



European
Commission

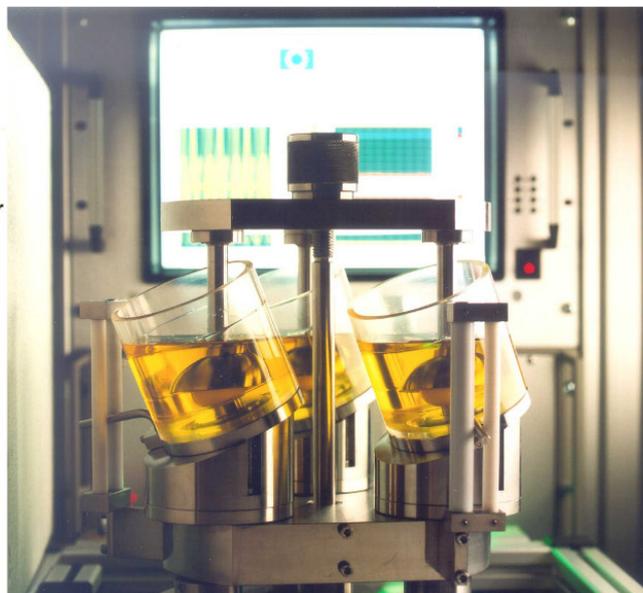
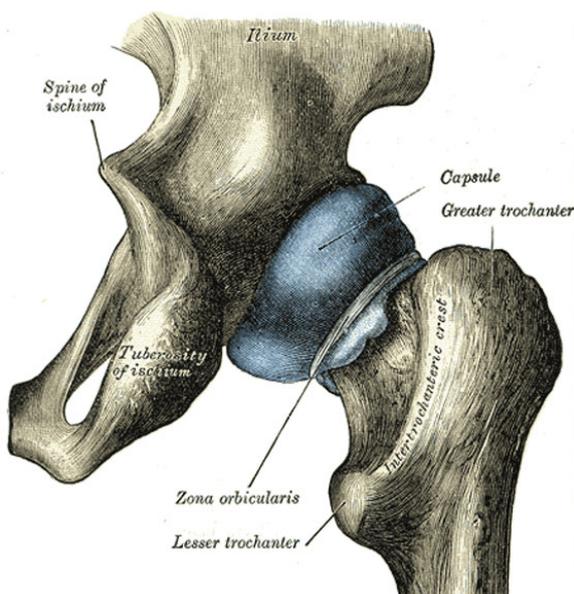
JRC SCIENTIFIC AND POLICY REPORTS

Total Hip Arthroplasty

*State of the Art,
Challenges and
Prospects*

Uwe Holzwarth
Giulio Cotogno

July 2012



Joint
Research
Centre

European Commission
Joint Research Centre
Institute for Health and Consumer Protection

Contact information

Uwe Holzwarth

Address: Joint Research Centre, Via Enrico Fermi 2749, TP 500, 21027 Ispra (VA), Italy

E-mail: uwe.holzwarth@jrc.ec.europa.eu

Tel.: +39 0332 78 5194

Fax: +39 0332 78 9385

<http://ihcp.jrc.ec.europa.eu/>

<http://www.jrc.ec.europa.eu/>

This publication is a Scientific and Policy Report by the Joint Research Centre of the European Commission.

Legal Notice

Neither the European Commission nor any person acting on behalf of the Commission is responsible for the use which might be made of this publication.

Europe Direct is a service to help you find answers to your questions about the European Union
Freephone number (*): 00 800 6 7 8 9 10 11

(*) Certain mobile telephone operators do not allow access to 00 800 numbers or these calls may be billed.

A great deal of additional information on the European Union is available on the Internet.
It can be accessed through the Europa server <http://europa.eu/>.

JRC72428

EUR 25378 EN

ISBN 978-92-79-25280-8 (print)

ISBN 978-92-79-25279-2 (pdf)

ISSN 1018-5593 (print)

ISSN 1831-9424 (online)

doi: 10.2788/31286

Luxembourg: Publications Office of the European Union, 2012

Cover pictures (from left to right):

Reproduction of a lithograph plate from Gray's Anatomy of the Human Body, published in the U.S. in 1918.

Courtesy of Wikimedia Commons: <http://commons.wikimedia.org/wiki/File:Gray343.png>.

Three station hip simulator developed at the JRC-IHCP, Ispra. Copyright © European Union 2012.

Hip-joint, total replacement, insertion without bone-cement. Photo by: Scuba-limp.

Courtesy of Wikimedia Commons: <http://commons.wikimedia.org/wiki/File:Hueftgelenk-Endoprothese.jpg>.

© European Union, 2012

Reproduction is authorised provided the source is acknowledged.

Printed in Italy

Table of Contents

Table of Contents	1
Executive Summary	3
1. Introduction	5
1.1. Objective of the report	5
1.2. The principle of total hip arthroplasty	5
1.3. The history of total hip arthroplasty	6
1.4. Incidence of total hip arthroplasty	7
1.5. The challenge of patients' expectations in an ageing population	8
1.6. Intended improvements may cause unexpected new problems	9
2. Materials used for hip joint prostheses	13
2.1. Biocompatibility and device modularity	13
2.2. Material properties and material selection	13
2.2.1. Metals	13
2.2.2. Polymers - Ultra High Molecular Weight Polyethylene	14
2.2.3. Ceramics	14
2.3. Components of modular hip prosthesis	15
2.3.1. The femoral stem	15
2.3.2. The femoral head	15
2.3.3. The acetabular cup – liner	16
2.3.4. The acetabular cup - shell	16
3. Design criteria for hip joint prostheses	17
3.1. Fixation strategies: cemented and non-cemented prostheses	17
3.2. Fatigue resistance and stiffness of the stem	17
3.3. Femoral head diameter and range of motion	18
3.4. Bone conservation: resurfacing versus conventional joint replacement	18
3.5. Biomechanical loading conditions and testing	19
4. Tribology of hip joint prostheses	21
4.1. Wear, wear processes and lubrication conditions	21
4.2. Tribological material combinations in total hip arthroplasty	23
4.3. Corrosion and wear effects	24
5. Clinical aspects	27
5.1. Indications for total hip arthroplasty	27
5.2. Choice of prosthesis	27
5.3. Surgical aspects	27
5.4. Clinical results and possible complications	28
6. Wear, corrosion and potentially related cancer risk	31
6.1. Exposure to wear debris and corrosion products	31
6.1.1. Origin and dissemination of wear debris	31

6.1.2.	Aseptic loosening	31
6.1.3.	Size and size effects of wear debris	32
6.1.4.	Nanoparticles and metal ions from MoM prostheses	32
6.2.	Total hip arthroplasty and potential cancer risk	34
7.	Economic and regulatory issues.....	37
7.1.	Health economics aspects	37
7.2.	Arthroplasty registers	37
7.3.	Clinical investigation and regulatory framework	38
8.	Research needs and challenges	41
8.1.	Evaluation and assessment problems	41
8.2.	Research needs in THA	41
8.3.	Prospects and challenges	43
9.	Conclusions	45
10.	Literature	47
11.	Annex	55
11.1.	Glossary	55
11.2.	List of abbreviations	57
11.3.	List of figures	58
11.4.	Authors	59

Executive Summary

Recent problems with certain metallic hip joint prostheses have raised concerns about their safety. This report provides a scientific overview of the state-of-the-art knowledge in total hip arthroplasty from a biomedical engineering point of view and identifies areas where further research and actions are needed.

Importance of Total Hip Arthroplasty

Every year, about one million patients worldwide undergo total hip arthroplasty (THA) surgery. This is considered a successful, safe and cost-effective medical intervention to restore functionality of the hip joint and to regain pain-free mobility in patients suffering from severe joint disease or trauma. The number of people undergoing primary THA and revision surgery is expected to increase further due to an ageing population, decreasing average age at the first operation and the limited life span of prostheses.

THA is the replacement of both articulating surfaces of a degenerated hip joint. This means that the spherical part of the joint is either completely replaced (conventional approach) or it is trimmed and covered by a metallic cap (resurfacing approach). The counterpart of the joint is in both cases replaced by a semi-spherical shell.

Artificial hip joints are innovative, high-quality biomedical engineering products. Whereas they are designed to last for at least 20 years, their lifespan is limited by wear. Hip prostheses are subject to continuous research and development in order to increase lifespan and reduce the likelihood of complications and revision surgery. This is reflected by the large variety of hip prostheses on the market, and rapid innovation in the field.

Purpose of the present report

Increasing revision rates of certain types of metal-on-metal (MoM) hip prostheses introduced on the market during the last decade have recently created a high level of uncertainty concerning the safety and effectiveness of artificial hip joints. Notwithstanding the expectation that medical progress is generally a continuous process leading to improved medical treatment, problems occurred with some hip-resurfacing systems having failed to deliver the expected improvements.

To put the current challenges in context, this report reviews the historical development and current state-of-the-art in THA from a biomedical engineering point of view. It illustrates the large variety of materials available. MoM devices are in fact only one possibility of a number

of possible devices. The most commonly applied designs use metal femoral heads against polymeric acetabular cups, so called metal-on-polymer (MoP) prostheses. In most countries, the latter account for more than 60% of all implanted hip prostheses.

This report focuses on key principles and issues, rather than attempting a comprehensive literature review. Cross-references are made to other sources for detailed information where appropriate. Particular problems related to evaluating the safety and effectiveness of hip prostheses are discussed and further research needs are identified. The report is also intended to provide background information for risk assessors and risk managers.

Key findings

The clinical long-term outcome of THA depends on factors related to the applied type of prosthesis, the health status of the patient and his post-operative physical activities, and also depends critically on the expertise and practice of the surgeon.

The most important complication with metal-on-polymer (MoP) prostheses is aseptic loosening due to an inflammatory reaction against polymer wear debris. Aseptic loosening is much less frequently encountered in patients with metal-on-metal (MoM) or ceramic-on-ceramic (CoC) prostheses.

During the last years clinical problems have emerged related to hip-resurfacing prostheses, which preserve the femur and cover the trimmed femoral head with a metal cap. The most common complications with these types of devices are the formation of pseudotumours, presumably as adverse reaction to metallic wear debris, and high incidence rates of femoral neck fracture and avascular necrosis. Therefore, revision rates for some types of these devices are found to be several times higher than expected. Biomechanical design weaknesses are suspected to be the main reason for underperforming devices, such as shallow, not fully semispherical acetabular cups and too large femoral head diameters. Identified underperforming devices have already been withdrawn from the European market.

Conventional MoM hip prostheses, which replace the complete femoral head with a metal sphere anchored in the femur, have a long tradition and were not affected by this problem in the past. However, recently, significantly higher early failure rates are reported with such prostheses that use large femoral head diameters above 36 mm. Such designs have become popular in the

last decade as they match more closely the anatomy of the natural hip joint and promise increased joint stability and larger range of movement. However, the failure modes of these devices are not precisely described in literature, in contrast to the details known on failing hip-resurfacing systems. Common concerns with all MoM hip prostheses are related to the unclear role of long-term exposure to metal ions released into the human body. Additionally, there is increased awareness that the size of the released wear debris is in the range of nanometers and nanotoxicity effects may have to be considered.

Most patients with conventional MoM prostheses exhibit higher chromium- and cobalt-ion concentrations in blood, which are however, only very rarely related with pathologies. Nevertheless, little is known about long-term low-level exposure to such ions, and the presence of nanosized metallic particles may amplify a possible toxicity of wear debris.

Currently, there is no scientific evidence for an increased, statistically significant overall cancer risk after THA.

Prospects and challenges

Since the theoretically expected benefits of MoM hip-resurfacing THA cannot generally be realised in clinical practice, its use should be limited to specific cases where the surgeon can expect that the medical benefit outweighs the risk of early revision.

For conventional THA, many alternatives to MoM prostheses are available, such as metal-on-polymer (MoP), ceramic-on-ceramic (CoC) and ceramic-on-polymer (CoP) prostheses. Each design has its own specific risk-benefit profile on the basis of which surgeons and patients should select the most appropriate solution.

Arthroplasty registers aiming at a complete registration and follow-up of all THA procedures are essential in monitoring the long-term performance of hip prostheses, as well as in evaluating and benchmarking new hip prostheses and for providing early alerts on problematic THA devices. They are indispensable tools in medical quality assurance, and medical education and training, and they should be an integral part of each healthcare

system. Ideally, such registers should be coordinated at European level in order to ensure harmonised and comparable data sets and to acquire statistical significance in the quickest and most effective way.

Clinical investigations with a reasonable number of patients might be helpful to identify hip prostheses that expose patients to unexpected health risks with high incidence rate. They will however not be able to qualify the long-term effectiveness of hip prosthesis design since this would require a disproportionately large number of patients to be enrolled and follow-up times that are beyond the time horizon for introducing medical innovations.

Clinical investigations dedicated to ensure patient safety and to prevent significantly underperforming devices from large-scale market introduction, should contain an independent review element and should not be carried out only by the developing company and clinical partners linked to this company.

Considering the long lifetimes for which hip prostheses are designed, a reasonable clinical investigation of a new hip prosthesis design will only provide limited information about its long-term performance. The evaluation of the long-term performance to be expected from a new device can only be based on the combined knowledge gathered from all clinical investigations, clinical evaluations and arthroplasty register data that are available so far. Only such a knowledge pool, which must be continuously maintained and extended, can ensure that patients are not exposed to unjustifiable long-term risks and that the safety and effectiveness of new and innovative hip prostheses can be guaranteed to the best of one's knowledge.

It is likely that the increasing societal cost of musculoskeletal diseases can not be managed by improved medical technology alone. The development and implementation of efficient prevention programmes will be important. In view of the expected increasing demand for primary THA procedures and revision surgery procedures in an ageing population, adequate measures should be taken to reduce the demand for revision surgery and to delay primary THA as far as possible by preventive health care programmes.

1. Introduction

1.1. Objective of the report

Recently increasing revision rates of certain types of metal-on-metal (MoM) hip prostheses [1], introduced on the medical device market during the last decade, have created uncertainty concerning the safety and effectiveness of artificial hip joints [2]. Eventhough medical progress is generally expected to be a continuous process leading to improved medical treatment, problems occurred with some hip-resurfacing systems that failed to deliver the expected improvement. Moreover, this created severe health problems for many patients worldwide [2].

This report reviews the historical development and the state-of-the-art of total hip arthroplasty from a biomedical engineering point of view and illustrates the motivation for the efforts to improve the quality of hip prostheses. The report also aims at explaining the peculiar problems related to evaluating the safety and effectiveness of hip prostheses, which are supposed to last for at least 20 to 25 years. Furthermore, it addresses some medical and biological aspects of total hip arthroplasty (THA).

The objective of the present report is not just to review the state-of-the-art of THA, but in addition to identify further research needs and health economic and regulatory issues.

This report focuses on key principles and issues, rather than attempting a comprehensive literature review. Cross-references to other sources are made for detailed information where appropriate. We hope the report will provide useful information to the risk assessment and risk management community.

1.2. The principle of total hip arthroplasty

The concept of replacing parts of a hip joint - such as the femoral head - that become defective due to pathological alteration or accident by a prosthetic device, goes back to the 19th century. However, the major breakthrough of substituting a hip joint with a prosthesis was not achieved until the middle of the 20th century in a process based on “*empiricism and intuition*” [3]. It also became clear that successful treatment required substituting both articulating surfaces, which coined the term *total hip arthroplasty (THA)* for this treatment [3].

THA has now become so successful that it has been referred to as “*the operation of the century*” [4]. It is the main surgical procedure in orthopaedics [5] and it is a cost-effective treatment to recover pain-free mobility

in patients suffering from degenerative bone and joint diseases such as osteoarthritis [6, 7].

The basic principle of THA is depicted in Figure 1. The defective hip joint is replaced by an artificial *acetabular cup* and *femoral head*, which replace the damaged natural articulating surfaces. Therefore the materials must have low friction and withstand wear and oscillating mechanical load. The femoral head is anchored in the femur by the *stem*. The acetabular cup is anchored in the pelvis and is composed of a *shell* in which a *liner* is inserted that provides the load bearing articulating surface. This modular design allows using different materials with properties most suitable for their function [3, 4, 8].

Shell and stem have to provide good bone integration and are frequently made of titanium and titanium alloy, respectively. Titanium alloys are however not hard enough for low-friction wear-resistant articulating surfaces. Therefore other materials are combined to meet the requirements for the articulating interface between head and cup as will be outlined in chapter 2. The frequently used notations metal-on-metal (MoM), ceramic-on-ceramic (CoC) or the *classical* combination metal-on-polyethylene (MoP) refer to the sequence of materials used for the femoral head and the acetabular cup (liner), respectively.

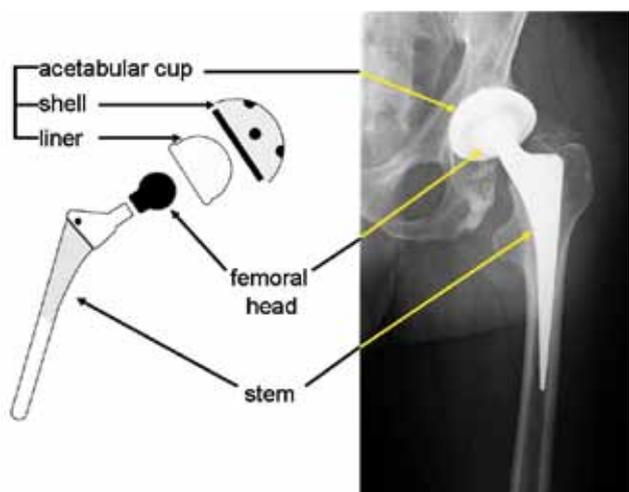


Figure 1: Modular hip prosthesis design consisting of femoral stem, femoral head, and acetabular cup composed of an outer shell and an inner liner. Shell and stem have to ensure good bone integration with the iliac bone of the pelvis and the femur, respectively. The femoral head and the liner provide the articulating surfaces. Their materials are selected for low friction and wear.

1.3. The history of total hip arthroplasty

The earliest documented attempt to replace a femoral head dates back to 1891 when Gluck used an ivory² prosthesis fixed with screws and cement [9, 10]. The procedure was however not as successful as expected and did not gain widespread use [3]. In 1938, a stainless steel prosthesis was introduced to replace the femoral head and the acetabular cup [11]. In 1940, a THA with an implant made of a cobalt-chromium alloy (developed for dental applications) was carried out, which was placed proximal to the femur and fixed by screws. This approach had been further developed into the *Austin Moore prosthesis*, introduced in 1952, which is still applied today in rare cases of revision surgery. MoM hip arthroplasty was introduced in clinical practice in 1953 however with poor early results [12]. The improved McKee-Farrar design, introduced in 1958, can be considered as the first generation of widely used MoM prostheses made of cobalt-chromium alloy. However, this design was soon discredited by a large number of failures [13]. MoM hip replacements were gradually phased-out by the mid 1970s due to the rising popularity of Charnley's MoP design, which showed lower rates of loose prostheses [14], and because of metal sensitivity found in patients with MoM hip designs [15].

Wroblewski et al. [16] stated that November 1962 would "mark the beginning of the era of a new speciality within orthopaedics – total hip joint replacement surgery". This was the first hip replacement surgery performed by Charnley, pioneering a prosthesis design based on a stainless steel femoral component and a polyethylene acetabular cup both fixed with acrylic bone cement. This so-called *low frictional torque arthroplasty* superseded the MoM approach in the 1960s.

Charnley's approach to use polyethylene as one load bearing surface was accompanied by the idea to reduce the diameter of the femoral head replacement in order to have a well defined centre of movement in the joint and to reduce wear. Charnley also pioneered the surgical techniques which are essential to obtain a biomechanically valid result [16]. Surgical skills, expertise and practice have major impact on clinical outcome. Charnley's prostheses were cemented in femur and pelvis using polymethylmethacrylate (PMMA) as bone cement [17]. In this way the prosthesis was fixed during surgery. Good fixation requires a homogeneous layer of bone cement around stem and acetabular cup in order to allow a uniform load transfer between bone and

prosthesis. Bone preparation, cementing and alignment require a high degree of surgical skill.

The success of Charnley's prostheses in recovering joint function and achieving pain relief was afflicted over time by an unexpected number of loose stems and/or acetabular cups. The phenomenon of *aseptic loosening* [18], i.e. a loss of fixation of the stem or the acetabular cup, is to date the main reason for revision surgery [16] and can affect patients 10 to 20 years after surgery. Other reasons for revision surgery such as infection, dislocation of the joint, fracture of the stem or the acetabular component, or unexplained pain, occur, but aseptic loosening is about five times more frequent than all these together.

Aseptic loosening is a consequence of polyethylene wear. Advanced wear-induced dimensional changes may impair the mechanical function of prostheses and wear debris may induce adverse tissue reactions leading to periprosthetic osteolysis. This *polyethylene disease* [19] triggered a lot of research to improve the wear resistance of polyethylene leading to the development of ultra-high molecular weight polyethylene (UHMWPE) and *crosslinked* UHMWPE (see chapter 2.2.2). It also led to the resurgence of MoM devices because osteolysis was not reported as failure mechanism in earlier MoM hip prostheses [12]. A second generation of MoM prostheses was developed and introduced in clinical practice in the late 1980s. However, in spite of the polyethylene wear debris problematic with the MoP design, it is still challenging to outperform Charnley-type prosthesis of which more than 50% are still performing satisfactorily after 27 years [16]. Patients who received this type of prosthesis from 1962 on were followed up for at least 35 years. It was found that even 78% of the patients still do well after 35 years and some patients exceeded 40 years with their primary hip replacement [20]. In spite of good results with second generation MoM hip prostheses [21], up to now no study could demonstrate that the expected reduced wear resulted in a superior performance. At best their performance is equivalent to MoP devices [14].

With THA becoming a well established and successful procedure to treat severe disabilities in elderly patients, expectations were raised in younger individuals, with degenerative joint diseases that compromise quality of life. Expectations are that THA could restore the same life-style with little or no restrictions on their physical activity. However, to fulfill such expectations, hip prostheses are required that can withstand higher load for extended time periods, thus mobilising a lot of research into materials with improved wear resistance [12, 22, 23].

This has led, since the late 1970s, to the development of CoC hip prostheses that exhibit excellent wear performance but initially also the risk of fragile fracture [24]. In the meantime the failure rate of ceramic components has been significantly reduced [24, 25]

1 Between the 1960s and the early 1980s San Baw in Burma performed hundreds of hip replacements using ivory. His prosthesis design was continuously improved and results ranked good or excellent have been reported in 88% of the cases. Ivory was chosen because its friction coefficient of 0.04 is close to that of cartilage (0.02). The material showed strong bonding to bone [10]. This can be explained by the biological nature of the material. Its surface properties and its elasticity, match the properties of surrounding bone better than any metallic engineering material.

and progress has been made to address the specific problems related to revision surgery in the rare cases of catastrophic ceramic failure [26]. Hence, CoC implants can be considered as a reasonable alternative to MoM or MoP prostheses [24, 27] and survivorship data of 94% and 84% have been reported after 9 and 21 years, respectively [28]. Currently, the main disadvantage seems to be an audible squeaking that occurs in 1-20% of the patients [28].

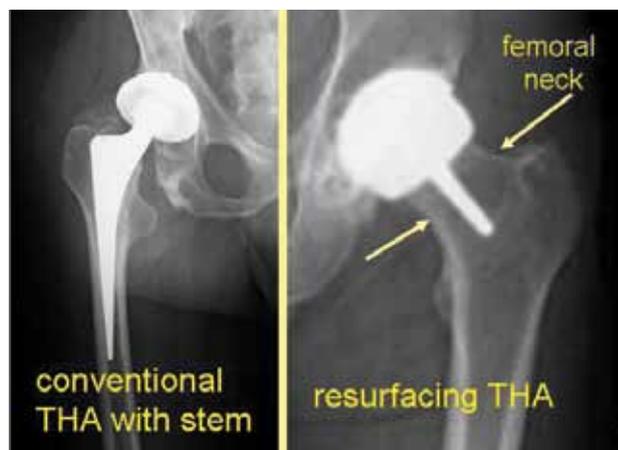


Figure 2: Hip-resurfacing THA covers the reshaped femoral head with a new metallic articulating surface. The femoral neck and the femoral bone mass are preserved. This allows using a conventional THA with a stem in future revision surgery. It can be recognised that the femoral head diameter in resurfacing is larger than in conventional THA.

Alternatively, for younger patients *hip resurfacing* has been advocated in the last 10 years because it promised to preserve the femoral bone as shown in Figure 2. This means that revision surgery, which is almost inevitable in patients younger than 50 years at the time of primary THA, consists of using a conventional stem design, thus intervening for the first time on the main femur mass [12, 29]. Additionally larger diameter femoral heads are used that give the joint more stability. It was expected to achieve lower failure rates because femoral stem loosening would be less probable. In particular, it was hoped that the improved wear resistance of the MoM bearings, which had been verified in laboratory tests, would pay off by an extended lifespan of resurfacing prostheses [12, 29, 30]. Thus, with the reintroduction of MoM bearings in hip resurfacing it was expected to

overcome problems with excessive wear, which had led to unfavourable results with earlier MoP resurfacing systems in the late 1970s and early 1980s [31]. The surgical procedure is however much more demanding [2, 32], and complications may occur due to the interruption of blood supply to the proximal femur (avascular necrosis), and a high incidence of femoral neck fracture is observed [32]. Moreover, excessive wear can trigger adverse tissue reactions [33, 34]. Early revision rates have been reported for some hip-resurfacing systems that are two to three times higher than normal [34], which creates a problem considering the large number of patients that underwent hip-resurfacing THA in the last 5 to 10 years.

1.4. Incidence of total hip arthroplasty

The importance of a medical treatment is reflected in the number of procedures carried out per year in a population. Figure 3 shows that in most industrialised countries THA has an incidence higher than 150 procedures per 100.000 habitants and year [35]. Thus, of the order of one million hips are replaced by prostheses worldwide every year. The rate of hip replacement increased by about 25% between 2000 and 2009 [35] and this trend is expected to continue in the next decades due to ageing population and improving medical care in developing countries.

Among OECD countries there are significant discrepancies between the number of THA procedures executed per year and per 100.000 habitants. Germany and Switzerland reach nearly twice the OECD average. There are no obvious reasons for such strong discrepancies in countries with similar quality of life and lifestyle. It may have to do with the medical judgement of *compromised quality of life* justifying the medical indication for THA and may also be due to more generous approaches taken by health insurers. While attracting attention from health policy makers in times of stressed health care budgets [36], the reasons for such national peculiarities have not yet been investigated.

While in the United States it is extrapolated that the increasing number of primary THA and revision procedures will increase the annual cost from 8.43 billion \$ in 2003 to 22.7 billion \$ in 2030 [37], there are to our knowledge no data available for the European Union.

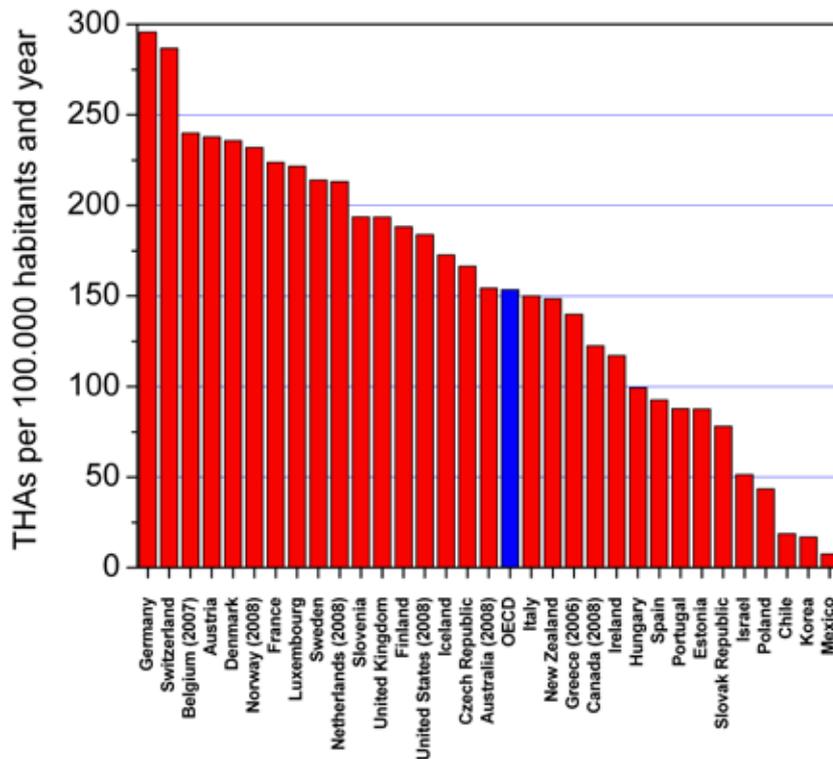


Figure 3: Number of THA procedures performed per 100.000 habitants in the year 2009 (or nearest year available). The mean incidence of THA in the OECD countries in 2009 was 156.6 per 100.000 habitants (data source [35]).

1.5. The challenge of patients' expectations in an ageing population

Generally, THA can be considered a safe intervention yielding high patient satisfaction. One year after surgery, more than 90% of the osteoarthritis patients declare that they are satisfied with the results of their THA [38] and most of them can return to normal life [39]. This success has led to high expectations among patients, orthopaedic surgeons and researchers, since progress in material science addressed many issues emerging during half a century of clinical experience with THA. However, the interaction of the human body with foreign materials that are subjected to alternating mechanical load in a highly corrosive environment still provides challenges. Patients will have to understand and accept that THA *"marks the beginning and not the end of treatment"* [16] despite almost immediate pain relief and gain in mobility that can be achieved.

Unlike natural joints that have some regenerative capacity a joint prosthesis is subject to wear from the very beginning of its implantation, and it will degrade. Thus, a joint prosthesis has a limited lifespan and must be replaced sooner or later by revision surgery (see Figure 4). As the population is ageing – especially in developed countries – the probability that patients outlive their primary THA is increasing. Moreover, the demand for primary THA in a younger population,

featuring a much higher level of physical activity, is increasing. In other words, the mean age of the patients selected for THA is decreasing whereas patients' life expectancy is increasing. This will inevitably lead to an increasing number of revision surgeries in the future.

It must be emphasised that the *lifespan* of a joint prosthesis is shorter the more it is used and the higher it is loaded [40]. Thus, its lifespan will be shorter in younger patients with a higher level of physical activity as illustrated in Figure 5. This explains the special focus in research on the young and (physically) active population, practicing sports and exercising physically demanding jobs, in order to provide more wear resistant materials and designs, as well as surgical methods to facilitate revision surgery and to improve its clinical outcome [26].

The continuous intense research efforts have produced thousands of hip prostheses designs that differ in the materials used, their shape and size, their surface properties and whether they are used with or without bone cement. Thus, prostheses in the current world-wide patient population reflect the whole history of THA. Some patients are still living with hip prostheses implanted in the 1960s [16], whereas new designs were not yet given the time to prove superior longevity. But with each design and at any time complications occurred, which may be related to patient specific issues and pre-existing co-morbidities, to inexperienced surgeons,

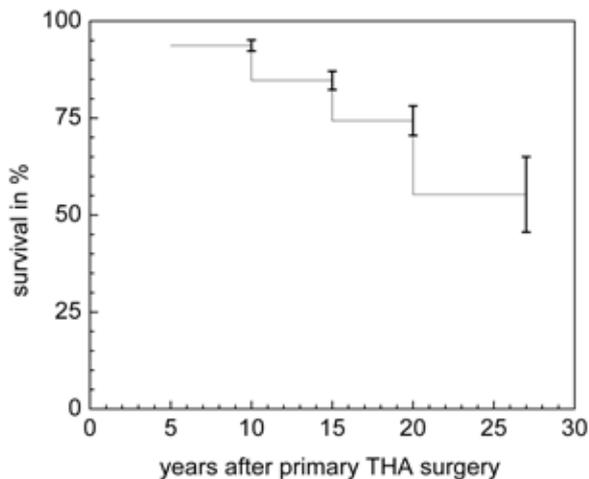


Figure 4: Kaplan-Meier plot for Charnley-type prostheses; endpoint is revision surgery (data of Wroblewski et al., 2006 [16]). Survival is defined as the percentage of prostheses that are still in place after a certain number of years. The percentage decreases when a prosthesis has to be replaced by revision surgery. The data cover 1434 primary THAs in 1092 patients aged less than 51 years at surgery, followed-up for 27 years.

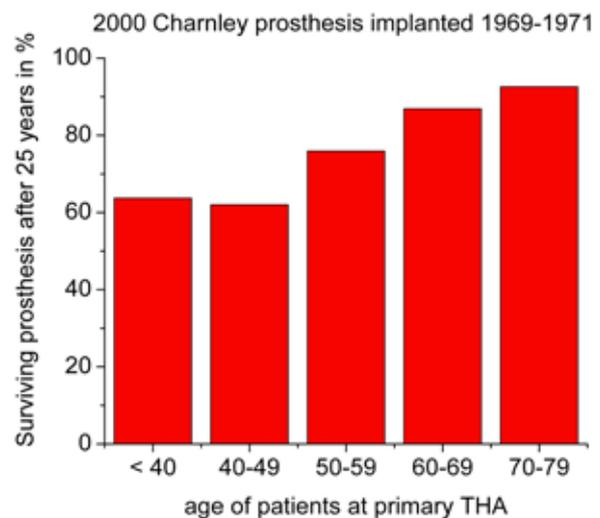


Figure 5: The longevity of Charnley-type hip prostheses increases with the age of patients at the time of primary THA because older patients exhibit lower levels of physical activity. This implies that the prostheses are loaded less frequently and less heavily. Therefore the percentage of prostheses that survives a given time span, is higher in older patients because their prostheses have been less “used”. Data of Berry et al.[41]

flaws in the hip prosthesis design, materials issues, or, usually, combinations thereof. It is therefore a statistical challenge to identify reasons for device failure, and sometimes unacceptably high early complication rates require designs to be removed from the market, before failure reasons can be clarified, and the concerned patient populations need to be followed-up for many years.

1.6. Intended improvements may cause unexpected new problems

Over the past years problems have emerged with some THA systems that belong to the family of third generation MoM implants and which have been designed as hip-resurfacing systems [2]. Many patients have developed *pseudotumours*, i.e. inflammatory lesions in periprosthetic soft tissues, and exhibit elevated concentrations of cobalt and chromium ions in blood [42] and subsequently require revision surgery. Currently the reasons for the high early failure rates are being analysed. Designs with unusually high short-term revision rates have been identified and removed from the orthopaedic device market. All other MoM designs are under close observation.

Each new THA implant is developed with the intention to outperform the Charnley-type MoP design, which provides the benchmark to date. The performance of hip prostheses may be compared by the percentage of prostheses that survive a certain number of years

before they need to be replaced by revision surgery. In Figure 6 survival data of MoM prostheses retrieved from literature are benchmarked against the survival of MoP Charnley-type prostheses, dealing with a group of younger patients with an average age of 32 years at the time of primary THA [43] and a group of older patients with an average age of 56 years at the time of primary THA [44]. The survival curves for older and younger THA patients show that the lifespan of a hip prosthesis is shorter in younger, more physically active patients. MoM designs were reintroduced with the intention to improve the survival of prostheses in younger patients and to achieve survival data at least between the two MoP benchmark curves and as close as possible to the *older patients curve* in Figure 6.

It is obvious that the first generation of MoM hip prostheses used in the late 1950s could not compete with the Charnley design. Data on second generation MoM implants, showing a 14 year survivorship of 94% of 138 MoM hip prostheses (Metasul™, Zimmer GmbH, Winterthur, Switzerland) implanted in 100 patients between March 1993 and July 1996, confirm that second generation MoM designs can perform as expected [53]. A general improvement from the first to the second generation of MoM implants is obvious.

Hip-resurfacing systems represent the third generation of MoM bearings. There is a large body of medical literature dealing with these devices, however, it is not completely comprehensive or indicative as it covers many different devices and only short follow-

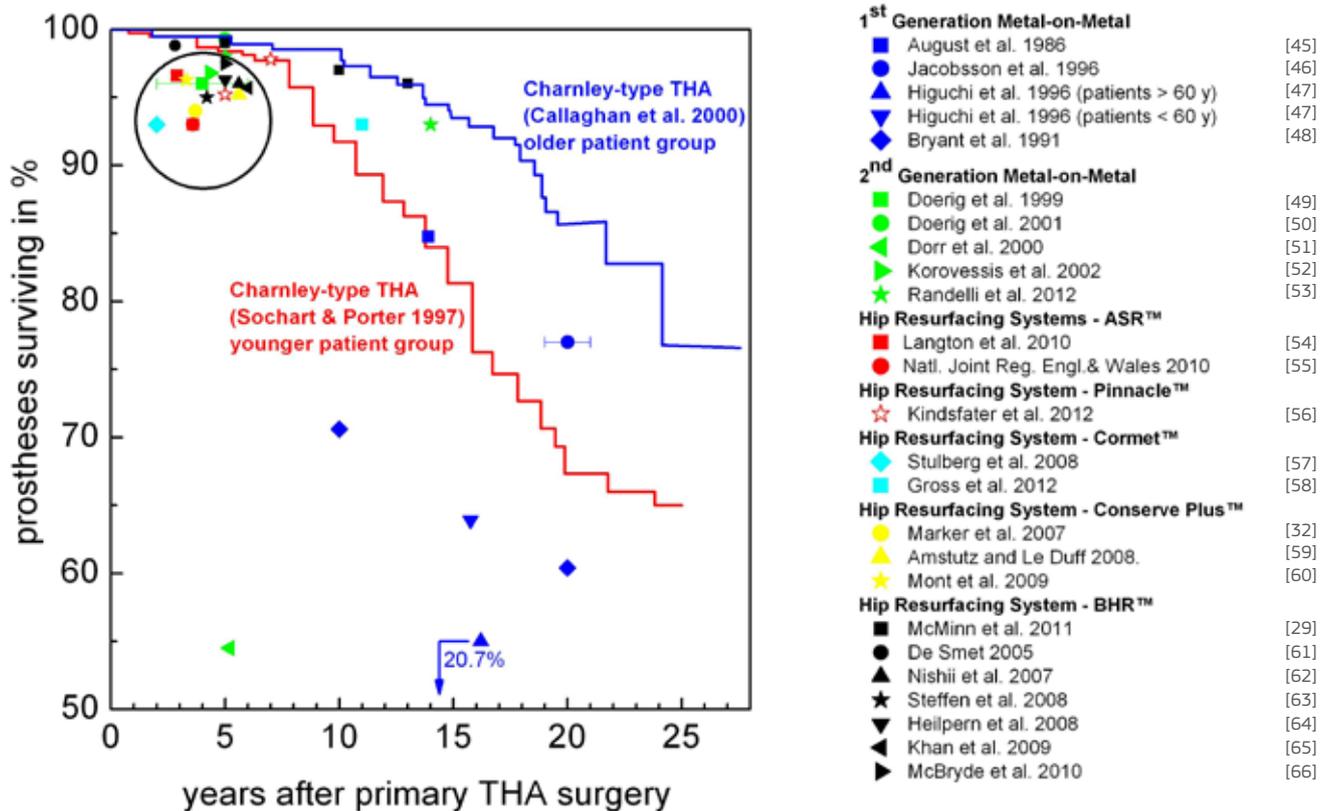


Figure 6: Graphical summary of currently available data on the survival of MoM hip prostheses. The performance of these devices is benchmarked against Charnley-type MoP prostheses. The red and blue curves present Kaplan-Meier survivorship data for Charnley prostheses in young and older patients retrieved from Sochart and Porter [43] and from Callaghan et al. [44], respectively. As explained, the aim of the MoM development was to outperform MoP designs in younger patients, i.e., to achieve a performance as close as possible to the blue curve. This has been achieved so far only in exceptional cases. The alarming data, indicating early device failure are indicated by the circle. The problems with recent MoM designs are confined to some hip resurfacing systems.

up periods of maximum 12 years. The survival data of hip-resurfacing devices as shown in Figure 6 indicate that (i) in general these implants have problems to perform better than Charnley-type MoP prostheses and (ii) that the Birmingham™ Hip Resurfacing (BHR) System performs better than most others. Some of the results obtained with the Birmingham™ Hip Resurfacing and the Pinnacle™ (DePuy, Warsaw, Indiana, USA) system indicate that also hip resurfacing has the potential to catch up with the longevity of MoP hip replacements. However, the reasons for frequent early failure of many MoM hip-resurfacing systems, as well as the role of metallic wear debris and elevated metal-ion concentrations, need to be established.

Gross et al. reported on their experience with 373 MoM hip-resurfacing arthroplasties of the type Cormet™ 2000 (Corin, Cirencester, Gloucestershire, UK): a survivorship of 93% was found after 11 years. These authors state that adverse reactions to wear debris are rare events with a probability of 0.5% after 6 to 11 years follow-up [58]. An analysis of survivorship after 7 years for the first 100, the second 100 and all further THA procedures showed an increase in survivorship from 93% to 98%

and illustrates the impact of increased experience of the surgeon on the clinical outcome of THA [58].

Kindsfater et al. [56] published a seven year follow-up on MoM total hip-resurfacing devices of the type Pinnacle™ in 95 patients and found a survivorship of 97.8% from 5 to 7 years after arthroplasty. The difference with respect to the less performing DePuy's Articular Surface Replacement implant (ASR™) is attributed to the fully hemispherical geometry of the Pinnacle™ acetabular cup design, which reduces the risk of *edge loading*, i.e., rubbing of the femoral head against the edge of the acetabular cup liner, and improves the mechanical stability of the modular acetabular cup design. No evidence was found for unusually high wear or adverse tissue reactions [56]. However the study does not report on blood serum metal-ion concentrations, which might have also become a problem with these devices as reported recently [2]. Such data are also not covered in the study of Randelli et al. [53], in which however only two patients were tested positively for metal allergies: one showed allergic skin reaction on nickel another one on cobalt. The patient reacting to cobalt had bilateral total hip arthroplasty and periprosthetic osteolysis was

observed bilaterally in the proximal part of the femur, but he was otherwise asymptomatic 11 years after surgery [53].

Recently also significantly increased rates for revision surgery are reported for conventional THA using MoM prostheses with femoral head diameters typically above 36 mm [67]. Already, before hip resurfacing was introduced such devices have become popular because they promised increased joint stability and larger range of movement because the size of such femoral heads corresponds geometrically better to the anatomy of the natural hip joint.

Whereas data from arthroplasty registers provide clear data on failure rates [67], the failure mechanisms and especially the factors that contribute to the formation of pseudotumours are still unclear and a matter of controversy. Large femoral head diameters in MoM devices are related to higher failure rates [67]. At the same time there appears to be a tendency towards lower metal-ion concentrations with increasing head diameter [68] and to higher metal-ion concentrations with increasing inclination angle of the acetabular cup

[68], which rather points to alignment problems during surgery than to a simple design issue. On the other hand there appears to be no clear correlation between the incidence of pseudotumours and the orientation of the acetabular cup in MoM hip prostheses [69] and not even with the incidence of well-functioning and painful MoM hip prostheses. Moreover, in one study pseudotumour have been diagnosed in 60% of all patients with MoM hip prostheses whether their implant was working properly or not and even with well-positioned acetabular cups [69].

The collected literature illustrates the difficulties in the assessment of clinical outcome of THA. The number of patients in short-term follow-up of newer devices is in many cases too low to draw statistically significant conclusions to pinpoint the reasons for early failure. However, it is felt necessary to protect patients by acting immediately if failure rates tend to be higher than average. Even assessing the long-term performance of THA devices that had been used widely in the past is difficult since frequently patients are lost for observation [70] and others suffer from co-morbidities that may distort statistical evaluation.

Summary of Chapter 1

- ▶ Total hip arthroplasty (THA) is generally considered a safe and cost-effective medical intervention to restore functionality of the hip joint after severe degenerative disease or trauma.
- ▶ In THA the damaged joint is replaced by an artificial femoral head articulating against an artificial acetabular cup liner. Both components are anchored in the femoral bone and the pelvis using a stem and an acetabular cup shell, respectively.
- ▶ In 2009, in the average of the OECD countries 150 hip joints were replaced by prostheses per 100.000 habitants, and this number is expected to increase. Worldwide of the order of one million THA procedures are performed per annum.
- ▶ The lifespan of hip prostheses is limited by wear and is therefore generally lower in patients with higher levels of physical activity.
- ▶ Hip prostheses are subject to continuous research and development efforts in order to increase their lifespan and to reduce the likelihood of revision surgery.
- ▶ Intense research and development has led to rapidly evolving designs over the last years and is reflected in a large variety of types of hip prostheses on the market that mainly differ by the materials used for the articulating surfaces and the diameter of the femoral head.
- ▶ Hip prostheses are categorised according to the material combination used for the combination femoral head on acetabular cup. The most common combinations are metal-on-polyethylene (MoP), metal-on-metal (MoM) and ceramic-on-ceramic (CoC).
- ▶ Hip resurfacing is an approach in which the femoral head is trimmed and then capped with a metal shell instead of replacing the complete femoral head. The conservation of the femoral bone is considered an advantage facilitating possible future revision surgery.
- ▶ Hip resurfacing requires a metal-on-metal (MoM) material combination.
- ▶ Recent evidence shows that with many devices the theoretical advantages of the hip-resurfacing approach cannot be realised to full extent. Some resurfacing devices have shown to exhibit high failure rates within the first five years due to adverse tissue reactions.
- ▶ Current problems with MoM hip-resurfacing devices were not seen in the past with conventional MoM prostheses, replacing the femoral head. However, elevated failure rates have recently been reported also from conventional MoM prostheses with large femoral head diameters above 36 mm.

2. Materials used for hip joint prostheses

2.1. Biocompatibility and device modularity

A *biocompatible material* can be defined as “any material used to make devices to replace a part or a function of the body in a safe, reliable, economic, and physiologically acceptable manner” [71]. The *biocompatibility* of a material has therefore to be assessed in function of its specific application. Its interaction with the body environment can range from no interaction, i.e. the bioinert case, to a maximum for *bioactive* or *bioresorbable* materials.

The term *bioinert* refers to any material that, once placed in the human body, has minimal interaction with its surrounding tissue [72]. Examples of these are stainless steel, titanium, alumina, partially stabilised zirconia, and ultra high molecular weight polyethylene (UHMWPE). As a consequence of initial inflammatory response on the foreign material, a fibrous capsule can be formed around a bioinert implant. Hence its biofunctionality relies on tissue integration of the implant.

Bioactive materials interact with surrounding tissue through a time-dependent kinetic modification of the surface after implantation. An example for such a material is synthetic hydroxyapatite $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$ used as a coating on metals to improve and/or accelerate their osteointegration [73]. An ion-exchange reaction between the hydroxyapatite and the surrounding body fluids results in the formation of a biologically active carbonate apatite layer on the implant that is chemically and crystallographically equivalent to the mineral phase of bone. *Bioresorbable* refers to a material that starts to dissolve after implantation and is slowly replaced by advancing tissue, for example tricalcium phosphate $[\text{Ca}_3(\text{PO}_4)_2]$.

In order to take over the physiological function of a hip joint, a hip prosthesis must feature three different compatibility requirements:

- *Structural requirements*: Since the hip is, after the knee, the body's second largest weight-bearing joint, the material must exhibit adequate mechanical strength and fatigue strength, i.e., it must resist millions of mechanical loading cycles without fracture.
- *Tribological requirements*: The articulating surfaces must ensure the correct relative motion of the musculoskeletal system without being compromised by wear.

- *Biological requirements*: Stem and shell must provide good osteointegration, all components must resist the highly corrosive body environment, and the inevitably released wear particles and corrosion products must not harm the organism.

Thus, the structural and bearing components should be bioinert, whereas, in the case of cementless fixation, stems and shell of the acetabular cup should exhibit bioactive surfaces for good osteointegration at the same time. To reduce wear, load bearing surfaces must be hard, whereas stem and shell should be as elastic as possible to better match the mechanical properties of the surrounding bone. These contradicting requirements require a modular design of hip prostheses. Additionally, coatings and surface modifications are frequently applied in order to stimulate bone growth and promote osteointegration for stable and durable fixation [73]. Examples are biomimetic titanium coatings, titanium porous surfaces [74], as well as hydroxyapatite plasma-spray coatings [75].

2.2. Material properties and material selection

2.2.1 Metals

Metals are required in orthopaedic applications because they exhibit elevated mechanical strength (see Table 2) and fracture toughness, i.e., the ability to contain a crack and to resist fracture. Today three groups of metals are prevailing for applications in joint replacements. These are [73, 76]:

- Austenitic *stainless steels* contain as main alloying elements chromium (Cr), nickel (Ni), molybdenum (Mo) and nitrogen (N) and in general exhibit good corrosion resistance. Composition, treatments and properties of wrought stainless steels are described in the standard ISO 5832-1 (implants for surgery – metallic materials) and in ISO 5832-9 (wrought stainless steels with high N content). ISO 5832-1 stainless steel alloys are economic but have limited resistance against localised crevice corrosion [73]. Moreover, their relatively high content of Ni represents a possible source of Ni sensitization for patients who have received a stainless steel hip implant. ISO 5832-9 stainless steel with increased N content, exhibit higher corrosion resistance and improved mechanical characteristics, which entail however more complicated manufacturing procedures and higher cost.

- *Cobalt-chromium-molybdenum* (CoCrMo) alloys, fall under two main categories: cast alloys (ISO 5832-4) and wrought alloys (ISO 5832-5,6,7,8,12). Cast CoCrMo exhibits elevated mechanical properties and optimal corrosion resistance under friction condition. Its main drawbacks are related to their poor fatigue resistance and their high cost. Wrought CoCrMo is even more expensive than cast material, but the higher cost can be justified by the enhanced corrosion and fatigue resistance [77]. The presence of Ni creates some concerns regarding possible nickel sensitization. In contrast to cast CoCrMo, the tribological properties of wrought CoCrMo are too poor for bearing surfaces.
- *Titanium* (Ti) is considered one of the most biocompatible metals, which has determined the success of pure Ti (ISO 5832-2) in dentistry. However, the poor mechanical properties of pure Ti, such as small Young's elastic modulus and low fracture stress [73, 78], have limited its application in joint replacement. However, titanium alloyed with aluminium (Al), vanadium (V) and niobium (Nb), mainly Ti6Al4V (ISO 5832-3) and Ti6Al7Nb (ISO-5832-11), are best suited for the production of uncemented femoral stems. The numbers in the formulas present the weight percentage of the alloying elements. The improved mechanical properties of Ti alloys are at the expense of a reduced biocompatibility due to the presence of potentially toxic elements, such as aluminium and vanadium. Another limitation of Ti and Ti alloys is the drastic reduction of its outstanding corrosion resistance under friction conditions [73].

2.2.2 Polymers - Ultra High Molecular Weight Polyethylene

Ultra high molecular weight polyethylene (UHMWPE) is a subset of semi-crystalline thermoplastic polyethylene materials [79, 80]. UHMWPE is a very tough material, with very high impact strength [79]. It is highly resistant to corrosive chemicals with the exception of oxidising acids, exhibits a very low friction coefficient, is self-lubricating and highly resistant to abrasion. Its friction coefficient is similar to that of polytetrafluoroethylene (PTFE), but UHMWPE has better abrasion resistance than PTFE [81]. The bulk material can be considered as inert *in vivo*, a judgement which is however not valid for its wear debris [19, 80].

As already mentioned in Chapter 1, UHMWPE was first employed by Charnley in the early 1960s [8, 16] after unsuccessful attempts to use PTFE as low friction material for the acetabular cup. The different hardness results in a preferential wear of the soft components minimising metal wear, avoiding the formation of metallic wear debris and therefore minimising metal-ion release. Moreover the viscoelasticity of UHMWPE can compensate for slight component misalignments

and poor working tolerances without causing excessive stresses on the bearing. The weakness of UHMWPE is its poor wear resistance and therefore many efforts have been made to improve it. [22, 23, 80, 82]

The use of gamma-ray sterilisation produced a series of early failing devices due to accelerated oxidative ageing of UHMWPE components. However, as a positive side effect of gamma-ray sterilisation, transversal links between polymeric chains were created, forming a network structure in the bulk material [22, 83]. This structural *crosslinking* has been optimised since the 1990s using gamma- or beta-ray irradiation, and new generations of crosslinked UHMWPE have been developed [22, 80, 83]. The crosslinked components are subsequently stabilised through thermal treatments (annealing or re-melting), or by addition of antioxidant agents, such as Vitamin E [23, 82] in order to eliminate the oxidative effects of irradiation and to fully exploit the benefits of the crosslinked structure. In laboratory tests such liners have demonstrated 95-99% less wear than other highly crosslinked UHMWPE liners [23, 82]. Crosslinked UHMWPE (also referred to as X-UHMWPE or XLPE), while losing some mechanical strength and becoming more brittle than UHMWPE, shows a significant enhancement of wear resistance [22, 23, 83], and is now the state-of-the-art processing for acetabular cup liners of MoP devices. However, the wear properties of UHMWPE are still limiting the lifespan of MoP hip replacements, due to the adverse reaction of bone tissue triggered by the release of UHMWPE wear debris *in vivo*.

2.2.3 Ceramics

Ceramics have been used in THA since the 1970s. Despite the critical brittleness of ceramics, both the hardness and the wettability of ceramic surfaces result in excellent abrasion and wear resistance [84], resulting in low wear rates. Three types of ceramic materials are used for hip prosthesis:

- *Alumina*, short for aluminium oxide (Al_2O_3). Alumina (ISO 6474-1) represents the gold standard for ceramics in THA thanks to its high compression strength, high hardness, and its resistance to abrasion and chemical attack. Its hydrophilicity plays an important role in the wettability of its surface and consequently on the lubrication efficiency under friction. However, aluminium oxide is a brittle material and cannot stand elevated tensile and impulsive stresses.
- *Zirconia* (zirconium oxide ZrO_2) ceramic has been used in orthopaedics since 1985. It exhibits lower hardness than alumina but higher fracture toughness. Zirconia has three stable crystallographic phases: monoclinic, tetragonal and cubic. Zirconia is commonly mixed with yttria (yttrium oxide, Y_2O_3) to stabilise its tetragonal crystal structure at room temperature. The tetragonal phase has the most suitable

mechanical properties, and thus the fabrication processes have been optimised to maximise this phase in the finished component. Standard ZrO₂ used in orthopaedic applications is therefore yttrium-stabilised tetragonal polycrystalline zirconia (Y-TZP).

- *Alumina-Zirconia Composite Ceramics* have been developed in order to improve the ageing behaviour of Y-TZP and to reduce the brittleness of Al₂O₃. They are commonly referred to as alumina-toughened-zirconia. The martensitic phase transformation of tetragonal ZrO₂ into monoclinic ZrO₂ is exploited to improve the mechanical properties of the composite material. Future progress in processing of nanocomposites may further improve the properties of Y-TZP [85].

2.3. Components of modular hip prosthesis

2.3.1. The femoral stem

After the resection of the femoral neck and after the drilling and reaming of the medullary canal of the femur, the stem is placed in the medullary canal [86]. The femoral stem firmly fixes the femoral side of the hip prosthesis to the femoral bone. It must ensure a uniform load transfer from the prosthesis to the lower limb. Stem fixation can be achieved either by a surrounding layer of bone cement, injected into the medullary canal before the stem is inserted, or by press-fitting the stem against the medullary canal walls. The fixation strategy influences the stem design, the choice of the material and the surface finishing. The stem is the component of the hip prosthesis subjected to the highest mechanical stresses. Its material must feature high mechanical strength and *fatigue resistance*. So far, metals are the only commercial option for stem manufacturing.

Stem *length* critically influences device stability. A longer stem would improve stability, however, more reaming of medullar canal would be required, cement would

have to be injected more distally and less bone would be available for revision surgery. In primary THA a stem in the range of 130 to 140 mm presents a reasonable compromise [3].

The stem *cross-section* is designed to ensure rotational stability and to reduce stress concentration around the device [3, 87-89]. Some femoral stems additionally feature a *collar* in correspondence of the calcar bone on the medial side, just underneath the femoral neck. The purpose of this structure is to ensure primary fixation of uncemented stems, to transfer loads to calcar bone and to avoid prosthesis subsidence [90].

The *neck angle* is an important parameter influencing the load transfer to the whole stem and its long-term resistance [3, 91]. In most cases femoral neck and stem are part of the same metal component. However there is a class of stems, known as modular, in which the two parts are independent and are coupled by means of a taper junction. Such a solution increases the degree of customization of a hip device to meet more closely patient anatomy in terms of neck length and orientation, especially in case of revision surgery [92]. However the increased number of components and taper junctions increase the risk of fretting corrosion [93].

Structural requirements of the stem, such as component stiffness and fatigue resistance are discussed in chapter 3.2.

2.3.2. The femoral head

The femoral head is coupled to the stem's neck by means of a taper junction. The *diameter* of the femoral head plays an important role in determining the achievable range of motion of the artificial joint and its stability against dislocation. Critical parameters for the manufacturing of the femoral heads are:

- the minimum achievable surface roughness, which influences friction and wear rate,
- the maximum outer diameter,

Component	Material class	Most used material
Femoral stem	Metal	CoCrMo-wrought, Ti-alloys, stainless steel
Femoral head	Metal	CoCrMo-cast, stainless steel
	Ceramic	Alumina (pure or zirconia-toughened), zirconia
Acetabular cup liner	Polymer	UHMWPE, XLPE
	Metal	CoCrMo-cast
	Ceramic	Alumina (pure or zirconia-toughened), zirconia
Acetabular cup shell	Metal	Commercially pure titanium, stainless steel

Table 1: Summary of material selection for THA components

- the mechanical resistance of the material to the tensile stresses generated along the taper junction.

Compared to metal femoral heads, ceramic heads feature the highest smoothness, resulting in the lowest friction coefficients, but their maximum diameter is limited by the manufacturing techniques to about 38-40 mm [94]. Increasing femoral head diameters improves the stability and increase the range of motion of the artificial hip joints [95, 96]. Their weak point is the low toughness, i.e. the risk of fragile fracture.

2.3.3. The acetabular cup – liner

The liner of the acetabular cup, also known as insert, or socket is the counterpart of the femoral head. It usually features a half-spherical cavity that represents the tribological surface worn by the action of the femoral head. In a hard-soft material coupling the cup represents the soft component. This means that it is the component preferentially worn out. This choice is a precaution, because in a spherical head-socket configuration it ensures that a geometrical change of the two mating surfaces caused by wear does not change too much the kinematics of the relative motion.

The liner is mechanically locked in the shell. A limiting factor for the choice of liner material is the minimum thickness of the shell, which has to ensure the mechanical stability of the acetabular cup. But its maximum external diameter is limited by the space available in the iliac

bone that has to host the acetabular cup. Therefore, femoral head diameters exceeding 36 mm can only be used with CoCrMo liners [97]. Otherwise the required minimum thickness of the liner and that of the shell, which has to provide the mechanical stability, would result in an acetabular cup, which is too large for most anatomical situations.

2.3.4. The acetabular cup - shell

The shell provides the outer face of the acetabular cup, which must be fixed into the pelvis, either by bone cement or by press-fitting. Its fixation can be enhanced by use of screws inserted into the massive pelvis bone. The design of the external surface is conditioned by the fixation strategy. Uncemented components present porous surface finishing (e.g. sintered Ti beads) or hydroxyapatite coatings to foster improved bone integration [73]. The stress levels reached in shells are lower than those in stems, which in many cases allow the fabrication out of commercially pure titanium.

For MoM couplings, shell and liner may be fabricated from the same material and the acetabular cup may consist of a single component. However, in case of revision surgery the replacement of a component that may still exhibit good bone integration should be avoided. Thus, the shell-liner modularity allows preserving a well fixed shell, replacing only a worn-out liner. When a UHMWPE or ceramic liner is used, the shell ensures the mechanical strength of the acetabular component [3].

Summary of Chapter 2

- ▶ The usage of different materials for the components of a hip prosthesis is necessary to meet the different requirements for each component.
- ▶ Stainless steel, cobalt-chromium-molybdenum or titanium alloys are the only materials that provide sufficient mechanical strength for the stem.
- ▶ Cast cobalt-chromium-molybdenum alloys, alumina or zirconia provide sufficient strength and hardness for femoral heads.
- ▶ The femoral head articulates against the acetabular cup liner. Lowest wear rates are achieved with cast cobalt-chromium-molybdenum alloys and alumina or zirconia.
- ▶ The acetabular cup has traditionally been fabricated from UHMWPE to reduce friction at the expense of a higher wear rate.
- ▶ Wear of UHMWPE can be significantly reduced by structural crosslinking by gamma- or beta-ray irradiation.
- ▶ The acetabular cup shell must provide good osteointegration and the mechanical stability for brittle ceramic or soft UHMWPE liners and is therefore mostly made of pure titanium.

3. Design criteria for hip joint prostheses

3.1. Fixation strategies: cemented and non-cemented prostheses

Fixation of the stem and acetabular cup component in THA can be achieved by using acrylic bone cement (*cemented prosthesis*) or by press-fitting against the bone (*non-cemented prosthesis*).

In *cemented* THA, the cement fixes the implant to the bone and assures uniform load transfer on the whole contact area between implant and bone in order to optimise the load-bearing capacity of the prosthesis-bone and the cement-bone system. Polymethylmethacrylate (PMMA) is the standard material used as bone cement.

Bone cement does not bond the prosthesis to bone. It rather acts as *filler* occupying the space between prosthesis and surrounding bone [3, 4], thereby it fixes the prosthesis in its position and creates a stable interlayer allowing a uniform mechanical load transfer between bone and prosthesis. A homogeneous and complete layer of bone cement between implant and bone is required to achieve this [3, 17] and to prevent high local stresses, leading could lead to local crushing of the bone (periprosthetic fractures), and implant loosening. Cemented stems and acetabular cups must exhibit smooth surfaces in order to avoid stress concentrations that may crack the PMMA layer. Moreover they must be sufficiently stiff to avoid mechanical loading of cement by elastic deformation of the metal.

The disadvantages of acrylic bone cements are related (i) to its dense polymerised structure, which does not allow osteointegration for improved bone fixation, and (ii) to its exothermal polymerisation reaction. A temperature peak during positioning of the implant may cause necrosis of surrounding bone tissue resulting in loosening of the implant. (iii) Necrosis of bone tissue can also be caused by released unreacted monomer molecules. (iv) Moreover, shrinkage during polymerisation of MMA may compromise the fixation of a component [95]. The timing of the preparation of bone cement, the injection technique and achieving a homogeneous thin layer completely filling up the space between implant and bone requires high surgical skills. The surgeon must also have experience in the preparation of the bone cement from the solid (a powder of pre-polymerised MMA) and liquid (the MMA monomer) components, which is done in a short time window just before the cement is needed to fix the implant. A slightly too low monomer content may reduce both toxicity and polymerization peak temperature, but it increases cement viscosity, reduces the available working-time before cement consolidation and makes it difficult to achieve a homogeneous and complete cement layer around the implant. A slightly

too high monomer content makes the cement too liquid and it distributes inhomogeneously because it has the tendency to flow. Both deviations may compromise fixation [33].

Non-cemented THA is characterised by a direct press-fit contact between implant components and surrounding bone. The close surface contact between bone and implant shall facilitate bone integration. In order to promote long-term osteointegration of non-cemented components their surface exhibits porous coatings or a porous surface finish, which are intended to be filled by newly forming trabecular bone tissue. Frequently the surfaces are coated with plasma-spray deposited hydroxyapatite [75, 99], Ti sintered beads or plasma-sprayed Ti that shall facilitate integration into hosting bone tissue [74]. The shape of uncemented stems exhibits edges and grooves, which are meant to mechanically enhance primary fixation.

Since the long-term stability relies on the patient's health status, factors reducing the capability of bone growth, such as age or pathological conditions, limit the application of uncemented THA. In older patients with less vital bone tissue, cement filling allows for a lower degree of accuracy in bone shaping and can compensate for bone defects. Since younger patients have biologically more active bone tissue, uncemented THA is preferred in younger patients. Moreover, this group will more likely undergo revision surgery, which is complicated by the presence of cement and cement debris [4]. The more sophisticated surface requirements for uncemented devices complicate their fabrication [74], which is reflected in the higher price compared with cemented prosthesis [100].

3.2. Fatigue resistance and stiffness of the stem

Mechanical *fatigue* describes the fact that a material subjected to oscillating mechanical load, as it is typical for a gait cycle, will fail after a certain number of load cycles even if the load is lower than the static load the material can support. The smaller the load amplitude the more load cycles the material will withstand before fracture. Materials usually exhibit a fatigue limit, which defines the load amplitude where the material will not fail even after many millions of load cycles. Material fatigue is a consequence of accumulating microstructural damage that nucleates microscopically small cracks which then grow and propagate until fracture. Shape and surface finish significantly affect the fatigue life. The shape defines where the material has to support the highest

stresses, and rough surfaces may locally concentrate the stress to levels that promote the formation of cracks. Square holes, sharp corners, scratches, and even laser marks may lead to elevated local stresses where fatigue cracks can initiate. The loading conditions of the femoral stem are so demanding that fatigue fracture can become a concern [101-103], as proven by several case reports giving evidence for fatigue failure initiating from producer laser marks on the implant surface, especially in the neck region [103-105].

The *stiffness* or rigidity determines the extent to which a component resists to deformation in response to an applied force [106]. Stiffness is determined by geometrical parameters, such as cross-sectional area, shape and length of a stem, and by the *elastic modulus* of the material. The stiffness of a femoral stem determines its interaction with the surrounding bone, which exhibits very different mechanical properties. Bone is a living tissue whose structure is continuously remodelled by the concurrent action of two classes of cells: the osteoblasts, which build up the bone structure, and the osteoclasts, which break it down [107]. Therefore, bone remodelling is a lifelong process where mature bone tissue is removed from the skeleton (*bone resorption*) or newly formed (*ossification*) in response to the local loading conditions. This means that bone may be locally resorbed, where it is not loaded, and recreated or strengthened where more load has to be carried. The implantation of a hip prosthesis is drastically changing the normal physiological load transfer leading to bone response [107, 108].

While the contribution of stem geometry to the structural stiffness can be controlled within certain limits by the design, there is a significant mismatch between the elasticity of bone and all major prosthesis materials. The typical Young's elastic modulus (see Table 2) of bone is about ten times smaller than that of metallic biomaterials. This mechanical mismatch may cause local *stress shielding* where the prosthesis does not transfer load to the surrounding bone. Insufficiently loaded bone responds to this by bone resorption [108]. Excessive bone loss caused in this way will compromise the long-term clinical performance of the prosthesis. Implant migration, aseptic loosening, and fractures around the prosthesis may be the consequences and will require revision surgery. The relationship between implant flexibility and the extent of bone loss is clinically well established. It has been confirmed that changes in bone morphology are a result of adaptive bone remodelling following stress shielding [107, 109].

The combination of these concepts with fixation strategies leads to different stiffness requirements for cemented and uncemented stems. For cementless stems the goal is to reduce stiffness in order to better match the properties of surrounding bone, cemented stems should feature a higher stiffness to reduce the amount

of stress transmitted to bone cement in order to avoid cement fracture. Therefore, frequently cemented stems are made of CoCrMo alloy or stainless steel and uncemented stems from Ti alloys, which have a significantly lower elastic modulus.

3.3. Femoral head diameter and range of motion

The last decade has seen a trend towards larger femoral head diameters, which comes closer to the anatomy of a healthy natural hip joint and yields enhanced stability against dislocation and a wider range of motion [95, 96]. Both factors determine the level of physical activity that can be accomplished by the patients. For metal or ceramic on UHMWPE joints an increased head size yields results in a larger sliding distance and higher sliding velocity on the articulating surfaces and thus on increased polymer wear. Therefore prosthesis with larger femoral head diameters cannot be realised with UHMWPE. Additionally, with a larger femoral head diameter, the inner and outer diameter of the acetabular liner would have to become larger too. If soft UHMWPE or brittle ceramic material would be used for the liner, the thickness of the shell would be reduced, because its external diameter is limited by the anatomy of the pelvis in which it has to fit. As a consequence a thinner shell could not provide sufficient mechanical stability to support a soft or brittle material for the liner. Thus large femoral head sizes require metallic acetabular cup liners or monoblock acetabular cups, where shell and liner are made of a single piece of metal, so called "monoblocks", to provide sufficient mechanical strength [94]. Since the maximum diameter of ceramic femoral heads that can be fabricated, without increased risk of brittle fracture, is currently limited to about 40 mm [94], MoM couplings are currently the only material choice for prostheses with large femoral-head diameters. Therefore, also all hip-resurfacing systems, which are available with head diameters up to 58-60 mm are MoM devices [12, 30].

3.4. Bone conservation: resurfacing versus conventional joint replacement

Hip-resurfacing prostheses have been developed for young and active patients with good bone quality that will outlive their prosthesis and very likely will undergo revision surgery [29, 30]. Revision THA is more complex than primary THA, is more invasive, has a higher risk and has usually poorer outcome, especially if the stem or the acetabular shell must be replaced [110]. The idea of hip resurfacing is to conserve femoral bone mass in primary THA by trimming the femoral head and covering it with a semi-spherical usually cemented metal cap. On the acetabular side the intervention is equivalent with conventional THA [31]. Hence, if revision will be required a stem can be placed in the femur for the first time, thus facilitating surgery.

Femoral head diameters in hip resurfacing of 45-55 mm should reduce the risk of dislocation and improve joint stability. However the trimming of the femoral head and the large head diameters are less forgiving for surgical inaccuracies and increase the risk of misalignments [2, 12]. This makes the surgical procedure more demanding and requires a high degree of surgical skills and experience. These difficulties in achieving biomechanically and anatomically proper joint function are reflected in a high rate of femoral neck fractures [32, 33]. Slight misalignments are more frequent than in conventional THA and may cause excessive wear. Since hip resurfacing requires MoM designs which entail the risk of metal ion release the method cannot be applied in cases of known metal allergy, hypersensitivity and should be avoided in patients with renal insufficiency [111, 112] and women of childbearing age [113]. This should also be considered in the selection of the femoral head diameter of conventional MoM hip prostheses [67].

3.5. Biomechanical loading conditions and testing

The knowledge of stress levels at bearing surfaces is fundamental for the prediction of wear behaviour of THA *in vivo*. The mechanical loads transferred from the pelvis to the femur during gait were measured and characterised by Paul in 1966 [114]. Paul identified a double-peak load curve that is still the reference for designing loading conditions for *simulator* wear testing of hip prostheses. ISO-14242 part 1 and part 3 standards have included the Paul curve in the set of wear test parameters. Considering the importance of wear processes, wear testing represents a fundamental step in the development of new hip prostheses designs. The test phase consists of two steps. In a screening phase the material combination exhibiting the lowest wear rate is determined, and in a second phase this combination is evaluated in the shape and size of the actual prosthesis in wear simulators [115].

Material	E in GPa	σ_y in MPa	σ_{uts} in MPa	ϵ_{max} in %	σ_f in MPa
Cortical bone	10-20		100-300	1-2	
PMMA* (bone cement)	3.3		80		
Stainless steel, type 316L	205-210	170-750	465-950		
CoCrMo (cast alloy)	220-230	450-530	655-890	11-17	207-310
CoCrMo (wrought, low C content)		875-995	1320-1450	19-26	670-800
CoCrMo (wrought, high C content)		≈ 1175	≈ 1510	≈ 10	
Commercially pure Ti ($\leq 0.4\% O$)	105	692	785	15-24	
Ti-4Al-6V	110	850-900	960-970	10-15	610-625
Ti-6Al-7Nb	105	921	1024	10	500-600
Ti-35.5Nb-5.7Ta-7.3Zr	55-66	793	827	20	265
Ti-13Nb-13Zr	79-84	863-908	973-1037	10-16	500
Al ₂ O ₃	350-380	350*	400 (flexural)	-	-
ZrO ₂ -TZP	150-210*	650*	900*(flexural)	-	-
UHMWPE [#]	0.8-2	≈ 21	≈ 50	≈ 400	

Table 2: Mechanical properties of biomaterials used in THA in comparison with cortical bone as host tissue. E denotes Young's elastic modulus, σ_y denotes the yield stress (start of plastic deformation), σ_{uts} the ultimate tensile strength (maximal stress before rupture), ϵ_{max} the maximum elongation of the material before rupture and σ_f the fatigue strength defined as the maximum stress amplitude the material supports for at least 10^7 load cycles. The data are taken from [78] unless marked with * (taken from [73]) or # (taken from [80]). The data are subject to variations depending on details of fabrication techniques, carbon, oxygen and nitrogen contents and heat treatments.

Despite the importance of standardised wear testing, *in vivo* loading conditions may differ from the idealised double peak load curve. This has been demonstrated in case of ceramic testing, where microseparation conditions along the contact surfaces resulted in phenomena not predicted by the Paul curve [116]. Thus, in spite of an already well elaborated system of standards and methods unexpected wear conditions do still occur.

Summary of Chapter 3

- ▶ The stem may be fixed to the femoral bone by using acrylic bone cement (cemented stem) or by press fit (non-cemented stem).
- ▶ Cemented stems require a thin homogeneous layer of bone cement between stem and femoral bone in order to achieve uniform load transfer.
- ▶ In order to avoid cement fracture, cemented stems must be stiff and must exhibit a smooth surface. Non-cemented stems exhibit rough and frequently coated surfaces in order to allow ingrowth of newly-formed bone tissue.
- ▶ Non-cemented stems require biologically active bone tissue. Cementation is preferred in older patients with biologically less active tissue and in patients with bone defects.
- ▶ In theory, larger femoral head diameters improve the stability of the hip joint and increase the range of motion, but size is limited by anatomical constraints and the mechanical properties of the materials used for the acetabular cup.
- ▶ In hip resurfacing the trimmed femoral head is capped with a metal shell, which results in femoral head diameters that are larger than for most conventional hip prostheses. Since the outer diameter of the acetabular cup is limited by anatomy, the required mechanical stability of the thin acetabular cup can only be achieved by metal-on-metal (MoM) coupling.
- ▶ The theoretical benefits of large femoral head diameters cannot be realised in many cases due to effects very likely caused by release of metal ions and wear debris.

4. Tribology of hip joint prostheses

4.1. Wear, wear processes and lubrication conditions

Wear is recognised as the most important limitation to long term stability of hip devices. Great attention is devoted to tribological aspects of THA [115, 117, 118]. Wear occurs when two surfaces in contact are subjected to a relative motion and material is released. The presence of a lubricant film in the contact region can mitigate surface damage. Wear depends on three factors:

1. the *load* compressing the two surfaces and determining their contact stress,
2. the *relative motion* that continuously modifies the location and extent of the contact area,
3. and the *lubricant* interrupting the direct contact of the two surfaces.

Different wear processes are distinguished [119-121]:

- *Adhesive wear* can be described as plastic deformation in very small areas of the surface layers. This results in increasing surface roughness and the creation of protrusions above the original surfaces. In THA this condition is given in the case of UHMWPE wear.
- *Abrasive wear* occurs when a hard rough surface slides across a softer surface and the softer material is abraded by the microscopic asperities on the harder surface.
- *Third body wear* is a particular case of abrasive wear caused by hard particles of a third material entrapped on the surface of the softer material. Its presence can cause damage even of the hard surface. Such a situation may be created after revision of a fractured CoC prosthesis, when residual ceramic fracture debris may cause massive wear on the replacement femoral head made of steel and a UHMWPE acetabular liner [122].
- *Surface fatigue* occurs when the surface is weakened by cyclic loading, and fatigue wear produces wear particles that are detached by cyclic crack growth from surface microcracks.
- *Corrosion related wear*, or tribocorrosion, is a material degradation process due to the combined effect of corrosion and wear, especially when friction destroys an oxide passivation layer and exposes fresh material to corrosion thereby creating new oxide on the surface which is then rubbed off again [123].

Lubrication is generally defined as the means of controlling friction and wear of interacting surfaces in relative motion under load [124]. The type of contact between the surfaces and the distribution of the lubricant in between them determines the efficiency of lubrication. The lubrication conditions can roughly be classified by three lubrication regimes as illustrated in Figure 7 [94, 121, 124]:

- *Boundary lubrication*: The interaction between the surfaces takes place over extended areas. This occurs in hard-soft couplings, when one surface is deformable and the other one is not.
- *Mixed lubrication*, also known as elastohydrodynamic lubrication: direct contact between articulating surfaces is limited to small regions. This occurs when at least one surface features some asperities allowing for penetration of a fluid lubricant forming a nearly complete layer.
- *Fluid-film lubrication*: the surfaces are completely separated and the load is fully supported by the fluid film of the lubricant. This configuration occurs in hard-hard couplings between non-deformable well-polished surfaces with optimal clearance².

Manufacturing technology plays a key role in achieving a low residual surface roughness and hence controlling clearance.

The desirable situation is fluid-film lubrication, due to a complete separation of the surfaces, which can be realised most easily in hard-hard tribological couplings. The use of a rather soft material, such as UHMWPE, coupled with either ceramic or metal, limits the regime of lubrication to the boundary condition. In this case, the wear of the soft material cannot be avoided. Technical improvements, such as crosslinking of UHMWPE result in a harder material and may improve lubrication conditions. The MoM coupling is much harder than MoP, but still softer than CoC. It is difficult to achieve an optimal surface finish for the MoM pairing and residual asperities favour the development of a mixed lubrication regime [125].

The best scenario is the fluid-film lubrication regime producing the lowest wear amounts. It can be realised

² Clearance means the distance between the articulating surfaces and defines the thickness of the lubricating fluid film. It is the difference between the diameters of the acetabular cup liner and the femoral head and therefore depends strongly on the achievable surface roughness and the fabrication tolerances for both components.

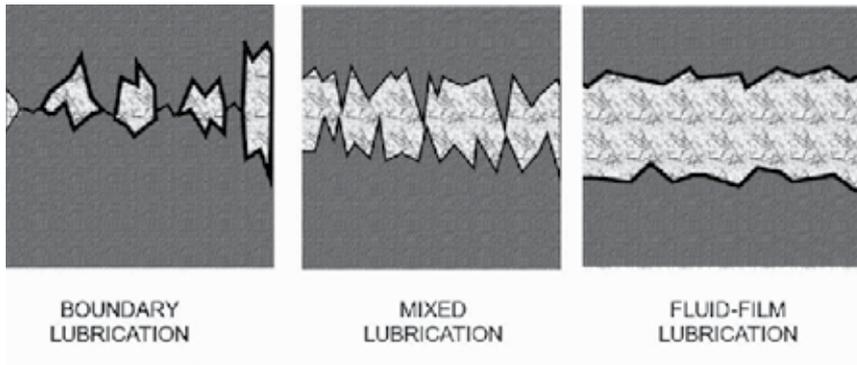


Figure 7: The lubrication regimes shown as a magnification of the contact point between the two coupling surfaces (e.g. the femoral head/liner (acetabular cup) contact).

with a CoC hard-hard pairing due to the extreme hardness of ceramics and the very low residual surface roughness that can be achieved.

CoM bearings feature a ceramic femoral head with an outstanding low surface roughness, and a hard metal acetabular cup with a rougher surface. Therefore, wear proceeds in two phases. In an initial *running-in period* metal asperities are polished away by the harder ceramic, and more wear can be expected than in CoC articulations, but less than in MoM devices. The following *steady-state phase* is characterised by a constant wear rate which is significantly lower than in MoM devices,

where both bearing parts exhibit the same hardness, which makes polishing during the running in phase less efficient, because there is no clear sacrificial surface [126].

In summary, CoC is the best choice for minimizing wear due to highest hardness, highest scratch resistance, high wettability and good lubrication. MoM bearings are however the only option for producing femoral heads with diameters above 38-40 mm [94]. A combination of both materials in CoM prostheses represents a good trade-off between low wear and articulation size [126, 127].

4.2. Tribological material combinations in total hip arthroplasty

In the following Table 3 a concise overview is given on the tribological couplings used in THA.

Combination	Pros	Cons	Remarks
MoP (UHMWPE)	<ul style="list-style-type: none"> • Most commonly used, longest experience and follow-up (> 40 years in some cases) • Most economic device 	<ul style="list-style-type: none"> • High polyethylene wear volumes • Late aseptic loosening possible in response to exposure to polyethylene wear debris • Insufficient longevity for patients younger 60-65 years 	<ul style="list-style-type: none"> • Wear rate \approx 0.1 mm/year [128]
MoP (crosslinked UHMWPE)	<ul style="list-style-type: none"> • Expectation of drastically reduced wear rate and reduced risk of aseptic loosening 	<ul style="list-style-type: none"> • Introduced 1998 [14] follow-up period still limited (< 10-15 years) 	<ul style="list-style-type: none"> • 0.01-0.02 mm/year [14]
MoM	<ul style="list-style-type: none"> • Low volumetric wear rate • Improved joint stability due to larger femoral head diameters (28 - 60 mm) • Low rate of aseptic loosening 	<ul style="list-style-type: none"> • Risk of metallosis, metal allergy and hypersensitivity • Unknown long-term effects of exposure to metal ions 	<ul style="list-style-type: none"> • 0.005 mm/year [14] • Used since the 1950s, reintroduced 1988 [14], FDA approval only in 1999, now used in about 1/3 of all THA procedures in the US [129].
MoM HRS	<ul style="list-style-type: none"> • Femoral bone conserved; facilitates revision surgery • Improved joint stability and range of motion due to larger femoral head size • Low volumetric wear rate 	<ul style="list-style-type: none"> • Surgically more delicate • Elevated risk of femoral neck fracture • Risk of excessive wear • Pseudotumours observed • Increased blood metal-ion concentrations • Possibly enhanced toxicity due to nanotoxic effects of nanosized wear debris 	<ul style="list-style-type: none"> • 0.005 mm/year [14] • Not recommended in case of renal insufficiency [112] or in women in childbearing age [113] • Hip resurfacing requires large femoral head diameters; this is only possible with MoM
CoP	<ul style="list-style-type: none"> • Wear rate reduced compared to MoP • Elasticity of UHMWPE mitigates fracture risk of ceramic femoral head 	<ul style="list-style-type: none"> • Still residual polyethylene wear with late risk of aseptic loosening 	<ul style="list-style-type: none"> • 0.03 – 0.1 mm/year [130, 131] • 0.01 mm/year with vitamin E stabilised XLPE
CoM	<ul style="list-style-type: none"> • Improved joint stability and range of motion due to larger femoral head size of up to 38-40 mm possible • Low volumetric wear rates 	<ul style="list-style-type: none"> • Catastrophic fragile fracture of ceramic components • No experience with metal-ion release; debris even smaller than with MoM (6-7nm) [127] 	<ul style="list-style-type: none"> • Reduced <i>in vitro</i> wear rates [132, 133] • CoCrMo acetabular cup components provide stability for larger ceramic femoral heads
CoC	<ul style="list-style-type: none"> • Highest wear resistance and lowest wear rate • Weak tissue interaction with ceramic wear debris [134] • Low risk of aseptic loosening [28] • High scratch resistance • Very low surface roughness • Good lubrication conditions • High wettability 	<ul style="list-style-type: none"> • Catastrophic fragile fracture of ceramic components • Tiny fracture debris may cause third body wear after revision • Squeaking affects 1 -20% of the patients [28] at least temporarily • Most expensive device 	<ul style="list-style-type: none"> • < 0.003 mm/year [14] • Used in Europe since the 1980s; FDA approval only recently [135] • With latest generation of ceramics head diameters up to 40 mm can be realised [24, 132, 133] • Head failure rates now below 0.02-0.004% [28]

Table 3: Summary of the most important advantages and disadvantages of tribological couplings in THA.

Table 4 gives some recent figures concerning the use of specific tribological couplings from the national arthroplasty registers in Denmark, Norway and England & Wales in 2010 [136-138]. It indicates significant regional differences, which do not necessarily reflect the situation in other countries. As shown in Table 4 it is evident that the MoP coupling is the most applied with an increasing use of cross-linked UHMWPE. In Norway CoP has gained popularity as an alternative. CoC and MoM (including hip-resurfacing devices) play a minor role compared to the use of polymer couplings.

4.3. Corrosion and wear effects

The human body is a chemically very aggressive environment and foreign implant materials are permanently exposed to extracellular tissue fluids, which are aqueous solutions of complex organic compounds, oxygen, sodium, chloride, bicarbonate, potassium, calcium, magnesium, phosphate, amino acids, and other corrosive species, such as peroxides [73, 139]. Only gold and a few other metals like platinum are electrochemically sufficiently resistant to corrosion under such conditions, but they are mechanically not strong enough for orthopaedic applications. From an electrochemical point of view, all metals currently used for orthopaedic implants can be oxidised by body fluids and become protected against further corrosion by an oxide layer. In electrochemistry this effect is called passivation [73, 76, 140]. It is the ability of a metal to form an ultra-thin surface layer of corrosion products, usually insoluble oxides, on the its surface,

acting as a barrier to further oxidation. Stainless steels, cobalt-chromium-molybdenum alloys (CoCrMo), pure titanium (Ti) and titanium alloys feature such passivation capabilities. Their corrosion resistance depends on the stability of the oxidised surface layer. Any chemical or mechanical breakdown of this layer causes localised corrosion phenomena such as crevice, pitting, fretting or tribocorrosion [73, 76, 140].

Compared to stainless steel and CoCrMo alloy the adhesion of the oxide layer on Ti-alloys is the weakest. Therefore Ti-alloys are suitable for manufacturing of structural components but they cannot be employed for tribological applications since the oxide layer would be quickly scraped off [73, 76, 140].

Galvanic corrosion occurs when two different metals are in electrical contact with each other and are immersed in a common electrolyte. This kind of corrosion may be an issue for modular prosthesis, wherever components made of different metals are put in contact e.g. at taper junctions between stem and femoral head.

Corrosion results in release of ions and/or debris particles especially when passivation layers are scraped off from surfaces exposed to wear or fretting. These corrosion products may cause adverse tissue reactions, which are among the most prominent clinical complications and may compromise the outcome of THA.

These biological consequences are described in further detail in chapter 6.1.

Couplings \ Country	Denmark	Norway	England and Wales
MoP	71%	44%	64%
CoP	8%	46%	11%
MoM	4%	2%	8%
CoC	3%	4%	13%
Others / Data missing	15%	4%	4%
Source	[136]	[137]	[138]

Table 4: Use of different tribological couplings in some European countries in 2010 according to national arthroplasty register data.

Summary of Chapter 4

- ▶ A theoretical understanding of the tribology of artificial hip joints is essential for reducing wear and corrosion of hip prostheses.
- ▶ The tribological performance of hip prostheses can be characterised by the wear rate in millimetres or cubic millimetres of material lost from the surfaces per year.
- ▶ Metal-on-polymer (MoP) and ceramic-on-polymer (CoP) prostheses exhibit the highest wear rates. If the UHMWPE is replaced by the highly crosslinked UHMWPE (XLPE), the wear rate can be reduced by a factor of 10.
- ▶ Metal-on-metal (MoM) and ceramic-on-ceramic (CoC) have wear rates that are again a factor of 5 to 10 lower than those of metal-on-highly crosslinked UHMWPE
- ▶ Ceramic material couplings have the most favourable tribological properties.

5. Clinical aspects

5.1. Indications for total hip arthroplasty

The most common medical indication for THA is advanced osteoarthritis, a degenerative joint disease, leading to pain, loss of mobility and disabilities. *Primary* osteoarthritis is related to ageing, as the cartilage becomes less resilient, and to heavy physical activity. A hereditary component may also be involved. When the disease can no longer be managed by moderate physical activity, weight reduction, manual therapy or medication with analgesics THA has to be envisaged. Osteoarthritis accounts for over two thirds of the THA procedures [141].

The second most common indication is rheumatoid arthritis, which is a systemic inflammatory disorder probably caused by a systemic autoimmune response. Severely affected joints are candidates for joint arthroplasty when medication with analgesics, anti-inflammatory drugs and steroids can no longer control the symptoms.

Other indications are the reconstruction of dysplastic hip joints or following bone defects caused by accidents or diseases, avascular necrosis (necrosis of bone tissue due to interruption of blood supply), and other rare diseases that compromise hip function [3, 7].

5.2. Choice of prosthesis

The first decision to be made is between a cemented or uncemented hip prosthesis [4]. Nowadays cementation is mainly used in patients aged above 60-65 years with compromised bone quality. Uncemented prostheses are preferred for younger patients with good bone quality since the stem and the acetabular cup shell are pressed fitted in the cavities prepared in the femur and the pelvis, respectively, and the bone must withstand the forces exerted by the press fit (see chapter 3.1).

Hip prostheses are available in various dimensions, geometries and with different diameters of the femoral head. Combinations should be used that best allow the reconstruction of the proper physiological function of the hip joint considering the anatomic situation of the patient. Bone shall be conserved as much as possible and geometries should be preferred allowing for this. For the femoral component a decision is required whether to apply a hip-resurfacing system, as advocated by some surgeons for younger patients [29, 31], or whether to use conventional THA systems with a stem.

An important decision concerns the material combination for the load bearing surfaces (see Table 3).

Surgeons frequently have their own material preferences and consequently individual experience profiles. Patients may influence the choice of the material combination by selecting the surgeon of their choice. There are contraindications for metal-on-metal devices [2] such as known metal allergies or hypersensitivity [30], also the usually increased metal ion concentrations in the blood [13, 14] have to be considered as risk factors, especially in patients affected by renal insufficiency [111, 112] or in women of childbearing age [113].

The large variety of components on the market is, to a certain extent, a necessity to find solutions matching patient specific requirements.

5.3. Surgical aspects

There are several surgical approaches for THA, which differ in the operative access to the hip joint. They have different implications concerning the preservation of the attachment of muscles to the joint [142] and they have different surgical risk profiles e.g. concerning possible nerve damage and immediate postoperative joint stability. The *traditional* surgical techniques – transtrochanteric approach (Charnley), anterior approach (Smith – Peterson), lateral approach (Haringe), anterolateral approach (Watson – Jones), posterior approach (Gibson) – have been recently compiled by Malhotra [143].

Preoperative planning, experience, practice and manual skills of the surgeon are a key factor in achieving good results [3, 12, 144, 145]. This holds especially for the more complex and difficult hip resurfacing [2, 12, 32]. Inexperienced surgeons may have difficulties achieving accurate positioning of the acetabular cup and the femoral head and deviations from the accurate position will lead to accelerated wear, edge loading and an increased risk of periprosthetic femoral neck fracture [32]. Femoral neck fracture alone accounts for about 40% of all revisions in hip resurfacing [12].

Gross et al. [58] demonstrated this by reporting their experience with 373 metal-on-metal hip-resurfacing arthroplasty procedures. An analysis of prostheses' survivorship after 7 years for the first 100, the second 100 and all further surgeries shows an increase of the survivorship from 93% to 98%. Surgeon-related data are rarely made available and would not even be necessarily conclusive since in hospitals more experienced surgeons usually deal with the more difficult cases.

Computer-assisted surgery [146] might help to improve the overall outcome but also use of this technology

has to be learnt, and surgeons have to be capable of performing well when, for whatever reason, such technology fails or is not applicable.

A new approach is *minimally invasive* hip surgery. Whereas minimal invasiveness may have its benefits in a lot of surgical procedures at the moment it appears that patients cannot benefit from it in THA [147]. Fehring et al. [148] reported of “*catastrophic complications of minimally invasive hip surgery*”. It is evident from the size of the implants and the delicate task to reconstruct a physiologically and biomechanically fully operative joint that full visualization of the anatomical landmarks in the operation field is important [3, 143]. The use of minimally invasive techniques is a matter of controversy [148, 149] since one should resist trying to realise short-term benefits at the expense of long-term outcome [150] since malpositioning of the artificial hip joint and soft tissue damage cannot be excluded. This does not contradict that especially gifted surgeons may achieve competitive results even by minimally invasive surgery.

5.4. Clinical results and possible complications

Patients expect from THA to recover pain-free mobility and to overcome restrictions in their private and professional activities. In this respect THA is a very successful treatment, since more than 80% of the patients are satisfied with the result after surgery [38, 151]. Nunley et al. [39] conducted a survey among 806 patients, followed up for a mean of (2.3 ± 0.8) years after surgery and having a mean age of (50 ± 7) years at the time of surgery. 94% of these patients returned to their usual job after surgery, and the number of patients with hip-related job restrictions dropped from 20% before to 3% after surgery [39].

The long-term clinical outcome of THA is determined by the materials and components used, by the surgeon and the patient himself. Durable solutions of THA can only be achieved if the surgeon manages to reconstruct the hip joint in a way that it can fulfil its proper function, and if a stable fixation of all components can be achieved. This requires a high degree of skill and practice.

Deviations from the perfect biomechanical alignment will increase hip loads and result in higher loosening rates [3, 4]. This may sometimes be compromised by the health conditions of the patient at the time of surgery. The mechanical load profile after surgery must avoid overload peaks or permanent overloading. Therefore, patients must be instructed adequately during rehabilitation [152]. Hip load is increasing linearly with body weight, and thus obesity is considered a risk factor that may compromise long-term performance of THA. However, with increasing walking speed, hip load increases exponentially [3], which makes THA more demanding for younger patients. Especially, frequent high peak loads

as they occur e.g. in contact sports challenge the clinical outcome of THA. Wroblewski et al. [16] emphasise that patients must be aware that “*operation of total hip arthroplasty marks the beginning and not the end of treatment*”, and this treatment should last for up to 200 million gate cycles in a young patient [94].

High rates of infection of up to 11% have been reported in the 1950s and 1960s [3]. Infection is still a serious complication, but not frequent. In 2003, surgery-related risks within 90 days after primary THA have been reported as 1.0% for mortality, 0.9% for pulmonary embolus, 0.2% for wound infection. They are higher after revision surgery with 2.6%, 0.8%, and 0.95%, respectively [153].

Dislocation, i.e., the physical disconnection between the femoral head and the acetabular cup, is a common complication in the first weeks after surgery (see Figure 8), when tissue strength has not yet been recovered and especially when small diameter femoral heads are used. The rates for dislocation within 90 days after THA are 3.1% after primary THA and 8.4%, after revision surgery. More experienced surgeons achieve lower dislocation rates [153]. Unequal leg length can be caused by improper selection of the stem dimensions or problems occurring during surgery. Temporary pain may occur after THA since the muscles of the compromised hip before surgery have to readapt to the anatomical normal condition that shall be recovered [3]. Chronic pain can be caused by nerve damage during surgery or by muscles rubbing against components of the prosthesis [142].

Breakage of stem has become a rare issue. It was observed more frequently in the past with cemented stems. Oscillating gait loads led to fatigue failure, when the distal part was well fixed with cement, whereas the proximal part was loose. These problems have been solved by improved cementing techniques [3].

The most frequent reason for revision surgery is the loosening of the stem and/or the acetabular cup, i.e., the loss of contact between bone and implant. The reasons are various, such as a misalignment of the cup that may increase hip loads and promote femoral loosening. An insufficient contact between bone and implant may locally cause *stress shielding*, because the implantation of a femoral stem results in a load transmission, which differs from the natural physiological loading conditions in the femur [109]. Where the bone-implant contact is weak, an adaptive remodelling occurs [107], and bone is locally resorbed where it no longer carries load.

The most important problem is *aseptic loosening*, which has been traced back in MoP prostheses to an inflammatory response to polyethylene wear debris. As polyethylene wear rates of 0.1 mm per year are to be considered normal, exposure to wear debris persists during the whole lifespan of the component. Wear particles larger than a certain critical size (0.2 - 0.8 μm [154]) are phagocytised by macrophages which initiates

an interleukin-induced activation of osteoclasts leading to periprosthetic osteolysis [18]. Aseptic loosening can affect patients even decades after surgery following a long period of subtle progression of periprosthetic tissue destruction in response to exposure to wear debris. Even asymptomatic patients may be candidates for revision surgery if there is radiological evidence for wear-induced abnormalities (see Figure 9). Since aseptic loosening has not been observed or reported as an important failure mechanism in first generation MoM implants [53], metallurgical improvements of CoCrMo alloys and reduced fabrication tolerances for prosthetic devices motivated the reintroduction of MoM hip implants.

While the risk of osteolysis is low with MoM hip implants, patients with such devices have permanently raised concentrations of chrome and cobalt metal ions in their blood, which was in general not associated with complications in the past [13]. Recently, in many patients with hip-resurfacing THA abnormal periprosthetic soft-tissue reactions have been observed [2, 42, 155]. These are sterile inflammatory lesions found in the soft tissues surrounding MoM hip implants with still unclear pathogenesis [155]. Since biopsy of such lesions is difficult to distinguish from necrotic tumour tissue, they were labelled as *pseudotumours*, but also other descriptions have been used in literature such as bursae, cysts or inflammatory masses [42].

An agreement on an unambiguous nomenclature would be desirable and also a systematic investigation in conventional MoM THA patients especially with large diameter femoral heads. At the moment there is no information available whether the early failure of conventional MoM prostheses with large femoral head diameters is also related with the formation of pseudotumours.

Pseudotumours may cause severe symptoms that frequently require revision surgery and also compromise the success of revision surgery [42]. In pseudotumour tissues tiny metal debris particles have been found [156] and their incidence is accompanied by increased metal ion concentrations in blood serum which points to excessive wear as possible reason [42, 54, 157]. However, available information is still limited and the impact on the management of patients with hip-resurfacing implants is a matter of controversy. Langton et al. [54] do not believe that the vast majority of resurfacing patients will experience severe soft-tissue reactions. These authors estimate that less than 1% of patients will develop reactions to *normally wearing* bearing surfaces, and Gross et al. [58] report that adverse reactions to wear debris are rare events with a probability of 0.5% after 6 to 11 years follow-up. Thus the problem would be confined to excessive wear. However, Matthies et al. [155] studied the effect of adverse cup position and in consequence increased wear rates and elevated metal-ion concentrations in blood, and could not attribute the occurrence of pseudotumours to these parameters. In their study also two thirds of the patients with well positioned

acetabular cups showed pseudotumours. Therefore, it is suggested that patient susceptibility would likely be more important [155] and that there may be an appreciable number of asymptomatic pseudotumours eventually becoming symptomatic [42].

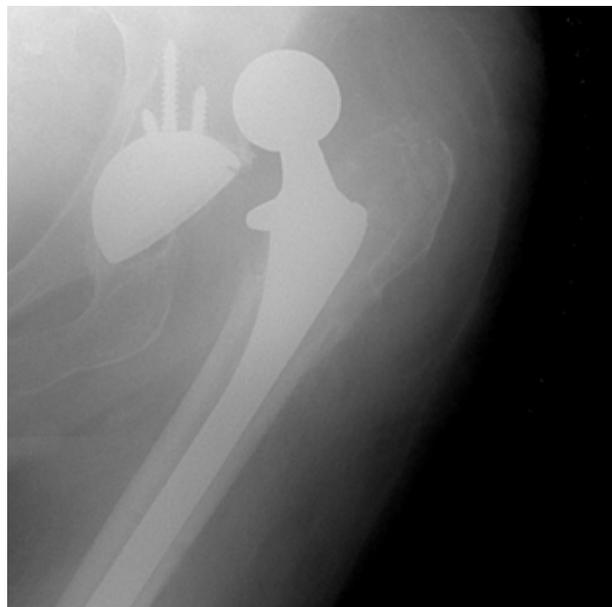


Figure 8: Dislocation of hip prosthesis



Figure 9: Focal osteolysis (see arrow) in proximal femur caused by polyethylene wear particles; eccentric position of femoral head within cup is consistent with polyethylene wear.

Summary of Chapter 5

- ▶ The most common medical indications for THA are osteoarthritis and rheumatoid arthritis.
- ▶ The proper choice of the type and design of prosthesis are essential for the long-term outcome of THA.
- ▶ Minimally invasive surgery is not yet sufficiently developed to ensure the same long-term benefits as obtained with the various commonly applied surgical methods.
- ▶ The long-term outcome of THA depends on factors that are related with the prosthesis that has been implanted. Furthermore, the expertise and practice of the surgeon are of utmost importance, but also the health status of the patient and his postoperative physical activities.
- ▶ The most important complication, which limits the lifespan of metal-on-polyethylene (MoP) prosthesis, is aseptic loosening due to an inflammatory reaction against polyethylene wear debris that can occur even many years after surgery.
- ▶ Aseptic loosening is much less frequent in patients with metal-on-metal (MoM) and ceramic-on-ceramic (CoC) prostheses.
- ▶ Adverse tissue reactions, such as the formation of pseudotumours of unclear pathogenesis, are frequent complications in patients with hip-resurfacing devices.

6. Wear, corrosion and potentially related cancer risk

6.1. Exposure to wear debris and corrosion products

6.1.1. Origin and dissemination of wear debris

Currently used prosthetic materials are the result of a long optimisation and selection process [73, 80] and revolutionary improvements are unlikely in the near future. For some recent innovations, such as the introduction of crosslinked UHMWPE, the follow-up periods are still too short to assess their long-term advantages over hitherto used UHMWPE in clinical application.

Under the loading conditions prevailing in articulating surfaces of artificial hip joints polyethylene debris is created with a typical size of 0.2 μm to 5 μm , whereas metallic debris released from MoM prosthesis exhibits typically a size of 50 nm [159, 160].

Debris particles can also be generated and released from surfaces not designed for tribological applications, such as conical taper *junctions* (Figure 10) or in case of micromotion between stem and bone or stem and cement along the stem surface and analogously on interfaces on the acetabular side that should not be subjected to movements under normal conditions [93, 161].

Whatever materials are used, the dissemination of wear particles to liver, spleen or abdominal lymph nodes after hip or knee replacement is a common feature [161]. But

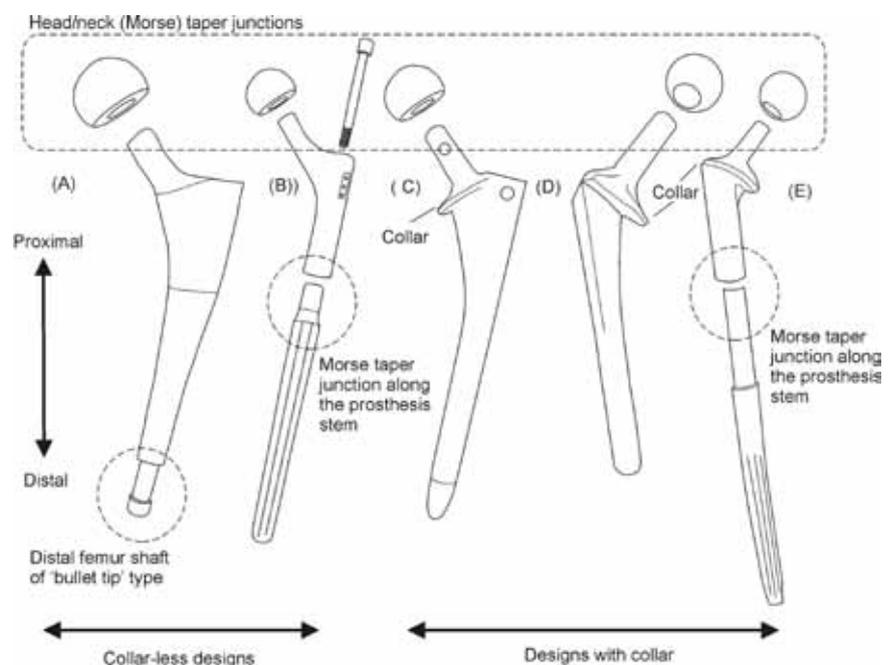
usually size and concentration of such disseminated debris particles appears to be pathologically not relevant [161]. The disseminated particles found by Urban et al. [161] were mostly *not* generated from articulating surfaces. They had been generated by wear of metal against bone cement, metal against bone or in taper junctions (see Figure 10) between femoral head and stem, or by micromotion between shell and liner of the acetabular cup. Since femoral components with large head diameters increase the mechanical stress at the taper junction between stem and head, such geometries could also increase the release of small metallic debris from these areas [2]. This implies that even for CoC bearings a certain amount of metallic debris particles can be disseminated in the body.

6.1.2. Aseptic loosening

Polyethylene wear limits the lifespan of Charnley-type hip prostheses. It is the dominating long-term complication in THA and the main reason for aseptic loosening [19]. Polyethylene wear debris starts a subtle inflammatory response, which becomes more pronounced as osteolysis progresses [18, 154].

Polyethylene particles above a critical size of about 0.2 μm to 0.8 μm can be phagocytosed by macrophages [154] and initiate a series of physiological reactions illustrated in Figure 11, which finally lead to osteolysis and aseptic loosening of the implant. This particle-induced periprosthetic osteolysis may affect both the acetabular and the femoral prostheses' components.

Figure 10: Small debris can also be released from conical taper junctions in use to join the femoral head with the femoral stem or to assemble stem components when patient specific requirements have to be met. [158].



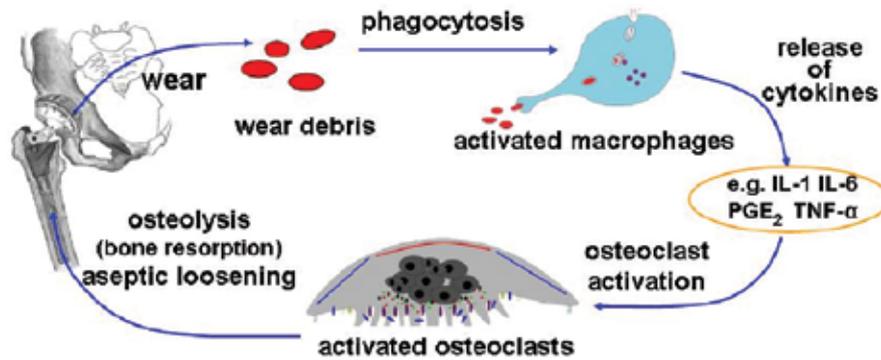


Figure 11: Simplified schematic of inflammatory response triggered by wear debris leading to bone resorption and aseptic loosening

6.1.3. Size and size effects of wear debris

In order to avoid periprosthetic osteolysis ascribed to exposure to polyethylene debris MoM devices were reintroduced in the late 1980s, and wear resistant CoC bearings were developed. [30]. As can be recognised from Table 5 the wear volumes realised with MoM combinations are much lower than those with MoP and CoP devices. However, metal debris is much smaller than polyethylene debris and therefore, in spite of drastically reduced wear volumes, in a given time period the number of metallic particles is much higher than the corresponding number of polyethylene. A quantitative analysis of wear particles obtained by simulator testing is becoming increasingly difficult with decreasing particles size because the particles have to be collected and isolated from the lubricant while preserving their characteristic properties and size distribution [162]. The simulator data are however supported by analysing periprosthetic tissue samples. In biopsy samples, *nanoparticles* of 10 nm to 50 nm size were found in phagosomes of macrophages [156]. The particles were rich in Cr and free of Co [156, 160].

Due to its small size, metallic wear debris may be internalised by cells in different ways than polyethylene particles, e.g. by pinocytosis instead of phagocytosis, which likely changes its biological effect [162]. With first and second generation MoM prostheses no significant osteolysis and aseptic loosening has been observed or reported [12, 163]. This has been interpreted as the absence of pathologically relevant toxicity [13]. Individual cases of osteolysis had been explained however by cytotoxicity of small metallic wear debris [14, 164].

The high mobility of small metallic debris particles and the damage they may cause was known before they had been classified as nanoparticles (< 100 nm) and a lot of research had started in *nanotoxicology*. As early as 1993, Haynes et al. [165] found that CoCr nanoparticles

are toxic to macrophages. Case at al. [166] reported on small metallic wear debris particles infiltrating periprosthetic tissues like regional lymph nodes, and it was supposed that high doses of CoCr wear particles could cause cytotoxicity and genotoxicity and were responsible for tissue necrosis in bone marrow, periprosthetic connective tissue and in lymph nodes [166]. Allen et al. [167] found that CoCr nanoparticles affect the growth of osteoblasts and could therefore interfere with bone formation [168]. Papageorgiou et al. [169] found that the toxicity of CoCr-alloy particles would be reduced after such particles had been phagocytosed by macrophages. It has been hypothesised that this effect is brought about by a modification of the particles surface that reduces further ion release. However, the authors studied this effect with particles of $(2.13 \pm 0.9)\mu\text{m}$ in diameter that are not representative for those generated by MoM hip prostheses.

6.1.4. Nanoparticles and metal ions from MoM prostheses

As can be seen from Table 5 metallic wear debris is significantly smaller than 100 nm. Current problems with MoM prostheses emerge in a period of increasing knowledge on nanotoxicology. The nanotoxicity of nanosized wear debris in MoM THA has recently been reviewed by Polyzois et al. [171] and Gill et al. [172] (see also citations there). It is possible that nanosized CoCr wear debris can induce DNA damage and lead to chromosomal aberrations [172], but knowledge is still incomplete, fragmented and insufficient for a risk-benefit analysis of MoM prostheses. Moreover nanotoxicity is usually studied with commercially available nanoparticles or nanoparticles synthesised in the laboratory instead of using particles from hip simulator experiments that may significantly differ in size distribution and morphology [173].

Combination	Wear volume per 10 ⁶ wear cycles	Particle size	Number of particles per 10 ⁶ wear cycles	Source
MoP (UHMWPE)	(40 - 80) mm ³	(0.1 - 8) μm	5 · 10 ¹¹	[127]
MoP (crosslinked)	(5 - 40) mm ³			[127]
MoM (high C > 0.2%)	(0.03 - 0.04) mm ³	(25 - 36) nm	4 · 10 ¹²	[126]
MoM (low C < 0.07%)	(0.3 ± 0.1) mm ³		6 · 10 ¹³	[126]
MoM	(1.2 ± 0.5) mm ³	(14 ± 0.7) nm (30 ± 2.) nm		[127] [170]
MoM		≈ 15 nm Cr ₂ O ₃ 30 - 80 nm CoCr		[160]
CoP (zirconia)	(31 ± 4) mm ³	(0.3 ± 0.2) μm (85%) 30% of mass > 10 μm		[170]
CoM	≈ 0.01 mm ³	(6.1 ± 0.4) nm		[127]
CoC (alumina)	(0.05 ± 0.02) mm ³	(9 ± 0.5) nm		[170]

Table 5: Wear volumes and particle size for various material combinations determined by hip simulator testing. The wear volume and the number of particles is given for one million simulated gait cycles.

Exposure conditions	Metal-ion concentrations		Source
	Chromium	Cobalt	
Control group without medical implants	< 0.25 μg/L	0.25 μg/L	[179]
Extreme value 3 months after hip resurfacing	46 μg/L	49 μg/L	
Values of the same patients after 2 years	2.7 μg/L	1.6 μg/L,	
Concentrations considered normal in patients with conventional MoM THA	1 - 5 μg/L	1 - 5 μg/L	[179, 181]
Concentrations associated with excessive wear in hip resurfacing THA	17 μg/L	19 μg/L	[182]
Hip resurfacing patients with pseudotumours	(4 - 23) μg/L	(5 - 23) μg/L	[42]
Hip resurfacing patients, asymptomatic	(1 - 9) μg/L	(1 - 9) μg/L	[180]
Patients with conventional MoM THA	(0.1 - 3.0) μg/L	(1 - 5.2) μg/L	
UK limits for professional exposure to hard metals MAC values	17 μg/L (erythrocytes)	5 μg/L (whole blood)	[2]

Table 6: Overview of metal-ion concentrations in blood of conventional MoM THA and hip-resurfacing MoM THA patient groups.

Already before hip-resurfacing THA was introduced, significantly increased chromosomal translocations in peripheral blood lymphocytes were reported in patients with CoCr-alloy implants that were in place for decades before revision surgery was required [174]. Chromosomal changes in bone marrow cells have been ascribed to the presence of metal implants [175]. Moreover, it was stated that corrosion products of CoCr alloy can induce osteolysis [176, 177]. The data of Andrews et al. [178] suggest that increased Co and Cr ion concentrations may affect the activities of osteoblasts and osteoclasts in a way that may explain aseptic loosening. However,

permanently raised concentrations of chrome and cobalt metal ions in MoM patients are known for a long time without being associated with a significant risk of osteolysis [13].

Table 6 summarises some examinations dealing with chromium and cobalt-ion concentrations in blood. In patients with conventional unilateral and bilateral MoM THA and in patients treated by resurfacing THA, the evolution of Co, Cr and Mo ion concentrations was compared over a period of two years [179]. The concentrations in patients with conventional THA exhibited a maximum

in the observation period and decreased in the second year. In patients treated by hip resurfacing a progressive increase of metal-ion concentrations in the whole observation period was reported [179].

However, it seems to be necessary to control metal-ion concentrations in MoM patients periodically, as one patient exhibited extremely high values three months after surgery, which decreased to “normal” values two years after surgery without clinical or radiographic evidence for implant loosening [179].

The values found by Kwon et al. [42] in hip-resurfacing patients with pseudotumours exhibit a large range slightly overlapping with the range considered “normal” for MoM patients. Moreover, the metal concentrations in patients with conventional MoM and hip-resurfacing devices were found not to be significantly different [180]. As shown in Table 6 only the measured maximum concentrations are higher in hip-resurfacing patients. It is interesting to note that the maximum Co-ion concentration tolerated in the UK for workers professionally exposed to hard metals (MAC) is in the same range (Table 6). In individual patients these values may however be exceeded.

No clear answer can be given concerning long-term risks related to MoM hip prostheses, but it is argued that higher concentrations of metal ions in patients bearing MoM hip joints as compared to patients with MoP or CoC implants might indicate a higher risk of complications increasing over time after implantation [14]. The elevated metal-ion load may cause continued stress on kidneys, thus MoM prostheses cannot be recommended for patients with chronic renal disease [111, 112] and women of childbearing age [113].

There is still no conclusive evidence whether hypersensitivity against metallic implant components does affect the performance and survivorship of hip prostheses [14]. Lymphocytic infiltration in tissue around second generation MoM implants appears typical for this kind of hip prostheses [183, 184]. For the first generation of MoM hip prostheses, Evans et al. [185] found a metal sensitivity in 9 out of 14 patients with aseptic loosening and concluded that it could be causal for loosening. However, it is difficult to diagnose metal hypersensitivity prior to THA because dermal metal sensitivity diagnosed by patch tests is not necessarily predictive for metallic prostheses [184, 186].

Ceramic wear particles have a typical size of 0.1 μm to 1 μm , but also a tiny mass fraction is released as nanoparticles with a size of 5 nm – 20 nm [184]. There are however no indications that ceramic wear debris could be responsible for aseptic loosening [134] or systemic toxicity [187].

6.2. Total hip arthroplasty and potential cancer risk

The evaluation of cancer risk related with THA requires a long follow-up of a large patient population. Most of the available studies are based on data from the Scandinavian arthroplasty registers [188-193] that have accumulated follow-up data on large patient populations. Most studies, including a recent meta-analysis [194], did not reveal an increased *overall* cancer risk in patients after THA. However, THA seems to affect the risk profile of cancer since the incidence of malignant melanoma [188, 189, 194], multiple myeloma, prostate and bladder cancer [189] appears to be slightly increased, whereas the incidence of stomach cancer [188] seems to be decreased compared with the general population. Olsen et al. [188] suggested that the reduced stomach cancer risk might be related to the use of antibiotics in THA patients that may eliminate helicobacter pylori, which is considered as a major risk factor in stomach cancer. Meyskens [195] pointed out that the increased incidence of melanoma in THA patients points towards an effect of metal release from implants since metals play a role in the pathogenesis of melanoma [195].

Only two studies compare cancer risk after MoM and MoP THA [190, 191]. The earlier study found that the cancer risk of patients after MoM THA is 1.2-fold that of patients with MoP THA. For leukaemia the risk in the MoM group was even 3.8-fold higher, but the authors [191] stated that this difference was still not statistically significant. This shows the difficulty to achieve sufficient statistical power even if well-developed arthroplasty registers can be consulted and linked to national cancer registers. The most recent investigation did not distinguish between different cancer types, but concluded that the cancer mortality in MoM patients is higher during the first 20 years after surgery than in MoP patients [192]. This underlines the difficulties to draw valid conclusions from the data available today.

The slight changes of the cancer risk profile that might so far be associated with THA will not change the medical indications for hip joint replacement since the benefits for the patients’ quality of life outweigh the marginal increase of risk for a few specific cancers.

Nevertheless, cancer risk is a topic that requires close observation since chromosome aberrations have frequently been observed in vitro as response to exposure to wear debris [171, 172, 196, 197].

Moreover disease caused by wear debris or metal ions may have long latency periods [144].

Additionally, Wagner et al. [193] found a significantly increased cancer risk after *knee* arthroplasty analysing all patients in Sweden that underwent *knee* surgery between 1975 and 2006.

This significant discrepancy of cancer risk between *hip* and *knee* arthroplasty, in which the same materials are involved, indicates that some elements in the possible relationship between joint replacement and cancer have

not yet been understood and deserve closer investigation. As the knee is the most loaded articulation of the body, overweight and obesity might also play a role in explaining this difference.

Summary of Chapter 6

- ▶ Release of polyethylene debris in the size between 0.1 and 8 μm may cause periprosthetic osteolysis and aseptic loosening of the stem or the acetabular component. It is the most important long-term complication with metal-on-polyethylene (MoP) prostheses.
- ▶ Wear, corrosion and fretting lead to a release of fine and even nanosized particles, that can be disseminated within the body, e.g. to liver and spleen.
- ▶ Metallic debris generated from metal-on-metal (MoM) prostheses is generally nanoparticulate ($< 100 \text{ nm}$) and may therefore exhibit enhanced toxicity.
- ▶ Metal concentrations in asymptomatic patients with conventional MoM and hip-resurfacing devices were found not to be significantly different. It is worth noting that similar values are tolerated in workers professionally exposed to metals e.g. in foundries.
- ▶ MoM patients with pseudotumours may exhibit significantly higher metal-ion concentrations than asymptomatic patients. However, the concentration ranges are overlapping. Therefore, measuring “normal” values is not sufficient to exclude the existence of a pseudotumour.
- ▶ Currently available literature gives no evidence for an increased overall cancer risk after THA, underlining the difficulties to draw valid conclusions.

7. Economic and regulatory issues

7.1. Health economics aspects

It is generally accepted that primary THA is a cost-effective medical treatment and that the cost for quality-adjusted life years – QALYs – compares favourably with other health interventions [6, 7, 100, 198]. The economics of revision THA have also been investigated. As discussed before in detail in Chapter 5, revision THA is technically and surgically more complex, more expensive and less successful in restoring long-term pain-free joint function compared to primary THA [37, 110]. It is, nevertheless, considered cost-effective. However, the growing number of primary THA procedures and patients' increased life expectancy will lead to an increasing number of patients that will outlive their first hip prosthesis. Therefore, an increasing number of revision THA procedures will be inevitable in the future, and this may increase stress on health care budgets [37, 141, 199].

It is therefore essential to investigate possible sources of cost savings by using those prostheses which promise longest survival and lowest complication rates, and by choosing the most economical way of patient management [152, 200]. Additionally, this requires a high performance of surgeons and clinical centres specialised in THA. Since failure and complication rates of specific systems are essential inputs for health-economic assessments, an as complete as possible follow-up of all THA patients is mandatory.

In spite of the rising number of hip-resurfacing THA procedures carried out in the last decade, the statistical evidence of health-economic analyses did not allow to conclude on the cost-effectiveness of MoM resurfacing THA [198, 201]. Only the increasing failure rates that became more obvious during the last four years provide evidence that cost-effectiveness will be compromised. However, it is still not possible to provide sound data on the method of hip resurfacing as such because many different systems are on the market that seem to significantly differ in performance. On the other hand, a health technology assessment from the US, performed in 2011, concluded that hip resurfacing with some of the most used devices does not yield significant improvement in comparison to conventional total hip arthroplasty [202].

In order to gain a complete overview of the cost-effectiveness and to allow a comparison between specific devices and surgical methods, health economists frequently emphasise that arthroplasty registers need to be adopted worldwide [37]. Moreover, economic variables should be included in the registered data sets [6]. Since illness causes various types of costs that all have to

be covered by society, health-economic assessments should be made from a societal point of view [141] because financial benefits of THA to societies have to be factored into the decision making process [203]. Cost optimisation in subsystems, e.g. on the hospital level, could lead to practices such as discount negotiations between hospitals and prosthesis suppliers, which restrict the medical decision margins of the surgeon [204] and could compromise long-term clinical outcome.

Considering the financial constraints currently faced by European countries, different revision rates are immediately reflected in the cost of disease management, which is becoming increasingly relevant as the number of THA procedures is expected to increase due to ageing population and growing number of interventions in younger patients. Sedrakyan [205] calculated that the 2-3 times higher revision rates in the US, compared to Sweden, accounts for more than a billion dollars in additional cost per year.

Despite efforts to gather all data on THA procedures, achieving statistical evidence to evaluate and predict clinical outcome for specific prosthetic devices will remain cumbersome. This is especially true in view of “10.000 products on the market for the same purpose” [205]. Except for some obviously underperforming devices, failure rates are low, designs evolve quickly and tracking is difficult [206].

In addition, health economists complain that *state-of-the-art health economic methods* could not be applied because data from prospective randomised clinical trials are lacking, which are practically impossible to provide for implantable medical devices that involve surgery. In other words, certain authors argue that health economics lacks the proper methods to deal with implantable medical devices [145, 207, 208]. Sedrakyan et al. suggested an assessment framework to overcome the methodological problems related to evidence evaluation in implantable device studies [209].

7.2. Arthroplasty registers

The primary goal of arthroplasty registers is a complete registration of all patients that undergo THA. Additionally, registers should provide a comprehensive follow-up in order to obtain quality improvements by continuous feedback, which is expected to yield reduced revision rates and cost reductions. Therefore such registers should become an integral part of any health care system [145]. The feedback that can be supplied by an arthroplasty register will be affected by particularities of

national health care systems such as preferences given to certain surgical methods, cemented or uncemented prosthesis and the management of patients during rehabilitation. Hence, the comparability of data from different countries may be limited even if the same types of data are registered [145]. Therefore, clinical outcome comparisons based even on harmonised data acquisition sets may still provide country specific discrepancies [145].

In many countries national arthroplasty registers have been set up. The Scandinavian countries have introduced arthroplasty registers very early, not only limited to THA (Sweden 1975, Finland 1980, Norway 1987 and Denmark 1995). They have accumulated a nearly complete data base for the long-term follow-up of arthroplasty procedures and the assessment of long-term performance of joint prostheses.

Most European countries followed this example and have introduced arthroplasty registers. The European Federation of National Associations of Orthopaedics and Traumatology (EFORT) has launched the *European Arthroplasty Register* EAR project, organised in the Austria-based scientific non-profit association EFORT-EAR. The EAR acts as a coordinating centre in a voluntary cooperation of National Arthroplasty Registers. Its mission is to “*support the development of national register projects, supranational cooperation, for example, by process standardisation, and conduct scientific research focused on outcome research methodology*” [210]. In order to keep the additional workload of an arthroplasty register for surgeons within reasonable limits while ensuring the comparability of data, EFORT developed minimal datasets for primary and revision hip arthroplasty [211, 212], which could be the basis for harmonised data acquisition in Europe.

Arthroplasty register data are indispensable to evaluate clinical outcome in devices that require long follow-up periods and to verify the reproducibility of clinical studies [145, 207, 208, 213]. Clinical studies are still important to answer specific questions, but they are usually carried out at specialised centres and tend to “*present good results achieved in small series*”. It is argued that the results of such studies may be affected by “hidden confounders” and even by “specific practices in the peer-review procedure” [207, 208].

It has been argued that a refined evaluation of clinical outcome would require an extended clinical data set including comorbidities of patients. This raises the fear that the consequently increased workload of the surgeons could compromise the acceptance of registers [214]. On the other hand, lack of such data could also misestimate the quality of health care that can be provided [214]. Attempting to find the additionally required data in electronic form in the hospitals’ patient documentation, Baglio et al. [214] found that especially comorbidities and complications are “under-coded” in

clinical information systems, because they are in many cases not relevant for the hospitals’ reimbursement. Such an extension of the register data set would require systematically more complete clinical patient dossiers and an automatic link to the register must be made compatible with personal data protection legislation.

Since hip arthroplasty registers data sets are a method standardised, recently Labek et al. [208] proposed to establish comparability of data. This was performed by calculating the number of revisions per observed 100 prostheses years. The notion of “prostheses years” is the sum over all patients of all years they live with their primary prosthesis until today or until they underwent revision surgery. Labek based his analysis on the cumulative data available for Denmark, Norway, Finland, Sweden, Australia and New Zealand, which yields a mean number of revisions of 1.3 for 100 component years, which corresponds to revision rates of 6.5% after 5 years and 13% after 10 years [208]. However, revision rates varied significantly from country to country. Sweden has shown the lowest revision rate per 100 implant years of 0.72 and Finland the highest with 4.06. Even within Sweden the revision rates varies by a factor of 2.5 between various hospitals and medical centres [208]. This should prompt a closer study to identify the reasons for such differences. The overall national performance indicates that Sweden has been more efficient in using its arthroplasty register data to improve the quality of its health care system [145].

The set-up of an arthroplasty register is a long-term investment as several years of data collection are required before useful data can be obtained. Moreover, any modification of the data set may compromise the utility of the data for future evaluation. Therefore, such a project requires stable datasets and stable resources being guaranteed for a long period of time [145].

Ideally, such an arthroplasty register should be organised on a European level, in order to rapidly pool a sufficient number of quality-ensured and harmonised data, to guarantee a high level of patient safety by issuing early quality alerts and health equity across the European Union. This could also allow understanding the differences in the number of THA procedures across Europe. It will be essential to find adequate ways of involvement of all stakeholders (surgeons, medical device industry and patients). Involvement of surgeons is particularly important to provide the medical expertise to analyse and interpret the data sets [145].

7.3. Clinical investigation and regulatory framework

Patients have the expectation that a therapy they undergo is safe. At the same time patients expect medical progress and innovation, which entails preclinical and clinical testing of new methods and devices. Recent

problems with certain medical devices, including MoM hip-resurfacing devices for THA, have led to discussions concerning the appropriateness of the regulatory and governance framework for medical devices to reconcile fast innovation with high safety.

Macpherson and Breusch [12] stated: *“The push for resurfacing by so-called champion surgeons and the manufacturers and the resulting patient demand have led to between 6 and 8% of all hip arthroplasty procedures being a metal-on-metal resurfacing (MoMHR)”*.

In this context, it should be understood whether market mechanisms might have played a role in the rush to develop hip-resurfacing systems that might not have achieved full maturity before market introduction. This raises the question whether more clinical investigations would be necessary to avoid problems of this type.

In the particular case of hip prostheses, which are designed to perform over decades, however, extremely long clinical investigations involving large numbers of patients would be required. Havelin [215] has shown that a prospective study would require more than 13.000 patients to determine a 1% difference in outcome between two implants after 10 years (95% confidence interval, 80% statistical power). To reveal a 2% difference still 3000 patients are required. This is not feasible for a treatment involving surgery. Heck et al. [206] calculated that for the event of stem fracture a prospective study capable of revealing a 33% reduction in fracture rate, e.g. caused by improved material processing, more than 100.000 patients would need to be followed-up.

Thus, regulation can only be based on a permanently evolving knowledge base as indicated in Figure 12, which is increasing due to systematic post-market follow-up studies and establishment of arthroplasty registers that should be co-ordinated on an international level. This is challenging for producers, patients and regulators since any regulatory approval will inevitably have a prelimi-

nary character. The limited clinical evidence that can be obtained in clinical investigations involving several hundred patients prospectively has to be compensated by a complete follow-up of all patients and should be considered as an obligation shared by patients, surgeons and device producers.

The current European regulatory framework is set by Council Directive 93/42/EEC, which is currently under revision to further improve the safety and effectiveness of medical devices.

Directive 2005/50/EC has already made regulation in this sector more stringent by reclassifying total hip, knee and shoulder joints from class b to the higher risk class III.

As the implementation of Directive 93/42/EEC is managed by Competent Authorities and Notified Bodies on national level, a more stringent implementation and a stronger degree of European coordination is envisaged to ensure a more harmonised approach in the implementation of the regulatory framework.

A recent study comparing the regulatory systems in the USA and the European Union concluded that there are significant differences between both systems [216]. Both systems combine premarket testing and postmarket vigilance, however, with significant differences in the enforcement. It is therefore desirable to harmonise these approaches – preferably on an international scale – as the medical device market is global, highly innovative and a driving force for improving public health.

Overregulation should be avoided as it can slow down an improvement of the total benefit-risk balance in case regulation prevents industries to introduce novel medical devices. Technical innovations should be made available to patients as quickly as possible while preserving their legitimate safety expectations.

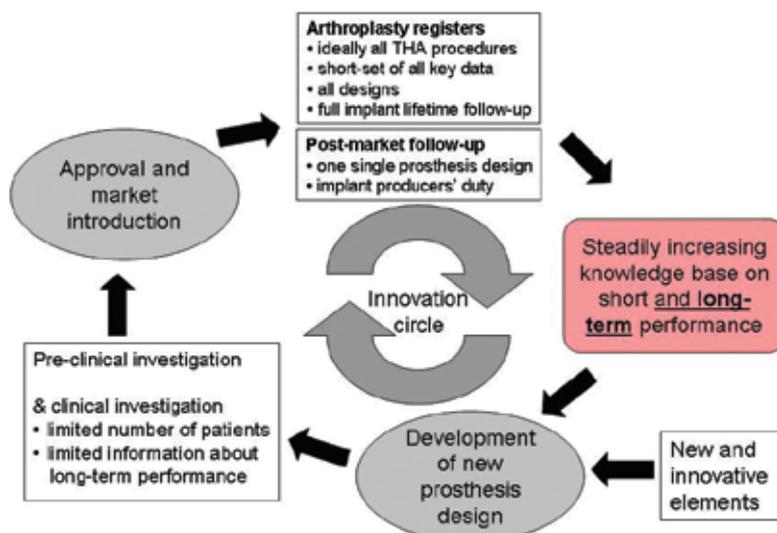


Figure 12: Innovation circle of long-lived implantable devices such as hip prostheses. Risks of new and innovative improvements can be managed by a clinical investigation only if they have a high incidence and become apparent shortly after implantation. They can prevent approval and market introduction. The feed back on long-term risks may be very slow. The more complete all relevant data are gathered the earlier a faulty design and the cause of the problem can be identified, and the product can be substituted by a more safe and improved one. Positive and negative feedback increase the knowledge base.

Summary of Chapter 7

- ▶ Primary THA is generally considered a cost-effective medical treatment. This holds also for revision surgery, however, higher surgical complexity, higher cost and poorer clinical outcome compromise cost-effectiveness compared to primary THA.
- ▶ The number of primary THA and revision surgery procedures is expected to increase due to the limited lifespan of prostheses, increasing life expectancy and decreasing age of patients at the time of primary THA.
- ▶ Gathering of comprehensive data in hip arthroplasty registers, including a complete follow-up of all patients, appears to be the only way to provide sufficient data to compare the cost-effectiveness of individual hip prosthesis designs.
- ▶ Register data can be used to identify new and underperforming devices early, to benchmark hip prosthesis designs, surgical methods and orthopaedic medical centres. They can therefore play an essential role in medical quality assurance, in guiding medical research and regulatory management.
- ▶ The set-up of arthroplasty registers is a long-term commitment and requires stable resources and harmonized datasets.
- ▶ Regulation has to keep the balance between patient safety and encouraging medical innovation.
- ▶ Preclinical testing would require the follow-up of a large patient group over many years to predict the long-term safety of hip prostheses, which are designed to perform over 20 to 25 years.
- ▶ An integrated approach of reasonable preclinical testing in combination with post-market follow-up studies and hip arthroplasty registers is required to ensure safety and effectiveness of hip prostheses.
- ▶ Overregulation should be avoided to supply patients with highly innovative medical devices as quick and as safe as possible.

8. Research needs and challenges

As discussed in the previous chapters, the current issues with some types of MoM prostheses and the concerns about their long-term safety reveal some problems concerning safety evaluation and assessment and point to specific research needs to overcome them.

In the following, we propose a number of research tasks – based on the conclusions from scientific literature –, which either have emerged in the wake of problems with MoM prostheses or which did not obtain sufficient attention in the past. In some cases, where problems cannot be completely avoided research, may also focus on mitigating their health consequences.

8.1. Evaluation and assessment problems

As already discussed above, overall failure rates of THA procedures are low and large patient populations need to be followed-up over a long period before the performance of novel devices and designs can be benchmarked against prostheses already on the market. To facilitate this, co-ordinated and harmonised arthroplasty registers at European and international level should be adopted. This would lead to the reduction of the probability of setbacks that may affect thousands of patients.

Initiatives such as the *European Arthroplasty Register EAR* [210] should be supported as much as possible and in a sustainable manner, since the involvement of diligent and professional organisations appears to be an efficient approach for reducing rates of revision surgery [145, 208].

Arthroplasty system should additionally feature an early warning system for detecting new and underperforming devices. Such a system would allow surgeons to indicate problems they encounter in patients with new devices and which yield an increased post-operative medical treatment effort [2]. In this way problems may already be recognised before surgeons proceed to revision surgery after having exhausted all non-surgical treatment options. Revision surgery must however be kept as a clearly defined end point of prosthesis life in the register [2]. Similarly, device-related problems during surgery could be flagged.

The way and extent to which patient data on comorbidities could be electronically linked to arthroplasty register data sets should be examined. Such data have proven utility in statistical evaluations on the clinical outcome of THA and in the identification of patient related risk-factors. A manual co-registration together with THA would however create an excessive workload.

Economic data should also be included in the register in order to facilitate cost-effectiveness and cost-benefit analysis in the framework of a specific health care system [6].

To summarise: the data of single or clustered arthroplasty registers that provide a continuous feedback of qualified data are important to accomplish the following tasks [145]:

- early warning of underperforming medical devices,
- supporting regulatory authorities in decision making,
- guidance for technological development and innovation and benchmarking of devices,
- identification of best-performing devices, hospitals and medical centres or health systems,
- improving the quality of health care by learning from the best,
- assessment of long-term cancer risk and other risk related to medical implants,
- health economic decision making.

The importance of arthroplasty registers for regulators has to be seen in the light of limited utility of clinical investigations in the case of implantable devices that are designed for a lifespan exceeding 20 years. In the present case of early failing hip-resurfacing systems it took three to five years and several tens of thousands of patients to realise the full dimension of the problem.

8.2. Research needs in THA

Metal-ion toxicity and nanotoxicity, long-term low-level exposure

Assessment of the possible toxicity arising from MoM implants has traditionally been focused on the toxicity of metal ions. Wear of MoM implants is still judged on the basis of metal-ion concentrations revealed in blood, serum or urine [182]. In this context, the release of nanoparticles is only considered as a mechanism of accelerated metal dissolution due to the high specific surface of the debris. Aspects of a direct toxicity of the nanoparticulate debris have so far been widely neglected and deserve more attention [217] in the light of increasing knowledge on nanotoxicology [171, 172].

Since the toxicity of nanoparticles depends on their size, their shape and surface morphology, such studies should be carried out with wear debris collected from hip simulator experiments [173].

Research should include titanium alloys that are currently not under criticism, but which may contain impurities such as nickel with a high allergic potential [218]. In this context metal hypersensitivity or metal allergies should be examined aiming at a better understanding and the development of reliable predictive test that can be applied prior to THA [184].

Knowledge on the long-term low-level exposure to metal ions is rather poor. Since it is known that MoM THA patients exhibit permanently raised metal-ion concentrations [13], a follow-up of such patients could significantly increase the knowledge base in this field.

Pathogenesis and incidence of pseudotumours

In hip-resurfacing THA, adverse tissue reaction against metal wear and corrosion products results in the formation of pseudotumours, i.e., inflammatory painful soft-tissue lesions with unknown aetiology. In order to reassure the safety of conventional MoM THA, patients bearing conventional MoM prostheses should be screened for elevated metal-ion concentrations in blood and for the presence of asymptomatic pseudotumours.

According to the authors' knowledge there are so far no scientific publications giving evidence of the occurrence of pseudotumours related to the use of conventional MoM hip prostheses, whilst there are first reports about early failure and revision of conventional MoM hip prostheses with large-diameter femoral heads [67]. Revision rates are reported to increase significantly with increasing femoral head diameters above 36 mm [67]. In analogy to the findings after hip-resurfacing THA adverse tissue reactions caused by wear debris and elevated metal-ion concentrations are made responsible for early failure [67].

A prominent feature of hip-resurfacing prostheses is the use of large femoral heads with diameters typically in the range between 45 mm to 58 mm. However, a recent investigation finds a tendency towards lower metal-ion concentrations with increasing femoral head diameter [68]. Such a finding would rather point to a nanotoxicity effect caused by tiny metallic wear debris. Therefore, the role of nanosized metallic wear debris in the pathogenesis of pseudotumours deserves special attention, as well as its origin that could be related to fretting along interfaces between metal and bone cement or metal and bone [161].

The role of nanosized metallic wear debris and metal ions in the pathogenesis of pseudotumours has to be investigated.

Understanding aseptic loosening and developing medication

A maximum revision rate of 10% after ten years is an ambitious benchmark [145, 208, 219], which can however be achieved with most MoP hip prostheses. In order to delay or to avoid revision surgery in the large number of patients bearing MoP implants, the understanding of polyethylene particle induced osteolysis should proceed to a point where it could be attempted to develop a medication to stop or delay osteolysis and prevent aseptic loosening [18].

Bioengineering solutions for facilitated revision surgery

The problem of possible fracture of ceramic components of CoC devices seems to be resolved with the ceramic materials currently in use [28]. However, for those few patients, in which catastrophic ceramic failure is encountered, revision procedures need to be further elaborated in order to safely manage problems caused by residual ceramic fracture debris [26]. This may lead to a broader acceptance of CoC hip prostheses, which is expected to significantly reduce the incidence of osteolysis and of adverse tissue reactions to corrosion and wear products.

Impact of prostheses design on incidence of adverse tissue reactions

Additional studies are required addressing the role of femoral head size in the evolution of metal ion concentrations and the formation of pseudotumours. A recent study, based on the arthroplasty register of England and Wales, provides statistical evidence for revision rates that increase significantly with femoral head diameters above 36 mm [67]. On the other hand, a meta analysis published in 2011 concludes that "at the end of ten years, the MoM bearing shows maximum survival rate and superiority compared to MoP and CoC bearings" [220]. This conclusion may be biased by poor statistics, compared to an analysis based on plenty of register data, and also by reflecting the use of MoM devices until 2004/2005, when large diameter femoral heads only started to become popular [67].

Since there are significant differences in the performance of various hip-resurfacing systems, their biomechanical behaviour should be compared by mathematical modelling methods, frequently applied in engineering and materials science, in order to determine stress distributions, elastic deformations, possible occurrence of surface fatigue or fretting and the likelihood of edge loading. This requires exact manufacturer data on the mechanical and surface properties of these components. The simulations should include deviations from the design

specifications as they may occur during surgery, affecting implant alignment and joint clearance.

Based on the experience of the authors, the hypothesis should be examined whether the increased femoral diameter is weakening the acetabular cup (whether mono-block or shell/liner modular design) by limiting its thickness. The consequence of a mechanically too weak acetabular component could be cyclic bending in the micrometer range, causing fretting between acetabular cup and bone, oscillating clearance between femoral head and cup, thus compromising lubrication, and possibly acetabular cup loosening. Finite element simulations of the acetabular cup deformation during the gait cycle should give a first indication whether this hypothesis has to be examined more closely or whether it can be rejected.

Lubrication and wear

It has been reported that a certain fraction of patients with Charnley-type prostheses showed *no* significant wear after 25 years of follow-up [128]. Whereas the reasons for excessive wear can usually be identified, more attention should be paid to investigate those cases of extraordinary low wear rate. In some retrieved MoM implants a graphite-type layer was found that ‘naturally’ formed on femoral heads acting as solid lubricant [221]. The formation of such layers and their impact on wear properties deserves further investigation.

8.3. Prospects and challenges

It is likely that the recent problems with hip-resurfacing systems that motivated the present report may be considered in future as an episode in the history of THA and that medical progress proceeds as expected. Especially the introduction of cross-linked UHMPWE is expected to improve the longevity of MoP devices. However, much longer follow-up times have to be reached for a final judgement, and also CoC devices require more time to gain broader acceptance among patients and, price-wise, among health care providers. However, several other aspects may challenge the future of THA.

Increasing demand for primary and revision THA

As already mentioned in the previous chapters, expected pronounced increase in the number of annually performed THA procedures and longer life expectancies will inevitably lead to an increasing number of revision surgeries since the number of patients that outlive their prostheses will grow [37, 199]. Thus, it is economically

mandatory to use every possibility to increase the life-span of joint replacements and to reduce revision rates. But this will probably not be enough.

It is known that e.g. in Anglo-Saxon countries the overall cost related to musculoskeletal diseases accounts already for up to 3.5% of the gross national product [141]. THA has evolved from a treatment for elderly, infirm patients, crippled by diseases such as osteoarthritis, into a treatment to regain compromised quality of life in younger patients [4]. The excellent results in elderly patients have led to the frequently exaggerated expectation that the same excellence can be achieved in younger patients with demanding high physical activity profiles. In many countries with a high number of THA procedures this necessitates a review of the medical indication that are currently accepted for THA [36, 141].

Health prevention and education

Increasing demand for joint arthroplasty and associated higher costs do not match with future health care budget constraints. Thus the development of educational programmes aiming at the prevention of musculoskeletal diseases should obtain proper attention.

Moreover, it is expected that the number of total *knee* arthroplasty (TKA) procedures will increase much faster than THA [199]. Since TKA is more expensive and less cost-effective than THA [7] this will create an even larger burden to public health systems. Even of greater concern is the finding that TKA, in contrary to THA, may be related with a significantly *higher overall* cancer risk [193] – most probably due to a number of reasons including obesity – entailing additional burden for public health care systems.

Covering the demand of well-trained surgeons

Fehring et al. [222] analysed the number of trained surgeons available in the USA for THA procedures and concluded that by 2016 the skilled medical workforce will no longer meet the increasing demand – at least in the USA. Since joint arthroplasty work is “*mentally and physically demanding*” [222], patient expectations are high, liability is an issue when operations are not successful, and because reimbursement (in the US) is decreasing and “*low compared to other orthopaedic subspecialties*”, only 45% of the arthroplasty fellowships could be filled by graduates in 2007 [222]. Considering the decisive impact of experience and practice of the surgeon on the clinical outcome of THA, the working environment of orthopaedic surgeons in our health care systems must be sufficiently attractive, also in future, to cover the demand in terms of quantity and quality.

9. Conclusions

THA is an orthopaedic sub-specialty, which is in continuous evolution concerning improvements in surgical techniques and the materials and designs applied in the production of hip prostheses. The current state-of-the-art knowledge documented in this report allows drawing the following conclusions, partly in addition to those at the end of the preceding chapters:

- THA is a successful, safe and cost-effective medical intervention to restore functionality of the hip joint and to regain pain-free mobility in patients suffering from severe joint disease or trauma.
- Hip prostheses are subject to continuous research and development efforts in order to increase their lifespan and to reduce the likelihood of complications and revision surgery. This is reflected in a large variety of hip prostheses designs on the market and rapidly changing designs.
- The clinical long-term outcome of THA depends on factors related to the prosthesis design, to the health status of the patient and his post-operative physical activities. Additionally it depends critically on the expertise and practice of the surgeon.
- The most commonly applied designs use metal femoral heads against polymeric acetabular cups, the so-called metal-on-polymer approach (MoP). In most countries they account for more of 60% of all implanted hip prostheses.
- The most important complication with metal-on-polymer (MoP) prostheses is aseptic loosening due to an inflammatory reaction against polymer wear debris. This can occur many years after primary surgery and may require revision surgery.
- Aseptic loosening is much less frequently encountered in patients with metal-on-metal (MoM) or ceramic-on-ceramic (CoC) prostheses.
- The currently discussed problems with early failing hip prostheses are limited to certain types of hip-resurfacing devices and conventional metal-on-metal (MoM) prostheses with femoral head diameters, typically larger than 36 mm. Hip-resurfacing preserves the femoral bone and only covers the trimmed femoral head with a metal cap. In both cases the metal femoral head articulates against a metallic acetabular cup component.
- The most common complications in hip-resurfacing patients are the formation of pseudotumours, causing pain and compromising the function of the hip joint, femoral neck fracture and avascular necrosis. In these cases revision surgery becomes inevitable.
- It is currently unclear whether pseudotumours are as frequently observed in patients with early failing large femoral head conventional metal-on-metal (MoM) prostheses as in patients with failing hip-resurfacing prostheses.
- The pathogenesis of pseudotumours is unclear, but very likely related to the toxicity of nanosized wear debris and the release of metal ions.
- The unclear role of metal ions and nanosized wear debris concerns not only hip-resurfacing devices but also conventional metal-on-metal (MoM) hip prostheses and possibly MoM prostheses used for other articulations.
- THA patients with conventional metal-on-metal (MoM) prostheses, and femoral head diameters even below 36 mm, generally exhibit elevated metal-ion concentrations in their blood, which could however only rarely be related to pathological alterations in the past.
- There is little known on pathologies caused by long-term low-level exposure to cobalt, chromium and other metal ions but also of metal nanoparticles released from hip prostheses.
- Currently there are no scientific indications for an increased, statistically significant overall cancer risk after THA.

- Biomechanical design weaknesses are suspected to be the main reasons for underperforming hip-resurfacing devices, in particular shallow, not fully semispherical acetabular cups and too large femoral head diameters.
- Obviously underperforming devices have already been removed from the medical device market.
- Since the theoretically expected benefits of hip-resurfacing THA cannot generally be realised in clinical practice its use should be limited to specific cases where the surgeon can expect that the medical benefit outweighs the risk of early revision.
- Patients being worried about hip-resurfacing THA or conventional metal-on-metal (MoM) THA will find durable metal-on-polymer (MoP), ceramic-on-polymer (CoP) or ceramic-on-ceramic (CoC) alternatives on the market.
- Arthroplasty registers aiming at a complete registration and follow-up of all THA procedures are indispensable tools in medical quality assurance, medical education and training. They should be an integral part of each healthcare system. Ideally they should be coordinated at a European level and linked to an international system, as potential problems with THA occur on a global level.
- Arthroplasty registers are essential in monitoring the long-term performance of hip prosthesis, in the evaluation and benchmarking of new hip prostheses and for providing early alerts on problematic THA devices.
- Clinical investigations with a reasonable number of patients might be helpful to identify hip prostheses that expose patients to unexpected health risks with high incidence rate. They will not be able to qualify the long-term effectiveness of hip prosthesis design since this would require a disproportionately high number of patients to be enrolled and follow-up times that are beyond the time horizon for introducing medical innovations.
- Clinical investigations, dedicated to ensure patient safety and to prevent significantly underperforming devices from large scale market introduction, should contain an independent review element and not be carried out only by the developing company and clinical partners linked to this company.
- Considering the long lifetimes for which hip prostheses are designed, a reasonable clinical investigation of a new hip prosthesis design will only provide limited information about its long-term performance. The evaluation of the long-term performance to be expected from a new device can only be based on the combined knowledge gathered from all clinical investigations, clinical evaluations and arthroplasty register data that are available so far.
- It is very likely that the increasing societal cost of musculoskeletal diseases can not only be managed by improved medical technology alone. The development and implementation of efficient prevention programmes will become a major challenge.

10. Literature

- [1] K. L. Weber and F. Shuttari-Khan, "Modern Metal-on-Metal Hip Implants and Modern Metal-on-Metal Hip Resurfacing" *Tech. Rep.*, American Academy of Orthopaedic Surgeons, December 2011.
- [2] C. Heneghan, D. Langton, and M. Thompson, "Ongoing problems with metal-on-metal hip implants" *BMJ*, Vol. 344, p. e1349, 2012.
- [3] R. A. Brand, J. J. Callaghan, and R. C. Johnston, "Total hip reconstruction, *Iowa Orthop J*, Vol. 11, pp. 19–42, 1991.
- [4] I. D. Learmonth, C. Young, and C. Rorabeck, "The operation of the century: total hip replacement," *Lancet*, Vol. 370, pp. 1508–1519, 2007.
- [5] J.-P. Courpied and J. Caton, "Total hip arthroplasty, state of the art for the 21st century," *Int Orthop*, Vol. 35, pp. 149–150, 2011.
- [6] K. J. Bozic, K. J. Saleh, A. G. Rosenberg, and H. E. Rubash, "Economic evaluation in total hip arthroplasty: analysis and review of the literature," *J Arthroplasty*, Vol. 19, pp. 180–189, 2004.
- [7] P. Räsänen, P. Paavolainen, H. Sintonen, A.-M. Koivisto, M. Blom, O.-P. Rynnänen, and R. P. Roine, "Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs," *Acta Orthop*, Vol. 78, pp. 108–115, 2007.
- [8] J. Charnley, "Fracture of femoral prostheses in total hip replacement. A clinical study," *Clin Orthop*, Vol. 111, pp. 105–120, 1975.
- [9] T. Gluck, "Report on the development of a new surgical experiment with positive results concerning the seam and the replacement of large tissue defects as well as in the use of resorbable and living tampons in the surgery," *Arch Klin Chir*, Vol. 41, pp. 187–239, 1891.
- [10] U. San Baw, "Proceedings and reports of universities colleges, councils and associations - Ivory prostheses for ununited fractures of neck of femur," *J Bone Joint Surg Br*, Vol. 52-B, pp. 177–178, 1970.
- [11] P. Wiles, "The surgery of the osteoarthritic hip," *Br J Surg*, Vol. 45, pp. 488–497, 1958.
- [12] G. Macpherson and S. Breusch, "Metal-on-metal hip resurfacing: A critical review," *Arch Orthop Trauma Surg*, Vol. 131, pp. 101–110, 2011.
- [13] P. Triclot, "Metal-on-metal: history, state of the art (2010)," *Int Orthop*, Vol. 35, pp. 201–206, 2011.
- [14] J. H. Dumbleton and M. T. Manley, "Metal-on-Metal total hip replacement: what does the literature say?," *J Arthroplasty*, Vol. 20, pp. 174–188, 2005.
- [15] M. K. Benson, P. G. Goodwin, and J. Brostoff, "Metal sensitivity in patients with joint replacement arthroplasties," *BMJ*, Vol. 4, pp. 374–375, 1975.
- [16] B. M. Wroblewski, P. D. Siney, and P. A. Fleming, "The Charnley hip replacement – 43 years of clinical success," *Acta Chir Orthop Traumatol Cech*, Vol. 73, pp. 6–9, 2006.
- [17] J. Charnley, "The bonding of prostheses to bone by cement," *J Bone Joint Surg Br*, Vol. 46-B, pp. 518–529, 1964.
- [18] Y. Abu-Amer, I. Darwech, and J. Clohisy, "Aseptic loosening of total joint replacements: mechanisms underlying osteolysis and potential therapies," *Arthritis Res Ther*, Vol. 9, Suppl 1, p. S6, 2007.
- [19] W. H. Harris, "Conquest of a worldwide human disease: particle-induced periprosthetic osteolysis," *Clin Orthop Relat.Res*, Vol. 429, pp. 39–42, 2004.
- [20] B. J. J. Callaghan, P. Bracha, S. S. Liu, S. Piyaworakhun, D. D. Goetz, and R. C. Johnston, "Survivorship of a Charnley Total Hip Arthroplasty," *Bone*, Vol. 91, pp. 2617–2621, 2009.
- [21] K.-T. Hwang, Y.-H. Kim, Y.-S. Kim, and I.-Y. Choi, "Cementless total hip arthroplasty with a Metal-on-Metal bearing in patients younger than 50 years," *J Arthroplasty*, Vol. 26, pp. 1481–1487, 2011.
- [22] D. W. Manning, P. Chiang, J. Martell, J. Galante, and W. Harris, "In vivo comparative wear study of traditional and highly cross-linked polyethylene in total hip arthroplasty," *J Arthroplasty*, Vol. 20, pp. 880–886, 2005.
- [23] E. Oral, S. D. Christensen, A. S. Malhi, K. K. Wannomae, and O. K. Muratoglu, "Wear resistance and mechanical properties of highly cross-linked, ultrahigh-molecular weight polyethylene doped with vitamin E," *J Arthroplasty*, Vol. 21, pp. 580–591, 2006.
- [24] G.-C. Lee and J. P. Garino, "Reliability of ceramic components," *Semin Arthroplasty*, Vol. 22, pp. 271–275, 2011.
- [25] P. Bizot and L. Sedel, "Alumina bearings in hip replacement: Theoretical and practical aspects," *Oper Tech Orthop*, Vol. 11, pp. 263–269, 2001.
- [26] M. Pospischill and K. Knahr, "Strategies for head and inlay exchange in revision hip arthroplasty," *Int Orthop*, Vol. 35, pp. 261–265, 2011.
- [27] A. Kress, R. Schmidt, U. Holzwarth, R. Forst, and L. Mueller, "Excellent results with cementless total hip arthroplasty and alumina-on-alumina pairing: minimum ten-year follow-up," *Int Orthop*, Vol. 35, pp. 195–200, 2011.
- [28] D. Hannouche, A. Zaoui, F. Zadegan, L. Sedel, and R. Nizard, "Thirty years of experience with alumina-on-alumina bearings in total hip arthroplasty," *Int Orthop*, Vol. 35, pp. 207–213, 2011.

- [29] D. McMinn, J. Daniel, H. Ziaee, and C. Pradhan, "Indications and results of hip resurfacing," *Int Orthop*, Vol. 35, pp. 231–237, 2011.
- [30] J. Tipper, E. Ingham, Z. Jin, and J. Fisher, "(iv) The science of metal-on-metal articulation," *Curr Orthopaed*, Vol. 19, pp. 280–287, 2005.
- [31] P. Roberts, P. Grigoris, H. Bosch, and N. Talwaker, "(iii) Resurfacing arthroplasty of the hip," *Curr Orthopaed*, Vol. 19, pp. 263–279, 2005.
- [32] D. R. Marker, T. M. Seyler, R. H. Jinnah, R. E. Delanois, S. D. Ulrich, and M. A. Mont, "Femoral neck fractures after Metal-on-Metal total hip resurfacing: A prospective cohort study," *J Arthroplasty*, Vol. 22, Suppl. 7, pp. 66–71, 2007.
- [33] F. Falez, F. Favetti, F. Casella, M. Papalia, and G. Panegrossi, "Results of hip resurfacing," *Int Orthop*, Vol. 35, pp. 239–243, 2011.
- [34] G. H. Prosser, P. J. Yates, D. J. Wood, S. E. Graves, R. N. de Steiger, and L. N. Miller, "Outcome of primary resurfacing hip replacement: evaluation of risk factors for early revision," *Acta Orthop*, Vol. 81, pp. 66–71, 2010.
- [35] OECD, "Health at a glance 2011," Report, OECD Publishing, 2011.
- [36] "Bahr will Zahl von Operationen begrenzen," *Financial Times Deutschland*, 02 May 2012, p.11.
- [37] A. W. Burns and R. B. Bourne, "(vi) Economics of revision total hip arthroplasty," *Curr Orthopaed*, Vol. 20, pp. 203–207, 2006.
- [38] R. Gandhi, J. R. Davey, and N. Mahomed, "Patient expectations predict greater pain relief with joint arthroplasty," *J Arthroplasty*, Vol. 24, pp. 716–721, 2009.
- [39] R. M. Nunley, E. L. Ruh, Q. Zhang, C. J. Della Valle, C. A. Engh, M. E. Berend, J. Parvizi, J. C. Clohisy, and R. L. Barrack, "Do patients return to work after hip arthroplasty surgery," *J Arthroplasty*, Vol. 26, pp. 92–98.e3, 2011.
- [40] T. P. Schmalzried, E. F. Shepherd, F. J. Dorey, W. O. Jackson, M. dela Rosa, F. Fa'vae, H. A. McKellop, C. D. McClung, J. Martell, J. R. Moreland, and H. C. Amstutz, "Wear is a function of use, not time," *Clin Orthop Relat Res*, Vol. 381, pp. 36–46, 2000.
- [41] D. Berry, W. Harmsen, M. Cabanela, and B. Morrey, "Twenty-five-year survivorship of two thousand consecutive primary Charnley total hip replacements: Factors affecting survivorship of acetabular and femoral components," *J Bone Joint Surg Am*, Vol. 84, pp. 171–177, 2002.
- [42] Y.-M. Kwon, S. J. Ostlere, P. McLardy-Smith, N. A. Athanasou, H. S. Gill, and D. W. Murray, "Asymptomatic pseudotumors after Metal-on-Metal hip resurfacing arthroplasty: Prevalence and metal ion study," *J Arthroplasty*, Vol. 26, pp. 511–518, 2011.
- [43] D. H. Sochart and M. L. Porter, "The long-term results of Charnley low-friction arthroplasty in young patients who have congenital dislocation, degenerative osteoarthritis, or rheumatoid arthritis," *J Bone Joint Surg Am*, Vol. 79, pp. 1599–1617, 1997.
- [44] J. J. Callaghan, J. C. Albright, D. D. Goetz, J. P. Olejniczak, and R. C. Johnston, "Charnley total hip arthroplasty with cement. Minimum twenty-five-year follow-up," *J Bone Joint Surg Am*, Vol. 82, pp. 487–97, 2000.
- [45] A. August, C. Aldam, and P. Pynsent, "The McKee-Farrar hip arthroplasty. A long-term study," *J Bone Joint Surg Br*, Vol. 68-B, pp. 520–527, 1986.
- [46] S.-A. Jacobsson, K. Djerf, and O. Wahlström, "20-year results of McKee-Farrar versus Charnley prosthesis," in *Metasul: a metal-on-metal bearing* (C. Rieker, M. Wyndler, and U. Wyss, eds.), Vol. 329, p. 61, Bern, Switzerland: Hans Huber Verlag, 1996.
- [47] F. Higuchi, A. Inoue, and M. Semlitsch, "Metal-on-Metal CoCrMo McKee-Farrar total hip arthroplasty: Characteristics from a long-term follow-up study," *Arch Orthop Trauma Surg*, Vol. 116, pp. 121–124, 1997.
- [48] M. Bryant, R. Mollan, and J. Nixon, "Survivorship analysis of the ring hip arthroplasty," *J Arthroplasty*, Vol. 6, Suppl., pp. S5–S10, 1991.
- [49] M. Doerig, E. Odstrcilik, M. Janukovic, and K. R., "Uncemented Alloclassic-Metasul total hip arthroplasty: early results after 2–6 years," in *Metasul: a metal-on-metal bearing* (U. W. C. Rieker, M. Wyndler, ed.), p. 157, Bern, Switzerland: Hans Huber Verlag, 1999.
- [50] M. Doerig, R. Kratter, T. Ritzler, and O. E., "Ceramic-on-polyethylene versus metal-on-metal: a clinical follow-up study, five to ten years after implantation," in *World Tribology Forum in Arthroplasty* (C. Rieker, S. Oberholzer, and W. U., eds.), p. 197, Bern, Switzerland: Hans Huber Verlag, 2001.
- [51] L. D. Dorr, Z. Wan, D. B. Longjohn, B. Dubois, and R. Murken, "Total hip arthroplasty with use of the Metasul metal-on-metal articulation. Four to seven-year results," *J Bone Joint Surg Am*, Vol. 82, pp. 789–798, 2000.
- [52] P. Korovessis, G. Petsinis, M. Repanti, Z. Papazisis, P. Iliopoulos, and P. Soucacos, "Short-term results with the Zweymueller-SL metal-on-metal total hip arthroplasty," *Eur J Orthop Surg Traumatol*, Vol. 12, pp. 81–89, 2002.
- [53] F. Randelli, L. Banci, A. D'Anna, O. Visentin, and G. Randelli, "Cementless Metasul Metal-on-Metal total hip arthroplasties at 13 years," *J Arthroplasty*, Vol. 27, no. 2, pp. 186–192, 2012.
- [54] D. J. Langton, T. J. Joyce, S. S. Jameson, J. Lord, M. Van Orsouw, J. P. Holland, A. V. Nargol, and K. A. De Smet, "Adverse reaction to metal debris following hip resurfacing: the influence of component type, orientation and volumetric wear," *J Bone Joint Surg Br*, Vol. 93, pp. 164–171, 2011.
- [55] "Wales (2010) Sixth Annual Report," Tech. Rep., National Joint Registry for England and Wales <http://www.njrcentre.org.uk/>, 5th July 2010.
- [56] K. A. Kindsfater, C. J. Sychterz Terefenko, T. A. Gruen, and C. M. Sherman, "Minimum 5-year results of modular metal-on-metal total hip arthroplasty," *J Arthroplasty*, Vol. 27, pp. 545–550, Apr 2012.

- [57] B. N. Stulberg, K. K. Trier, M. Naughton, and J. D. Zadzilka, "Results and lessons learned from a United States hip resurfacing investigational device exemption trial," *J Bone Joint Surg Am*, Vol. 90 Suppl 3, pp. 21–26, 2008.
- [58] T. P. Gross, F. Liu, and L. A. Webb, "Clinical outcome of the metal-on-metal hybrid Corin Cormet 2000 hip resurfacing system: an up to 11-year follow-up study," *J Arthroplasty*, Vol. 27, pp. 533–538, 2012.
- [59] H. C. Amstutz and M. J. Le Duff, "Eleven years of experience with Metal-on-Metal hybrid hip resurfacing: A review of 1000 Conserve Plus," *J Arthroplasty*, Vol. 23, pp. 36–43, 2008.
- [60] M. Mont, D. Marker, J. Smith, S. Ulrich, and M. McGrath, "Resurfacing is comparable to total hip arthroplasty at short-term followup," *Clin Orthop Relat Res*, Vol. 467, pp. 66–71, 2009.
- [61] K. A. De Smet, "Belgium experience with metal-on-metal surface arthroplasty," *Orthop. Clin. North Am.*, Vol. 36, pp. 203–213, 2005.
- [62] T. Nishii, N. Sugano, H. Miki, M. Takao, T. Koyama, and H. Yoshikawa, "Five-year results of metal-on-metal resurfacing arthroplasty in Asian patients," *J Arthroplasty*, Vol. 22, no. 2, pp. 176–183, 2007.
- [63] R. T. Steffen, H. P. Pandit, J. Palan, D. J. Beard, R. Gundle, P. McLardy-Smith, D. W. Murray, and H. S. Gill, "The five-year results of the Birmingham hip resurfacing arthroplasty," *J Bone Joint Surg Br*, Vol. 90-B, no. 4, pp. 436–441, 2008.
- [64] G. N. A. Heilpern, N. N. Shah, and M. J. F. Fordyce, "Birmingham hip resurfacing arthroplasty," *J Bone Joint Surg Br*, Vol. 90-B, no. 9, pp. 1137–1142, 2008.
- [65] M. Khan, J.-H. Kuiper, D. Edwards, E. Robinson, and J. B. Richardson, "Birmingham hip arthroplasty: Five to eight years of prospective multicenter results," *J Arthroplasty*, Vol. 24, pp. 1044–1050, 2009.
- [66] C. W. McBryde, K. Theivendran, A. M. Thomas, R. B. Treacy, and P. B. Pynsent, "The influence of head size and sex on the outcome of Birmingham hip resurfacing," *J Bone Joint Surg Am*, Vol. 92, pp. 105–112, 2010.
- [67] A.J. Smith, P. Dieppe, K. Vernon, M. Porter, A.W. Blom, "Failure rates of stemmed metal-on-metal hip replacements: analysis of data from the National Joint Registry of England and Wales," *Lancet*, in press, 2012, DOI:10.1016/S0140-6736(12)60353-5
- [68] N.M. Desy, S.G. Bergeron, A. Petit, O.L. Huk, J. Antoniou, "Surgical variables influence metal ion levels after hip resurfacing," *Clin Orthop Relat Res*, Vol. 469, pp. 1635–1641, 2011
- [69] A.J. Hart, K. Satchithananda, A.D. Liddle, S.A. Sabah, D. McRobbie, J. Henckel, J.P. Cobb, J.A. Skinner, and A.W. Mitchell, "Pseudotumors in association with well-functioning metal-on-metal hip prostheses - A case-control study using three-dimensional computed tomography and magnetic resonance imaging," *J Bone Joint Surg Am*, Vol 94, pp.317-325, 2012
- [70] D. Biau and M. Hamadouche, "Estimating implant survival in the presence of competing risks," *Int Orthop*, Vol. 35, pp. 151–155, 2011.
- [71] J. Park and R. Lakes, "Introduction," in *Biomaterials*, pp. 1–16, Springer New York, 2007.
- [72] G. Heness and B. Ben-Nissan, "Innovative bioceramics," *Mater Forum*, Vol. 27, pp. 104–114, 2004.
- [73] E. Wintermantel and S. Ha, *Biokompatible Werkstoffe und Bauweisen: Implantate für Medizin und Umwelt*. Springer, 1998.
- [74] G. Ryan, A. Pandit, and D. P. Aptsidis, "Fabrication methods of porous metals for use in orthopaedic applications," *Biomaterials*, Vol. 27, pp. 2651–2670, 2006.
- [75] Y. Abe, T. Kokubo, and T. Yamamuro, "Apatite coating on ceramics, metals and polymers utilizing a biological process," *J Mater Sci Mater Med*, Vol. 1, pp. 233–238, 1990.
- [76] A. Cigada, R. Chiesa, M. Pinasco, and K. Hisatsune, "Metallic Materials," in *Integrated Biomaterials Science* (R. Barbucci, ed.), pp. 255–296, Springer US, 2002.
- [77] P. Sürý and M. Semlitsch, "Corrosion behavior of cast and forged cobalt-based alloys for double-alloy joint endoprostheses," *J Biomed Mater Res A*, Vol. 12, pp. 723–741, 1978.
- [78] R. M. Pilliar, "Metallic Biomaterials," in *Biomedical Materials* (R. Narayan, ed.), pp. 41–81, Springer US, 2009.
- [79] H. Stein, "Ultrahigh molecular weight polyethylenes (UHMWPE)," *ASM International, Engineering Plastics. Engineered Materials Handbook*, Vol. 2, pp. 167–171, 1988.
- [80] S. Kurtz, *UHMWPE Biomaterials Handbook: Ultra High Molecular Weight Polyethylene in Total Joint Replacement and Medical Devices*. Academic, 2009.
- [81] K. G. Budinski, "Resistance to particle abrasion of selected plastics," *Wear*, Vol. 203–204, pp. 302–309, 1997.
- [82] E. Oral and O. Muratoglu, "Vitamin E diffused, highly crosslinked UHMWPE: a review," *Int Orthop*, Vol. 35, pp. 215–223, 2011.
- [83] G. Lewis, "Properties of crosslinked ultra-high-molecular-weight polyethylene," *Biomaterials*, Vol. 22, pp. 371–401, 2001.
- [84] C. Zietz, D. Klues, P. Bergschmidt, M. Haenle, W. Mittelmeier, and R. Bader, "Tribological aspects of ceramics in total hip and knee arthroplasty," *Semin Arthroplasty*, Vol. 22, pp. 258–263, 2011.
- [85] J. Chevalier, P. Taddei, L. Gremillard, S. Deville, G. Fantozzi, J. Bartolomé, C. Pecharroman, J. Moya, L. Diaz, R. Torrecillas, and S. Affatato, "Reliability assessment in advanced nanocomposite materials for orthopaedic applications," *J Mech Behav Biomed Mater*, Vol. 4, pp. 303–314, 2011.
- [86] J. Park and R. Lakes, "Hard tissue replacement - ii: Joints and teeth," in *Biomaterials*, pp. 395–458, Springer New York, 2007.
- [87] M. G. Joshi, S. G. Advani, F. Miller, and M. H. Santare, "Analysis of a femoral hip prosthesis designed to reduce stress shielding," *J Biomech*, Vol. 33, no. 12, pp. 1655–1662, 2000.

- [88] X. Li, D. Li, Q. Lian, H. Guo, and Z. Jin, "The effect of stem structure on stress distribution of a custom-made hip prosthesis," *Proc Inst Mech Eng H*, Vol. 224, pp. 1275–1284, 2010.
- [89] M. Pawlikowski, K. Skalski, and M. Haraburda, "Process of hip joint prosthesis design including bone remodeling phenomenon," *Comput Struct*, Vol. 81, pp. 887–893, 2003.
- [90] G. Demey, C. Fary, S. Lustig, P. Neyret, and T. A. si Selmi, "Does a collar improve the immediate stability of uncemented femoral hip stems in total hip arthroplasty? A bilateral comparative cadaver study," *J Arthroplasty*, Vol. 26, pp. 1549–1555, 2011.
- [91] T. S. Wik, "Experimental evaluation of new concepts in hip arthroplasty," *Acta Orthop*, Vol. 83, S345, pp. 1–26, 2012.
- [92] M. Kopec, A. Pemberton, J. Milbrandt, and G. Allan, "Component version in modular total hip revision.," *Iowa Orthop J*, Vol. 29, pp. 5–10, 2009.
- [93] P. Schaaff, "The role of fretting damage in total hip arthroplasty with modular design hip joints -evaluation of retrieval studies and experimental simulation methods," *J Appl Biomater Biomech*, Vol. 2, pp. 121–135, 2004.
- [94] A. Cigada, G. Cotogno, and R. Chiesa, "The ceramic-on-metal coupling in total hip replacements for young patients: a review study," *J Appl Biomater Biomech*, Vol. 9, pp. 2–10, 2011.
- [95] S. L. Smith, D. Dowson, and A. A. J. Goldsmith, "The effect of femoral head diameter upon lubrication and wear of metal-on-metal total hip replacements," *Proc Inst Mech Eng H*, Vol. 215, pp. 161–170, 2001.
- [96] A. Malviya, J. R. Ramaskandhan, R. Bowman, M. Hashmi, J. P. Holland, S. Kometa, and E. Lingard, "What advantage is there to be gained using large modular metal-on-metal bearings in routine primary hip replacement?," *J Bone Joint Surg Br*, Vol. 93-B, pp. 1602–1609, 2011.
- [97] F.-W. Shen, Z. Lu, and H. McKellop, "Wear versus thickness and other features of 5-Mrad crosslinked UHMWPE acetabular liners," *Clin Orthop Relat Res*, Vol. 469, pp. 395–404, 2011.
- [98] M. A. Puska, L. V. Lassila, T. O. Närhi, A. U. O. Yli-Urpo, and P. K. Vallittu, "Improvement of mechanical properties of oligomer-modified acrylic bone cement with glass-fibers," *Appl Compos Mater*, Vol. 11, pp. 17–31, 2004.
- [99] J.-P. Vidalain, "Twenty-year results of the cementless Corail stem," *Int Orthop*, Vol. 35, pp. 189–194, 2011.
- [100] M. Marinelli, A. Soccetti, N. Panfoli, and L. de Palma, "Cost-effectiveness of cemented versus cementless total hip arthroplasty. A Markov decision analysis based on implant cost," *J Orthop Traumatol*, Vol. 9, pp. 23–28, 2008.
- [101] J. Gilbert, C. Buckley, J. Jacobs, K. Bertin, and M. Zernich, "Intergranular corrosion-fatigue failure of cobalt-alloy femoral stems. A failure analysis of two implants," *J Bone Joint Surg*, Vol. 76 A, pp. 110–115, 1994.
- [102] A. Gonzalez Della Valle, B. Becksac, J. Anderson, T. Wright, B. Nestor, P. Pellicci, and E. Salvati, "Late fatigue fracture of a modern forged cobalt chrome stem for total hip arthroplasty," *J Arthroplasty*, Vol. 20, pp. 1084–1088, 2005.
- [103] S. Woolson, J. Mibauer, J. Bobyne, S. Yue, and W. Maloney, "Fatigue fracture of a forged cobalt-chromiummolybdenum femoral component inserted with cement. A report of ten cases," *J Bone Joint Surg*, Vol. 79-A, 12, pp. 1842–1848, 1997.
- [104] E. Lee and H. Kim, "Early fatigue failures of cemented, forged, cobaltchromium femoral stems at the neck shoulder junction: a case report," *J Arthroplasty*, Vol. 16, p. 236, 2001.
- [105] A. Ong, K. Wong, M. Lai, J. Garino, and M. Steinberg, "Early failure of precoated femoral components in primary total hip arthroplasty," *J Bone Joint Surg Am*, Vol. 84, pp. 786–792, 2002.
- [106] F. Baumgart, "Stiffness - an unknown world of mechanical science?," *Injury*, Vol. 31, Suppl. 2, pp. 14 – 84, 2000.
- [107] R. Huiskes, H. Weinans, and M. Dalstra, "Adaptive bone remodeling and biomechanical design considerations for noncemented total hip arthroplasty," *Orthopedics*, Vol. 12, pp. 1255–1267, 1989.
- [108] H. Gong, W. Wu, J. Fang, X. Dong, M. Zhao, and T. Guo, "Effects of materials of cementless femoral stem on the functional adaptation of bone," *J Bionic Eng*, Vol. 9, pp. 66–74, 2012.
- [109] K. L. Markolf, H. C. Amstutz, and D. L. Hirschowitz, "The effect of calcar contact on femoral component micromovement. A mechanical study," *J Bone Joint Surg Am*, Vol. 62, pp. 1315–1323, 1980.
- [110] G. Holt, S. Hook, and M. Hubble, "Revision total hip arthroplasty: the femoral side using cemented implants," *Int Orthop*, Vol. 35, pp. 267–273, 2011.
- [111] M. Corradi, J. Daniel, H. Ziaee, R. Alinovi, A. Mutti, and D. McMinn, "Early markers of nephrotoxicity in patients with metal-on-metal hip arthroplasty," *Clin Orthop Relat Res*, Vol. 469, pp. 1651–1659, 2011.
- [112] W. Brodner, , P. Bitzan, V. Meisinger, A. Kaider, F. Gottsauner-Wolf, and R. Kotz, "Serum cobalt levels after metal-on-metal total hip arthroplasty," *J Bone Joint Surg Am*, Vol. 85-A, pp. 2168–73, 2003.
- [113] N. Maffulli, A. D. Buono, and V. Denaro, "Hip arthroplasty: A transient reason not to be pregnant," *Surgeon*, Vol. in press, pp. –, 2012.
- [114] J. P. Paul, "Paper 8: Forces transmitted by joints in the human body," *Proc Inst Mech Eng Conf Proc*, Vol. 181, pp. 8–15, 1966.
- [115] S. Affatato, M. Spinelli, M. Zavalloni, C. Mazzega-Fabbro, and M. Viceconti, "Tribology and total hip joint replacement: Current concepts in mechanical simulation," *Med Eng Phys*, Vol. 30, pp. 1305–1317, 2008.
- [116] T. D. Stewart, J. L. Tipper, G. Insley, R. M. Streicher, E. Ingham, and J. Fisher, "Severe wear and fracture of zirconia heads against alumina inserts in hip simulator studies with microseparation," *J Arthroplasty*, Vol. 18, pp. 726–734, 2003.

- [117] H. Bhatt and T. Goswami, "Implant wear mechanisms - basic approach," *Biomed Mater*, Vol. 3, pp. 042001, 2008.
- [118] C. Brockett, S. Williams, Z. Jin, G. Isaac, and J. Fisher, "Friction of total hip replacements with different bearings and loading conditions," *J Biomed Mater Res B Appl Biomater*, Vol. 81B, pp. 508–515, 2007.
- [119] I. Hutchings, *Tribology: friction and wear of engineering materials. Metallurgy and materials science*, Edward Arnold, 1992.
- [120] K. Kato and K. Adachi, "Wear mechanisms," in *Modern Tribology Handbook* (B. Bhushan, ed.), Vol. 1, pp. 273–300, CRC Press, 2000.
- [121] J. Williams, *Engineering Tribology*. Oxford Science Publications, Cambridge University Press, 1994.
- [122] I. Kempf and M. Semlitsch, "Massive wear of a steel ball head by ceramic fragments in the polyethylene acetabular cup after revision of a total hip prosthesis with fractured ceramic ball," *Arch Orthop Trauma Surg*, Vol. 109, pp. 284–287, 1990.
- [123] Y. Yan, A. Neville, D. Dowson, S. Williams, and J. Fisher, "Tribo-corrosion analysis of wear and metal ion release interactions from metal-on-metal and ceramic-on-metal contacts for the application in artificial hip prostheses," *Proc Inst Mech Eng J*, Vol. 222, pp. 483–492, 2008.
- [124] S. Hsu and R. Gates, "Boundary lubrication and boundary lubricating films," in *Modern Tribology Handbook* (B. Bhushan, ed.), Vol. 1, pp. 455–492, CRC Press, 2000.
- [125] W.-Z. Wang, Z. M. Jin, D. Dowson, and Y. Z. Hu, "A study of the effect of model geometry and lubricant rheology upon the elastohydrodynamic lubrication performance of metal-on-metal hip joints," *Proc Inst Mech Eng J*, Vol. 222, pp. 493–501, 2008.
- [126] P. Firkins, J. Tipper, M. Saadatzaheh, E. Ingham, M. Stone, R. Farrar, and J. Fisher, "Quantitative analysis of wear and wear debris from metal-on-metal hip prostheses tested in a physiological hip joint simulator," *Biomed Mater Eng*, Vol. 11, pp. 143–157, Jan. 2001.
- [127] P. Firkins, J. Tipper, E. Ingham, M. Stone, R. Farrar, and J. Fisher, "A novel low wearing differential hardness, ceramic-on-metal hip joint prosthesis," *J Biomech*, Vol. 34, pp. 1291–1298, 2001.
- [128] J. Caton and J. Prudhon, "Over 25 years survival after Charnley's total hip arthroplasty," *Int Orthop*, Vol. 35, pp. 185–188, 2011.
- [129] K. J. Bozic, S. Kurtz, E. Lau, K. Ong, V. Chiu, T. P. Vail, H. E. Rubash, and D. J. Berry, "The epidemiology of bearing surface usage in total hip arthroplasty in the United States," *J Bone Joint Surg Am*, Vol. 91, pp. 1614–1620, 2009.
- [130] S. Kurtz, H. Gawel, and J. Patel, "History and systematic review of wear and osteolysis outcomes for first-generation Highly Crosslinked Polyethylene," *Clin Orthop Relat Res*, Vol. 469, pp. 2262–2277, 2011.
- [131] Y. L. Jung and S. Y. Kim, "Alumina-on-Polyethylene bearing surfaces in Total Hip Arthroplasty," *Open Orthop J*, Vol. 4, pp. 56–60, 2010.
- [132] C. L. Barnes, D. DeBoer, R. S. Corpe, S. Nambu, M. Carroll, and I. Timmerman, "Wear performance of large-diameter differential-hardness hip bearings," *The Journal of Arthroplasty*, Vol. 23, Suppl. 6, pp. 56–60, 2008.
- [133] S. R. Williams, J. J. Wu, A. Unsworth, and I. Khan, "Wear and surface analysis of 38-mm ceramic-on-metal total hip replacements under standard and severe wear testing conditions," *Proc Inst Mech Eng H*, Vol. 225, pp. 783–796, 2011.
- [134] L. Savarino, N. Baldini, G. Ciapetti, A. Pellacani, and A. Giunti, "Is wear debris responsible for failure in alumina-on-alumina implants?," *Acta Orthopaedica*, Vol. 80, pp. 162–167, 2009.
- [135] "United States Food and Drug Administration. Device Approval: Ceramic TRANSCEND® Hip Articulation System - P010001." http://www.accessdata.fda.gov/cdrh_docs/pdf3/p010001a.pdf, February 3rd 2003.
- [136] "Annual Report 2011," Danish Hip Arthroplasty Register, 2011.
- [137] "Report June 2010," The Norwegian Arthroplasty Register, 2010.
- [138] "8th NJR Annual Report 2011," National Joint Registry for England and Wales <http://www.njrcentre.org.uk/>, 31st December 2010.
- [139] D. C. Hansen, "Metal corrosion in the human body: the ultimate bio-corrosion scenario," *Electrochem Soc Interface*, Vol. 17, no. 2, pp. 31–34, 2008.
- [140] P. Pedferri, Corrosione e protezione dei materiali metallici. No. v. 2 in *Corrosione e protezione dei materiali metallici*, Polipress, 2010.
- [141] H. Merx, K. Dreinhöfer, P. Schröder, T. Stürmer, W. Puhl, K.-P. Günther, and H. Brenner, "International variation in hip replacement rates," *Ann Rheum Dis*, Vol. 62, pp. 222–226, 2003.
- [142] B. Hansen, R. Hallows, and S. Kelley, "The Rottinger approach for total hip arthroplasty: Technique and review of the literature," *Curr Rev Musculoskelet Med*, Vol. 4, pp. 132–138, 2011.
- [143] R. Malhotra, ed., *Mastering Orthopedic Techniques - Total Hip Arthroplasty*. Mastering Orthopedic Techniques, Jaypee Brothers, Medical Publishers, 2011.
- [144] I. D. Learmonth and C. P. Case, "Metallic debris from orthopaedic implants," *Lancet*, Vol. 369, pp. 542–544, 2007.
- [145] G. Labek, W. Janda, M. Agreiter, R. Schuh, and N. Böhler, "Organisation, data evaluation, interpretation and effect of arthroplasty register data on the outcome in terms of revision rate in total hip arthroplasty," *Int Orthop*, Vol. 35, pp. 157–163, 2011.
- [146] A. M. I. DiGioia, B. Jaramaz, and B. D. Colgan, "Computer assisted orthopaedic surgery: Image guided and robotic assistive technologies," *Clin Orthop Relat Res*, Vol. 354, pp. 8–16, 1998.

- [147] T. Smith, V. Blake, and C. Hing, "Minimally invasive versus conventional exposure for total hip arthroplasty: a systematic review and meta-analysis of clinical and radiological outcomes," *Int Orthop*, Vol. 35, pp. 173–184, 2011.
- [148] T. K. Fehring and J. B. Mason, "Catastrophic complications of minimally invasive hip surgery. A series of three cases," *J Bone Joint Surg Am*, Vol. 87, pp. 711–714, 2005.
- [149] J. Laffosse, P. Chiron, F. Molinier, H. Bensafi, and J. Puget, "Prospective and comparative study of the anterolateral mini-invasive approach versus minimally invasive posterior approach for primary total hip replacement. Early results," *Int Orthop*, Vol. 31, pp. 597–603, 2007.
- [150] D. Berry, "'Minimally invasive' total hip arthroplasty," *J Bone Joint Surg Am*, Vol. 87, pp. 699–700, 2005.
- [151] M. Fortina, S. Carta, D. Gambera, E. Crainz, P. Ferrata, and P. Maniscalco, "Recovery of physical function and patient's satisfaction after total hip replacement THR surgery supported by a tailored guide-book," *Acta Biomed*, Vol. 76, pp. 152–156, 2005.
- [152] Y. Bulthuis, S. Mohammad, L. M. A. Braakman-Jansen, K. W. Drossaers-Bakker, and M. A. F. J. Van De Laar, "Cost-effectiveness of intensive exercise therapy directly following hospital discharge in patients with arthritis: results of a randomized controlled clinical trial," *Arthritis Rheum*, Vol. 59, pp. 247–254, 2008.
- [153] N. N. Mahomed, J. A. Barrett, J. N. Katz, C. B. Phillips, E. Losina, R. A. Lew, E. Guadagnoli, W. H. Harris, R. Poss, and J. A. Baron, "Rates and outcomes of primary and revision total hip replacement in the United States medicare population," *J Bone Joint Surg Am*, Vol. 85-A, pp. 27–32, 2003.
- [154] E. Ingham and J. Fisher, "Biological reactions to wear debris in total joint replacement," *Proc Inst Mech Eng H*, Vol. 214, pp. 21–37, 2000.
- [155] A. K. Matthies, J. A. Skinner, H. Osmani, J. Henckel, and A. J. Hart, "Pseudotumors are common in well-positioned low-wearing metal-on-metal hips," *Clin Orthop Relat Res*, Vol. 4701, pp. 1895–1906, 2012.
- [156] Z. Xia, Y.-M. Kwon, S. Mehmood, C. Downing, K. Jurkschat, and D. W. Murray, "Characterization of metal-wear nanoparticles in pseudotumor following metal-on-metal hip resurfacing," *Nanomedicine*, Vol. 7, pp. 674–681, 2011.
- [157] Y.-M. Kwon, S. J. Mellon, P. Monk, D. W. Murray, and H. S. Gill, "In vivo evaluation of edge-loading in metal-on-metal hip resurfacing patients with pseudotumours," *Bone Joint Res*, Vol. 1, pp. 42–49, 2012.
- [158] P. Schaaff and U. Holzwarth, "Characterization of loading and damage modes of fretting and the role of fretting damage in medical implants," A Literature report, EUR 20555 EN, European Commission, Joint Research Centre, 2003.
- [159] P. Doom, P. Campbell, J. Worrall, P. Benya, H. McKellop, and H. Amstutz, "Metal wear particle characterization from metal on metal total hip replacements: Transmission electron microscopy study of periprosthetic tissues and isolated particles," *J Biomed Mater Res A*, Vol. 42, pp. 103–111, 1998.
- [160] R. Pourzal, I. Catelas, R. Theissmann, C. Kaddick, and A. Fischer, "Characterization of wear particles generated from CoCrMo alloy under sliding wear conditions," *Wear*, Vol. 271, pp. 1658–1666, 2011.
- [161] R. M. Urban, J. J. Jacobs, M. J. Tomlinson, J. Gavriloic, J. Black, and M. Peoc'h, "Dissemination of wear particles to the liver, spleen, and abdominal lymph nodes of patients with hip or knee replacement," *J Bone Joint Surg Am*, Vol. 82, pp. 457–476, 2000.
- [162] F. Billi, P. Benya, E. Ebramzadeh, P. Campbell, F. Chan, and H. A. McKellop, "Metal wear particles: What we know, what we do not know, and why," *SAS J*, Vol. 3, pp. 133–142, 2009.
- [163] H. G. Willert, M. Semlitsch, H. G. Willert, and M. Semlitsch, "Tissue reactions to plastic and metallic wear products of joint endoprostheses," *Clin Orthop Relat Res*, Vol. 333, pp. 4–14, 1996.
- [164] J. H. Dumbleton, M. T. Manley, and A. A. Edidin, "A literature review of the association between wear rate and osteolysis in total hip arthroplasty," *J Arthroplasty*, Vol. 17, pp. 649–661, 2002.
- [165] D. R. Haynes, S. D. Rogers, S. Hay, M. J. Pearcy, and D. W. Howie, "The differences in toxicity and release of bone-resorbing mediators induced by titanium and cobalt-chromium-alloy wear particles," *J Bone Joint Surg Am*, Vol. 75, pp. 825–834, 1993.
- [166] C. Case, V. Langkamer, C. James, M. Palmer, A. Kemp, P. Heap, and L. Solomon, "Widespread dissemination of metal debris from implants," *J Bone Joint Surg Br*, Vol. 76-B, pp. 701–712, 1994.
- [167] M. Allen, B. Myer, P. Millett, and N. Rushton, "The effects of particulate cobalt, chromium and cobalt-chromium alloy on human osteoblast-like cells in vitro," *J Bone Joint Surg Br*, Vol. 79, pp. 475–482, 1997.
- [168] S. Goodman, P. Aspenberg, Y. Song, G. Knoblich, P. Huie, D. Regula, and L. Lidgren, "Tissue ingrowth and differentiation in the bone-harvest chamber in the presence of cobalt-chromium-alloy and high-density-polyethylene particles," *J Bone Joint Surg Am*, Vol. 77, pp. 1025–1035, 1995.
- [169] I. Papageorgiou, V. Shadrack, S. Davis, L. Hails, R. Schins, R. Newson, J. Fisher, E. Ingham, and C. P. Case, "Macrophages detoxify the genotoxic and cytotoxic effects of surgical cobalt chrome alloy particles but not quartz particles on human cells in vitro," *Mutat Res*, Vol. 643, pp. 11–19, 2008.
- [170] J. Tipper, P. Firkins, A. Besong, P. Barbour, J. Nevelos, M. Stone, E. Ingham, and J. Fisher, "Characterisation of wear debris from uhmwpe on zirconia ceramic, metal-on-metal and alumina ceramic-on-ceramic hip prostheses generated in a physiological anatomical hip joint simulator," *Wear*, Vol. 250, pp. 120–128, 2001.
- [171] I. Polyzois, D. Nikolopoulos, I. Michos, E. Patsouris, and S. Theocharis, "Local and systemic toxicity of nanoscale debris particles in total hip arthroplasty," *J Appl Toxicol*, Vol. 32, pp. 255–269, 2012.
- [172] H. Gill, "Molecular and immune toxicity of CoCr nanoparticles in MoM hip arthroplasty," *Trends Mol Med*, Vol. 18, pp. 145–155, 2012.

- [173] F. Billi and P. Campbell, "Nanotoxicology of metal wear particles in total joint arthroplasty: A review of current concepts," *J Appl Biomater Biomech*, Vol. 8, pp. 1–6, 2010.
- [174] A. T. Doherty, R. T. Howell, L. A. Ellis, I. Bisbinas, I. D. Learmonth, R. Newson, and C. P. Case, "Increased chromosome translocations and aneuploidy in peripheral blood lymphocytes of patients having revision arthroplasty of the hip," *J Bone Joint Surg Br*, Vol. 83-B, pp. 1075–1081, 2001.
- [175] C. P. Case, "Chromosomal changes after surgery for joint replacement," *J Bone Joint Surg Br*, Vol. 83-B, pp. 1093–1095, 2001.
- [176] S.-H. Lee, F. R. Brennan, J. J. Jacobs, R. M. Urban, D. R. Ragasa, and T. T. Glant, "Human monocyte/macrophage response to cobalt-chromium corrosion products and titanium particles in patients with total joint replacements," *J Orthop Res*, Vol. 15, pp. 40–49, 1997.
- [177] R. M. Urban, J. J. Jacobs, J. L. Gilbert, and J. O. Galante, "Migration of corrosion products from modular hip prostheses. Particle microanalysis and histopathological findings," *J Bone Joint Surg Am*, Vol. 76, pp. 1345–1359, 1994.
- [178] R. E. Andrews, K. M. Shah, J. M. Wilkinson, and A. Gartland, "Effects of cobalt and chromium ions at clinically equivalent concentrations after metal-on-metal hip replacement on human osteoblasts and osteoclasts: Implications for skeletal health," *Bone*, Vol. 49, pp. 717–723, 2011.
- [179] W.-C. Witzleb, J. Ziegler, F. Krummenauer, V. Neumeister, and K.-P. Guenther, "Exposure to chromium, cobalt and molybdenum from metal-on-metal total hip replacement and hip resurfacing arthroplasty," *Acta Orthop*, Vol. 77, pp. 697–705, 2006.
- [180] M. T. Clarke, P. T. H. Lee, A. Arora, and R. N. Villar, "Levels of metal ions after small- and large-diameter metal-on-metal hip arthroplasty," *J Bone Joint Surg Br*, Vol. 85-B, pp. 913–917, 2003.
- [181] C. E. Pelt, A. G. Bergeson, L. A. Anderson, G. J. Stoddard, and C. L. Peters, "Serum metal ion concentrations after unilateral vs bilateral large-head Metal-on-Metal primary total hip arthroplasty," *J Arthroplasty*, Vol. 26, pp. 1494–1500, 2011.
- [182] K. De Smet, R. De Haan, A. Calistri, P. A. Campbell, E. Ebramzadeh, C. Pattyn, and H. S. Gill, "Metal ion measurement as a diagnostic tool to identify problems with metal-on-metal hip resurfacing," *J Bone Joint Surg Am*, Vol. 90 Suppl. 4, pp. 202–208, 2008.
- [183] H. Willert, G. Buchhorn, A. Fayyazi, and C. Lohmann, "Histopathological changes in tissue surrounding metal/metal joints – signs of delayed type hypersensitivity?," in *World Tribology Forum in Arthroplasty* (C. Rieker, S. Oberholzer, and W. U., eds.), pp. 147–166, Bern, Switzerland: Hans Huber, 2001.
- [184] P. J. Cousen and D. J. Gawkrödger, "Metal allergy and second-generation metal-on-metal arthroplasties," *Contact Dermatitis*, Vol. 66, pp. 55–62, 2012.
- [185] E. M. Evans, M. A. R. Freeman, A. J. Miller, and B. Vernon-Roberts, "Metal sensitivity as a cause of bone necrosis and loosening of the prosthesis in total joint replacement," *J Bone Joint Surg Br*, Vol. 56-B, pp. 626–642, 1974.
- [186] N. Hallab, K. Merritt, and J. J. Jacobs, "Metal sensitivity in patients with orthopaedic implants," *J Bone Joint Surg Am*, Vol. 83-A, pp. 428–436, 2001.
- [187] M. Germain, A. Hatton, S. Williams, J. Matthews, M. Stone, J. Fisher, and E. Ingham, "Comparison of the cytotoxicity of clinically relevant cobalt–chromium and alumina ceramic wear particles in vitro," *Biomaterials*, Vol. 24, pp. 469–479, 2003.
- [188] J. H. Olsen, J. K. McLaughlin, O. Nyren, L. Mellekjær, L. Lipworth, W. J. Blot, and J. F. Fraumeni, "Hip and knee implantations among patients with osteoarthritis and risk of cancer: a record-linkage study from Denmark," *Int J Cancer*, Vol. 81, pp. 719–722, 1999.
- [189] L. B. Signorello, W. Ye, J. P. Fryzek, L. Lipworth, J. F. Fraumeni, W. J. Blot, J. K. McLaughlin, and O. Nyrén, "Nationwide study of cancer risk among hip replacement patients in Sweden," *J Natl Cancer I*, Vol. 93, pp. 1405–1410, 2001.
- [190] T. Visuri, H. Borg, P. Pulkkinen, P. Paavolainen, and E. Pukkala, "A retrospective comparative study of mortality and causes of death among patients with metal-on-metal and metal-on-polyethylene total hip prostheses in primary osteoarthritis after a long-term follow-up," *BMC Musculoskelet Disord*, Vol. 11, p. 78, 2010.
- [191] T. Visuri, E. Pukkala, P. Paavolainen, P. Pulkkinen, and E. B. Riska, "Cancer risk after metal on metal and polyethylene on metal total hip arthroplasty," *Clin Orthop Relat Res*, Vol. 329, pp. S280–S289, 1996.
- [192] T. Visuri, P. Pulkkinen, P. Paavolainen, and E. Pukkala, "Cancer risk is not increased after conventional hip arthroplasty," *Acta Orthop*, Vol. 81, pp. 77–81, 2010.
- [193] P. Wagner, H. Olsson, L. Lidgren, O. Robertsson, and J. Ranstam, "Increased cancer risks among arthroplasty patients: 30-year follow-up of the Swedish Knee Arthroplasty Register," *Eur J Cancer*, Vol. 47, pp. 1061–1071, 2011.
- [194] T. Onega, J. Baron, and T. MacKenzie, "Cancer after total joint arthroplasty: A meta-analysis," *Cancer Epidemiology Biomarkers & Prevention*, Vol. 15, pp. 1532–1537, 2006.
- [195] F. L. Meyskens, P. J. Farmer, and H. Anton-Culver, "Etiologic pathogenesis of melanoma," *Clin Cancer Res*, Vol. 10, pp. 2581–2583, 2004.
- [196] E. Dunstan, D. Ladon, P. Whittingham-Jones, R. Carrington, and T. W. Briggs, "Chromosomal aberrations in the peripheral blood of patients with metal-on-metal hip bearings," *J Bone Joint Surg Am*, Vol. 90, pp. 517–522, 2008.
- [197] J. Ponti, E. Sabbioni, B. Munaro, F. Broggi, P. Marmorato, F. Franchini, R. Colognato, and F. Rossi, "Genotoxicity and morphological transformation induced by cobalt nanoparticles and cobalt chloride: an in vitro study in Balb/3T3 mouse fibroblasts," *Mutagenesis*, Vol. 24, pp. 439–445, 2009.
- [198] K. J. Bozic, C. M. Pui, M. J. Ludeman, T. P. Vail, and M. D. Silverstein, "Do the potential benefits of Metal-on-Metal hip resurfacing

- justify the increased cost and risk of complications?," *Clin Orthop Relat Res*, Vol. 468, pp. 2301–2312, 2010.
- [199] S. Kurtz, K. Ong, E. Lau, F. Mowat, and M. Halpern, "Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030," *J Bone Joint Surg Am*, Vol. 89, pp. 780–785, 2007.
- [200] F. Krummenauer, K. P. Gunther, and W. C. Witzleb, "The incremental cost effectiveness of in-patient versus out-patient rehabilitation after total hip arthroplasty – results of a pilot investigation," *Eur J Med Res*, Vol. 13, pp. 267–274, 2008.
- [201] L. McKenzie, L. Vale, S. Stearns, and K. McCormack, "Metal on metal hip resurfacing arthroplasty. An economic analysis," *Eur J Health Econ*, Vol. 4, pp. 122–129, 2003.
- [202] "Metal on Metal Hip Resurfacing as an alternative to Total Hip Arthroplasty," Tech. Rep., California Technology Assessment Forum, San Francisco, CA, USA, October 2012.
- [203] C. J. Lavernia, V. H. Hernandez, and M. D. Rossi, "Payment analysis of total hip replacement," *Curr Opin Orthop*, Vol. 18, pp. 23–27, 2007.
- [204] C. M. Metz and A. A. Freiberg, "An international comparative study of total hip arthroplasty cost and practice patterns," *J Arthroplasty*, Vol. 13, pp. 296–298, 1998.
- [205] A. Sedrakyan, "Metal-on-metal failures - in science, regulation, and policy," *Lancet*, Vol. 379, pp. 1174–1176, 2012.
- [206] D. A. Heck, C. M. Partridge, J. D. Reuben, W. L. Lanzer, C. G. Lewis, and E. M. Keating, "Prosthetic component failures in hip arthroplasty surgery," *J Arthroplasty*, Vol. 10, pp. 575–580, 1995.
- [207] G. Labek, "QoLA Study Group: Quality of publications regarding the outcome of revision rate after arthroplasty," in *Final Report of the QoLA Project presented at the EFORT Congress 2011 in Copenhagen*, 2011.
- [208] G. Labek, M. Thaler, W. Janda, M. Agreiter, and B. Stöckl, "Revision rates after total joint replacement," *J Bone Joint Surg Br*, Vol. 93-B, pp. 293–297, 2011.
- [209] A. Sedrakyan, D. Marinac-Dabic, S.-L. T. Normand, A. Mushlin, and T. Gross, "A framework for evidence evaluation and methodological issues in implantable device studies," *Med Care*, Vol. 48, pp. S121–S128, 2010.
- [210] "European Arthroplasty Register EAR http://www.ear.efort.org/ear_about_us.aspx."
- [211] "EFORT minimal dataset hip arthroplasty primary form <http://www.ear.efort.org/downloads/efort-ear-minimal-dataset-the-primary.pdf>."
- [212] "EFORT minimal dataset hip arthroplasty revision form <http://www.efort.org/ear/downloads/efort-ear-minimal-dataset-the-revision.pdf>."
- [213] "Age.na.s HTA Report - Prostheses for primary total hip replacement in Italy," *Age.na.s*, Rome, September 2008.
- [214] G. Baglio, F. Sera, S. Cardo, E. Romanini, G. Guasticchi, G. Labek, and T. M., "The validity of hospital administrative data for outcome measurement after hip replacement," *Ital J Public Health*, Vol. 6, pp. 114–127, 2009.
- [215] L. Havelin, "Hip arthroplasty in Norway 1987 – 1994: the Norwegian Arthroplasty Register," Ph.D thesis, University of Bergen, Bergen, 1995.
- [216] D. B. Kramer, S. Xu, and A. S. Kesselheim, "Regulation of medical devices in the United States and European Union," *New Engl J Med*, Vol. 366, pp. 848–855, 2012.
- [217] G. M. Keegan, I. D. Learmonth, and C. P. Case, "A systematic comparison of the actual, potential, and theoretical health effects of cobalt and chromium exposures from industry and surgical implants," *Crit Rev Toxicol*, Vol. 38, pp. 645–674, 2008.
- [218] A. Schuh, P. Thomas, W. Kachler, J. Göske, L. Wagner, U. Holzwarth, and R. Forst, "Das Allergiepotenzial von Implantatwerkstoffen auf Titanbasis," *Orthopade*, Vol. 34, pp. 327–333, 2005.
- [219] "NICE issues guidance on hips," *Br J Perioper Nurs*, Vol. 10, p. 285, 2000.
- [220] V. Shetty, B. Shitole, G. Shetty, H. Thakur, M. Bhandari, "Optimal bearing surfaces for total hip replacement in the young patient: a meta-analysis," *Int Orthop*, Vol. 35, pp. 1281–1287, 2011.
- [221] Y. Liao, R. Pourzal, M. A. Wimmer, J. J. Jacobs, A. Fischer, and L. D. Marks, "Graphitic tribological layers in Metal-on-Metal hip replacements," *Science*, Vol. 334, pp. 1687–1690, 2011.
- [222] T. K. Fehring, S. M. Odum, J. L. Troyer, R. Iorio, S. M. Kurtz, and E. C. Lau, "Joint replacement access in 2016: a supply side crisis," *J Arthroplasty*, Vol. 25, pp. 1175–1181, 2010.

11. Annex

11.1. Glossary

Acetabulum: the cup-shaped cavity formed by the iliac, pubic and ischiac bones of the pelvis in which the femoral head of the hip joint fits.

Arthroplasty: an orthopaedic surgical procedure that replaces or remodels a defective natural joint.

Aseptic loosening: the mobilization of a prosthesis caused by bone resorption in absence of any infection process (sepsis).

Avascular necrosis: the consequence of temporary or permanent cessation of blood flow to the bones. The absence of blood causes the bone tissue to die, resulting in fracture or collapse of the entire bone

Brittle fracture: a rupture mechanism that takes place without any previous apparent plastic deformation of the loaded material

Calcar bone: a bony spur springing from the underside of the neck of the femur above and anterior to the lesser trochanter, adding to the strength of this part of the bone.

Co-morbidity: (literally "additional morbidity"), describes the effect of all other diseases an individual patient might have other than the primary disease of interest.

Cortical bone: the compact bone of the shaft of a bone that surrounds the medullary canal. For its compact structure it differs from the spongy bone (cancellous bone) which is, on the contrary, less dense, softer, and organised in trabeculae (small tissue elements in the form of a small beam, strut or rod). Cortical bone facilitates bone's main functions: to support the whole body, protect organs, provide levers for movement, and store and release chemical elements, mainly calcium.

Crevice corrosion: a corrosion occurring in spaces to which the access of the working fluid from the environment is limited. These spaces are generally called crevices. Typical examples of crevices are gaps and contact areas between parts.

Degenerative joint disease: see *Osteoarthritis*

Dislocation: displacement of a bone from its normal position, especially at a joint.

Distal: anatomically located far from a point of reference, such as an origin, a point of attachment, or the midline of the body. Opposed to Proximal

Edge loading: a particular loading condition that occurs when the femoral head interacts only with the rim of the acetabular cup.

Femoral head: the rounded proximal articulating extremity of the femur constituting part of the hip joint.

Femoral neck: the column of bone connecting the head of the femur and the shaft

Femur: a bone of the leg situated between the pelvis and knee in humans. It is the largest and strongest bone in the body. It articulates with the pelvis through the femoral head, which constitutes, together with the acetabulum, the hip joint.

Fibrous capsule: also referred as foreign body granuloma, a layer of connective tissue formed as part of the biological response to an implanted foreign material. It consists primarily of collagen fibres, but may also contain a variety of inflammatory cell types and new capillaries, depending on the degree of the response.

Hip resurfacing: a particular type of hip prosthesis that is anchored to the natural femoral neck (see chapter 3.4).

Mechanical fatigue: a material subject to a cyclic loading, whose maximum value is below material's yield stress, can show fatigue effects due to progressive crack propagation, up to a point when the component is so weakened that it suddenly breaks (see chapter 3.2).

Medullary canal: also known as medullary cavity or marrow cavity, it is the central cavity of bone shafts where bone marrow is stored. Located in the main shaft (cortical bone) of a long bone (diaphysis) (consisting mostly of compact bone), the medullary cavity has walls composed of spongy bone (cancellous bone) and is lined with a thin, vascular membrane (endosteum).

Melanoma: a dark-pigmented, usually malignant tumour arising from a melanocyte and occurring most commonly in the skin.

Modular device: a device made of different components and/or materials

Myeloma: a malignant tumor formed by the cells of the bone marrow.

Natural joint: the location at which two or more bones make contact. Joints are constructed to allow movement and provide mechanical support. Some of them are hip, knee, shoulder, wrist, ankle and elbow.

Osteoarthritis: a form of arthritis, occurring mainly in elder persons, that is characterized by chronic degeneration of the cartilage of the joints. Also called degenerative joint disease.

Osteointegration: the direct structural and functional connection between living bone and the surface of a load-bearing implant.

Periprosthetic tissue: the tissue surrounding the prosthesis.

Press-fitting: a match between the size and shape of two parts, such that force is required for assembly as one part is slightly larger than the other.

Primary THA: the first surgical intervention during which the natural hip joint is replaced by an artificial prosthesis. The following surgeries, aimed either at the partial or total replacement of the artificial joint, are called revisions.

Prosthesis survival: the percentage of prostheses that are still in place after a certain number of years. The percentage decreases when a prosthesis has to be replaced by revision surgery.

Proximal: nearer to a point of reference such as an origin, a point of attachment, or the midline of the body. Opposed to Distal

Pseudotumour: a non-neoplastic enlargement that resembles a tumour; it may result from inflammation, accumulation of fluid, or other causes, and may or may not regress spontaneously.

Revision rate: the frequency of revision surgery; it is frequently expressed as the percentage of hip prostheses that had to be replaced after a given number of years.

Revision surgery: see *Primary THA*

Stainless steel: any of various alloys of iron that contain chromium, nickel, and small amounts of carbon. They may also contain minor amounts of other elements, such as molybdenum. Stainless steel is resistant to rusting and corrosion.

Stiffness: a property of a mechanical component. It determines the extent to which a component resists to deformation in response to an applied force. Typically the stiffness describes how easily a piece can be bent (see chapter 3.2).

Total Hip Arthroplasty: replacement of both articulating surfaces of a degenerated hip joint. On the acetabular side an artificial acetabular cup is inserted and on the femoral side, the femoral head is replaced completely by a spherical component, which can be anchored in the femur with a stem (*conventional THA*), or the femoral head is trimmed and covered with a metal cap that provides the new articulating surface (see *hip resurfacing THA*).

Tribology: the science and engineering of interacting surfaces in relative motion. It includes the study and application of the principles of friction, lubrication and wear. Tribology is a branch of mechanical engineering.

Trochanter: a broad, flat ledge on the femur, at the upper end of its lateral surface (greater trochanter), or a short conical ledge on the posterior border of the base of its neck (lesser trochanter).

Viscoelasticity: property of a material which is viscous but which also exhibits certain elastic properties such as the ability to store energy of deformation, and in which the application of a stress gives rise to a strain that approaches its equilibrium value slowly

Young's elastic modulus: also referred as modulus of elasticity, the ratio of the stress applied to a body to the strain that results in the mechanical body in response to it. In particular Young's modulus is the ratio of the longitudinal strain to the longitudinal stress.

11.2. List of abbreviations

CoC Ceramic femoral head on Ceramic acetabular cup hip prosthesis

CoCrMo Cobalt Chromium Molybdenum alloy

CoM Ceramic femoral head on Metal coupling acetabular cup hip prosthesis

CoP Ceramic femoral head on Polymer coupling acetabular cup hip prosthesis

DNA DeoxyriboNucleic Acid

EAR European Arthroplasty Register

EFORT The European Federation of National Associations of Orthopaedics and Traumatology

EU European Union

EUDAMED EUropean DAtabank on MEdical Devices

FDA Food and Drug Administration

HRS Hip Resurfacing System

ISO International Organization for Standardisation

MoM Metal femoral head on Metal coupling acetabular cup hip prosthesis

MoMHR MoM Hip Resurfacing

MoP Metal femoral head on Polymer coupling acetabular cup hip prosthesis

OECD Organisation for Economic Co-operation and Development

PMMA PolyMethylMethAcrylate

PTFE PolyTetraFluoroEthylene

QUALY QUality-Adjusted Life Year

THA Total Hip Arthroplasty

THR Total Hip Replacement

TKA Total Knee Arthroplasty

UHMWPE Ultra High Molecular Weight PolyEthylene

UK United Kingdom

US United States

USA United States of America

XLPE Cross Linked ultra high molecular weight PolyEthylene

X-UHMWPE Cross Linked Ultra High Molecular Weight PolyEthylene

Y-TZP Yttrium-stabilised Tetragonal Polycrystalline Zirconia

11.3. List of figures

- Figure 1** **Modular hip prosthesis design**
Photo by: Scuba-limp
Courtesy of Wikimedia Commons:
<http://commons.wikimedia.org/wiki/File:Hueftgelenk-Endoprothese.jpg>
- Figure 2** **Hip-resurfacing THA covers the reshaped femoral head with a new metallic articulating surface**
On the left: Photo by Scuba-limp
 Courtesy of Wikimedia Commons:
 <http://commons.wikimedia.org/wiki/File:Hueftgelenk-Endoprothese.jpg>
On the right: Copyright © European Union 2012
- Figure 3** **Number of THA procedures performed per 100.000 habitants in the year 2009 (or nearest year available)**
Copyright © European Union 2012
- Figure 4** **Kaplan-Meier plot for Charnley-type prostheses**
Copyright © European Union 2012
- Figure 5** **The longevity of Charnley-type hip prostheses increases patients exhibiting lower levels of physical activity**
Copyright © European Union 2012
- Figure 6** **Graphical summary of currently available data on the survival of MoM hip prostheses**
Copyright © European Union 2012
- Figure 7** **Lubrication regimes between the two coupling surfaces**
Copyright © European Union 2012
- Figure 8** **Dislocation of hip prosthesis**
Photo by: Bill Rhodes
Courtesy of Wikimedia Commons:
http://upload.wikimedia.org/wikipedia/commons/7/76/Dislocated_hip_replacement.jpg
- Figure 9** **Focal osteolysis in proximal femur caused by polyethylene wear**
X-ray from source: <http://www.radiologyassistant.nl/en/431c8258e7ac3>
- Figure 10** **Debris release from taper junctions**
Copyright © European Union 2012
- Figure 11** **Simplified schematic of aseptic loosening**
Copyright © European Union 2012
- Figure 12:** **Innovation circle of long-lived implantable devices such as hip prostheses**
Copyright © European Union 2012

11.4. Authors

Uwe Holzwarth received his degree in physics at the University of Stuttgart in 1989 and obtained his Ph.D. in natural sciences from the University of Stuttgart in 1992. He worked as a materials scientist at the Max-Planck-Institute for Metal Research from 1989 until 1994 and held a post-doctoral fellowship at the Institute for Advanced Materials at the Joint Research Centre at Ispra in 1994/95. After two years in the Institute for Radiation and Nuclear Physics at the University of Bonn he returned to the JRC's Institute for Advanced Materials in 1997. Since 1998 he is scientist in the Institute for Health and Consumer Protection and is currently working in the Nanobiosciences Unit.

His work areas of specialism are physics, materials science, nuclear methods in materials science, biomedical materials, biomedical radioisotope production, radiotracer studies and clinical engineering.

Giulio Cotogno studied biomedical engineering at the Politecnico di Milano and obtained his degree in 2002. Since 2003 he has held various positions in the Institute for Health and Consumer Protection at the Joint Research Centre in Ispra and during this time worked on the development and testing of materials for total hip and knee arthroplasty.

He is an expert on wear simulation and wear debris characterisation. Currently he is responsible for quality assurance and quality control.

Acknowledgements

The authors would like to thank Francesca Cattaneo, Orla O'Hanlon, Carla Caprioli, Alexander Riedl and Elke Anklam for their valuable contributions and support in finalising this report.

European Commission
EUR 25378 – Joint Research Centre – Institute for Health and Consumer Protection

Title: Total Hip Arthroplasty

Authors: Uwe Holzwarth, Giulio Cotogno

Luxembourg: Publications Office of the European Union

2016 – 68 pp. – 21.0 x 29.7 cm

EUR – Scientific and Technical Research series – ISSN 1018-5593 (print), ISSN 1831-9424 (online)

ISBN 978-92-79-25280-8 (print)

ISBN 978-92-79-25279-2 (pdf)

doi:10.2788/31286

Abstract

Recent problems with metallic hip joint prostheses have raised concerns about their safety. This report provides a scientific overview of the state-of-the-art knowledge in total hip arthroplasty and identifies areas where further research and actions are needed.

As medical progress is generally expected to be a continuous process leading to improved medical treatment, the question must be asked why setbacks sometimes occur such as those recently witnessed with certain types of hip prostheses which were expected to be an important innovation, especially for younger and physically more active patients.

The present report reviews the historical development and the state-of-the-art knowledge in total hip arthroplasty, mainly from a bio-medical engineering standpoint. It explains reasons for the high innovation rate of devices for total hip arthroplasty, and deals with the problems related to early performance assessment of hip prostheses that are designed for a lifespan exceeding 20 years. Despite THA being considered a safe and cost-effective health intervention, further efforts are required to increase the longevity of hip prostheses and to reduce the incidence rate of complications in order to keep up with the increasing demand in an ageing population combined with increasing public health care budgetary restraints.

As the Commission's in-house science service, the Joint Research Centre's mission is to provide EU policies with independent, evidence-based scientific and technical support throughout the whole policy cycle.

Working in close cooperation with policy Directorates-General, the JRC addresses key societal challenges while stimulating innovation through developing new methods, tools and standards, and sharing its know-how with the Member States, the scientific community and international partners.

Key policy areas include: environment and climate change; energy and transport; agriculture and food security; health and consumer protection; information society and digital agenda; safety and security, including nuclear; all supported through a cross-cutting and multi-disciplinary approach.

doi:10.2788/31286

ISBN 978-92-79-25279-2

