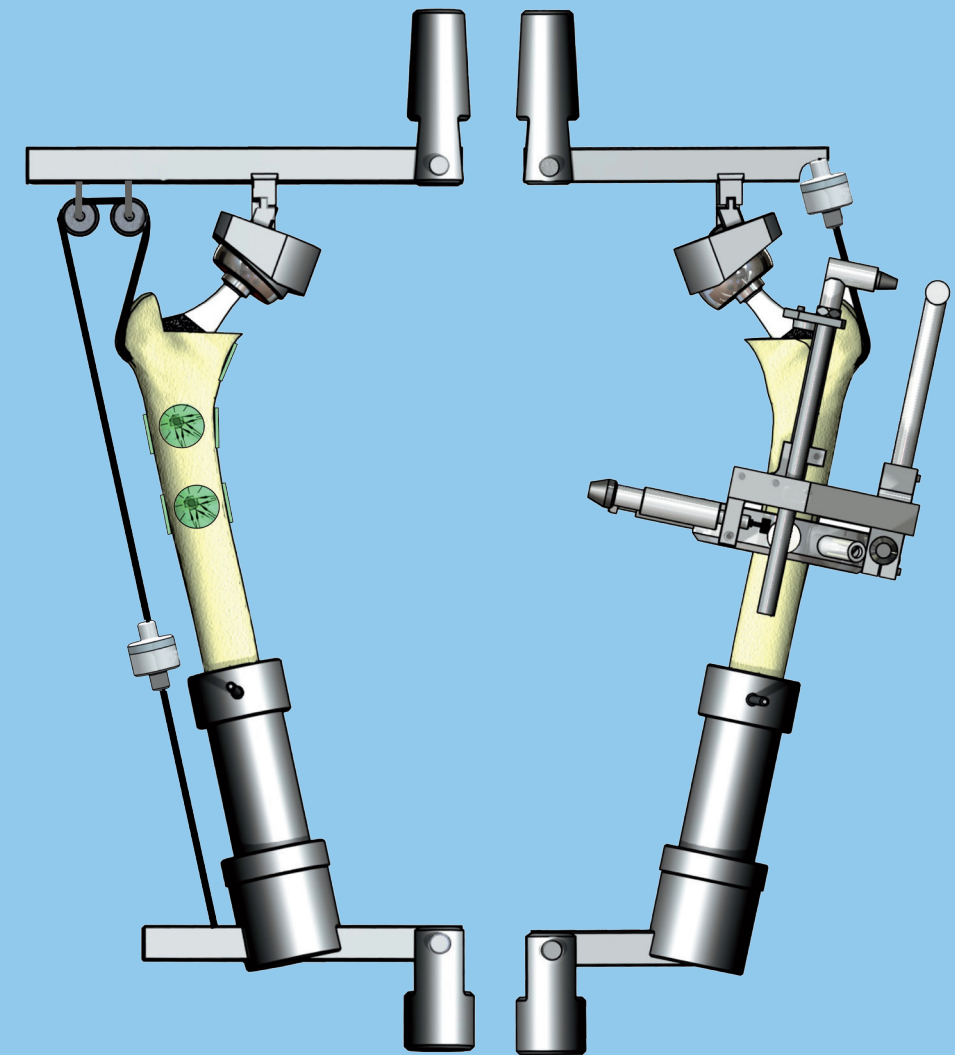


Acta Orthopaedica

Experimental evaluation of new concepts in hip arthroplasty

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ACTA ORTHOPAEDICA SUPPLEMENTUM NO. 345, VOL. 83, 2012

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The Doctoral Thesis was defended in June 2011.

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DOI 10.3109/17453674.2012.678804

Printed in England
Latimer Trend & Company Limited
2012

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Acknowledgements

This thesis has been carried out from 2007 to 2010 during my employment as residence and research fellow at the Department of Orthopaedic Surgery, Trondheim University Hospital. The work has been carried out at the Norwegian Orthopaedic Implant Research Unit (NKSOI). Implants and surgical instruments for this project have been provided by DePuy Int. Ltd, Leeds.

Many people have been involved in this project, and I would like to express my sincere gratitude to all of them. Supervisor was Professor Arild Aamodt, head of NKSOI was Dr.med Olav A. Foss, and head of the biomechanical laboratory at NKSOI was Jomar Klaksvik.

Abbreviations

BMD	Bone mineral density
BW	Bodyweight
BWm	Bodyweight meter
CoCr	Cobalt chrome
CT	Computer tomography
DXA	Dual-energy X-ray absorptiometry
E-modulus	Elastic modulus or Young's modulus
ε_1	Principal tensile strain
ε_2	Principal compressive strain
$\bar{\varepsilon}$	Equivalent strain or von Mises strain
FCE	Femoral condyle endoprosthesis
FE	Finite element

GPa	GigaPascal, or 10^9 Pascal
HA	Hydroxyapatite
HU	Hounsfield Unit
MPa	MegaPascal, or 10^6 Pascal
$\mu\varepsilon$	Microstrain, or 10^{-6} m/m
μm	Micrometer, or 10^{-6} m
N	Newton
Nm	Newtonmeter
N/mm²	Newton per square millimetre, $1 \text{ N/mm}^2 = 1 \text{ Pascal}$
THA	Total hip arthroplasty
Ti	Titanium
3D	Three dimensional

List of papers

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

- I Wik T S, Østbyhaug P O, Klaksvik J, Aamodt A. Increased strain in the femoral neck following insertion of a resurfacing femoral prosthesis. *J Bone Joint Surg (Br)* 2010; 92(3): 461-7.
- II Wik T S, Enoksen C, Klaksvik J, Østbyhaug P O, Foss O A, Ludvigsen J, Aamodt A. *In vitro* testing of the deformation pattern and initial stability of a cementless stem coupled to an experimental femoral head, with increased offset and altered neck angles. *Proc Inst Mech Eng H* 2011; 225(8): 797-808.
- III Pettersen S H, Wik T S, Skallerud B. Subject specific finite element analysis of stress shielding around a cementless femoral stem. *Clin Biomech* 2009; 24(2): 196-202.
IIIb: Corrigendum in: *Clin Biomech* 2011; 26(4): 429.
- IV Wik T S, Foss O A, Havik S, Persen L, Aamodt A, Witsø E. Periprosthetic fracture caused by stress shielding after implantation of a Femoral Condyle Endoprosthesis in a transfemoral amputee. A case report. *Acta Orthop* 2010; 6: 765-7.

Summary

In this thesis we evaluated two different hip arthroplasty concepts through *in vitro* studies and numerical analyses.

The cortical strains in the femoral neck area were increased by 10 to 15 % after insertion of a resurfacing femoral component compared to values of the intact femur, shown in an *in vitro* study on human cadaver femurs. There is an increased risk of femoral neck fracture after hip resurfacing arthroplasty. An increase of 10 to 15 % in femoral neck strains is limited, and cannot alone explain these fractures. Together with patient specific and surgical factors, however, increased strain can contribute to increased risk of fracture.

An *in vitro* study showed that increasing the neck length in combination with retroversion or reduced neck shaft angle on a standard cementless femoral stem does not compromise the

stability of the stem. The strain pattern in the proximal femur increased significantly at several measuring sites when the version and length of neck were altered. However, the changes were probably too small to have clinical relevance.

In a validation study we have shown that a subject specific finite element analysis is able to perform reasonable predictions of strains and stress shielding after insertion of a femoral stem in human cadaver femurs. The usage of finite element models can be a valuable supplement to *in vitro* tests of femoral strain pattern around hip arthroplasty.

Finally, a patient case shows that bone resorption around an implant caused by stress shielding can in extreme cases lead to periprosthetic fracture.

Introduction

General background

Total hip arthroplasty (THA) is a successful treatment of osteoarthritis and other destructive diseases of the hip joint, relieving pain and restoring the function of the joint. In Norway approximately 7000 patients undergo primary hip replacement every year. The incidence of hip surgery is steadily increasing. The recent decade the number of patients undergoing hip surgery in Norway has increased by nearly 30% and the share of patients younger than 70 years is expanding (The Norwegian Arthroplasty Register 2010).

The history of hip implant surgery goes back to 1923, when the Norwegian-American Orthopaedic surgeon Marius Smith-Petersen implanted a glass mould interposition to treat severe hip arthritis. These implants had a tendency to break, and it was first in 1938 using vitallium, a cobalt chrome alloy, the mould arthroplasty had some success (Law and Manzoni 1970, Smith-Petersen 1978). One may still encounter patients with an intact Smith-Petersen cup, free of pain and well-functioning, more than 50 years after surgery (Wright et al. 2006, Northover and Maqsood 2008). In the 1960's Sir John Charnley revolutionised THA surgery with a new principle; the Charnley low friction arthroplasty (Charnley 1972). This cemented prosthesis is today widely used with good results, and has extensive documentation (Aamodt et al. 2004, Allami et al. 2006, Buckwalter et al. 2006, Hulleberg et al. 2008). However, although the Charnley prosthesis was the start of a very successful treatment for arthritis, osteolysis and aseptic loosening became a considerable problem. The osteolysis was believed to be caused by "cement disease" and led to a search for other fixation methods than cement (Jones and Hungerford 1987). Today, osteolysis is in general recognized as the cellular response to wear debris, including metal, cement and polyethylene particles (Harkess 2003).

Cementless stems gained popularity throughout the 1980's. The fixation of cementless stems is provided by bony ingrowth into the surface layer of the implant (Cross and Spycher 2008). Over the last twenty years there has been extensive research into how conditions can be made favourable for bony ingrowth and long-term survival of uncemented implants. Today most uncemented femoral stems have a porous surface layer covered with an osteoinductive material, typically hydroxyapatite. Still cementless implants are dependent on excellent primary stability to achieve bony fixation and long term stability of the implant (Cross and Spycher 2008).

The problems of wear-induced osteolysis in the proximal femur have declined with improved bearings and focus on reduc-

tion of wear particles. However, periprosthetic bone resorption due to stress shielding is often observed for the cementless stems, especially in the bone surrounding the coated part of the implant. In the case of stress shielding bone resorption is seen as diffuse atrophy of the periprosthetic bone, whereas wear-induced osteolysis is observed as localised or lacunar areas of bone resorption. Different stem designs have been launched in effort to avoid bone resorption due to stress shielding, including short-stemmed implants and resurfacing implants.

Due to the excellent performance of many established prostheses, the documentation of new implants is increasingly important (Viceconti et al. 2009). For cementless stems two demands stand out; the desire to preserve proximal bone stock and the necessity to provide excellent primary stability of the stem.

Experimental evaluation of hip implants

Strain and bone remodelling

Periprosthetic bone resorption around THA is extensively documented (Bobyk et al. 1992, Sychterz and Engh 1996, Engh et al. 1999, Yamaguchi et al. 2000, Prendergast 2001, Rahmy et al. 2004, Glassman et al. 2006). Bone resorption is also described for total knee arthroplasty and tumour prostheses (Lan et al. 2000, Li and Nilsson 2000, van Loon et al. 2001). The bone loss around the femoral stem is commonly explained by bone remodelling due to stress bypass of the proximal femur, also called stress shielding.

Revision surgery in severely stress shielded bone can be technical challenging, and the lack of bony support for the revision implant can be of concern. Although periprosthetic bone resorption is commonly observed around cementless implants, there has not yet been documented any increased risk of aseptic loosening or periprosthetic fracture in clinical series (Engh et al. 2003, Karachalios et al. 2004, Glassman et al. 2006, Engh et al. 2009). Nevertheless, the preservation of proximal bone stock is a fundamental goal in THA, and many of the new hip implant designs specifically aim to preserve a physiological load transfer to the femur. Both the number of primary THAs and the share of younger patients increase, leaving a rising population of younger patients receiving femoral implants. This emphasizes the importance of increasing the longevity of implants and preservation of proximal bone stock to ease later revision surgery.

The deformation pattern, or strain pattern, of bone is controlled by functional loading. Typically the femur compresses

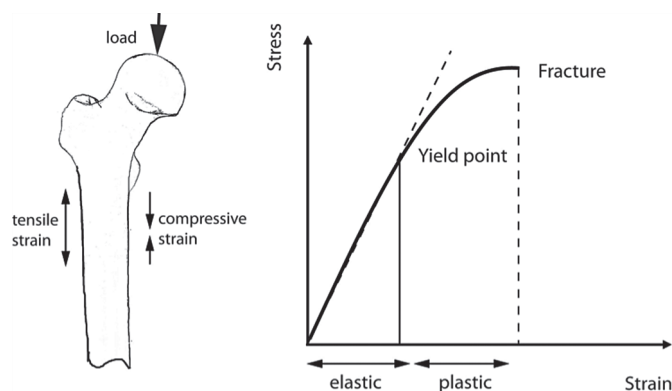


Figure 1. The stress-strain relationship for bone. The slope of the curve represents the elastic modulus of the bone.

on the medial side and stretches on the lateral side (Aamodt et al. 1997). The relationship between stress and strain is illustrated in Figure 1.

Most materials such as metals and bone can be described as linear-elastic, meaning that there is a linear relationship between stress and strain (Hooke's law):

$$\sigma = \varepsilon \times E \quad (1)$$

where σ = stress, ε = strain and E = modulus of elasticity or Young's modulus. Stress and Young's modulus are given by dimensions force per area, usually expressed as N/mm², MPa or GPa. Strain is the relative deformation of the object and is dimensionless, but it is common to give the dimension as microstrain ($\mu\epsilon$), or 10⁻⁶m/m. Young's modulus denotes the stiffness of a material, and is given by the slope of the stress-strain curve (Figure 1).

As long as the femur is deformed elastically, it will recapture its original shape when unloaded. However, if load exceeds a certain level, the deformation becomes irreversible, i.e. plastic. The transition from elastic to plastic deformation is defined as the yield point of bone, and from this point the stress curve flattens out. When strains increase even further the bone will eventually fracture. The maximum strain and stress that the bone can sustain are called the ultimate strain and strength, respectively. The area under the stress-strain curve is a measure of the amount of energy needed to cause a fracture (Turner and Burr 2001).

Even though the exact cellular mechanisms are unclear, it is widely accepted that dynamic strain is the controlling stimulus of bone remodelling (Martin et al. 1998, Ruimerman et al. 2005, Lanyon 2008, Xu and Robinson 2008). The adaptive remodelling phenomenon of bone was early recognised. Already in the 17th century Galileo made a point of the mechanical implications of the shape of bones. Bell observed early in the 19th century that the structure of cancellous bone had "reference to the forces acting on the bone" (Martin et al. 1998). Later the same century Wolff published several papers

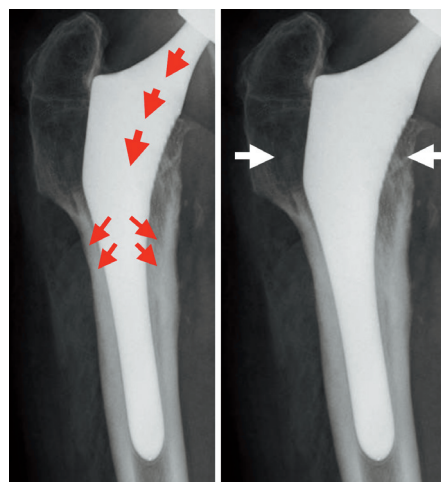


Figure 2. To the left the red arrows indicate the pattern of load transfer of a proximally coated uncemented stem. To the right the white arrows indicate the bone resorption occurring in the area where the periprosthetic bone is bypassed.

on the alignment of trabeculae with principal stress directions, and his main work "The law of Bone Remodelling" (Das Gesetz der Transformation der Knochen) was published in 1892. Today the self-regulation of bony structures by cells responding to a mechanical stimulus is referred to as Wolff's law, even though the understanding of the law has been modernised by several researchers later (Roesler 1987, Martin et al. 1998, Frost 2004).

The clinical observation is that bone adapt to loading by increased bone density when load increases, and reduced bone density when load reduces. Strain protection induced by bed rest or space flights is known to lead to bone mineral resorption (Bloomfield 1997, Collet et al. 1997, Sibonga et al. 2007). Strain protection of periprosthetic bone occurs after insertion of a femoral stem into the femur, since the load of the hip joint will pass through the stiffest material, in this case the stem, and thereby bypass the periprosthetic bone (Prendergast 2001, Glassman et al. 2006). This leads to bone resorption, which is observed around cementless stems, and often referred to as "stress shielding" (Figure 2).

The research into bone remodelling around THA has been extensive. It is shown that the stiffness of the femoral stem is one of the main determinants in bone remodelling around an implant (Bobyn et al. 1992, Engh et al. 1999, Glassman et al. 2006). The stiffness of a material is defined as the resistance of an elastic body to deflection or deformation by an applied force (Cross and Spycher 2008) and is the combined effect of the material properties and the geometry of the object. Usually femoral stems in THA are made of stainless steel, cobalt chrome alloys (CoCr), titanium (Ti) or titanium alloys. The material properties of implants depend on the composition of the metal alloy. Stainless steel have a Young's modulus of 200 GPa, cobalt chrome alloys of 200–250 GPa and titanium

of 55–110 GPa (pure titanium 105 GPa) (Cross and Spycher 2008). Cortical bone has a Young's modulus of approximately 20 to 25 GPa, while the elastic modulus of cancellous bone in the human femur is reported at a range from 1 to 20 GPa (Rho et al. 1993, Turner et al. 1999, Zysset et al. 1999, Guo 2001, Bayraktar et al. 2004, Huiskes and Van Rietbergen 2005). The typical implant materials are thus five to ten times stiffer than cortical bone.

The geometry of the stem is probably more determining for the stiffness than the stem-material itself. The bending stiffness is dependent of the cross sectional moment of inertia, which again is dependent on the radius powered by four (Engh and Bobyn 1988, Bobyn et al. 1992, Martin et al. 1998). The design of the stem is therefore important, and more bulky stems would shield more strain than slimmer stem designs. Bone resorption is also observed around cemented stems, but not to the same extent as in cementless stems, due to differences in stem diameters (Huiskes 1990).

Another important factor is the interface between implant and bone. When two materials are combined, the stiffest material will bear the majority of the load (Glassman et al. 2006). A strong mechanical bond between the implant and the bone would contribute to more stress shielding. When the bone has grown into the surface of a stiff stem, the surrounding bone will be shielded more extensively in the area of bone ingrowth, than where ingrowth has not occurred. Bone resorption therefore typically occurs in the areas of coating and bone ingrowth (Bobyn et al. 1992, Blunn et al. 2000, Yamaguchi et al. 2000, Werner et al. 2005, Glassman et al. 2006). Stems with proximal coating tends to preserve more bone distal to the level of coating compared to extensively coated stems, however they offer no protection of bone resorption in the proximal area (Yamaguchi et al. 2000, Sychterz et al. 2002, Glassman et al. 2006).

To ensure the initial stability the proximally coated stems often have a wider diameter and a more bulky design in the metaphyseal area. Some stems with a wide proximal metaphyseal part and undersized distal stem, have been designed to selectively load the proximal femur. However, the wide metaphyseal part of the stem in anatomical and proximal coated stems are substantial stiffened, which potentially increase the stress shielding in the proximal metaphyseal area, even though the implant was designed to preserve proximal bone stock (Glassman et al. 2006).

A low preoperative bone mineral density, either locally or systemic, would additionally contribute to increased bone resorption (Kerner et al. 1999, Venesmaa et al. 2003, Rahmy et al. 2004, Alm et al. 2009). It thus seems as the larger the difference in stiffness between bone and implant gets, the more pronounced the stress shielding will be, and consequently the periprosthetic bone resorption is intensified.

The CoCr stems are twice as stiff as titanium stems, which would generally induce more stress shielding (Bobyn et al. 1992). Femoral stems with lower stiffness such as isoelastic

stems have proven to reduce stress shielding of the proximal femur (Vail et al. 1998, Karrholm et al. 2002). However, flexible implants will have increased interface stresses and micromotion which can lead to debonding and increased loosening rates (Huiskes et al. 1992, Trebse et al. 2005, Kontinen et al. 2008).

The stresses in bones during loading can indirectly be evaluated by measuring the cortical deformation pattern through different techniques. The most common technique for measuring strains of bones is the electrical resistance strain gauge (Miles and Tanner 1992, Cristofolini 1997). The main advantage of the strain gauges is the accuracy of the method and that they provide direct quantitative measures. The main disadvantage is that they provide information from the attachment site only. Other techniques such as the photoelastic coating technique provide full-field surface measurements. However, these methods have lower accuracy and only qualitative or semi-quantitative analyses are possible (Cristofolini 1997, Glisson et al. 2000, Huiskes and Stolk 2005). The mentioned strain measurement techniques obtain two-dimensional surface strains at the surface where the sensors are applied, typically at the cortical surface. Strains in the trabecular bone can in such cases not be evaluated. Strains in the cement mantle can be evaluated by embedding strain gauges within the cement. Finite element models which are discussed later can give three-dimensional strain values as well as strain values for both cortical and trabecular bone.

Micromotion and primary stability

The success of a cementless implant is dependent on, beyond the mechanical properties of the implant itself, rigid initial stability and osseous integration (Cross and Spycher 2008). The stability of the femoral stem is dependent on the implant design, which must resist rotational forces and initial sinking. Surface roughness of an implant has also a determining effect on bone-implant contact and hence the initial stability of the implant (Shalabi et al. 2006). Other factors that influence the initial stability of an implant are planning, surgical technique, press-fit, cancellous compaction and the quality of bone.

To ensure bony ingrowth into cementless femoral stems there must be direct contact between the implant and surrounding bone, and the micromovements on the bone-implant interface must be as small as possible. Pilliar et al. showed in a retrieval study that implants which were clinically stable had micromovements on the implant-bone interface less than 28 μm (Pilliar et al. 1986). Loose stems had excessive micromotion more than 150 μm . This is supported by a similar study conducted by Jasty et al. who found full ingrowth into implants that were exposed to micromovements less than 20 μm , and partial ingrowth between 20 and 40 μm (Jasty et al. 1997). A fibrous tissue layer was formed when the micromotion were larger than 150 μm . Also Søballe et al. have shown that micromotions over 150 μm inhibits bone ingrowth for both titanium and hydroxyapatite-coated implants (Søballe et

al. 1992a). These studies indicate that the threshold for acceptable interfacial micromovements is less than 150 μm .

The addition of a bioactive calcium phosphate to the porous coating such as hydroxyapatite (HA), facilitates the osseointegration by being osteoinductive (Cross and Spycher 2008). Søballe and co-authors have performed several animal studies discussing the effect of HA and porous coating. They have shown that the HA coating is superior to porous coatings in animal models regarding capability to induce ingrowth (Søballe et al. 1991, Søballe et al. 1992a, Søballe et al. 1992b, Søballe et al. 1993, Mouzin et al. 2001), and that porous coating with HA has a better sealing effect both in stable and unstable implants (Rahbek et al. 2005).

Excessive micromotion have adverse effects, since the formation of fibrous tissue includes inflammatory cells such as macrophages that phagocytises the HA coating (Overgaard et al. 1998). It is however shown that in the presence of a fibrous tissue layer the HA coating induces ongrowth on parts of the implant in spite of excessive micromotion (Søballe et al. 1993, Rahbek et al. 2005). It is also shown that loading enhances bone ingrowth on HA-coated implants if the implant is stable, presumably in the same way that bone cells adapt to functional loading (Mouzin et al. 2001). The addition of HA can thus seem to enhance the stem's ability to become osseointegrated in spite of micromovements. However, a critical limit of 150 μm in preclinical evaluations still seems reasonable.

Finite element analysis

The numerical investigation into material properties and behaviour is extensively used in construction and industry. In orthopaedic research it has been increasingly utilised to investigate the properties of bone and implant and their interface (Prendergast 1997). A finite element (FE) analysis is based on modelling the structure as a grid or a mesh of many small simple structures, i.e. "finite elements". According to Brand et al. the FE model principally needs 1) a sufficiently refined mesh reflecting the geometry of a structure, 2) boundary conditions reflecting external constraints or loads surrounding the structure, 3) material properties describing each element and 4) proper modelling of interfaces of differing material, such as the bone-implant interface (Brand et al. 2003).

Strain gauge rosettes reflect the deformation of the cortical surface at the exact place where they are attached. The FE method enables analyses of stress and strain in areas of the bone that are not accessible for strain gauge measurements. Traditionally, and still today, the FE analyses have been based on the geometry of a standard composite femur, representing an average anatomy of the femur. By combining computer tomography (CT) scans of cadaver femurs with FE modelling, subject specific finite element analyses can be performed. The CT scans are used to model the geometry of the bone, and the grey-scale values are used to estimate the local material properties for the FE model. These analyses enable us to account for some of the natural variations in mechanical properties

and geometries between specimens. The subject specific FE analyses have been used in several studies, but usually intact femurs are modelled to investigate for example normal strain distribution or fracture strength (Bessho et al. 2007, Schileo et al. 2007, Schileo et al. 2008, Taddei et al. 2008, Bessho et al. 2009, Trabelsi et al. 2009, Cong et al. 2010). The recent year however, it seems as if the subject specific finite element analyses have become more common concerning numerical analyses of stresses and strains around implants (Helgason et al. 2009, Dickinson et al. 2010, Taddei et al. 2010, Tarala et al. 2010).

The set-up in a finite element model is versatile, in the sense that load configurations that are difficult to replicate in *in vitro* experiments can be analysed, for example by simulating muscle attachments and forces, or different resultant hip forces and directions. One may also choose the contact areas between the implant and bone, and thereby simulate a situation of bony attachment of an uncemented implant, whereas in an *in vitro* experimental set-up with cadaver bones, only the immediate postoperative situation is simulated.

The main limitation of the finite element analysis is that it represents an idealisation of the physical reality (Sharir et al. 2008, Cristofolini et al. 2010b). The assumption of isotropy and homogeneity of bone is often made in FE models, although this is really not the case. The inhomogeneity of bone is accounted for in the subject specific finite element analysis. However, isotropy of bone remains an assumption. The elastic modulus of bone is smaller for circumferential tension and compression than longitudinal tension and compression (Martin et al. 1998). After implantation of a femoral stem, the implant will tend to wedge into the femoral canal during loading. Assuming isotropy of an implanted femur in a finite element analysis might therefore lead to underestimation of the hoop strain in the proximal femur.

Combination of finite element analysis and in vitro experiments

The research into the mechanical behaviour of bones lies in the crossroad of natural science and physics. Traditionally surgeons and biologists have been concerned with empirics and engineers with more theoretical approaches such as numerical analyses. Over the recent years the number of publications of finite element analyses evaluating the bone-implant complex has increased enormously. *In vitro* experiments using bone specimens are both time consuming and expensive and for practical reasons the numerical investigations can be favourable. Measuring single point strain misses the local variations, whereas the numerical models relies on the knowledge of material properties that are not known, and must be assumed (Sharir et al. 2008). The two methods each have their limitations and advantages, and are not fully overlapping. Cristofolini and co-authors have in particular focused on the advantage in combining the experimental and numerical methods, and that this may have synergistically effects (Viceconti et al.

2009, Cristofolini et al. 2010b). The *in vitro* experiments may improve the finite element analysis by improving input details such as relevant scenarios and indicators, boundary conditions and more detailed material properties. Conversely, finite ele-

ment models may improve *in vitro* experiments by identifying relevant loading conditions and placements of sensors, explore multiple scenarios, optimize boundary conditions and identify acceptable simplifications.

Aims of the study

The general aims of this thesis were to evaluate some bio-mechanical aspects of strain pattern in the proximal femur after THA and to examine initial stability of different femoral implant designs.

The specific aims of the papers were:

- 1) to measure strains on the femoral neck and proximal femur in human cadaver femurs before and after implantation of a femoral resurfacing component, and relate the results to the risk of periprosthetic neck fracture (paper I).
- 2) to evaluate the influential effect of the co-factors age and bone mineral density (BMD) on the change in strains in the neck region after resurfacing arthroplasty (paper I)
- 3) to investigate the changes of strain in the proximal femur after implantation of a standard uncemented femoral stem coupled to a femoral head with increased offset and altered neck version or femoral neck-shaft angle (paper II).
- 4) to investigate the micromotion of a standard uncemented femoral stem coupled to a femoral head with increased offset and altered neck version or femoral neck-shaft angle (paper II).
- 5) to predict the strain pattern of the proximal femur before and after insertion of a cementless femoral stem by use of a subject specific finite element model of human cadaver femurs, and to validate the FE model with experimental strain gauge measurements on the same cadaver femurs (paper III).
- 6) to report a clinical failure of a femoral condyle endoprosthesis implanted in the distal residual femur of a transfemoral amputee, caused by severe bone resorption. We present the features proposed as risk factors for stress shielding and bone resorption (paper IV).

Material and methods

Implant systems

Resurfacing total hip arthroplasty

The resurfacing arthroplasty has been reintroduced as an alternative in total hip replacement. These implants are thought to preserve proximal bone stock in two ways; first there is a minimal removal of bone during primary surgery. Second the implants are designed to preserve a physiological load transfer and thereby maintain a physiological bone remodelling. Resurfacing arthroplasty with metal-polyethylene articulations were used in the 1980's, however, the clinical results were poor. The large number of revisions of this generation of hip resurfacing is most likely associated with excessive polyethylene wear due to the large bearing surfaces. New metal tribology allowed for the introduction of metal-on-metal articulations in the late nineties. This opened for a reintroduction of resurfacing arthroplasty with metal-on-metal bearings. The metal-on-metal articulation in THA is still not a conventional treatment, lacking long-term clinical documentation and perhaps especially long-term consequences of elevated metal ions found in patients with such articulations. In addition there have been reports of pseudotumours in the same patient group (Pandit et al. 2008, Grammatopoulos et al. 2009, Langton et al. 2010).

Periprosthetic neck fracture is the most frequent short-term complication after resurfacing arthroplasty (Shimmin and Back 2005, Carrothers et al. 2010). In paper I we used the ASRTM resurfacing femoral component (DePuy Int Ltd, Leeds, England) (Figure 3). The femoral component is made of CoCr alloy and has a central pin that is not weight bearing. The femoral component is fixed with a thin layer of high viscosity cement and cementing of the central pin is carefully avoided.



Figure 3. The ASRTM resurfacing hip implant.

Modularity of femoral neck version and neck-shaft angle

The accuracy in reconstruction of the hip joint anatomy and biomechanics is another objective in total hip arthroplasty. The reconstruction of anteversion, femoral offset and leg length are features that probably increase longevity of the implant and restores the function of the hip joint. Modular necks have been introduced as a concept allowing variations in neck length, neck version and neck-shaft angles. In paper II we made such alterations by use of a large diameter experimental femoral head. The head consisted of two parts, one outer spherical part and an inner sleeve (Figure 4). The insert of the sleeve was placed eccentrically into the outer part. This allowed for an eccentric displacement of the entry for the taper of the femoral neck. The maximum displacement was 8 mm, which corresponds to a change in femoral neck angle of 6 degrees, which could be adjusted in any desired direction.

In paper II we tested this experimental head in two positions; Position 1 was a maximal anterior displacement of the taper into the femoral head, corresponding to 6 degree of retroversion of the femoral neck axis. Position 2 was a maximal superior displacement of the taper, which corresponded to a reduction of the neck-shaft angle from 130 to 124 degrees.

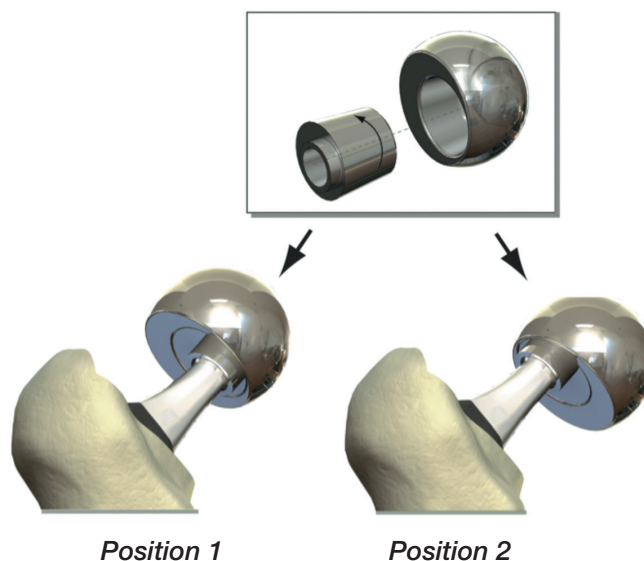


Figure 4. The experimental femoral head allowed eccentric displacement of the entry of the taper of the femoral neck. In position 1 the taper is maximal anteriorly displaced, corresponding to 6 degrees retroversion of the neck axis. In position 2 the taper is superiorly displaced, corresponding to a 6 degrees reduction of the neck-shaft angle.

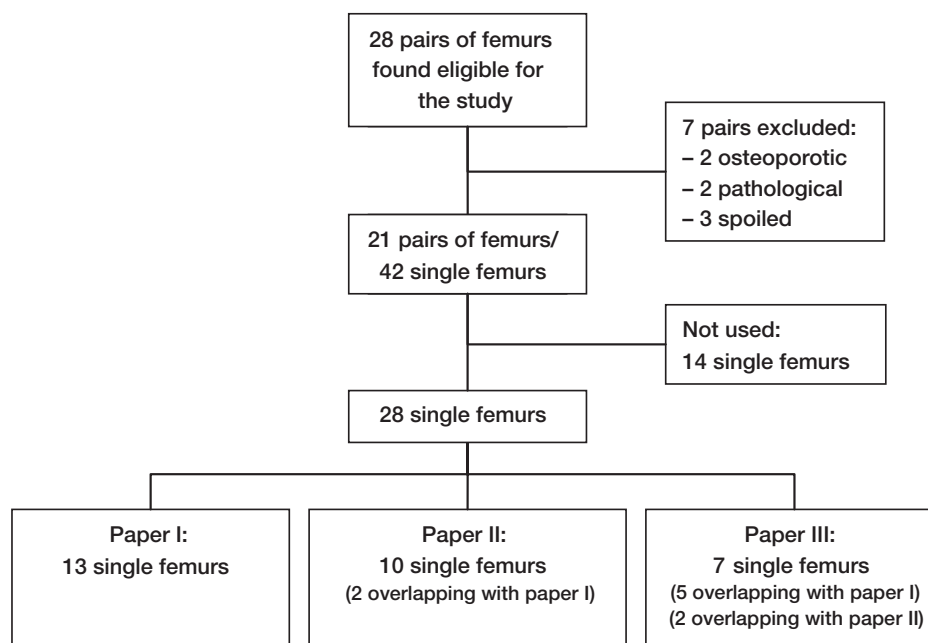


Figure 5. Flow chart showing inclusions and exclusions of specimens in the study.

The experimental head had 10.5 mm increased neck length compared to the standard head. These two femoral head configurations were compared to a standard head. All three configurations were coupled to a straight uncemented stem (Summit™ high offset, DePuy Int Ltd, Leeds, England).

Human cadaver femurs

In this thesis a total of 28 single human cadaver femurs were included. Figure 6 displays the inclusions and exclusions of femurs in the studies. The cadaver femurs were collected from recent deceased during post-mortem examinations. Before collection, consent from the relative of the departed was given. Most of the subjects in this thesis were collected at Stavanger University Hospital. A minority of them were collected at Trondheim University Hospital. Human cadaver bones are an exclusive resource as the availability is limited due to a decline in number of post-mortem examinations. The upper age limit of the donors was of 75 years.

There was some overlapping of subjects between the studies as they were used for implantation of a femoral stem after resurfacing arthroplasty. In addition two of the femurs in the finite element analysis in paper III were overlapping with the specimens in paper II.

Handling and preparation of the femurs

The handling and preparation of the femurs is earlier described (Aamodt et al. 2001). The specimens were removed from the

subjects within 24 hours, packed in saline-soaked towels, and stored at -20°C . Radiographs were obtained preoperatively to rule out localised skeletal pathologies. Bone mineral density in the neck, trochanter, and intertrochanteric area was obtained by dual-energy X-ray absorptiometry (DXA) (Hologic Discovery A, Bedford, USA) and a total value for the proximal femur was given. Femurs with T-scores for the total proximal femur below -2.5 were classified as osteoporotic and not included in paper I. In paper II this inclusion criterion was restricted to T-scores above -2.0 .

Before testing, the femur was thawed at room temperature, and remaining soft tissue was removed. The frontal plane of the femur was defined by placing the femur on a horizontal surface resting on the posterior condyles and the greater trochanter. Prior to resection of the condyles the anteversion was determined for later guidance to recreate frontal and sagittal planes of the femur.

After resection of the condyles, the distal part of the remaining femur was fixed into a steel cylinder with bone cement (Meliodent, Heraeus, Hanau, Germany). The cementing was performed in a jig ensuring that the centre axis of the femur through fossa piriformis coincided with the centre axis of the cylinder.

The distance from the tip of the greater trochanter to the cylinder was 25 cm. To simulate the hip abductor muscles a 40 mm nylon strap was attached to the lateral aspect of the greater trochanter using epoxy glue (X60, HBM, Darmstadt, Germany) and 5–6 small screws. The femur was kept humid during testing by a saline-soaked towel to avoid excessive drying of the bone (Figure 6).



Figure 6. Photo illustration of a femur mounted in the hip simulator.

Hip simulator

During testing the femur was loaded in a material testing machine (MTS 858 MiniBionix II, MTS Systems Corporation, Eden Prairie, Minnesota, USA). The hip simulator allowed the femur to rotate freely around its longitudinal axis, and to tilt freely in the medial-lateral plane. This was to avoid unphysiological bending moments. The femur was tilted 12 degrees into valgus, corresponding to physiological inclination during one-leg stance (McLeish and Charnley 1970). The intact femoral heads, the resurfacing femoral components (paper I) and the experimental femoral heads (paper II) articulated with an acetabular cup (DePuy ASR™, DePuy Int Ltd, Leeds, England) with the corresponding diameter. Finally, the standard heads in paper II articulated with an acetabular cup with a 32 mm polyethylene liner. For all experiments the acetabular cup had an inclination of 45 degrees and 0 degrees anteversion. The centre of the acetabular cup was positioned 110 mm lateral to the load axis. Load was applied to the femoral head by a lever arm connected to the piston of the testing machine. The trochanter strap was fixed to the lever arm at an angle of 15 degrees to the load axis (McLeish and Charnley 1970). Torsional load was applied to the distal part of the femur through a weight-and-pulley system acting on a transverse crossbar connected to the metal cylinder holding the specimen. The ilioti-

bial band was simulated by a wire running from the trochanter strap via two pulleys and attached to the distal femur (Figures 6 and 7). The iliotibial band was abandoned during measurement of micromotion due to the jig design (Figure 7).

We simulated two activities during both strain and micromotion measurement; single leg stance and stair climbing. A single vertical force that was applied through the actuator of the material testing machine to the femur simulated the single leg stance, while stair climbing was simulated by a combined vertical and torsional force (Figure 7). At each load level the femur was preloaded with the current vertical force while the trochanter band and iliotibial band were adjusted. The specimen was thereafter unloaded and strain gauges levelled to zero before testing.

In paper I and III the femurs were subjected to two loading levels. The low loading level had a vertical force of 600 N and the high loading level 900 N. The stair climbing situation was simulated by adding a torque of 10 and 15 Nm to the vertical force, in the low and high loading level, respectively. In paper II the femurs were tested only in the low loading level. In the micromotion part of paper II the torque was adjusted to 13.8 Nm, since the iliotibial band was abandoned.

Load cells monitored the force exerted by the femoral head in the acetabular cup and the forces in the trochanter strap and iliotibial band. These forces were used in the calculation of hip resultant force.

The resultant forces of the experiments are reported in each paper. The hip simulator including the trochanter strap was constructed to simulate a physiological loading situation. Applying a vertical force of 5/6 Bodyweight (BW), the weight of the lower extremity subtracted, yields a physiological resultant force of the hip joint (Martin et al. 1998). Thus for the micromotion measurement test set-up the 600 N vertical force corresponds to a person weighing 73 kg, and the resultant force of the hip joint is 244% BW in single leg stance and 253% BW in stair climbing. These forces correspond well to values obtained in telemetric studies (Davy et al. 1988, Kotzar et al. 1991, Bergmann et al. 2001). The torsional moment in stair climbing was 1.9% BWm in the test set-up with the trochanter band. This is somewhat less than the torsional moment of 2.24% BWm that Bergmann et al reported in their telemetric study (Bergmann et al. 2001).

The inclusion of the iliotibial frame in the strain measurement test set-up leads to an increased lever arm and a reduction in the resultant hip joint force. The resultant hip joint force is therefore no longer physiological corresponding to the vertical force applied in the simulator. Because of the reduction in resultant hip joint force the torque was adjusted from 13.8 Nm in the micromotion measurement test set-up to 10 Nm in the strain measurement test set-up.

In both the strain and micromotion measurement the experiment followed the same test sequence: First, a vertical load, second a combined vertical and torsional load, and third an “unloaded” condition.

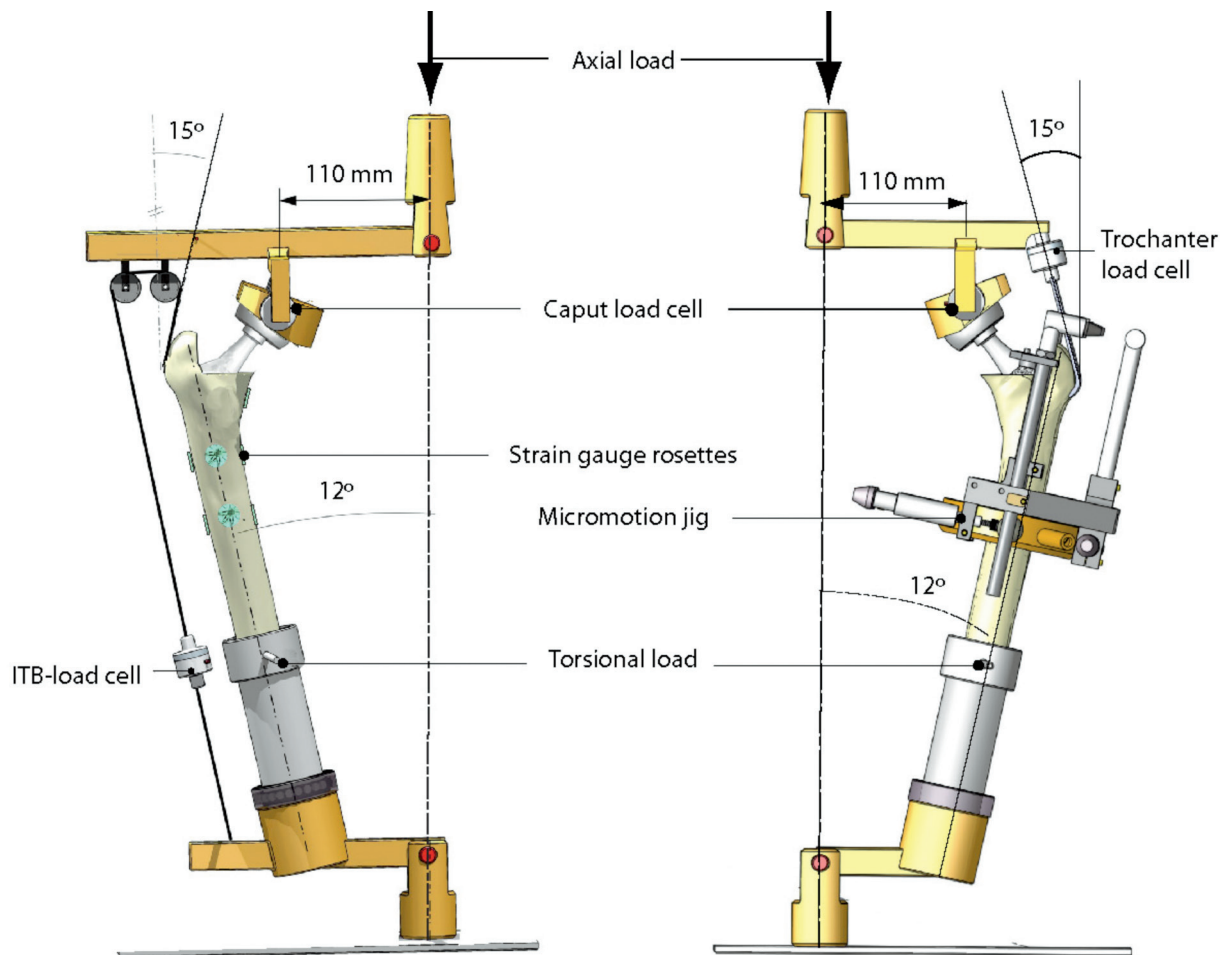


Figure 7. Schematic illustration of the hip simulator. To the left: the test set-up for strain measurement to the left including trochanter band and iliotibial band. To the right: the test set-up for micromotion measurement, including only the trochanter band, and the micromotion measurement device.

Strain gauge measurements

For strain measurements prewired triaxial strain gauge rosettes (FRA-3-23, Tokyo Sokki Kenkyujo Co., Ltd., Japan) were used. Each rosette consisted of three strain gauges, each at 45 degrees angle apart (Figure 8). Gauge 2 was always perpendicular to the longitudinal axis of the femur. For the evaluation of strain in the proximal femur and femoral neck after resurfacing arthroplasty (paper I) we bonded ten rosettes to the femur at four horizontal levels (Figure 8).

Three gauge rosettes were attached on the medial, lateral and anterior aspect of the femoral neck (N). Another seven rosettes were bonded to the proximal femur at three horizontal levels, 14 (A), 34 (B) and 64 (C) mm below the most caudal part the femoral head. At the A-level, one strain gauge rosette was attached at the medial aspect of the femur. At the B and C-level, strain gauge rosettes were attached to the anterior, medial and lateral aspect of the femur. The positions of the strain gauges on the proximal femur correspond to the Gruen

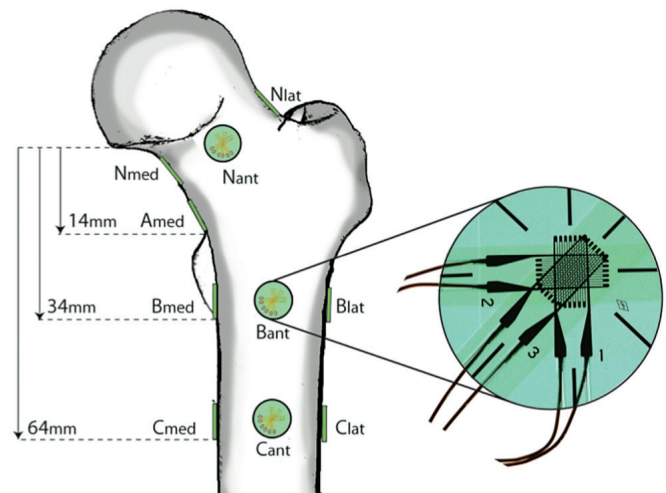


Figure 8: Placement of strain gauge rosettes in the femoral neck area (N) and in three horizontal levels of the proximal femur (A, B and C). To the right a photo of the strain gauge rosette.

zones and have been described and evaluated earlier by Aamodt et al. (Aamodt et al. 2001). For evaluation of strain in paper II and III only the seven strain gauge rosettes on the proximal femur were used, as the neck was resected during surgery. The attachment of strain gauge rosettes is an established procedure (Aamodt et al. 2001) which includes a thorough preparation of the cortical surface. Soft tissue was carefully removed and the surface was smoothened with sandpaper and degreased with acetone and etchant (Scotchbond™ Etchant, 3M ESPE, St Paul, Minnesota), and dried with N₂-gas. After priming the surface (Scotchbond™ Multipurpose Primer, 3M ESPE, St Paul, Minnesota), the rosettes were bonded with epoxy glue (X60, HBM, Darmstadt, Germany). The rosettes were finally covered with waterproof sealing for protection (Vitremer™ Finishing Gloss, 3M ESPE, St Paul, Minnesota). The accuracy of the strain gauges was ± 1 . The strain measurement was first performed for the intact femur in single leg stance and stair climbing, and thereafter repeated for the operated femur. The measurement of strain values was repeated three times. Principal strains were continuously calculated during data acquisition according to the following equation (Irgens 1985):

$$\varepsilon_{1,2} = \frac{\varepsilon_a + \varepsilon_c}{2} \pm \sqrt{\frac{1}{2}(\varepsilon_a^2 - \varepsilon_c^2) + \varepsilon_b(\varepsilon_b - \varepsilon_a - \varepsilon_c)} \quad (2)$$

where ε_1 and ε_2 are principal strains in two directions, perpendicular to one another. ε_a , ε_b and ε_c are the strain output from the three gauges in the rosette oriented 45° apart. Principal direction 1 (ε_1) is always the algebraically larger numerical value. The largest value (positive) value can be denoted as tensile strain, and the smallest (negative) value (ε_2) as compressive strain. In the present thesis we look at the compressive strain on the medial side and the tensile strain on the anterior and lateral side (Aamodt et al. 1997). The strain values are presented as computed percentage values relative to the intact strain values, for each load configuration, and is later referred to as percentage of intact strain.

Micromotion measurement

For measurement of micromotion of the stem relative to the bone, the micromotion jig was attached to the hip simulator (paper II). The test configuration was identical for strain and micromotion measurements except for the iliotibial frame which could not be combined with the micromotion jig.

The micromotion measurement device is previously described and validated by Østbyhaug et al (Østbyhaug et al. 2010). The micromotion jig was based on two main components; a ring attached to the femur and a transducer frame attached to the shoulder of the femoral stem (Figure 9).

The femoral ring consisted of three 18 mm ceramic hemispheric ball probes fixed to a circular frame. The circular frame was locked to the bone with three screws equally spaced around the femur, without perforating femoral cortex.

A guide ensured proper alignment and centering of the ring. The transducer frame was attached to the shoulder of the prosthesis through a yoke and could move freely along the femur in the superior/inferior direction which allowed micromotion measurement at any level along the prosthesis. Altogether six Linear Variable Displacement Transducers (LVDTs) (HBM, Darmstadt, Germany) obtained complete three-dimensional motion with six degrees of freedom. Three were positioned parallel to and three were perpendicular to the length axis of the prosthesis. The accuracy of the LVDTs were $<1\mu\text{m}$.

For each testing sequence micromotion measurements were obtained 5 mm from the proximal and distal border of the coated zone of the femoral stem (Figure 10).

This method enabled measurements of translational motion in three directions (x, y and z) and three rotations (around each of the three previous axes) of the implant relative to the bone at each measurement level. These measurements were then used to calculate total point motion at the anterior (P_{ant}), lateral (P_{lat}) and posterior (P_{post}) aspects of the prosthesis (Figure 10). The total point motion was based on calculation of the movement from a specific prosthetic point with original coordinates $\mathbf{p}$ (x, y, z) to a new point with coordinated $\mathbf{p}'$ (x', y', z') using the equation:

$$\Delta P = \sqrt{(x' - x)^2 + (y' - y)^2 + (z' - z)^2} \quad (3)$$

A more detailed mathematical basis for the micromotion jig and the measurements is found in the supplementary material of Østbyhaug et al's publication (Østbyhaug et al. 2010).

Each loading sequence was repeated for 5 cycles, and relaxation intervals between successive loadings were approximately 10 seconds. The translational and rotational micromotion outcome was the difference between the values of loaded and unloaded condition for each cycle. An average value of the four last cycles was calculated.

Finite element analysis

In the subject-specific finite element analysis (paper III), the geometries of seven subjects were retrieved from CT-scans. The CT scans were optimized by using thin slice thicknesses (0.75 mm), and small distances between the image slices (0.7 mm). Together this gave enough CT-pixels to determine the bone density of each element. The pixel values are given in Hounsfield Units (HU). Inner and outer contours of the femur were extracted from the CT scans based on grey scale transition values described in the thesis of the first author of paper III (Pettersen 2009). The bone-prosthesis assemblies were modelled in SolidWorks and meshed in CosmosWorks (Solidworks Corporation, Concord, USA). The FE models were analysed in ABAQUS 6.7 (Simulia, Providence, USA).

The three dimensional (3D) models were meshed using 2nd order tetrahedral elements with a global size of 3 mm. The

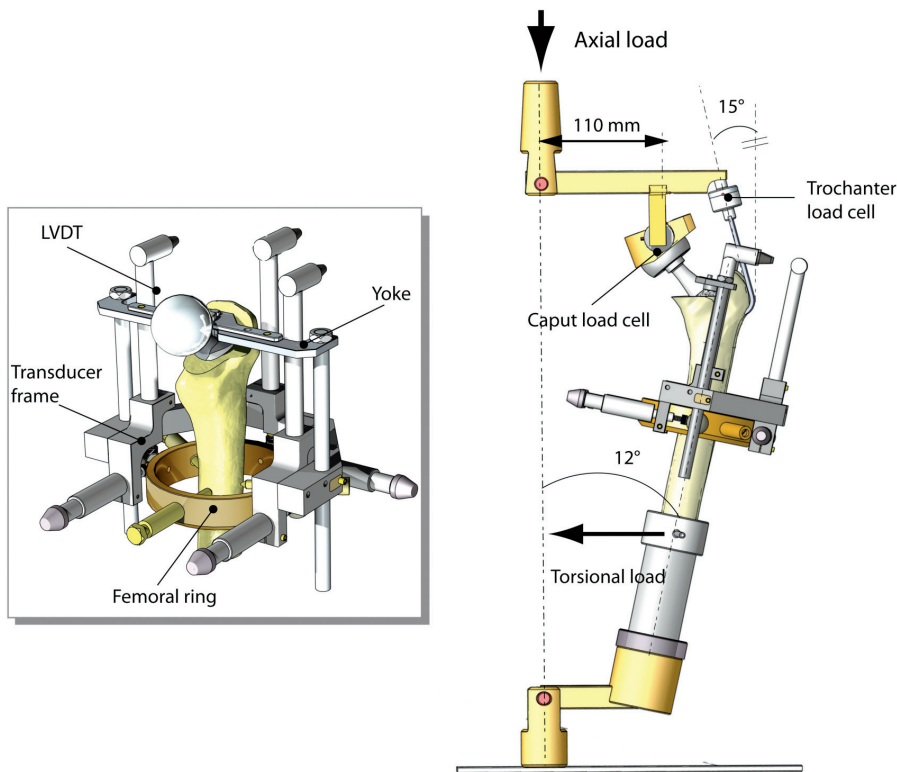


Figure 9. Schematic illustration of the micromotion device coupled to the specimen to the left. To the right the micromotion jig and specimen is mounted in the hip simulator.

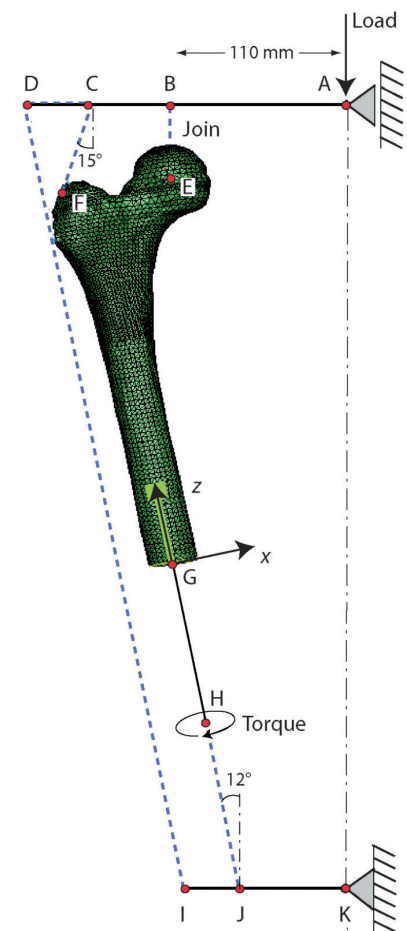


Figure 11. Finite element model of the hip simulator

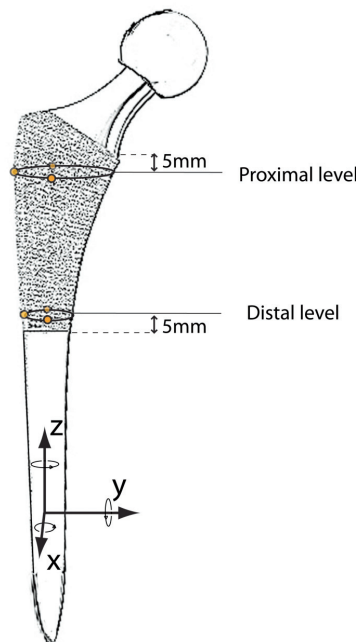


Figure 10. Proximal and distal level for micromotion measurement. Yellow balls mark measurement sites for total point motion. The coordinate system shows the three translational directions, where z is directed along the stem axis, y is directed in the mediolateral plane, and x in the anteroposterior plane.

process of identifying the pixels, i.e. the bone density, located inside the tetrahedral element is described by Zannoni et al. (Zannoni et al. 1998). The material properties of the elements were then given by a density-stiffness relationship introduced by Verhulp et al. (Verhulp et al. 2006). The node coordinates of the FE model were transformed to achieve the orientation of the femur used in the *in vitro* testing.

The hip simulator was modelled using structural elements (Figure 11). The boundary conditions of the hip simulator including the femur were set to mimic the boundary conditions of the experimental load jig. Thus the material flow of the slip ring elements, used between F, C, D and I to simulate the pulley system, was constrained in point F and I. In point K rotation around the y-axis allowed the femur to tilt in the mediolateral direction. In point A displacement in the vertical direction and rotation around y-axis was allowed. The points E, F and G were defined by the rotational centre of the femoral head, the midpoint of the greater trochanter and the midpoint of the distal end of the femur respectively. Single leg stance was simulated by applying load to point A, and stair climbing by adding a torque to point H.

The geometry of the Summit™ stem was provided by the manufacturer (DePuy Int Ltd, Leeds, UK). The Young's modulus of the prosthesis was in the original paper set to 200 GPa (CoCr). The Summit stem is made of a titanium alloy, and the material stiffness has later been corrected accordingly to 110 GPa (Ti alloy), and the finite element models have been reanalyzed. Regrettably paper III was published with the incorrect material stiffness. The corrected finite element analysis is published as a Corrigendum in *Clinical Biomechanics* (paper IIb).

The inner contour of the endosteal surfaces and photographs of the implanted femurs were used to position the implants. In addition, the model positions were confirmed by postoperative radiographs.

The Poisson ratio was set to 0.3. Surface interaction between bone and the stem was simulated assuming a frictional factor of 0.4 and a normal contact stiffness of 1200 N/mm.

The strain values from the FE analyses are three-dimensional. In order to compare strain from finite element analysis to surface strain values obtained by strain gauges, post-processing of the data was necessary. The strain values from the FE analysis was transformed to the local coordinate system of the strain gauges and principal surface strains were calculated. To assess the stress shielding at the different strain gauge locations, the equivalent strain or von Mises strain, ϵ , was calculated. The strain values of the operated femurs were expressed as relative to the strain values of the unoperated femurs.

A case report

A 48-year-old transfemoral amputated woman had an uncemented Femur Condyle Endoprosthesis (FCE) implanted in her residual femur. The purpose of this implant was to make the amputation stump endbearing when using an artificial limb. The condyle plateau was designed to resemble the plateau size of the human femoral condyles. The implant was customized, and the stem design was based on the experience from a customized femoral stem for THA (Unique™, Scandinavian Customized Prosthesis AS, Trondheim, Norway). Preoperative cross-sectional CT images were used to retrieve the inner contours of the femoral diaphysis, and the stem was designed to fit closely into the femoral canal (Figure 12). The stem was fully coated with a dual layer of titanium and hydroxyapatite.

The patient signed an informed consent and the study was approved by the regional medical research ethics committee. The patient was thus followed with X-rays and clinical follow-ups at regular time intervals.

Statistics

Power analysis was performed to identify appropriate sample size for study I. In paper II the number of ten subjects was



Figure 12. Preoperative computer-based construction of the femoral endoprosthesis inside the residual femur.

chosen based on experience from previous experiments by the same research group.

The behaviour of the bone surface and the bone-implant interface will be correlated from one measuring site to another. This means that the results from the different measuring sites of strain gauge rosettes and point motion will be dependent of each other. This has been a topic of discussion in the choice of statistical analysis. However, since we are interested in the measured values at the specific sites of measurement we have chosen to look at the measuring sites as independent incidents, and one-group t-tests was used for statistical comparisons in paper I.

The multiple measuring sites and loading configurations, lead to more complex models regarding statistical analysis due to multiple comparisons and repeated measurements. The corrections for multiple comparisons by for example Bonferroni's method are known to be too strict. A significance level somewhere in between Bonferroni's level and the conventional level of 0.05 can be a good compromise. In paper I and II the multiple comparisons are accounted for by an adjustment of the significance level to $P < 0.01$.

In paper II we tested three different implant configurations in the same specimen, and in addition the testing was repeated for two loading configurations. This study therefore had a factorial design, which was employed in a linear mixed model.

The linear mixed model uses all available data and is unaffected by randomly missing data. In addition the linear mixed model provides a general framework for analysis of repeated measures and is advantageous when the results within each subject tend to be closer in value to another than the observations collected from the different subjects would be (Gueorguieva and Krystal 2004).

In paper I we also chose to evaluate the influence on change in strain from the co-factors age and BMD by the use of multiple linear regression analysis. For this analysis a significance level of $P < 0.05$ was chosen.

The data for the group of subjects in paper I and II was checked by Q-Q plots and found to be normally distributed. In addition the residuals of the change in strain between the

intact and resurfaced femur in paper I were found to be normally distributed and with a constant variance, meaning that the assumptions for multiple linear regression were fulfilled.

Linear regression was used in paper III to evaluate the agreement between the finite element results and the experimental results. The agreement could be considered perfect if the goodness of fit, $R^2 = 1$, the slope $\beta_1 = 1$ and the intercept $\beta_0 = 0$. The 95 % confidence intervals were used to evaluate the statistical significance of the slope and intercept. The slope was considered not significantly different from 1 if the 95% interval included the value 1, and the intercept was considered not significantly different from 0 if the interval included the value 0.

Discussion

General discussion

In this thesis the strain pattern of the proximal femur has been evaluated following insertion of a resurfacing femoral component in human cadaver femurs. Also, the changes in cortical strain pattern was studied after insertion of a standard uncemented stem coupled to three different femoral head configurations, including increased offset and altered neck angles. The standard stem with the three head configurations was also evaluated with regard to initial stability. The third paper validated subject-specific finite element analyses against experimentally obtained strain data. This thesis shows that these experimental methods can be versatile as different implant designs can be evaluated. The fourth paper shows the consequences of dramatic bone loss around an experimental implant inserted into the residual femur of a transfemoral amputee. Perhaps this could have been avoided through pre-clinical evaluation.

A variety of research questions, such as preclinical validation, clinical observations and failure scenarios can be addressed in the experimental methods used in the present thesis. The experimental evaluation of implants can be successfully improved by integration of *in vitro* testing and numerical analysis. *In vitro* testing, numerical analysis and the combination of these methods, is an important piece in the puzzle of biomechanical evaluation of implants, as adverse effects of the implant could be detected at an early stage and clinical observations could be explained. It is however important to emphasize that the experimental testing is only a part of the whole picture of implant evaluation, from material testing to randomized clinical trials.

Both standard composite femurs and human cadaver bones are commonly used in experimental research. The composite bones are easy to handle, as they require no specific storage and they are more easily prepared for testing than cadaver femurs. The cadaver femurs will require storage at least below -20°C . The preparation of cadaver femurs is time consuming, and sometimes grooves and ridges on the cortical surface make the strain gauge positions difficult to replicate. The variation between the cadaver specimens is large, which means that quite large samples are needed for statistical analyses. In addition the collection of cadaver femurs requires necessary authorization, and declining post-mortem examinations reduces the availability. The composite femurs, however, represent a standard geometry and will not reflect the natural variation between specimens. In a study where the main goal is to make a basic comparison between two implant systems,

composite bones can increase the sensitivity of the study by eliminating the variation between the specimens. However, human cadaver femurs are more clinically relevant, and thus in most cases preferable, since they will constitute a more representative population sample.

When comparing two implant systems in cadaver femurs the study should have a paired contralateral design, where the two implants are randomized between the right and the left femur, to increase the power of the study. In paper I we chose a different approximation as the strain pattern after inserting the resurfacing prosthesis was compared to the intact strain pattern, thus only single femurs needed to be investigated. In paper II we compared three different femoral head configurations coupled to the same femoral stem. Also in this study only single femurs were tested, and the femurs served as their own control.

In vitro experiments are simplifications of the *in vivo* situation. In order to replicate the *in vitro* experiments, as many variables as possible need to be standardised. There is no agreement in the literature on which muscles should be included in the experimental set-up of a hip simulator, except for the inclusion of an abductor force (Cristofolini et al. 1995, Cristofolini 1997, Duda et al. 1998, Stolk et al. 2001, Britton et al. 2003, Pancanti et al. 2003, Bitsakos et al. 2005, Kassi et al. 2005, Park et al. 2010).

Duda et al. performed a FE study and concluded that there are nearly no difference in stress and strain pattern between inclusion of all muscles or only abductors and iliotibial band in the interthrochanteric area (Duda et al. 1998). Stolk et al. concluded that even the iliotibial band seems unnecessary in reconstruction of a physiological loading condition (Stolk et al. 2001).

There seems to be a larger controversy considering stability measurements (Cristofolini and Viceconti 2006). Some investigators conclude that active simulation of muscle forces as opposed to no simulation of muscles considerably affect the primary stability of uncemented hip prostheses and that simulation of muscles should be included in preclinical experimental set-ups (Britton et al. 2003, Kassi et al. 2005). This is in opposition to Pancanti et al. who in their study used a simplified load case replacing the major muscle groups with only the hip contact force. They found that this only altered the bone-implant micromotion by $2\text{ }\mu\text{m}$ (Pancanti et al. 2003). A recent study concluded that the abductor muscle has a stabilising effect during simulation of stair climbing, but not as much during single leg stance (Park et al. 2010).

Recent *in vitro* studies of both deformation pattern and primary stability of implants, have a tendency towards being as

simple as possible, including only the abductor muscle studying the proximal femur and the metaphysis (Ganapathi et al. 2008, Deuel et al. 2009, Long et al. 2009, Ostbyhaug et al. 2009, Ostbyhaug et al. 2010, Park et al. 2010, Tayton et al. 2010). Some studies indicate that the bone strength and strain distribution in the proximal metaphysis are not altered when no muscles are simulated (Keyak et al. 2005, Cristofolini et al. 2007a), and some investigators have therefore used a test set-up without the abductor muscles when studying the proximal metaphyseal area of the femur (Cristofolini et al. 2009a, Cristofolini et al. 2009b, Pal et al. 2009). In our test set-up, the hip simulator including only the trochanter band constitutes a physiological loading situation where the individual anatomy of the femur is allowed to influence the resultant hip joint force. Thus when the bodyweight is applied as vertical force, the hip simulator yields physiological hip contact forces, which corresponds to available telemetric measurements of the hip joint force (Bergmann et al. 2001). For future studies, when investigating strain in the proximal femur after insertion of various implant designs and micromotion between implant and bone, it seems reasonable to have an experimental set-up simulating the abductor muscle force, but not the iliotibial band.

In our test set-up the torque during stair climbing simulation is kept constant. The consequence of a constant torque when the lever arm is changed, for example as in paper II where the offset was increased in the experimental femoral head, can be that the micromotion is somewhat underestimated. Stair climbing is seen as the most critical simulation for initial stability tests (Pancanti et al. 2003, Kassi et al. 2005). Therefore, in future experiments on different implant designs that alter the offset or neck angles, one should consider adjustments to the torsional moment in stair climbing and implement this in the protocol.

The loading of a specimen in a hip simulator remains a topic for discussion. There is more information about the forces in the proximal femur and the hip joint than for many other anatomical regions, probably due to the extensive research done to the field of THA (McLeish and Charnley 1970, Davy et al. 1988, Kotzar et al. 1991, Kotzar et al. 1995, Cristofolini 1997, Bergmann et al. 2001, Bergmann et al. 2004, Cristofolini et al. 2009b).

Bergmann and co-authors presented telemetric hip joint forces in routine activities recorded only for four persons (Bergmann et al. 2001). From their publication it is evident that the individual variation is large. However, it seems as there is agreement between these measurements and previous telemetric studies (Davy et al. 1988, Kotzar et al. 1991). Although the diversity in loading characteristics still is large in the literature, several authors acknowledge the work of Bergmann and co-authors and use their measurements as basis for relevant resultant hip joint forces (Britton et al. 2003, Kassi et al. 2005, Cristofolini et al. 2007b, Radcliffe and Taylor 2007, Andreaus and Colloca 2009, Cristofolini et al. 2009a, Fottner et al. 2009, Cristofolini et al. 2010a, Park et al. 2010). In our micromotion

test set-up simulating stair climbing, the torsional moment is approximately 1.9 % BWm. This is somewhat less than the telemetric measured value of 2.24% BWm, but we consider this as a realistic physiological situation. In addition a slight reduction in torque is necessary to reduce the risk of experimental failure.

Another issue is whether the femurs should be loaded at a standardised equal load, or loaded individually corresponding to the bodyweight of the donor. The latter seems reasonable since absolute strain values are dependent on the cortical thickness as well as the BMD of the specimens. However, as long as the strain values are presented as relative to the intact values, the specific loading is probably less significant for strain measurements. Cortical strains are linear to increasing load (Harrington et al. 2002, Cristofolini et al. 2007a, Cristofolini et al. 2009b), and some authors therefore advocate loading the femurs with only a fraction of the physiological resultant force in order to avoid failures. Due to linearity of strain the results can be scaled by the donor's individual bodyweight to obtain the absolute strain data (Cristofolini et al. 2009b).

Considering micromotion measurements it seems as an improvement of the method to load the femurs at their individual bodyweight. Individual loading will also yield a more correct picture of the femurs individual absolute strain values, as it can prevent incorrectly high strain values for the smallest femurs.

Discussion of papers

The resurfaced femur in *paper I* displayed a strain pattern in the proximal femur very similar to the strains in the proximal part of the unoperated femur. This has also been shown in another *in vitro* study (Deuel et al. 2009). Bone resorption due to the stress shielding effect should therefore not be expected in the proximal femoral shaft after resurfacing arthroplasty. In the femoral neck area however, the strain gauge measurements showed an increase in compressive strain on the medial aspect and increased tensile strain on the lateral aspect of the femoral neck. This has also been shown in other finite element and *in vitro* studies (Gupta et al. 2006, Taylor 2006, Little et al. 2007, Ganapathi et al. 2008, Cristofolini et al. 2009a, Long et al. 2009, Pal et al. 2009). However, Vail et al. found by the use of photoelastic strain measurements a reduction of strain in the femoral neck after inserting a resurfacing component in neutral position (Vail et al. 2008). Even though there are some discrepancies in the results regarding the femoral neck strain pattern after resurfacing arthroplasty, there is a predominance of papers demonstrating increased strain and stress. Whether the increased strain implies an increased risk of fracture is not agreed on in the literature.

In our study we found an increase of strain after implanting the resurfacing component up to 15% compared to the intact values. The measured values are well below suggested critical

damage limits (Pattin et al. 1996). However, together with surgical factors and patient-related factors the increased strains in the femoral neck may contribute to the risk of neck fractures. In addition, we found that higher age is significantly correlated to increased strain in the femoral neck after resurfacing arthroplasty and further that increased BMD protected against increase of strain. These findings support the intention of careful selection of patients receiving resurfacing arthroplasty.

In *paper II* we analysed the changes of the femoral strain pattern and the bone-implant micromotion after insertion of an uncemented stem coupled to a femoral head of increased offset and retroversion or reduced neck-shaft angle. In general the standard stem gave a stress shielding effect with reduced strains especially in the medial proximal femur, which can be expected for uncemented implants. The particular implant used in this study is clinically well documented, therefore the standard head coupled to this stem could be considered as a reference situation. The differences in strain and micromotion between the three femoral head configurations were generally very small. Even though the experimental head configurations gave a significant increase of strains compared to the standard head, the largest significant increase was only 14.2%. The experimental head gave an increase of the neck length of 10.5 mm and thus the lever arm of the femur-implant assembly was increased. This led to a reduction in resultant hip joint force compared to the standard head situation. Changes in resultant hip joint force can thus not explain the increase in strain observed. However, the increased bending moment would probably contribute to increase in strain.

The micromovements between the femur and the femoral stem remained small for all three femoral head configurations, and for both loading conditions. A recent registry report have shown increased revision rate for femoral stems with modular necks (Australian Orthopaedic Association National Joint Replacement Registry 2010). Together with case reports on femoral modular neck fractures (Skendzel et al. 2010, Wilson et al. 2010, Wright et al. 2010) there are some concerns on the long-term performance of these implants. The findings in the present study cannot explain these failures. It seems as increasing femoral offset and retroversion or reduced neck shaft angle on the particular femoral stem used in this study do not have clinically important effects on the strain and micromotion pattern.

Since the *in vitro* experiment is quite time consuming and human cadaver femurs are an exclusive resource, FE analyses has over the recent decades become increasingly popular. In *paper III* we used the results from *in vitro* strain gauge measurements to validate the predictions of a subject specific finite element analysis. In this study CT scans of the human cadaver femurs tested in the laboratory, enabled us to retrieve the geometry and density of the subjects, and thereby model the femurs with a stiffness adjusted to the local density of the element of the model. This gives the model the advantage of accounting for the variation of geometry and stiffness

in human specimens. The results from the FE analysis were fairly good with an agreement of $R^2=0.94$ for intact femurs. The operated femurs had an agreement of $R^2=0.86$.

However, the FE model still assumes isotropy of the bone, which in reality is not true. The other major limitation of this study was the lack of a method for accurately verifying the positions of the femoral stem in the FE models. This study successfully described the overall stress shielding effect of the prosthesis, and even though FE analyses can not replace *in vitro* testing, this study supports that FE models can be considered as a valuable supplement to the *in vitro* analysis (Cristofolini et al. 2010b).

In the original article the material of the femoral stem was assumed to be CoCr with a corresponding stiffness of 200 GPa. This was unfortunately incorrect, and we have later reanalyzed the simulations with the correct material stiffness of 110 GPa, corresponding to Titanium alloy. The reduced material stiffness gave only minor changes to the results. The correlation between experimental data and finite element analyses were not altered and the significance of the results was not changed. The conclusions of the study were thus maintained.

Paper IV describes a periprosthetic fracture due to severe bone resorption. We believe this bone resorption occurred because of stress shielding. Risk factors associated with stress shielding such as wide stem diameter (Bobyn et al. 1992, Engh et al. 1999, Glassman et al. 2006) and extensive implant coating (Bobyn et al. 1992, Blunn et al. 2000, Yamaguchi et al. 2000, Werner et al. 2005, Glassman et al. 2006) both applied to this implant. In addition the patient's residual femur must be expected to be osteoporotic (Sherk et al. 2008), and low preoperative bone mineral density is also known to increase the stress shielding effect (Kerner et al. 1999, Venesmaa et al. 2003, Rahmy et al. 2004, Alm et al. 2009).

A similar implant has been inserted into transhumeral amputees (Witso et al. 2006). This implant design had a cemented intramedullar stem, and periprosthetic bone resorption has not been observed in this patient group. The stem of the FCE had to be uncemented due to calculations that showed a risk of material fatigue failure at the stem-plateau junction if the stem was too slim compared to the size of the condyle plateau. Therefore a customized press-fit stem was chosen. The diameter of the stem is determining for the stiffness of the implant which means that a wider uncemented stem can have dramatic consequences for the periprosthetic bone resorption compared to a slimmer cemented stem. In a patient with a wide or osteoporotic femoral canal the difference between a cemented and press-fit stem can be expected to be even larger.

In our opinion this patient case emphasizes the necessity of preclinical evaluation through experimental studies. The knowledge on risk factors for stress shielding have become more established throughout the last decade, and should be taken into consideration in planning new implant designs. The stiffness of the implant seems to be a key factor aggravating stress shielding in periprosthetic bone.

Further perspectives

New hip implant designs will continue to be introduced to patients and surgeons. This justifies preclinical research on implants and further development of experimental methods.

The experience from this thesis has led to several interesting methodological questions, where some can easily be answered for, whereas others have a more complex background.

- The hip simulator can be simplified by only simulating the abductor muscle force both in strain and micromotion measurements.
- The femurs should be loaded by the donor's individual bodyweight.
- The distance from the body centre axis to the rotational centre of the acetabulum is possible to obtain from donors, and is another possibility to individualize the hip simulator.
- The strain gauge measurement method simulates the immediate postoperative situation, before the implant has reached osseointegration and secondary stability. Bone ingrowth and bone adaptive remodelling have been simulated both in *in vitro* experiments, animal models and in finite element analyses (McNamara et al. 1997, Waide et al. 2003, Huiskes and Stolk 2005, Tarala et al. 2010). Further integration of *in vitro* experiments, finite element models and animal models could take the stress shielding research a step further.
- Even though stress shielding is extensively investigated, many questions on risk factors and how to prevent bone

resorption are still to be answered. A study on how bone mineral density around a femoral stem is affected by high intensity exercise and different surgical approaches is under planning.

- At the moment it seems important to further integrate the subject specific finite element models and *in vitro* experiments. Finite element models could be useful to predict optimal positioning of the strain gauge rosettes in new *in vitro* experiments.

The specific studies included in this thesis give cause to further investigations.

- The modularity of femoral necks should be further investigated on different stem sizes and different stem designs.
- Excessive valgus and varus positions of the resurfacing component could be advantageous to investigate.
- The experimental implant for transfemoral amputees could have benefited of a smaller stem diameter, preferably a cemented stem. This could have been possible by making the condyle plateau smaller or by use of a stiffer implant material such as cobalt chrome. If these changes were compatible with full endbearing, then probably the extreme stress shielding could have been avoided. This could theoretically have been investigated *in vitro* or in an animal model.

Conclusions

1. The implantation of a resurfacing component increases strains significantly on the medial and the lateral aspect of the femoral neck, compared to the strain values of the intact femur. In the proximal femur a physiological strain pattern was preserved. The changes of strain in the femoral neck area were too small to cause neck fracture alone; however they may contribute to the risk of fracture when combined with patient-specific or surgical factors.
2. Reduced BMD and higher age significantly increased the change of strain in the femoral neck area after resurfacing arthroplasty.
3. The increase of medial offset in combination with retroversion or reduced neck-shaft angle increases the cortical strain of the proximal femur significantly compared to a standard head. The differences in strain are however too small to be considered clinically important.
4. The total point motions of the standard uncemented stem were not influenced by the different femoral head configurations tested. The specific femoral stem in this study was very stable in all test situations.
5. The subject specific finite element models in this study successfully described the overall stress shielding effect of the implant. On the proximal medial side of the femur the finite element model underestimated the stress shielding effect compared to the experimental data, and on the lateral side there was some degree of overestimation of stress shielding. The FE model should be improved further and can be a valuable supplement of *in vitro* testing.
6. Stress shielding can lead to severe bone resorption, which subsequently can lead to implant failure, such as the periprosthetic fracture experienced in our patient. Known risk factors for stress shielding applied to this particular case. This case report supports preclinical testing of novel implant designs.

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