct and the elimination of backside wear

(160;161). A monoblock cup with a thin titanium backing and direct compression molded polyethylene has a 10 year clinical record with favourable results (162;163). The lack of acetabular modularity may have restricted the use of these implants. Acetabular modularity allows the surgeon to choose between different liner inserts and hence provides a slightly wider safety margin. However, in my point of view the anticipated, and to a point proven assets of the one-piece uncemented implants call for further investigations of this concept.

11.2 Documentation of hip prostheses

Ideal papers (scientific level I or II, National Health and Medical Research Council, www.nhmrc.gov.au/) are not prevailing the orthopaedic research fields, and surgeons can quite easily find support for approaches which they for reasons such as economy, experience, local routines, etc prefer. The majority of studies on outcome and effectiveness of hip prostheses are observational studies, and a large proportion of implants do not have any peer-reviewed clinical documentation (44). Unlike drugs, medical devices such as joint implants are not subject to strict evaluation in several steps before they can be used in human beings. Testing according to required standards (International Organization for standardization (ISO), Communauté Européenne (CE), and Food and Drug Administration (FDA)) merely documents the mechanical quality of the implant materials. To my knowledge, the relationship between performance in these tests and clinical performance has not been documented.

Reviews of the scientific literature on effectiveness and outcome of total hip arthroplasty have uncovered a lack of substantial evidence on which surgeons may base their choice of implants (43;44;164). Aamodt et al propose the development of a system for the choice of prostheses and an algorithm for introduction of new implants (44). In accordance to Malchau (105), a stepwise introduction of new implants should be undertaken. After pre-clinical testing according to accepted standards, controlled trials should be done. Initially, studies of high accuracy such as RSA-studies with

small number of patients and short follow-up time should be done. If favourable results in this first step, larger-scale prospective trials and ultimately surveillance through large registers should be done until long-term clinical performance is documented.

It is evident that inferior implants have been used, still are used, and will continue to be used in the lack of an obligatory system for the introduction and choice of prostheses for clinical practice. Health authorities should engage in the development of such systems. While waiting for the authorities, the research communities together with the orthopaedic associations should strive to influence this process and outline suggestions for future evaluation systems.

11.3 Is there a need for further improvement?

THA is a very effective and cost-effective surgical procedure. Good results, meaning survival at 10 years exceeding 90%, are documented for several implant systems. Why the continuous efforts to develop new devices? There are several reasons for this. Some reasons are related to the interest of the patients, others to the interest of surgeons or society and some related to the interest of the medical industry. Human beings, both orthopaedic surgeons and osteoarthritic patients, tend to believe in continuous progress; new inventions are thought to be superior to older technology. Furthermore, the medical industry may make higher profits on new and “improved” implants than they do on older implants, and market shares might drop when a company does not come up with the latest cutting edge technology. These mechanisms compete with scientific evidence when implants, bone cements, techniques and routines are considered. Thus, new implants with little or no clinical documentation, but with supposed improvements, are often preferred to well-proven older ones.

The incidence of primary total hip arthroplasty in Norway in 2005, was 145 per 100.000. In the United States of America about 200 000 primary total hip arthroplasties were performed in the year 2002, resulting in an incidence of 69 /

100.000 (165). The numbers in both countries are increasing. The revision rates have not been significantly reduced during the last decades; thus there is an increase in the total number of revisions. The results of primary hip arthroplasty are generally very good. Revision surgery on the other hand, has variable success with regards to clinical outcome, but is invariably an expensive procedure and a burden to the patient. Thus, a reduction of the failure rates of only a few percents can, due to the large number of patients, have a vast influence on the accumulated costs and patient suffering (166). Therefore, a continuous effort to improve the outcome of THA, with the ultimate goal of creating prostheses that last a lifetime, is justified. In the slow evolution towards the perfect THA however, as few patients as possible should be subjected to novel, un-proven principles. Unless they are participants in controlled trials, patients should be treated according to existing knowledge with prostheses that have proven good long-term results.

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Paper I

High wear rates and extensive osteolysis in 3 types of uncemented total hip arthroplasty

A review of the PCA, the Harris Galante and the Profile/Tri-Lock Plus arthroplasties with a minimum of 12 years median follow-up in 96 hips

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Submitted 04-12-06. Accepted 06-02-11

Background High wear rates and femoral and acetabular osteolysis have been—and still are—the main problems in uncemented total hip replacement. We reviewed 96 consecutive cementless total hip replacements of 4 different designs.

Patients and methods 21 PCA, 25 Harris Galante Porous/Harris Galante I (stem/cup), 25 Profile pressfit/Tri-Lock Plus (stem/cup) and 25 Profile HA-coated/Tri-Lock Plus (stem/cup) prostheses were included. The operations were performed in the period 1984–1991. Median follow-up ranged from 12–16 years. Wear and osteolysis were measured.

Results Mean linear wear rates ranged from 0.17 to 0.21 mm/year in the 4 groups, and there were no statistically significant differences between the groups ($p = 0.9$, ANOVA). Moderate or extensive osteolysis was found in 46 of the 96 hips included. The association between high and low wear rates (more or less than 0.20 mm/year) and extent of osteolysis was statistically significant ($p < 0.001$, t-test). We found poor 12-year survival of the primary prostheses in all 4 groups (50–70%), mainly due to revisions because of wear of the polyethylene liner and/or osteolysis. The infrequently documented Profile/Tri-Lock Plus systems did not perform differently from the PCA and the HG.

Interpretation The poor long-term results with these uncemented total hip arthroplasties illustrate the necessity of regular radiographic evaluation in order to detect osteolysis and liner failure, which are both generally asymptomatic until catastrophic failure appears.

Cementless total hip arthroplasty was introduced partly in the belief that periprosthetic osteolysis could be eliminated by eliminating the need for cement (Willert et al. 1974, Jones and Hungerford 1987). However, numerous studies have reported alarming periprosthetic osteolysis in cementless total hip replacement (Tanzer et al. 1992, Xenos et al. 1995, Kim et al. 1999, Thanner et al. 1999, Crowther and Lachiewicz 2002). Polyethylene wear debris has been suggested by many authors as a major cause of osteolysis (Santavirta et al. 1990, Willert et al. 1990). Others believe that unstable components cause osteolysis by pumping joint fluid into the surrounding bone tissue at high pressure (Mjöberg 1994, Aspenberg and van der Vis 1998). The relationship between wear rate and extent of osteolysis (Dowd et al. 2000, Barrack et al. 2002, Orishimo et al. 2003b) has been established. The high wear rate and high incidence of osteolysis in some metal-backed uncemented acetabular cups (Harris 1994, Nashed et al. 1995, Sychterz et al. 1996) is a major concern in cementless total hip replacement, in addition to the mechanical problems of wear alone (instability and leg shortening). We compared the wear rates and incidence and patterns of osteolysis in 4 cementless total hip systems, 2 of which (the Profile/Tri-Lock Plus systems) have virtually no clinical documentation. Furthermore, we evaluated the influence of femoral head size, cup abduction, sex and body weight on wear rates, and the asso-

Table 1. Patient characteristics: age at surgery, gender, body weight, femoral head diameter, duration of follow-up, and diagnosis

	PCA (n = 21)	HG (n = 25)	Profile/Tri-Lock (n = 25)	Profile HA/Tri-Lock (n = 25)
Age at surgery, median (range)	43 (24–60)	47 (19–62)	56 (25–74)	56 (30–65)
Gender (F/M)	15/6	13/12	15/10	20/5
Body weight (kg), median (range)	65 (52–104)	72 (50–90)	63 (48–100)	70 (50–106)
28-mm femoral head (number of hips)	0	0	13	17
32-mm femoral head (number of hips)	21	25	12	8
Follow-up ^a (years), median (range)	16 (9–18)	15 (7–17)	12 (7–14)	12 (7–14)
Diagnosis				
Primary coxarthrosis	4	6	8	11
Sequel, hip fracture	10	2	6	–
Sequel, childhood hip disease	6	10	10	7
Rheumatoid arthritis	1	3	2	5
Others	1	5	3	2

^a Follow-up until first revision of any component, including exchange of liner and femoral head.

ciation between the rate of wear and the extent of osteolysis.

Material and methods

The 4 designs of prosthesis studied were the Porous-Coated Anatomic (P.C.A.; Howmedica, Rutherford, NJ), the Harris/Galante Porous stem/Harris Galante I cup (HG; Zimmer, Warsaw, IN), the Profile pressfit stem/Tri-Lock Plus cup and the Profile hydroxy-apatite coated stem/Tri-Lock Plus cup (Profile and Profile HA, respectively; DePuy, Warsaw, IN).

The PCA stem was made of cobalt-chrome, was relatively short, collarless, and anatomically shaped with a circumferential proximal porous coating. The cup used in the period 1984–1986 was single-assembly, cobalt-chrome, porous-coated and also fixed to bone by pegs. From August 1986, a two-piece cup with a hexagon locking mechanism was used (8 hips). The porous coating was Vitallium and applied by sintering. The liner was fixed to the shell by a central polyethylene locking peg. The UHMWPE liner was not heat-treated, but sterilized by gamma irradiation in air.

The HG (Harris/Galante Porous Hip Prostheses) stem was a straight titanium alloy (Titanium Ti-6Al-4V) stem with a collar and non-circumferential proximal fiber-mesh pads made of pure titanium. The acetabular component was a modular, hemispherical press-fit cup with a sintered titanium

fiber-mesh at the bone-implant interface and holes for transacetabular screws. 2 or 3 transacetabular screws were used in all hips. The liner was sterilized by gamma irradiation in air.

The Profile stem was a modular anatomic titanium alloy stem with two different surfaces. One had a gritted surface with proximal circumferential microtexture (hereafter referred to as Profile). The other had a proximal, circumferential microtexture finish made of hydroxy-apatite (hereafter referred to as Profile HA). The Tri-Lock Plus cup is a hemispherical titanium shell with porous coating and holes for peripheral screw fixation. The liner was sterilized by gamma irradiation in air.

In the PCA and HG groups, the femoral head was a 32-mm modular cobalt chromium head in all hips. In the Profile/Tri-Lock hips, both 28-mm and 32-mm heads were used; see Table 1.

Between 1984 and 1991, these components were used in our department in younger patients, most of them less than 60 years of age. The PCA was inserted in 26 hips. 2 of these were revision arthroplasties, 2 patients died within 7 years of surgery, and radiographs of 1 patient were missing. This left 21 hips in 18 patients in the PCA group. We then aimed for groups of similar sizes (25 patients) in the 3 other groups. The HG was used in 47 hips. We included the first (consecutive) 25 hips (20 patients) with available data and minimum follow-up of 7 years. Revision arthroplasties and former resurfaced hips were excluded. The Profile/Tri-Lock Plus and Profile HA/Tri-Lock

Plus were used in 191 hips in the period 1989–1994. In the same manner, we included the first 25 patients in each of these groups. Thus, we included 25 Profile/Tri-Lock Plus combinations in 23 patients and 25 Profile HA/Tri-Lock Plus in 21 patients. The total number of hips included was 96 (82 patients) (Table 1). A proportion of the patients in all 4 groups were referred from other regions for uncemented total hip arthroplasty, which, at that time, was done only at selected clinics. The follow-up, however, was often done at the patient's local hospital. According to Norwegian law, radiographs of patients not re-examined in our radiology department within 10 years of the index examination were destroyed. Thus, in these patients the postoperative radiographs were not available and the patients were therefore excluded.

The patients who received the PCA were followed radiographically for a median of 16 (9–18) years. Similarly, those who received the HG were followed for a median of 15 (7–18) years, the Profile/Tri-Lock Plus for a median of 12 (7–14) years, and the Profile HA/Tri-Lock Plus for a median of 12 (7–14) years. The median follow-up was longer in the PCA and HG groups. In the PCA group, sequel after hip fracture was the most common diagnosis whereas sequel after childhood hip disease (developmental dysplasia of the hip, Legg-Perthes disease, slipped capital epiphysis) and primary osteoarthritis predominated in the other groups. The average age of patients in the PCA and HG groups was lower than in the Profile/Tri-Lock Plus groups (ANOVA, $p = 0.03$). Otherwise, the 4 groups were reasonably well matched. All the operations were performed in the lateral decubitus position using a direct lateral Hardinge approach without trochanteric osteotomy, by three experienced surgeons. Postoperatively, the patients were allowed partial weight bearing from day 2 and full weight bearing after 3 months.

Standard radiographs, including an AP pelvic view, and AP and lateral views of the hip within three months of surgery, and the films from the latest follow-up or the latest films prior to revision were evaluated by one of the authors (GH). GH did not operate any of the patients.

Linear wear was measured on AP pelvic views using the method described by Livermore et al.

(1990). The direction of linear polyethylene wear in the frontal plane was measured referenced to a line through the center of the femoral head that was perpendicular to the inter-teardrop line. A manual caliper was used, measuring to the nearest 0.05 mm, and the known diameter of the femoral head was used to correct for magnification. Rather than measuring the thickness of the polyethylene directly, we measured the distance from the center of the femoral head to the outer surface of the metal backing, assuming negligible wear of the head and backing. Assuming a cylindrical wear track, volumetric wear was calculated from the formula $v = r^2w$, in which v is the change of volume of the polyethylene, r is the radius of the head, and w is the linear wear. The average volumetric wear rate (in mm^3/year) was then calculated based on the follow-up time of the liner.

The angle of abduction of the cup was the angle measured between a line drawn along the opening of the cup and the inter-teardrop line on the postoperative AP pelvic radiograph. The influence of femoral head size on wear rate and extent of osteolysis was evaluated in the Profile/Tri-Lock Plus groups only, in which both 28- and 32-mm heads were used.

Presence and extent of osteolysis was recorded on the AP and pelvic films since the quality of the lateral views was poor in many cases. Any punched-out area of reduced bone density that was not present on the initial radiographs was interpreted as osteolysis. The area of osteolysis was measured by multiplying the length by the width of the lesions. Osteolysis was labeled extensive when the area was 10 cm^2 or more, intermediate when between 2.5 and 10 cm^2 , and mild when less than 2.5 cm^2 (Hubble et al. 1997). The distribution in femoral and acetabular regions was recorded according to Gruen et al. (1979) and Charnley (1976).

Statistics

Statistical evaluation was performed using SPSS version 10.0 software. We used the Student t-test and ANOVA (analysis of variance) to compare means. Survival analysis was performed by the Kaplan-Meier method and by Cox regression analyses. Survival rates for the primary prostheses were calculated based on revision as end-point. Revision was defined as removal or exchange of any part of

Table 2. Wear characteristics and extent of osteolysis

	PCA (n = 21)	HG (n = 25)	Profile/Tri-Lock (n = 25)	Profile HA/Tri-Lock (n = 25)
Linear wear rate (mm/year), mean	0.20	0.20	0.21	0.17
Linear wear (mm), mean	2.2	2.3	1.81	1.75
Volumetric wear (mm ³), mean	1,817	1,841	1,286	1,297
Volumetric wear rate (mm ³ /year), mean	159	159	144	117
Number of hips with osteolysis	13	16	12	12
Osteolysis, mean total area (cm ²)	15	10	7	8
Osteolysis, severity (n)				
Mild (< 2.5 cm ²)	0	1	3	3
Intermediate (2.5–10 cm ²)	4	12	5	5
Extensive (> 10 cm ²)	9	3	4	4

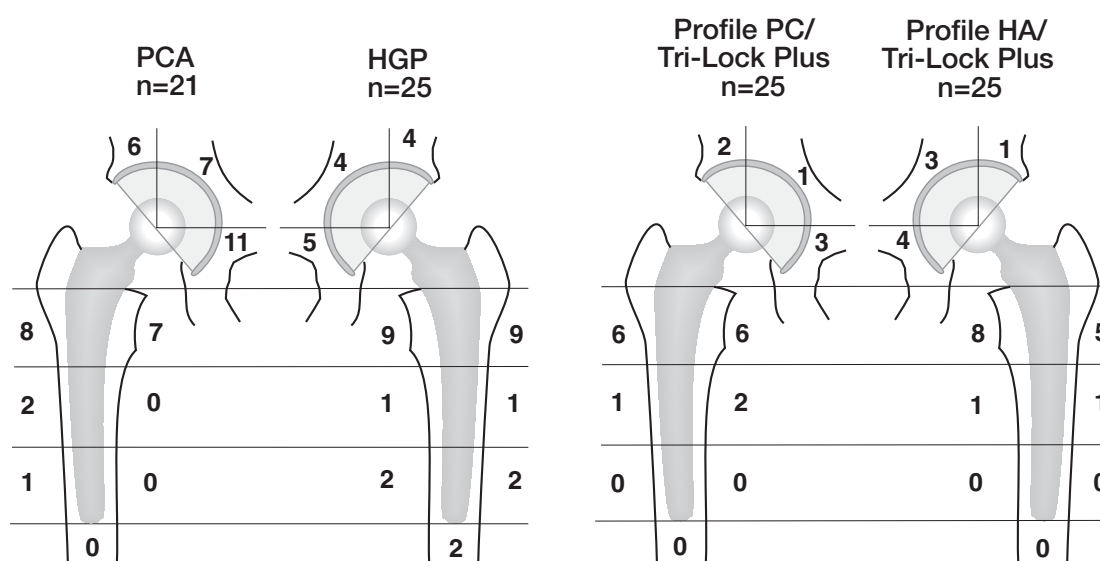


Figure 1. Distribution of osteolysis. Distribution of osteolytic lesions in regions according to Gruen, and Charnley and DeLee. Figures in each region show the number of hips in which osteolytic lesions were found in that specific region. Lesions spanning more than one region have been registered in all regions involved.

the total hip, including liner and head exchange. We also did separate survival analyses with aseptic loosening as the endpoint. The survival data were collected from the patient files. For calculation of the survival of the prostheses, we used date of revision for any cause as the failure date and date of last control as the censoring date.

Results

The mean rate of linear wear ranged from 0.17 to 0.21 mm/year in the 4 groups (Table 2). There were no statistically significant differences between the groups regarding linear or volumetric wear rates ($p = 0.9$ and 0.7 , ANOVA).

In the 2 Profile/Tri-Lock Plus groups, there were 30 hips with a 28-mm femoral head and 20 with a 32-mm head. The volumetric wear rates were 124 mm³/year and 140 mm³/year, respectively, and the difference was not significant ($p = 0.7$, t-test). Gender and body weight had no statistically significant influence on wear rates ($p = 0.3$ and $p = 0.3$, t-test).

Extensive osteolysis occurred in all 4 groups (Table 2, Figure 1). Femoral osteolysis was found primarily in the proximal regions (regions 1 and 7). Distal femoral osteolysis (regions 3, 4 and/or 5) was found in 3 HG hips and in 1 PCA hip (Figures 2 and 3). In the latter, clinical signs of loosening preceded osteolysis by several years, and during revision the stem was found to be loose (Figure 2).



Figure 2. PCA with distal osteolysis. The patient had clinical signs of aseptic stem loosening, starting several years before the osteolytic lesion developed.



Figure 3. Harris-Galante stem showing moderate distal osteolysis. Radiographically, the stem is otherwise well fixed.

Table 3. Revisions and survival rates

	PCA (n = 21)	HG (n = 25)	Profile/Tri-Lock (n = 25)	Profile HA/Tri-Lock (n = 25)
All revisions	12	13	10	11
Liner/head exchange	6	9	7	9
Metal shell exchange	6	–	1 ^a	2
Stem exchange	5	4	3	1
12-year survival, any revision (%)	70 (50–90)	58 (38–78)	56 (20–77)	50 (26–73)

^a Well-fixed metal shell revised because of wear in a highly abducted cup (70°).

Thus, in this case, the osteolysis was possibly secondary to instability. In the acetabulum, the lesions were equally distributed in the three regions.

The cup inclination was median 48° (32–56) in the PCA, median 44° (33–73) in the HG, median 45° (35–64) in the Profile/Tri-Lock Plus, and median 49° (35–70) in the Profile HA/Tri-Lock Plus. There were no statistically significant differences between the groups (all $p > 0.05$, ANOVA). There was no statistically significant association between cup abduction and linear or volumetric wear rate ($p = 0.1$ and $p = 0.2$, ANOVA).

The association between wear rates—both linear and volumetric—and osteolysis was statistically

significant in Cox regression analyses ($p = 0.004$ and $p = 0.001$). Dividing the whole material into 2 groups defined by linear wear rate greater or less than 0.20 mm/year, we found statistically significantly more osteolysis in the high-wear group ($p = 0.006$, t-test). In hips with a wear rate of > 0.20 mm/year, the mean area of osteolysis was 9.5 cm² (95% CI 6.4–13) as compared to 3.1 cm² (95% CI 1.7–4.5) in the low-wear group.

The 12-year survival of the prostheses ranged from 50% to 70% (Table 3), but there were no statistically significant differences (all $p > 0.05$, log rank test). 31 of 46 revisions were liner and head exchange procedures because of wear and

Table 4. Reasons for revision

	PCA (n = 21)	HG (n = 25)	Profile/Tri-Lock (n = 25)	Profile HA/Tri-Lock (n = 25)
Wear	9	6	7	9
Osteolysis	10	4	4	5
Aseptic loosening, cup	6	–	–	2
Aseptic loosening, stem	5	3	3	1
Others ^a	–	1	–	1

^a Others: pain, instability

liner failure. In more than half of these revisions (n = 18), we performed autologous bone impaction grafting for osteolysis in the femur, the acetabulum or both. Revision for aseptic loosening of the cup was done in 6 PCA hips, in 2 Tri-Lock Plus hips (n = 50) but in no HG hips. Stem revision for aseptic loosening was done in 5 PCA hips, in 4 HG hips, in 3 Profile hips and in 1 Profile HA hip (Table 4).

Discussion

We found high wear rates, extensive osteolysis, and poor long-term survival in all 4 groups. Furthermore, we found a statistically significant association between wear and osteolysis. The poor performance of the PCA and the HG prostheses is well documented (Tanzer et al. 1992, Kim et al. 1993, Xenos et al. 1995, Kim et al. 1999, Tanner et al. 1999, Bojescul et al. 2003). The Profile stems and the Tri-Lock Plus cup have very little clinical documentation (Kim et al. 2003). The second generation Profile/Tri-Lock Plus THAs did not perform statistically significantly different from the first-generation PCA and HG prostheses. The extent of osteolysis was less, however, in the Profile groups. Whether this was implant-related or due to a shorter time of follow-up, we do not know.

Conventional radiographic measurement of wear in acetabular components has limited reproducibility and precision. The intraobserver variability of Livermore's method is reported by the author to be 0.075 mm (Livermore et al. 1990). On the other hand, other studies have reported the variability to be from 0.3 mm (Callaghan et al. 1995) to as high as 0.6 mm (Ebramzadeh et al. 2003). Moreover, the metal backing of the acetabular components made

visualization of the femoral head difficult in some cases, especially in the PCA group. This may be a source of variability in the wear measurements. The wear rate of metal-backed uncemented cups has been shown in numerous studies to be higher than in cemented all-polyethylene cups (Harris 1994, Nashed et al. 1995, Sychterz et al. 1996). The mean linear wear rates spanning from 0.17 to 0.21 mm/year found in the current study are similar to those reported in other studies (Hernandez et al. 1994, Røkkum and Reigstad 1998, Dowd et al. 2000). They are higher than the 0.08–0.1 mm/year reported for the cemented Ogee UHMWPE sterilized in air with the Charnley 22.2-mm stainless steel head (Halley and Glassman 2003, Wroblewski et al. 2004).

This patient material was made up of 4 relatively small groups. Thus, the power to detect differences between groups was low. We could not confirm the relationship between large femoral heads and volumetric wear, as reported previously (Livermore et al. 1990, Kesteris et al. 1996, Oparaugo et al. 2001). Even so, we believe—based on broad documentation—that the use of large femoral heads with conventional polyethylene liners is not advisable. When performing liner exchange revisions, we used thicker inlays and smaller heads to reduce wear and postpone future liner exchange. Until further long-term documentation of low-wear articulations using metal-on-metal, highly cross-linked polyethylene and/or ceramic bearings, large-diameter heads should be avoided unless the risk of dislocation outweighs the risk of excessive wear, as in older patients with low compliance and/or fracture sequels (Furnes et al. 2001, Byström et al. 2003).

The relationship between wear rates and occurrence of osteolysis reported by others (Shih et al. 1997, Dowd et al. 2000, Barrack et al. 2002) was

confirmed in our study. Also, revision rates have been shown to correlate strongly with volumetric wear rates of polyethylene (Oparaugo et al. 2001). In 18 of the 31 liner-exchange revisions, we also performed autologous bone impaction grafting of osteolytic lesions. The identification of osteolytic lesions and the differentiation towards stress shielding and osteoporosis is crude in conventional X-rays. The extent of osteolysis as judged by routine radiographic evaluation is generally underestimated, especially on the acetabular side (Claus et al. 2003). Preoperative computerized tomographic scans help delineate pelvic osteolytic lesions (Puri et al. 2002, Stulberg et al. 2002) and are useful in deciding the need for grafting, and whether or not to exchange the metal shell.

According to Schmalzried and others (Schmalzried et al. 1992, Emerson et al. 1999), the effect of circumferential proximal coating of the stem is important in reducing the effective joint space and hence distal femoral osteolysis. The HG stem lacks such a coating, and has been shown to display distal osteolysis (Kim and Kim 1992, Hubble et al. 1997). In our material of 25 HG, we found distal femoral osteolysis (regions 3–5) in 3. These findings support the belief that uncemented stems should have circumferential coating. The other designs in this study all feature proximal circumferential coatings of different kinds. With the exception of 1 PCA stem, we did not find distal femoral osteolysis in the Profile stems or in the PCA stems. In the PCA-case, we suspect that osteolysis is secondary to loosening, as clinical signs of loosening preceded radiographic osteolysis by several years (Figure 2).

5 patients in our material had identical bilateral hip replacements. In 3 of these, sudden accelerating wear appeared after 7–12 years in one hip whilst the other had a linear wear pattern. The reason for this sudden acceleration is poorly understood. Third body wear and increasing roughness of the femoral head are probably important cofactors. Orishimo et al. (2003a) demonstrated that 40% of wear variance in total hip replacement is dependent on factors other than those related to the patient, such as sex, weight, age and activity level. Furthermore, the association between early and late wear rates in the individual case has been shown to be low (Hopper et al. 2003). Thus, the rate of wear

in an individual patient cannot be predicted and cannot be expected to be linear. Patients are usually asymptomatic unless synovitis or instability develops. All patients with these uncemented total hip arthroplasties should thus be frequently and systematically evaluated radiographically to assess wear and to avoid severe bone loss that would complicate later revisions.

The association between wear and osteolysis shown in our study and others gives no answer to the fundamental question of what causes osteolysis. The findings may imply a simple coexistence rather than a causative relationship between the two. It seems that the orthopedic community has accepted the theory of wear-induced osteolysis, and contemporary research on hip implant technology regards wear particles as the major problem to be solved. Some authors have advocated the theory of early loosening, according to which osteolysis is caused by unstable components pumping joint fluid under high pressure into the surroundings (Mjöberg 1994, Aspenberg and van der Vis 1998). It has been shown by use of radiostereometric analysis that early micromotion of implants predicts loosening several years later (Kärrholm et al. 1994, Ryd et al. 1995). Experiments have shown polyethylene particles to be rather incapable of causing bone resorption, whereas osteolysis in the same set-up was easily induced by mechanical instability (Aspenberg and Herbertsson 1996). The findings in our study neither support nor contradict any of these theories; they simply underscore the magnitude of wear and osteolysis as clinical problems. We believe more research is needed regarding our fundamental understanding of osteolysis, in order to accurately address the clinical problems of bone loss and loosening. The apparent consensus on the theory of wear-induced osteolysis may suppress further knowledge in this field, and may even misguide the orthopedic research community in its effort to improve clinical results of hip arthroplasty.

Liner exchange procedures are usually not presented in the literature when reporting survival of primary hip replacements. We believe that survival of metal-backed uncemented cups should be reported with exchange of liner or shell as an endpoint. In our view, a liner exchange procedure is not a minor procedure. Although it is technically

simple, the implications for the patient regarding pain and rehabilitation, the cost of the procedure, the risk of infection, soft tissue complications and the substantial risk of postoperative dislocation (Huo and Brown 2003) make the procedure a considerable burden to the patient and to society. Furthermore, the association between wear and osteolysis means that bone impaction grafting is frequently indicated when performing liner exchange, as was the case in 18 of 31 liner exchange revisions in the current study. We definitely consider this procedure to be major surgery. It should be regarded a revision when reporting survival of total hip replacements.

Our department used the PCA, the HG and the Profile/Tri-Lock Plus hip prostheses in young patients in the eighties and early nineties in the belief that they would provide better long-term results than cemented hips used at that time. Poor clinical results based on high wear rates and osteolysis were the reason for these prostheses being abandoned.

The Scandinavian joint replacement registries have shown 95% 10-year survival of the best performing cemented total hip replacement (Havelin et al. 2000, Malchau et al. 2002). 10-year survival of cemented total hips, in patients less than 60 years of age, also exceed 90% with third-generation cementing technique and high-viscosity, well-documented bone-cements (Havelin et al. 2000, Furnes et al. 2001). These results are superior to those of contemporary uncemented prostheses (Havelin et al. 2002, Malchau et al. 2002).

Several modern uncemented stems do very well, with medium-term survival rates higher than 95% (Havelin et al. 2000, Garcia-Cimbrelo et al. 2003). It seems that the problems to be addressed in uncemented hip replacement surgery are the acetabular component and the bearing surfaces. Wear and osteolysis, and subsequent aseptic loosening of the cup constitute the major challenges in uncemented total hip replacements. Nearly half of the hips in our study had been revised one or more times. New articulations with improved materials will hopefully show better long-term clinical results in contemporary uncemented total hip arthroplasty. Until then, we will continue to use cemented total hip arthroplasties for primary hip replacements in all patients, regardless of age.

Contributions of authors

GH planning, conducting and first writer. SAL planning (statistics), writing (statistics), reviewing the writing process. LIH idea, planning, writing.

No competing interests declared.

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Paper II

Palamed G compared with Palacos R with gentamicin in Charnley total hip replacement

A RANDOMISED, RADIOSTEREOMETRIC STUDY OF 60 HIPs

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We performed a randomised, radiostereometric study comparing two different bone cements, one of which has been sparsely clinically documented. Randomisation of 60 total hip replacements (57 patients) into two groups of 30 was undertaken. All the patients were operated on using a cemented Charnley total hip replacement, the only difference between groups being the bone cement used to secure the femoral component. The two cements used were Palamed G and Palacos R with gentamicin. The patients were followed up with repeated clinical and radiostereometric examinations for two years to assess the micromovement of the femoral component and the clinical outcome.

The mean subsidence was 0.18 mm and 0.21 mm, and the mean internal rotation was 1.7° and 2.0° at two years for the Palamed G and Palacos R with gentamicin bone cements, respectively. We found no statistically significant differences between the groups. Micromovement occurred between the femoral component and the cement, while the cement mantle was stable inside the bone. The Harris hip score improved from a mean of 38 points (14 to 54) and 36 (10 to 57) pre-operatively to a mean of 92 (77 to 100) and 91 (63 to 100) at two years in the Palamed G and Palacos R groups, respectively. No differences were found between the groups.

Both bone cements provided good initial fixation of the femoral component and good clinical results at two years.

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©2006 British Editorial Society of Bone and Joint Surgery
doi:10.1302/0301-620X.88B9.18008 \$2.00

J Bone Joint Surg [Br]
2006;88-B:1143-8.
Received 10 April 2006;
Accepted 31 May 2006

The long-term performance of cemented total hip replacement (THR) is dependent on many factors, including the characteristics of the patient, the surgical technique, the choice of prosthesis, the cementing technique and the properties of the bone cement used. The impact of modern cementing technique on the survival of cemented THRs has been documented.^{1,2} Although all bone cements used in current clinical practice are based on methylmethacrylate, their performance differs physically and clinically. Poor results with some low-viscosity cements^{1,3} and particularly with Boneloc cement (Biomet, Warsaw, Indiana)^{4,5} have demonstrated the importance of the selection of the correct cement for clinical practice. Several high-viscosity antibiotic-loaded bone cements have given good long-term results in the Scandinavian arthroplasty registers.^{1,3,6}

One of the well-documented high-viscosity bone cements is Palacos R with gentamicin (Schering Plough, Labo nv Belgium), hereafter referred to as Palacos R. Palamed G (Biomet Merck, Darmstadt, Germany) is a high-viscosity antibiotic-loaded bone cement based on Refobacin-Palacos R from the same com-

pany.^{3,6} Since the conduct of this study the distribution of the two bone cements has changed (September 1995). This is commented on at the end of the article. Palacos R has an initially reduced viscosity which allows mixing without pre-chilling, yielding a homogeneous cement with reduced porosity.^{7,8} It has been mechanically tested, reaching standards superior to the ISO 5833 (International Standards 5833/1-2) concerning compressive strength, Young's modulus and bending strength. The maximum temperature, the penetration of the cement and the elution of gentamicin are also found to be comparable or superior to other Palacos-based bone cements.^{9,10} Based on *in vitro* evidence of good physical and chemical properties, we wished to evaluate the clinical performance of Palamed G bone cement.

The relationship between early migration and late aseptic loosening has been documented using conventional radiography^{11,12} and radiostereometric analysis (RSA).¹³⁻¹⁵ The latter is a highly accurate method for the evaluation of prosthetic migration allowing the assessment of new implants, cements or surgical technique using only small numbers of

Table I. Details of the hips in both groups

	Palamed G	Palacos R
Mean age in yrs (range)	74 (62 to 82)	74 (63 to 84)
Gender		
M:F	5:23	7:23
Mean body weight in kg (range)	67 (48 to 95)	69 (55 to 100)
Charnley class (A:B:C)*	19:9:0	12:13:5
Diagnosis†		
Osteoarthritis	18	19
Post-traumatic	7	5
Rheumatoid arthritis	2	7
Acute fracture	2	1

* A, unilateral hip disease with no other disability; B, bilateral hip disease with no other disability; C, unilateral or bilateral hip disease with generalised systemic factors affecting function

† more than one diagnosis was recorded in some of the patients

patients.¹⁶ The degree of micromovement during the first one or two years has been shown to correlate with the medium- or long-term performance of cemented joint prostheses and can thus be used as a predictor in early clinical evaluation.^{13,15,17}

Our aim was to evaluate the early migration of a cemented femoral component using Palamed G bone cement, using Palacos R as a reference. The null hypothesis was that the stability of the stem was equal in the two study groups. Furthermore, we wished to determine whether the micromovement occurred at the cement-stem interface or between the cement mantle and the bone. The study was approved by the Regional Ethical Committee.

Patients and Methods

A total of 60 hips in 57 patients was randomised to receive either Palamed G or Palacos R for fixation of a Charnley femoral component (DePuy International Ltd, Leeds, United Kingdom). The three bilaterally operated patients, as an effect of randomisation, received the same cement in both hips. Two of these were in the Palacos R group and one in the Palamed G group. Two patients (two hips) were excluded; one because of post-operative dislocation and infection, and the other died before the three-month examination. Both patients were in the Palamed G group, leaving 28 hips in this group and 58 overall.

The diagnosis and details of the patients are given in Table I.

Operative technique. Four surgeons (LIH, AS, OF, GH) operated on all the patients, and randomisation was arranged so that each operated on an equal number of patients in the two groups. This was done to avoid the influence of the surgeon on the results. A stainless-steel, monoblock 22 mm head Charnley flanged 40 femoral component was used in all patients. It was supplied with tantalum markers on its tip and shoulder from the manufacturer. The centre of the femoral head was used as a third point for the three-dimensional assessment of the stem in calculations of movement. The acetabular component used was a Charnley Ogee cup

with an outer diameter of 40 mm or 43 mm (DePuy International Ltd) inserted with Palacos R with gentamicin cement in all patients. The procedure was standardised using a modified direct lateral approach¹⁸ with the patient in the lateral decubitus position. We used a third-generation cementing technique (high-pressure lavage, femoral cement restrictor, retrograde cement injection with cement gun and cement pressurisation). An envelope with the type of cement to be used in the femur was opened after preparing the femur and performing trial reduction, leg-length measurement and testing of stability.

Palamed G cement was stored at a constant temperature of 20°C in a temperature storage cabin and Palacos R cement at 8°C in a refrigerator. The cements were taken out immediately before use, and mixing was done using the Optivac system (Biomet). This is a closed vacuum-mixing system producing homogeneous cement with low porosity (macroporosity below 0.5%, microporosity below 1 pore per 100 mm³).⁸ Insertion of the femoral stem was performed at 4.5 minutes after mixing for Palamed G, and at six minutes for Palacos R, according to the manufacturers' recommendations. The temperature of the operating room was between 20°C and 21°C.

All patients received systemic prophylactic antibiotics (four doses of cefuroxime 2 g, or two doses of clindamycin 0.6 g in the presence of penicillin allergy). For thromboprophylaxis, 2500 units of Dalteparin was given intra-operatively after spinal anaesthesia and was continued for ten days at a daily dose rate of 5000 units. The patients were allowed to mobilise, partially weight-bearing with crutches, from the first post-operative day.

Radiostereometry. Seven or eight tantalum markers (RSA Biomedical Innovations, Umeå, Sweden) with a diameter of 1.0 mm were inserted into the proximal femur. Additional tantalum markers 0.8 mm in diameter were inserted into the cement restrictor (two) and into the cement mantle (approximately six) during cementing and insertion of the stem.

The initial RSA examination was performed three and five days (mean 4.3) after operation with repeat examinations at 3, 6, 12 and 24 months. The patient was supine and the uniplanar technique (cage 43, RSA Biomedical) was used with the calibration cage under the examination table. Simultaneous exposures were obtained with one gantry-mounted and one portable x-ray tube. Using the UmRSA Digital measure version 5.0 software (RSA Biomedical) the three-dimensional position of the markers and the translations and rotations of the gravitational centre of the segment of the stem were computed. The upper limit for the mean error of rigid-body fitting was set at 0.35 mm and that for the condition number at 150.¹⁹ These limits ensured that there was proper stability and distribution of the tantalum markers. A condition number higher than 150 implies poor distribution of the tantalum markers in bone and/or cement. This adversely affects the accuracy of migration measurements. Validation of the precision of our

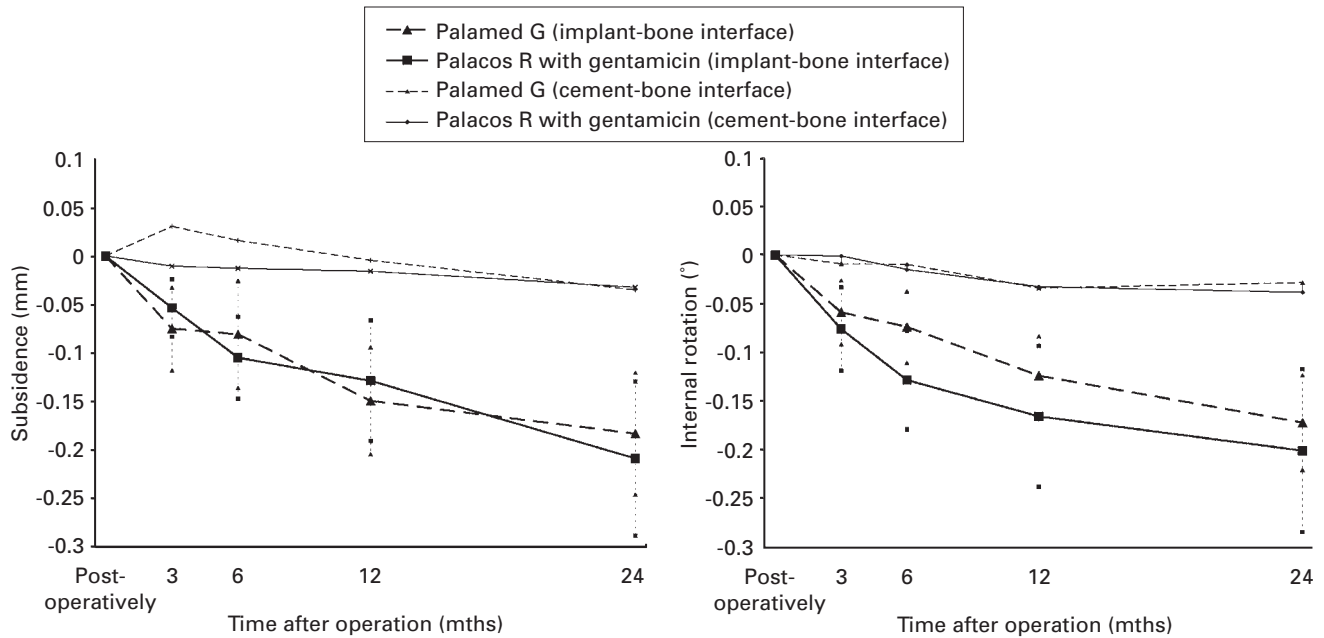


Fig. 1a

Fig. 1b

Observed mean values of a) subsidence and b) internal rotation of the femoral components with the two cements at the cement-bone interfaces (with standard error of means).

RSA technique was done by double examinations of 27 patients at the 12-month examination.²⁰

Clinical follow-up. Clinical evaluation using the Harris hip score (HHS)²¹ was performed pre-operatively, at 3, 12 and 24 months post-operatively, and will in due course take place at five and ten years in conjunction with conventional radiological examinations.

Statistical analysis. Limits for significant translations and rotations were calculated as the 99% confidence interval (CI) of the absolute mean values from analyses of the double examinations. The effects of the cement (Palamed G, Palacos R) and the time (3, 6, 12 and 24 months) on the RSA migration data and on the clinical outcome data were investigated in a mixed-effects model.²² Assumptions for the mixed-effects analyses were assessed based on residual plots and normal probability plots of the residuals and of the estimated random effects. Analyses were performed using the statistical package S-Plus (Insightful Inc., Seattle, Washington). Differences were regarded as being statistically significant if the p value was less than 0.05. The data presented in the Tables and Figures are observed data, whereas the p values are based on estimates from the mixed-effects model.

Results

Radiostereometric analysis. Femoral components in both groups subsided and rotated into internal rotation. Subsidence (negative translation along the y-axis; distal migration) at two years was 0.18 mm and 0.21 mm, and internal rotation (negative rotation around the y-axis; retroversion) was

1.7° and 2.0° for the Palamed G and Palacos R groups, respectively (Fig. 1). Micromovements in the other directions were all of minor magnitude. The mixed-effects analyses showed no consistent differences between the cements with time, and at one and two years follow-up we observed no statistically significant differences ($p = 0.2$ to $p = 0.9$). Table II gives the micromovement observed in translations and rotations relative to three axes (x, y and z) at two years for the three interfaces. Most micromovement occurred at the cement-stem interface. In the Palacos R group, the cement mantle rotated -0.2° around the x-axis (extension) relative to the femur. Movement of the cement mantle in all other directions was within the precision of the RSA measurements. We therefore concluded that the cement mantle was stable relative to the femur. We investigated the patients with internal rotation exceeding 3° (3.4° to 7.9°) and/or subsidence of more than 0.35 mm (0.38 to 0.93) separately. None of these patients had clinical evidence of loosening or radiological signs of loosening on conventional radiographs at follow-up at two years (Table III). The number of examinations suitable for the calculation of micromovement of all three segments (femoral component, cement and bone) at the different time intervals, are given in Table IV. At two years, 22 and 21 sets of examinations were included in each group. In measurements of the stem-bone segment, however, another six hips were included, thereby increasing the numbers available to 26 and 23 in the Palamed G and Palacos R groups, respectively. The reasons for the exclusion of patients and missing two-year RSA data are given in Table V.

Table II. Observed mean values for micromovement at the three interfaces at radiostereometric analysis (RSA) follow-up at two years. Rotation around the x-axis is flexion-extension, about the y-axis external-internal rotation and about the z-axis abduction-adduction. Translation at the x-axis is medial to lateral, in the y-axis distal to proximal and in the z-axis posterior to anterior. We defined positive values for the right limb

	Rotation (°)			Translation (mm)		
	x	y	z	x	y	z
Cement-stem						
Palamed G	-0.103	-1.635	0.165	0.048	-0.144	-0.244
Palacos R	-0.009	-1.820	0.184	0.078	-0.136	-0.201
Precision*	0.09	0.48	0.13	0.114	0.061	0.114
p value†	0.3	0.9	0.8	0.3	0.8	0.7
Stem-bone						
Palamed G	-0.136	-1.722	0.229	-0.010	-0.183	-0.259
Palacos R	-0.238	-2.008	0.324	0.027	-0.208	-0.273
Precision*	0.15	0.38	0.09	0.064	0.051	0.116
p value†	0.5	0.9	0.7	0.5	0.8	0.8
Cement-bone						
Palamed G	-0.050	-0.285	0.105	-0.029	-0.035	0.052
Palacos R	-0.210	-0.386	0.150	0.052	-0.032	0.108
Precision*	0.12	0.40	0.11	0.081	0.045	0.144
p value†	0.2	0.7	0.5	0.3	0.9	0.6

* calculation of precision is based on 27 double examinations

† mixed-effects model including all RSA examinations

Table III. Results for those hips when the femoral component rotated more than 3° and/or subsided more than 0.35 mm

Case	Cement	Subsidence (mm)	Rotation (°)	Harris hip score
4	Palacos R	0.38	-	96
13	Palacos R	0.93	7.82	100
18	Palamed G	-	4.83	98
20	Palamed G	0.39	-	100
25	Palamed G	0.58	-	91
30	Palacos R	-	3.86	100
49	Palacos R	-	7.91	96
52	Palacos R	0.39	3.41	100
54	Palamed G	0.50	4.75	98
57	Palamed G	0.46	3.38	93

Clinical results. In the Palamed G group the mean HHS increased from 38 points (14 to 54) pre-operatively to 88 (51 to 100) at one year and 92 (77 to 100) at two years. The corresponding scores for the Palacos R group were 36 (10 to 57), 87 (67 to 100) and 91 (63 to 100), respectively. There were therefore no statistically significant dif-

ferences between the groups (mixed-effects model, $p = 0.2$ to 0.9).

Discussion

During the two first years, the two bone cements performed equally well in fixation of the femoral component. A subsid-

Table IV. Number of examinations available for complete calculation of micromovement at the different time intervals. Numbers in brackets represent examinations available for the calculations of micromovement between the femoral component and bone

Months	Palamed G	Palacos R
Post-operatively	27	29
3	21 (24)	21 (25)
6	20 (24)	20 (25)
12	22 (27)	23 (23)
24	22 (26)	21 (23)

Table V. Radiostereometric analysis (RSA) examinations missing at two years, and exclusions

Number of patients	Palamed G/ Palacos R	Reason for missing RSA examination
9	4/5	Condition number > 150*
4	2/2	Death of patient†
2	1/1	Missing or inadequate index RSA examination
1	1/0	Post-operative dislocation. Excluded
1	0/1	Stem markers obscured at RSA at two years

* calculation of movement of the stem relative to the bone included in 7 of 9

† one patient died before three months after operation and was excluded

ence of 0.2 mm is considered by some authors to be safe with respect to long-term performance.^{13,14} The migration into internal rotation found in our study, however, is slightly larger than that in other studies. Grant et al²³ found internal rotation of 1.1° at two years with the Charnley Elite Plus (DePuy) using Palacos R with gentamicin bone cement. Alfaro-Adrián, Gill and Murray²⁴ found internal rotation of 1.3° at two years using the Charnley Elite stem and CMW bone cement (DePuy). Onsten et al²⁵ found 1.25 mm posterior migration of the centre of the femoral head using the Charnley stem and Palacos R bone cement. If it is supposed that there is an offset of 40 mm and rotation around the centre of the diaphyseal portion of the femoral stem; this corresponds with 1.8° ($\tan n \text{ degrees} = 1.25/40$).

Gill et al²⁶ proposed that there was a correlation between decreasing femoral component anteversion and posterior migration of the head. In our study we did not measure anteversion of the femoral components post-operatively and therefore do not know whether the degree of anteversion affected the degree of internal rotation at follow-up. Intra-operatively, we aimed at anatomical anteversion of the femoral component according to the cut femoral neck. On average, this would be approximately 10° of anteversion. In our study, the initial RSA examination was performed at three to five days after the operation and before vigorous mobilisation of the patient. The latter influences the initial micromovement,¹⁹ and an early initial examination may detect micromovement not seen when the initial examinations are delayed. The post-operative RSA examinations in the studies compared above were undertaken within seven days,²³ unspecified post-operatively²⁵ or between one and two weeks after operation.²⁵ The slightly higher internal rotation in our patients may be explained by their relatively early initial RSA examinations. The two-year RSA examinations in our study were actually performed in all patients more than two years after the operation, the mean delay being 61 days (10 to 190). The 24-month RSA follow-up was therefore actually a 26-month follow-up. Calculated values of translation and rotation would be expected to be slightly lower at 24 months. With a precision of 0.4° for internal rotation, and taking the previously mentioned aspects into account we believe that the internal rotation found in our study matches published results reasonably well.²³⁻²⁵

The rate of movement in our series was, as expected, highest initially. Between one and two years, the mean rate of internal rotation was 0.45°/year (0° to 2.1°) as compared with 1.44°/year (0° to 3.7°) in the first year. The mean rate of subsidence was 0.03 mm/year (0 to 0.45) in the second year but 0.14 mm/year (0 to 0.56) in the first year. We plan to re-examine our patients at five and ten years in order to further evaluate migration of the femoral component and clinical outcomes.

Knowing the technical difficulties in obtaining high-quality RSA examinations, our study was planned to allow for exclusions. The most frequent cause of excluded RSA

examinations was a high condition number. Poor distribution and visibility of cement markers caused the high condition number in most cases (6 of 9). The stem and bone markers, however, were properly placed and readily identified. In these six hips, high-precision measurements of movement at the stem-bone interface were undertaken while measurements at the cement-bone and stem-cement interfaces were excluded. Accurate placement of cement markers is difficult as the femoral stem easily obscures the markers in one or both projections. The precision in our study, also in the calculation of relative movement of the cement mantle (Table II), is still good, and is comparable with that found in other studies using similar RSA techniques.^{20,23,27}

In our study, the cement mantle was shown to be stable while the stem internally rotated and subsided inside the cement. Micromovement of the cement mantle has not been widely studied and, of the published studies, most have found the cement to be stable although the femoral component moves inside the cement.^{24,27,28} This corresponds with our findings.

The proportion of Charnley class-B and class-C hips was higher in the Palacos R group than in the Palamed G group (Table I) mainly because of a larger proportion of patients with rheumatoid arthritis in the former group. This should not influence migration of the Charnley stem, since migration in patients with rheumatoid arthritis has been found not to differ from that in those with primary osteoarthritis.²⁵ It might have been expected, however, that the clinical scores differed according to the somewhat skewed material, but this was not found to be the case.

Different designs of the femoral component may have different tolerance to the qualities of the bone cement. The Boneloc cement was better tolerated by the double-tapered, polished Exeter femoral component than by the Charnley femoral component although still yielding inferior results than high-viscosity cements.⁴ It cannot be assumed that the results of our study can be applied to all designs of cemented stem. New bone cements should, as new implants, be introduced in a stepwise manner, as proposed by Malchau.²⁹ Several bone cements (Boneloc (Biomet), CMW I and II (DePuy), Sulfix (Stryker Corp., Kalamazoo, Michigan)) which have fulfilled *in vitro* tests according to the ISO standard,³⁰ have proved to be clinically inferior to the best well-documented cements on the market.^{3,4,6} *In vitro* evidence of physical and chemical properties should not be considered to be evidence of good clinical results. Therefore, documentation of clinical performance is vital before considering widespread use. The only clinical investigation of the Palamed G bone cement which we have identified involved the fixation of tibial components in a series of 35 total knee replacements (TKR). This was not a randomised study and the published RSA follow-up was limited to one year. The authors concluded that migration with the Palamed G cement was comparable with results reported in other RSA studies in cemented TKR.³¹ In our

RSA study, micromovement of the Charnley stem using the Palamed G cement proved to be equal to that with Palacos R cement, the latter having documented good long-term clinical results.^{1,3,6} It is therefore anticipated that Palamed G cement should give similar long-term results given the supposed predictive nature of RSA studies. However, the performance of larger randomised trials with long-term follow-up, and ultimately prospective follow-up in national registries is advisable to ensure safe practice.

At the time of patient inclusion, the bone cements Palamed®G and Palacos®R with Gentamicin were distributed by Biomet and Schering Plough, respectively. The two bone cements are now both produced and traded by Heraeus Kulzer GmbH/Heraeus Medical. According to Heraeus Kulzer, their current bone cements, called Palamed® G and Palacos® R + G, have the same properties as the corresponding cements used in the study.

We wish to thank our radiographer, T. Stokke at the Department of Radiology for producing excellent RSA examinations, our study secretary A.-L. Salbu for keeping track of the patients and E. Dybvik and B. Espehaug at the Norwegian Arthroplasty Register for invaluable help and quality control of the statistics. We also acknowledge Biomet Merck for sponsoring the study and thank our colleagues and the operating staff for the patience required for this clinical study to be possible.

One or more of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article. In addition, benefits have been or will be directed to a research fund, foundation, educational institution, or other non-profit organisation with which one or more of the authors are associated.

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Paper III

**MEDIUM AND LONG-TERM PERFORMANCE OF
11 516 UNCEMENTED PRIMARY FEMORAL
STEMS FROM THE NORWEGIAN
ARTHROPLASTY REGISTER**

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Primary uncemented femoral stems reported to the Norwegian Arthroplasty Register in the period 1987-2005, were included in this prospective observational study. The material was comprised of 11 516 hips in 9 679 patients and 14 different stem designs. Kaplan-Meier survival probabilities and Cox regression were used to analyse the data. With aseptic loosening as the end-point, all currently used stem designs performed excellently with survival percentages of 96-100 at 10 years. With the end-point being stem revision of any cause, the long-term results of the different stem designs varied from very poor to excellent with 15-year survival ranging from 29% to 97%. Follow-up longer than 7 years was needed to identify some of the poorly performing stem designs. All the currently used stems had over 90% 10 years survival with this end-point, but there were differences between the designs. The Corail (n= 5456) was the most frequently used uncemented stem, and this design had a survival of 97% at 15 years. Male gender was associated with a 1.3 times increased risk of stem revision (95% CI 1.05-1.52). Age and diagnosis had no influence on the results in this study. Overall, we concluded that modern uncemented femoral stems performed well.

Moderate differences in survival between well-performing stems should be interpreted with caution since the differences may be caused by factors other than the femoral stem *per se*.

Paper IV

**Liner exchange procedures compared to whole
cup revisions in revision of uncemented
acetabular cups.**

**A study of 1649 revisions from the Norwegian
Arthroplasty Register**

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Abstract

We analyzed the results of different strategies in revision of primary uncemented acetabular cups reported to the Norwegian Arthroplasty Register. The aim was to compare the risk of further cup revisions after liner exchange procedures and whole cup revisions. Furthermore, we compared the results of exchanging well-fixed cups with those of exchanging loose cups.

The revisions were reported between September 1987 and April 2005. The following groups were compared: Group 1) Exchange of liner only (n=318), Group 2)

Exchange of well-fixed cups (n=398), and Group 3) Exchange of loose cups (n=933).

We found that the risk of a second cup revision was lower after revision of well-fixed cups (RR=0.56, 95 % CI [0.37-0.87]) and loose cups (RR=0.56 [0.39-0.80]),

compared to revision of liner only. The most frequent reason for second cup-revisions was dislocation, accounting for 28 % of the re-revisions. Other reasons for second cup revisions included pain (12%), cup loosening (11%) and infection (9%). Re-revisions due to pain were less frequent when whole cups (fixed or loose) were revised compared to liner-revisions (RR=0.20 [0.06-0.65] and RR=0.10 [0.03-0.30], respectively). Risk of second cup revisions due to infection however, did not differ between the groups.

In the present study exchange of liner only, had a higher risk of re-revision compared to revision of the whole cup. Our results suggest that the threshold for revising well-fixed cups in the case of liner wear and osteolysis should be lowered.