MECHANICAL CHARACTERISTICS IN IMPACTION ALLOGRAFTING –
THE ROLE OF GRAFT DENSITY AND CEMENT PENETRATION PROFILE

by

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Abstract

Revision total hip arthroplasty with femoral impaction allografting has an attractive potential for restoring bone stock in femurs with bone loss caused by the failure of hip implants. However, problematic implant subsidence is often reported after this procedure. A lack of understanding remains over the mechanisms that cause subsidence.

The objectives of this study were to: a) explore the relationships between subsidence and morphometric features of the graft and bone cement regions after femoral impaction allografting in a cadaveric femur model; b) characterize mechanical properties of the graft bed as a function of impaction force, and explore new alternative graft compaction methods; and c) develop a finite element model to investigate the key mechanisms that contribute to initial implant subsidence.

High levels of cement penetration into the graft bed were observed, resulting in extensive regions of cement contact with the host bone in a cadaveric femur model. The implant subsidence correlated negatively with the amount of cement-endosteum contact.

The density, compression stiffness and shear strength of the graft were proportional to the impaction force. A slower alternative graft compaction method resulted in higher graft stiffness and shear strength than traditional graft impaction, but the benefit of this new compaction method was small compared to the effect of increasing the impaction force.

In a finite element model, the relationship between graft density and subsidence was dependant on cement penetration profile. Without cement-endosteum contact, subsidence decreased with increasing graft density; however, graft density did not affect subsidence in constructs with cement-endosteum contact. Initial subsidence was primarily attributed to slippage at the stem-cement and endosteum interfaces, and the latter mechanism was greatly affected by changes in graft density and cement penetration profile.
This study demonstrated that extensive cement penetration can occur in femoral impaction allografting, which may compromise the potential for new bone formation but may be important in preventing excessive subsidence. The endosteum interface was identified as a key factor in the development of subsidence. Finally, our results indicate that the potential benefit of achieving a denser graft bed depends upon the cement penetration profile.
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This thesis is dedicated to my husband Jeff,
for his love and immeasurable support.
Co-authorship Statement

Sections of this thesis have been submitted or published as multi-authored papers in refereed journals. Details of the authors’ contributions are provided.

Chapter 2

Authors’ contributions: The origin of this project was a grant proposal written by Thomas Oxland, Goran Fernlund, Bassam Masri and Clive Duncan. Carolyne Albert was responsible for the design of this study based on ideas from the grant proposal, conduction of the experiments, analysis and presentation of the findings, and writing and editing of the original paper. Göran Fernlund and Thomas Oxland supervised the project and were the key editors of this paper. Sanjeev Patil conducted the surgical procedures on the cadaveric femora and provided editorial assistance. Hanspeter Frei stimulated discussions and provided editorial assistance. Bassam Masri and Clive Duncan provided clinical input and editorial assistance.

Chapter 3

Authors’ contributions: Carolyne Albert was responsible for the original ideas behind the paper, conduction of the experiments, analysis and presentation of the findings, and writing and editing of the original paper. Thomas Oxland provided guidance as well as editorial assistance. Bassam Masri and Clive Duncan provided editorial assistance. Göran Fernlund was the key editor on this paper.

Chapter 4

Authors’ contributions: Carolyne Albert was responsible for the original ideas behind the paper, construction of the finite element model, analysis and presentation of the findings, and writing and editing of the original paper. Göran Fernlund was the key editor on this paper. Thomas Oxland provided guidance as well as editorial assistance. Bassam Masri and Clive Duncan provided editorial assistance.
CHAPTER 1

INTRODUCTION
1.1 Total Hip Arthroplasty

Musculoskeletal conditions are the leading cause of long-term pain and physical disability, affecting hundreds of millions of people worldwide (Woolf and Pfleger, 2003). Approximately 4.4 million Canadians suffer from arthritis (Statistics Canada, 2008), which affects many aspects of their lives including daily and social activities, and their ability to work. Musculoskeletal conditions constitute the second most costly diagnostic category in Canada - in 1998, these conditions were responsible for an estimated CDN$16.4 billion in direct (medical expenses) and indirect (loss of productivity) healthcare costs in Canada (Health Canada, 1998). In the United States, the total annual healthcare costs of musculoskeletal conditions in 2004 was US$849 billion – almost 8% of the national gross domestic product (American Academy of Orthopaedic Surgeons, 2008). Moreover, the prevalence of musculoskeletal problems is rising due to the ageing population and sedentary lifestyles (American Academy of Orthopaedic Surgeons, 2008). The number of people who suffer from arthritis is expected to rise by more than 50% between the years 2001 and 2026 (Health Canada, 2003).

Total hip arthroplasty (THA) can be an effective treatment for musculoskeletal conditions affecting the hip, such as severe osteoarthritis, rheumatoid arthritis, congenital deformities, hip fractures, and femoral head necrosis (Karrholm et al., 2007). In THA, the diseased or injured hip joint is replaced with implants: an acetabular cup with an ultra-high molecular weight polyethylene liner, and a femoral stem which may be press-fit or cemented into the femur using polymethyl methacrylate bone cement (Figure 1.1).
In general, THA surgeries have very good outcome. Prior to undergoing THA, most patients experience continuous pain that limits their ability to perform common daily activities such as walking or kneeling. After surgery, most of them become pain free and are able to resume jobs as well as some physical activities. For this reason, THA surgeries have become popular around the world. Over 25,000 such procedures are performed annually in Canada (Canadian Institutes for Health Information, 2005). Moreover, the demand for THA is growing - Canadian hospitals have observed a 101% increase in hospitalizations for hip and knee replacements between 1996 and 2006 - and these procedures are performed increasingly in younger patients (Canadian Institute for Health Information, 2008).

1.2 Failure and Revision Options

Hip implants, however, have a finite life span. The survival rate of primary THA is 80 to 98% at 10 years post surgery (Karrholm et al., 2007). Failure of the femoral and/or acetabular component can require revision THA surgery to replace the failed component(s). Revisions represent 10-20% of all THA procedures (Karrholm et al., 2007; Kurtz et al., 2005), and they are becoming more and more common. In the United States, the number of revision THA surgeries performed annually increased by as much as 79% between 1990 and 2002 (Kurtz et al., 2005). The leading causes for revision THA are aseptic loosening, instability or
dislocation, and infection (Karrholm et al., 2007; Bozic et al., 2009). The most common indication for revision of the femoral component is aseptic loosening; i.e., a mechanical loosening of the implant from the surrounding bone (Bozic et al., 2009).

Loosening of the femoral component is often accompanied by bone loss, which can make revision procedures much more challenging than primary THA. The severity of the bone loss is variable; it can be classified, for example, using the Endo-Klinik classification system (Figure 1.2).

![Figure 1.2 Endo-Klinik classification system for femoral bone stock deficiency. Type I: radiolucent zone confined to the upper half of the cement mantle with clinical signs of loosening. Type II: generalized radiolucent zones and endosteal erosion of the proximal part of the femur, leading to widening of the medullary cavity. Type III: widening of the medullary cavity by expansion of the proximal part of the femur with possible perforation. Type IV: gross destruction of the proximal and middle third of the femur. Adapted from Engelbrecht E. and Heinert K., 1987.](image)

In the presence of significant bone deficiency in the proximal femur, a number of revision options are available to the surgeon (Figure 1.3). These include: Girdlestone arthroplasty, i.e., removal of the implants and allowing the formation of scar tissue without rebuilding the joint surfaces; the use of a longer/larger stem with or without cement; replacement of the proximal femur with a structural allograft or a megaprosthesis; and impaction allografting (Duncan et al., 1998).
Figure 1.3 Surgical options for revision THA. (a) Girdlestone arthroplasty. (b) Structural allograft. (c) Cemented revision. (d) Cementless revision with a larger prosthesis. (e) Replacement of the proximal femur with a megaprosthesis.

1.3 Femoral Impaction Allografting

1.3.1 Technique
In femoral impaction allografting, the bone deficient proximal femur is reconstructed with particles of cancellous bone graft, obtained from donors, before a new implant is cemented in place. The graft, usually harvested from femoral heads but occasionally from distal femurs or proximal tibiae, is morsellized with a bone mill. The failed femoral stem is first removed along with the bone cement if present, and the canal is cleared of any debris. A tight-fitting polyethylene plug (distal plug) is inserted in the femoral canal to a distance of approximately 2 cm distal of the most distal bone defect (Figure 1.4 a). The femoral cavity is gradually filled with the morsellized cancellous bone graft (MCB), impacted first using flat-headed distal impactors (Figure 1.4 b), then using proximal impactors which bear the oversized shape of the new stem (Figure 1.4 c). Once the medullary cavity is filled with impacted MCB, the proximal impactor is left in place temporarily while further MCB is packed around the impactor using proximal packers (Figure 1.5). After graft impaction, the neo-medullary canal (newly formed stem-shaped cavity) is filled with bone cement. The bone cement consists of a liquid (methyl methacrylate monomer) and a powder (polymethyl methacrylate) which, when mixed together, polymerize in an exothermic reaction within approximately 10 minutes after they are mixed.
together. The cement is injected into the canal early in the polymerization process, and is pressurized using a cement gun (Figure 1.4 d). Finally, when the cement has reached the desired ‘doughy’ consistency, the new stem is slowly and carefully inserted in place (Figure 1.4 e). A set of surgical instruments used for femoral impaction allografting (CPT, Zimmer Inc., Warsaw, Indiana) is shown in Figure 1.5.

![Figure 1.4 Impaction allografting technique. (a) Insertion of distal plug, with guide wire attached. (b) Distal impaction of the morsellized graft. (c) Proximal impaction of the graft. (d) Injection and pressurization of bone cement into the stem-shaped neo-medullary canal formed by the impacted graft. (e) Stem insertion.](image-url)
1.3.2 Indications and use of the technique
The femoral impaction allografting technique was introduced in the early 1990s as a means to reverse problematic bone loss that is often encountered after THA (Ling et al., 1993; Gie et al., 1993; Nelissen et al. 1995). Good clinical results have been reported, including alleviation of pain and improvement of function (Gie et al., 1993; Leopold et al., 1999), and this procedure is now performed in patients with varying degrees of bone loss, e.g., types I to IV according to the Endo-Klinik classification system (Sierra et al., 2008). Impaction allografting is also performed in patients of various ages, e.g., 31-89 years old (Gore, 2002; Piccaluga et al., 2002; Robinson et al., 2002; Wraighte and Howard, 2008). This procedure, however, is technically challenging and time-intensive (Morgan et al., 2004), and a high incidence of complications have been reported (Eldridge et al., 1997a; Pekkarinen et al., 2000). For these reasons, some surgeons reserve this procedure for a specific group of patients for whom reconstitution of bone stock is deemed important: young (<50 years old) and/or active patients with compromised bone stock (Duncan et al., 1998; Leopold et al., 1999; Morgan et al., 2004). Some surgeons have expressed concerns about performing such a lengthy operation in elderly
patients after an 88-year-old woman died due to a cerebrovascular accident six months after surgery (de Thomasson et al., 2005). Nonetheless, femoral impaction allografting has become a popular option for revision THA at many hospitals, particularly in Europe. This procedure accounted for most of the revisions performed between 1991-2003 at the Royal Devon and Exeter Hospital in the United Kingdom (Sierra et al., 2008), and many clinical studies of femoral impaction allografting have been published recently by British centres (e.g., Wraighte and Howard, 2008; Sierra et al., 2008; Aulakh et al., 2009; Hassaballa et al., 2009). To this day, over 90 clinical articles about femoral impaction allografting can be found in English through Pubmed (Table 1.1).

Table 1.1 Published clinical articles on femoral impaction allografting.

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Nonetheless, there are considerable problems associated with femoral impaction allografting. Bone graft sources are limited, and two to four donor femoral heads are required to create the allograft bed. There is also a risk of disease transfer from the graft (Sommerville et al., 2000). Moreover, incomplete graft remodeling (Linder, 2000), a high incidence of femoral fracture (Meding et al., 1997; Leopold et al., 1999; Pekkarinen et al., 2000; Ornstein et al., 2002), and
high levels of implant migration relative to the femur have been reported (Meding et al., 1997; Eldridge et al., 1997a; Masterson et al., 1997a; Masterson et al., 1997b; Nelissen et al., 2002).

### 1.3.3 Femoral fracture

Femoral fractures are common with impaction allografting and can occur intraoperatively (Gie et al., 1993; Meding et al., 1997; Masterson et al., 1997a; Pekkarinen et al., 2000; Knight and Helming, 2000; Ullmark et al., 2002; Robinson et al., 2002; Piccaluga et al., 2002; Ornstein et al., 2002) or postoperatively (Gie et al., 1993; Meding et al., 1997; Fetzer et al., 2001; Lind et al., 2002; Ornstein et al., 2002).

Postoperative fractures occur typically around the stem tip or more proximally, and usually lead to re-operation, i.e., either fracture repair or another revision THA (Leopold et al., 1999). In one study, a postoperative fracture rate of 9% was reported within five months of the surgery; most of these were alleged to have originated at a cortical window or perforation that was present at the time of the surgery (Ornstein et al., 2002).

Intraoperative fractures are especially common (Pekkarinen et al., 2000; Ornstein et al., 2002; Piccaluga et al., 2002; Frances et al., 2007) – these have been reported at rates up to 27% (Ornstein et al., 2002). Intraoperative fractures can occur during the removal of the cement from the primary THA, during graft impaction, or during trial reduction (Ornstein et al., 2002). Intraoperative fractures require subsequent cortical reinforcement using either cortical strut graft, synthetic mesh and/or cerclage wire (Masterson et al., 1997a; Leopold et al., 1999). Intraoperative perforation of the femoral shaft is also common, occurring typically during removal of the cement from the previous THA, and it is often treated with a cortical strut graft (Leopold et al., 1999). It has been found that greater bone stock deficiency and intraoperative perforation of the femur are risk factors for intra- and postoperative femoral fractures (Ornstein et al., 2002). To minimize the risk of fracture, several surgeons advocate prophylactic reinforcement of the femur with cables, meshes and/or plates, particularly in zones of extensive defect, prior to graft impaction (Duncan et al., 1998; Pekkarinen et al., 2000; Schreurs et al., 2005; Sierra et al., 2008).
1.3.4 Implant subsidence

Gradual distal migration of the stem within the femur, often referred to as subsidence, is not uncommon after impaction allografting (Franzen et al., 1995; Meding et al., 1997; Masterson et al., 1997a; Eldridge et al., 1997a; Leopold et al., 1999; van Biezen et al., 2000; Pekkarinen et al., 2000; Ornstein et al., 2000; Boldt et al., 2001; Robinson et al., 2002). While it is often less than 2 mm (Halliday et al., 2003), much higher levels of subsidence are often observed (Meding et al., 1997; Masterson et al., 1997a; Eldridge et al., 1997a; Pekkarinen et al., 2000; Gore, 2002). Subsidence up to 8 cm has been reported (Sierra et al., 2008).

Some implant subsidence within the cement mantle is expected to occur (Figure 1.6). The most common stems used in this procedure are double-tapered polished stems. Subsidence of these stems does not necessarily reflect a failure in fixation, as the implant may settle into a stable position (Gie et al., 1993; Elting et al., 1995; Nelissen et al., 2002; Ornstein et al., 2004). It is believed that the resulting radial compression generated as the stem subsides within the cement is beneficial in enhancing the rotational fixation of the implant (Gie et al., 1993). These tapered stems are often implanted with a centralizer, i.e., a polyethylene cap intended to leave a space into which the tip of the implant can migrate (Figure 1.6). It has been speculated that this process generates compression on the surrounding graft which may also be beneficial to the remodeling process (Gie et al., 1993). Nonetheless, a correlation between implant migration and the radiographic appearance of the graft has not been found (Ornstein et al., 2004). Furthermore, it is not clear whether the stem subsides mainly within the cement, or whether the whole construct subsides within the femur (van Biezen et al., 2000; Ornstein et al., 2001).
Figure 1.6 Settling of the stem within the cement mantle. A polyethylene centralizer (insert) is usually implanted at the tip of smooth tapered cemented stems to provide a space into which the stem tip can subside. Settling of the stem into the cement is expected to generate compressive radial stresses within the surrounding cement and graft regions.

In some patients, however, stem migration is progressive (Ornstein et al., 2001; Nelissen et al., 2002), and can cause further complications (Meding et al., 1997; Masterson et al., 1997a; Eldridge et al., 1997a; Masterson et al., 1997b; Robinson et al., 2002; Piccaluga et al., 2002). ‘Massive’ subsidence (>10 mm) has been associated with a risk of aseptic loosening of the stem (Meding et al., 1997), hip dislocation (Masterson et al., 1997a) and thigh pain (Eldridge et al., 1997a; Robinson et al., 2002; Piccaluga et al., 2002; Hassaballa et al., 2009), and is therefore regarded often as a clinical failure (personal communication with Dr. Bassam Masri, 2009).

The mechanisms through which subsidence develops after impaction allografting are not fully understood. Many mechanisms have been suggested to contribute to subsidence: settling of the stem within the cement (Gie et al., 1993; Elting et al., 1995; Karrholm et al., 1999; Knight and Helming, 2000; Ornstein et al., 2001; Schreurs et al., 2005; Yim et al., 2007; Wraighte and Howard, 2008), shear failure within the graft (Ornstein et al., 2001; Halliday et al., 2003), compression of the graft (Karrholm et al., 1999; Ornstein et al., 2000; Ornstein et al., 2001; Nelissen et al., 2002; Gore, 2002; Ornstein, 2002; Halliday et al., 2003), sliding at the endosteum interface (Ornstein, 2002; Frei et al., 2005a; Frei et al., 2005b), cement
fatigue/failure (Masterson et al., 1997a; Masterson et al., 1997a; Masterson et al., 1997b; Ullmark et al., 2002; Ornstein, 2002), allograft resorption (Karrholm et al., 1999; Ornstein, 2002), sliding at the graft/cement interface (Ornstein et al., 2001; Yim et al., 2007), and expansion of the femoral canal (Karrholm et al., 1999; Ornstein, 2002; Frei et al., 2005b).

Longitudinal fracture of the cement mantle can cause the stem to subside within the cement (Figure 1.7). Some stems with massive subsidence showed radiological evidence of cement mantle fracture (Masterson et al., 1997a). It was suggested that cement mantle defects (defined as a cement layer less than 2 mm thick) may be a risk factor for massive subsidence, as this would predispose the construct to fracture of the cement (Masterson and Duncan, 1997; Masterson et al., 1997a; Masterson et al., 1997b). Since these reports were published, impaction tools have been updated to accommodate a minimum cement mantle thickness of 2 mm (personal communication with Dr. Clive Duncan, 2009). Without cement fracture, however, it is not clear whether cement mantle defects influences subsidence. There appeared to be a relationship between subsidence and cement mantle defects in one study (Nelissen et al., 2002) while none was observed in another study (Ornstein et al., 2004).

![Figure 1.7 Stem subsidence relative to the cement due to longitudinal cement fracture.](image)

Postoperative compression of the graft has been speculated to cause implant subsidence (Figure 1.8 a), (Karrholm et al., 1999; Ornstein et al., 2000; Ornstein et al., 2001; Nelissen et al., 2002; Ornstein, 2002; Gore, 2002; Halliday et al., 2003). This is presumed because the
graft region has the lowest stiffness of all the regions in a femoral impaction allografting construct and it exhibits some creep deformation under compressive loading (Giesen et al., 1999; Voor et al., 2000; Voor et al., 2004).

Figure 1. 8 Subsidence due to compression deformation of the graft bed (left), shear failure in the graft bed (center), and slippage at the endosteum interface (right).

Shear failure, or slippage in the graft bed, is also believed to contribute to implant subsidence (Ornstein et al., 2001; Halliday et al., 2003; Ornstein et al., 2004). Particulate materials are well known to be susceptible to shear stresses. Under certain loading conditions, particulate materials form shear failure planes that essentially slide until the normal loads on those planes become so high that the shear strength exceeds the shear stress. This process may contribute to implant subsidence in impaction allografting, as the graft region surrounding the stem is subjected to shear loading (Figure 1.8 b).

It has also been suggested that subsidence may be associated with slippage at the endosteal interface (Figure 1.8 c), (Ornstein, 2002; Frei et al., 2005a; Frei et al., 2005b). The importance of this mechanism is implied by radiographic observations that the stem and cement appear to migrate together relative to the femur in some patients (Masterson et al., 1997a; Ullmark et al., 2002; Halliday et al., 2003; Yim et al., 2007).
Expansion of the femoral canal has been proposed as another possible contributor to subsidence (Figure 1.9), (Karrholm et al., 1999; Ornstein, 2002; Frei et al., 2005b). This mechanism could occur due either to the natural expansion of the femoral canal due to ageing (Ornstein, 2002; Ornstein et al., 2004), or to resorption or cancellization of the cortical bone at the endosteal (inner) surface caused by an interrupted vascular supply (Karrholm et al., 1999; Frei, 2003).

![Figure 1.9 Subsidence caused by expansion of the femoral canal, adapted from Frei, 2003.](image)

Finally, the graft incorporation process has been speculated to be the source of some subsidence (Karrholm et al., 1999; Ullmark et al., 2002; Ornstein, 2002; Ornstein et al., 2004). It is not known, however, whether MCB graft strengthens or weakens during the incorporation process (Ornstein et al., 2003).

Some clinical factors have been proposed to affect the subsidence. It is widely believed that a thorough packing of the graft is essential for initial stem stability (Halliday et al., 2003; Cabanela et al., 2003). Graft particle size distribution is also believed important (Halliday et al., 2003). In vitro studies have characterized the mechanical behaviour of MCB in shear (Tanabe et al., 1999; Brewster et al., 1999; Dunlop et al., 2003). It was concluded that shear strength was affected by the particle size distribution (Tanabe et al., 1999; Dunlop et al., 2003), and by washing of the graft (Dunlop et al., 2003). Nonetheless, aggregates for which the grading was closest to the theoretically ideal particle size distribution did not have superior
shear strength compared with a theoretically inferior mix (Dunlop et al., 2003). Others, on the other hand, have reported that larger (>4.5-5 mm) particles yielded better stability in in vitro tests compared with smaller particles (Wallace et al., 1997; Eldridge et al., 1997b); however, no quantitative information was provided about the grading of the particle batches being compared. Finally, whether grading or washing of the graft truly affect implant stability is not certain, nor whether shear failures truly occur postoperatively within the graft bed.

In some studies, there appeared to be a relationship between the severity of the bone stock deficiency and subsidence for the double-tapered Exeter stem (van Doorn et al., 2002; Nelissen et al., 2002; Halliday et al., 2003; Hassaballa et al., 2009). Other studies, however, did not observe such a relationship for the same stem (Meding et al., 1997; Ornstein, 2002; Ornstein et al., 2004; Gokhale et al., 2005), nor for collared stems (Leopold et al., 1999; Leopold et al., 1999; Boldt et al., 2001; Boldt et al., 2001; Ornstein, 2002; van Doorn et al., 2002; Ornstein et al., 2004; Gokhale et al., 2005; Gokhale et al., 2005). Similarly, it is unclear whether patient age at the time of revision plays a role in the development of subsidence. Some studies have reported higher angular stem displacement (Gokhale et al., 2005) and a higher incidence of massive distal subsidence (Hassaballa et al., 2009) in older patients. Nonetheless, age was not found to affect subsidence in other studies (Eldridge et al., 1997a; van Doorn et al., 2002; Frances et al., 2007).

In short, the relative impact of each proposed mechanism on the development of subsidence after impaction allografting remains unknown (Halliday et al., 2003; Gokhale et al., 2005), and the wide range of subsidence reported in the clinical literature is not fully understood.

1.3.5 Cement penetration into the graft bed

Several clinical studies, retrieval analyses, and in vitro studies that focus on the mechanical characterization of MCB are available. However, it was not until recently that the morphology of the cement/graft layer was described. In a recent in vitro study, extensive cement penetration into the graft bed was observed when impaction allografting was performed in a cadaveric femur model (Frei et al., 2004). It was found that cement penetration was deeper than anticipated, reaching the endosteal surface of the femur in the diaphysis region, especially
around mid-stem (Figure 1.10). A finite element study showed that cement penetration depth was related to cement viscosity (e.g., how soon after mixing the cement was injected), how much pressure was applied, and for how long the pressure was maintained (Frei et al., 2006). It was also shown that the apparent strength of the endosteal interface was proportional to the amount of cement contact at that interface (Frei et al., 2005a).

Figure 1.10 Extensive cement penetration observed after impaction allografting in a cadaveric femur model. (a) Cross-section taken from the metaphysis region, i.e., proximal femur. (b) Cross section from the diaphysis region, around mid-stem. Adapted from Frei et al., 2004.

1.4 Summary and Project Motivation
In summary, various mechanisms have been proposed to contribute to subsidence, but the relative importance of each mechanism on the development of subsidence is not known. The quality of the graft impaction, i.e., the graft density achieved, is believed critical to the initial stability of the implant. Nonetheless, it has been demonstrated that high levels of cement penetration into the graft bed can occur after impaction allografting, and the roles of cement profile and graft packing density on implant stability have not yet been determined.
1.5 **Objectives and Scope**
The focus of this thesis was to investigate the effects of impaction force and cement pressurization on morphological and mechanical characteristics of the femur-implant construct after impaction allografting.

The objectives of this study were to:
1. Examine the effect of cement penetration into the graft bed on the initial stability of the femoral stem after impaction allografting (CHAPTER 2).
2. Determine the effect of impaction force on the bone density, shear strength, compression stiffness, and creep behavior of morsellized cancellous bone graft (CHAPTER 3).
3. Explore two alternative methods to graft impaction as a means to improve the mechanical characteristics of the graft (CHAPTER 3).
4. Estimate the effect of graft density, cement penetration profile, and the status of the stem/cement and endosteal interfaces, i.e., bonded or sliding, on the shear stresses at the endosteal interface and the distal migration and micromotion of the stem (CHAPTER 4).
5. Estimate the relative contribution of each of the following mechanisms on the stem motion: sliding at the stem-cement interface; deformation of the graft and/or graft/cement composite region; and slippage at the endosteal interface (CHAPTER 4).

In Chapter 2, the effect of cement pressurization on cement penetration into the graft bed after impaction allografting was investigated in an *in vitro* human cadaveric femur model. The graft density, the cement penetration profiles, and the initial implant migration and micromotion were measured, and the relationships between these morphological and structural characteristics were studied. In Chapter 3, the effects of impaction force on density, compression stiffness and shear strength of the graft bed were examined using confined compression tests, simple shear tests, and histomorphometric analysis. Alternative graft compaction methods were proposed and these were compared with traditional impaction. Finally, in Chapter 4, a finite element model was used to estimate the relative importance of graft bed density, cement penetration profile, and debonding of the cement at the stem-cement and endosteal interfaces on the structural characteristics of the proximal femur after impaction allografting.
1.6 References


CHAPTER 2

CEMENT PENETRATION AND PRIMARY STABILITY OF THE FEMORAL PROSTHESIS

A BIOMECHANICAL STUDY IN THE CADAVERIC FEMUR

A version of this chapter has been published.

2.1 Introduction

Failure of the femoral component in total hip replacement is often associated with a loss of bone stock in the proximal femur which can make revision procedures challenging. Impaction allografting has gained popularity over the last decade because of its potential for reconstitution of bone stock, which is particularly important when dealing with young patients with moderate to severe bone loss (Duncan et al., 1998).

Impaction allografting, however, is associated with several clinical problems, including a high prevalence of intra- and postoperative fractures (Knight and Helming, 2000; Fetzer et al., 2001; Ornstein et al., 2002; Schreurs et al., 2005) and high levels of implant migration (> 10 mm) (Masterson and Duncan, 1997; Eldridge et al., 1997; van Biezen et al., 2000; Piccaluga et al., 2002). Although the mechanisms by which migration develops are not fully understood, inadequate compaction of the graft bed (Karrholm et al., 1999; Nelissen et al., 2002; Malkani et al., 1996; Gokhale et al., 2005), defects in the cement mantle (Nelissen et al., 2002; Masterson et al., 1997) and absorption of the endosteal surface (Frei et al., 2005b) are believed to be contributing factors.

Many studies have shown radiological evidence of remodelling of the graft following impaction allografting (Gie et al., 1993; Meding et al., 1997; Cabanela et al., 2003). However, histological reports from autopsies and biopsies have revealed that the graft bed had not fully remodeled into viable bone, even up to eight years after the impaction allografting procedure (Linder, 2000; Nelissen et al., 1995).

It has been shown in a cadaveric experiment that during femoral impaction allografting the penetration of cement into the graft bed is greater than expected, filling virtually the entire intramedullary canal at the level of mid-stem (Frei et al., 2004). Penetration of cement to the endosteal cortex is a limiting factor that prevents bone remodeling, as cement is not biodegradable (Frei et al., 2005b). Therefore, a construct having reduced cement penetration, particularly in the proximity of the endosteal surface, may enhance local vascularization and allow the formation of new bone in these cement-free areas. Results from a finite element analysis have suggested that lower levels of cement penetration could be achieved by reducing
cement pressure or increasing its viscosity (Frei et al., 2006). A potential drawback of reducing cement penetration in impaction allografting is that the shear strength at the endosteal interface is lower in the absence of cement contact (Frei et al., 2005a), which may lead to excessive migration of the stem. However, the importance of contact of the cement with the endosteal surface on the primary stability of the stem is not known.

This study aimed to examine the effect of the extent of cement penetration into the graft bed on the primary stability of the femoral stem after impaction allografting. We hypothesized that by not pressurizing the cement a reduction in penetration would be achieved versus the conventional pressurized cementing technique. We also hypothesized that there is a relationship between cement contact with the endosteum and the primary stability of the stem. We tested our hypotheses in the human cadaveric femur.

2.2 Methods
Impaction allografting was performed on eight pairs of human cadaveric femurs. The femoral heads were removed from the specimens and loss of bone was simulated with a high-speed burr. All the trabecular bone was removed from the proximal femur, and lytic defects were created in the cortical shell. The loss of bone achieved represented a class II defect according to the EndoKlinik classification system (Engelbrecht E. and Heinert K., 1987). Trabecular bone graft from 15 femoral heads and 15 femoral condyles was morsellized with a Lere bone mill (DePuy, Warsaw, Indiana), giving a particle size distribution of between 0.6 mm and 13 mm, with 50% by weight of the particles being smaller than 4 mm (Frei et al., 2004). The grafts were rinsed in saline and pooled together for better reproducibility. All the procedures were performed by a single surgeon (SP). Prophylactic application of Dall-Miles cables (Stryker Orthopaedics, Mahwah, New Jersey) was carried out to prevent iatrogenic fractures. For the impaction procedures the CPT instrumentation (Zimmer Inc., Warsaw, Indiana), with Simplex P bone cement (Stryker Howmedica Osteonics, Allendale, New Jersey) was used. In one femur from each pair, chosen randomly, the cement was pressurized, whereas in the other femur it was not. In both groups, the cement was injected in the neo-medullary canal in a retrograde fashion using a cement gun. In the pressure group, two packs of bone cement were used and the timing of pressurization was standardized. The cement was mixed for one minute,
injection began at two minutes from the onset of mixing, and pressurization at three minutes, ending at four minutes. Finally, ten seconds after the end of pressurization, an appropriate femoral component (CPT 12/14 Hip System, Zimmer Inc.) was inserted. In the no-pressure group, one pack of cement was used per specimen, and the same cement gun was used. The neo-medullary canal was filled with cement in a retrograde fashion, but the cement was not pressurized. Insertion of the stem began three minutes from the onset of cement mixing. Three specimens from two pairs fractured during the procedure, and therefore six pairs of specimens were included in the study (Table 2.1).

Table 2.1 Description of specimens.

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*EXT, extended offset

The femurs were potted in dental stone (Tru-Stone, Heraeus Kulzer, Armonk, New York) at 13° of adduction and subjected to cyclical loading on a biaxial servohydraulic testing machine (Instron Model 8874, Instron, Canton, Massachusetts). The loads applied simulated 50% of expected walking loads (2500 cycles) followed by 100% of walking loads (5000 cycles). Two force components were applied sinusoidally at 1 Hz: a craniocaudal component (F_{cc}) with peak values of 0.4 to 2.3 times body-weight, and an anteroposterior component (F_{ap}) with peak values of -0.1 to 0.3 times body-weight for the walking load cycles (Bergmann 2001 gait patterns). The loads were scaled for a 70 kg individual, and the two components were phased such that their maximum peak values coincided. The F_{cc} was applied at 13° from the longitudinal axis of the femur, resulting in a mediolateral component (F_{ml}) and a proximodistal component (F_{pd}) as shown in Figure 2.1. The anteroposterior load (F_{ap}) was applied with the rotary actuator by controlling the moment, M, with an offset of 32 mm between the femoral head and the line of action of the actuator. More details about the simulation of hip joint loading are provided in Appendix 1.1.
Figure 2.1 Diagram showing the loading set-up. The potted femur was mounted on a linear guide to avoid undesired horizontal reaction forces in the frontal plane. A craniocaudal load ($F_{cc}$) was applied with the linear actuator, generating the mediolateral ($F_{ml}$) and proximodistal ($F_{pd}$) components. The anteroposterior load ($F_{ap}$) was applied by controlling the moment, $M$, applied with the rotary actuator ($M = F_{ap} \times \text{offset}$).

The three-dimensional motion of the implant relative to the bone was measured at the reference point shown in Figure 2.1, using a custom-built system similar to designs used previously (Berzins et al., 1993; Chareancholvanich et al., 2002). The system, shown in Figure 2.2, consisted of six linear variable differential transformers (GCD-121-250, Shaevitz Sensors, Hampton, Virginia) mounted on an aluminum frame which was fixed rigidly to the femur with seven pyramid-tip set screws. In order to achieve adequate fixation of the screws to the femur, all local soft tissue was removed and the periosteal surface was sanded, cleaned with acetone, and sealed with cyanoacrylate. The set-screw-femoral interface was strengthened using polymethyl-methacrylate (Lecoset, LECO Corp, St Joseph, Michigan). The sensors measured the motion of a triangle that was rigidly fixed to the lateral side of the implant, 5 cm below its shoulder, with a 5 mm square steel pin through a hole in the femur. The relative motion between the implant and the bone was calculated from the measured motion of the triangle relative to the frame, using a custom program implemented in Matlab (MathWorks, Natick, Massachusetts). The measured motion was separated into migration (permanent) and micromotion (reversible), each of which had three translational components (posterior, lateral...
and distal), and three rotational components, (valgus/varus, flexion/extension, and retroversion/anteversion), see Appendix 1, Figure A1.9. Migration was defined as the difference between the initial position of the stem and the average unloaded position during the last ten cycles of loading, and micromotion was defined as the amplitude of reversible motion during the last ten cycles. The accuracy of the system in measuring translation was evaluated against a dial gauge micrometer by attaching the sensors to an over-reamed composite femur (Model 3303, Pacific Research Laboratories, Vashon, Washington), and applying translations to the implant relative to the bone along each of the three axes. The mean absolute error observed was 2.1 µm (0.4 to 5.8) in 12 translation measurements over a range of 200 µm. The accuracy of each sensor was also measured. A maximum error of 2.2 µm was observed over a range of 450 µm (mean 0.8 µm (0.0 to 2.2) for 60 measurements). The accuracy of rotation was evaluated analytically from the maximum individual sensor errors, yielding a maximum rotation error of 0.004°. More details about the implant motion measurement methods can be found in Appendix 1.2.

Figure 2.2 Photograph of the motion measurement system. Six linear variable differential transformers were mounted on an aluminum frame that was rigidly attached to the femur. They measured the motion of a triangle that was fixed rigidly to the lateral side of the implant through a hole in the femur. The relative motion between implant and bone was determined from that of the triangle, relative to the frame.
Non-parametric statistical analysis was used to compare the results between the two groups because the variances differed substantially between the groups for some of the motion components. Motion was compared between the pressure group and the no-pressure group using Wilcoxon’s matched-pairs tests, and a significance level of 0.05 was used. For the components that showed a significant difference between the pressure and no-pressure groups, linear regression models were used to examine the relationship between migration and micromotion.

After structural testing, the implant was removed and the cavity filled with coloured polymethyl-methacrylate (LECO Corp). The femurs were cut into transverse cross-sections, 7 mm thick, with a diamond saw (model 310 CP, Exakt Apparatebau, Norderstedt, Germany). The levels of cross-sections were matched between the specimens using the tip of the stem as the reference. Alternating cross-sections, corresponding to 11 levels, were processed for histomorphometric analysis. They were fixed in 10% buffered formalin for a minimum of two days, and dehydrated for four days: one day in 70% ethanol, one in 95% ethanol, and two in 100% ethanol (changing the solution after the first day). The cross-sections were embedded in resin (Buehler EpoThin, Lake Bluff, Illinois) to form blocks, which were mounted on a slide. Each block was cut to approximately 500 µm with a diamond saw and ground to 200 µm, and the slide was stained with a calcium stain, alizarin red S. Each slide was placed on a light box to enhance the contrast between graft and cement/voids, and photographed with a digital camera (resolution 3.2 megapixels). The graft porosity was characterized as the percentage of the graft area occupied by cement or void, using the Image-Pro 4.5 (Mediacybernetics, Silver Springs, Maryland) image analysis software. The slides were then placed on a green background, to distinguish more clearly the area of penetration of the cement within the graft bed. Each slide was photographed and the penetration of cement was measured using the Image-Pro 4.5 software. Penetration was characterized as the percentage of contact of the cement with the endosteal surface (cement contact, Equation 2.1) and the area of the canal occupied by cement (cement area, Equation 2.2):

\[
\text{Cement contact} = \frac{\text{length of contact between cement and endosteum}}{\text{endosteum perimeter}} \times 100\% \tag{2.1}
\]
Further details about the slide preparation, staining and photography methods are provided in Appendix 2.

The measurements of cement contact and cement area were performed by a single person (CA) and were each analyzed with a two-factor analysis of variance (ANOVA), in which the factors were group (pressure versus no-pressure), and level (defined as a repeated measure). The graft porosity was analyzed with a one-factor ANOVA (level) which was defined as a repeated measure. Student-Newman-Keuls analysis was used for post hoc comparisons, and the significance level was 0.05.

Linear regression models were used to examine the relationship between the mean cement contact and cement area from all 11 matched levels, and the components of the motion that were significantly different between the two groups.

2.3 Results
The cement contact and cement area results are shown in Figure 2.3 and Table 2.2 for each group at all cross-sectional levels. The main effect of pressure was significant for both cement contact and cement area (p = 0.0013 and p = 0.0014, respectively). There was an average of 30% more cement contact and 25% more cement area in the pressure group than in the no-pressure group. The effect of level was also significant (p < 0.001 for both variables). Levels 4 to 10 had significantly higher cement contact and cement area than levels 1, 2, 3 and 11 (p < 0.05), but they did not differ significantly between levels 4 and 10, or between levels 1, 2, 3 and 11. There was no interaction effect between the two factors (i.e., pressure group and level).

The results for graft porosity are shown in Table 2.2. The effect of level on graft porosity was significant (p < 0.001). Porosity was relatively constant along the length of the implant, averaging 66%, and did not differ significantly between levels 1 and 10 (post hoc comparisons with Student-Newman-Keuls p > 0.4). Below the tip of the implant, at level 11, the porosity

\[
\text{Cement area} = \frac{\text{area inside the cement penetration front}}{\text{total canal area}} \times 100\% \quad (2.2)
\]
was slightly lower than at all other levels (*post hoc* comparisons with Student-Newman-Keuls \( p < 0.01 \)).

---

**Figure 2.3** Graph showing cement contact with endosteum for the pressure and no-pressure groups, at eleven matched-level cross-sections. Means (standard deviations).
Table 2.2 Cement contact with endosteum, cement area and graft porosity for the pressure and no-pressure group at eleven matched-level cross-sections.

<table>
<thead>
<tr>
<th>Level</th>
<th>Cement contact (%)</th>
<th>Cement area (%)</th>
<th>Graft porosity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pressure group</td>
<td>No-pressure group</td>
<td>Pressure group</td>
</tr>
<tr>
<td></td>
<td>Mean (range)</td>
<td>Mean (range)</td>
<td>Mean (range)</td>
</tr>
<tr>
<td>1</td>
<td>26 (0 to 56)</td>
<td>9 (0 to 32)</td>
<td>52 (32 to 83)</td>
</tr>
<tr>
<td>2</td>
<td>32 (25 to 44)</td>
<td>7 (0 to 20)</td>
<td>53 (35 to 74)</td>
</tr>
<tr>
<td>3</td>
<td>42 (28 to 73)</td>
<td>20 (4 to 29)</td>
<td>57 (37 to 82)</td>
</tr>
<tr>
<td>4</td>
<td>59 (32 to 86)</td>
<td>41 (10 to 82)</td>
<td>73 (43 to 96)</td>
</tr>
<tr>
<td>5</td>
<td>71 (49 to 98)</td>
<td>46 (28 to 91)</td>
<td>83 (50 to 100)</td>
</tr>
<tr>
<td>6</td>
<td>70 (49 to 97)</td>
<td>36 (0 to 52)</td>
<td>80 (52 to 99)</td>
</tr>
<tr>
<td>7</td>
<td>72 (48 to 100)</td>
<td>40 (0 to 60)</td>
<td>80 (59 to 99)</td>
</tr>
<tr>
<td>8</td>
<td>82 (67 to 100)</td>
<td>40 (0 to 100)</td>
<td>87 (73 to 100)</td>
</tr>
<tr>
<td>9</td>
<td>80 (45 to 100)</td>
<td>36 (0 to 100)</td>
<td>89 (75 to 99)</td>
</tr>
<tr>
<td>10</td>
<td>81 (27 to 97)</td>
<td>25 (0 to 65)</td>
<td>91 (70 to 98)</td>
</tr>
<tr>
<td>11</td>
<td>26 (0 to 91)</td>
<td>11 (0 to 38)</td>
<td>50 (4 to 94)</td>
</tr>
</tbody>
</table>

The components of migration and micromotion for each group at the end of the cyclical loading are shown in Tables 2.3 and 2.4, respectively. Two of the migration components, distal translation and valgus rotation, differed significantly (p = 0.028) between the two groups (Figure 2.4). The median distal migration and valgus rotation migration were twelve and three times greater in the no-pressure group (Table 2.3). The resultant of the translational migration components ranged between 19 µm and 27 µm in the pressure group, and between 45 µm and 792 µm in the no-pressure group. Of all the micromotion components, only distal translation was significantly different between the groups (p = 0.028, Figure 2.4c). The median distal micromotion was almost five times greater in the no-pressure group (Table 2.4). The resultant of the translational micromotion components ranged between 10 µm and 31 µm in the pressure group, and between 22 µm and 70 µm in the no-pressure group. Distal migration also correlated significantly with the micromotion in the same direction (slope of the linear fit to the data (m) = 12.8, y-offset (b) = - 101 µm, R^2 = 0.78, linear regression, p < 0.001).

Table 2.3 Migration components for the pressure and no-pressure groups.

<table>
<thead>
<tr>
<th></th>
<th>Pressure group</th>
<th>No-pressure group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (Range )</td>
<td>Median (Range )</td>
<td></td>
</tr>
<tr>
<td>Posterior (µm)</td>
<td>8 (-15 to 22)</td>
<td>41 (-89 to 203)</td>
<td>0.60</td>
</tr>
<tr>
<td>Lateral (µm)</td>
<td>2 (-9 to 20)</td>
<td>7 (-34 to 38)</td>
<td>0.92</td>
</tr>
<tr>
<td>Distal (µm)</td>
<td>18 (-6 to 26)</td>
<td>218 (42 to 765)</td>
<td>0.028</td>
</tr>
<tr>
<td>Valgus/varus (°)</td>
<td>0.04 (0.02 to 0.11)</td>
<td>0.13 (0.11 to 0.20)</td>
<td>0.028</td>
</tr>
<tr>
<td>Flexion/extension (°)</td>
<td>0.02 (-0.08 to 0.05)</td>
<td>0.01 (-0.02 to 0.08)</td>
<td>0.46</td>
</tr>
<tr>
<td>Retro/anteversion (°)</td>
<td>0.01 (-0.01 to 0.05)</td>
<td>0.02 (-0.32 to 0.20)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Valgus, flexion and retroversion rotations are represented as positive rotations.
Table 2.4 Micromotion components for the pressure and no-pressure groups.

<table>
<thead>
<tr>
<th>Component</th>
<th>Pressure group</th>
<th>No-pressure group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (Range)</td>
<td>Median (Range)</td>
<td></td>
</tr>
<tr>
<td>Posterior (µm)</td>
<td>9 (4 to 21)</td>
<td>8 (5 to 26)</td>
<td>0.75</td>
</tr>
<tr>
<td>Lateral (µm)</td>
<td>7 (2 to 17)</td>
<td>8 (3 to 36)</td>
<td>0.75</td>
</tr>
<tr>
<td>Distal (µm)</td>
<td>7 (4 to 15)</td>
<td>32 (15 to 65)</td>
<td>0.028</td>
</tr>
<tr>
<td>Valgus/varus (°)</td>
<td>0.05 (0.02 to 0.08)</td>
<td>0.07 (0.04 to 0.13)</td>
<td>0.17</td>
</tr>
<tr>
<td>Flexion/extension (°)</td>
<td>0.02 (0.01 to 0.04)</td>
<td>0.03 (0.01 to 0.04)</td>
<td>0.60</td>
</tr>
<tr>
<td>Retro/anteversion (°)</td>
<td>0.03 (0.01 to 0.08)</td>
<td>0.06 (0.02 to 0.08)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Valgus, flexion and retroversion rotations are represented as positive rotations.

Figure 2.4 Graphs showing distal migration (left), valgus/varus rotation migration (center) and distal micromotion (right) for the two groups (medians and ranges). Valgus rotation is represented as a positive rotation. All of these motions (distal migration, valgus/varus migration and distal micromotion) displayed a significant difference between the two groups (p<0.05).

Distal migration and micromotion throughout the 5000 cycles of walking loads are shown in Figure 2.5. In the pressure group, distal micromotion was mainly constant (Figure 2.5 a). The trend of micromotion in the no-pressure group was more variable, being roughly constant in three specimens, increasing slightly in one, and decreasing in two. The implant settled more quickly in the pressure group, where most of the migration occurred within the first 2000 cycles (Figure 2.5 b). In the no-pressure group, the implants were still migrating distally at 5000 cycles, with a median migration of 10.9 µm (0.3 to 27.1) during the last 1000 cycles, compared with 0.5 µm (-1.1 to 3.4) in the pressure group.
Figure 2.5 Graph showing distal micromotion (top) and migration (bottom) versus number of walking cycles for all specimens tested. Note that the migration data presented include the migration that had previously developed during the 2500 cycles at 50% of expected walking loads.
The three motion components that differed between the pressure and the no-pressure groups (distal migration, valgus rotation migration and distal micromotion) correlated significantly with both cement contact and cement area (Table 2.5 and Figure 2.6). Two specimens, both of which were in the no-pressure group, showed substantially higher distal migration than the others, and corresponded to the two largest specimens in that group (Pairs 3 and 6, Table 2.1). The average cement contact with the endosteuum (averaged over the eleven levels) was correlated positively with the average cement area (slope = 1.07, R = 0.89).

Table 2.5 Pearson’s correlation coefficients (R) and slopes for the linear regressions between the motion components and the cement morphological parameters (average cement contact and average cement area).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Factor</th>
<th>Slope</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal migration (µm)</td>
<td>Cement contact</td>
<td>-9.557</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>Cement area</td>
<td>-14.090</td>
<td>0.83</td>
</tr>
<tr>
<td>Valgus rotation migration (°)</td>
<td>Cement contact</td>
<td>-0.0021</td>
<td>0.65</td>
</tr>
<tr>
<td></td>
<td>Cement area</td>
<td>-0.0028</td>
<td>0.75</td>
</tr>
<tr>
<td>Distal micromotion (µm)</td>
<td>Cement contact</td>
<td>-0.574</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>Cement area</td>
<td>-0.896</td>
<td>0.77</td>
</tr>
</tbody>
</table>

All slopes were significantly different from zero (p < 0.05).
Figure 2.6 Scattergraph showing distal migration as a function of: (top) the average cement contact with endosteum (averaged for each specimen over all 11 levels); (bottom) the average cement area. The regression parameters are given in Table 2.5.
2.4 Discussion
When using the impaction allografting technique penetration of cement through the graft bed has been observed to reach the endosteal surface of the femur, creating an extensive cement-host bone interface at mid-stem level (Frei et al., 2004). The presence of cement at the endosteal surface compromises the potential for incorporation of the graft at that site (Frei et al., 2005b), but its importance for primary stability of the implant is not known. In this study, we carried out impaction allografting on cadaveric femurs with and without pressurizing the cement to examine the effect of cement penetration on the motion of the implant under simulated walking loads.

In vitro mechanical tests are commonly performed to assess new hip implant designs or surgical techniques pre-clinically. The relevance of in vitro tests is supported by studies demonstrating that excessive micromotion at the bone-implant interface inhibits successful bone ingrowth in cementless implants, which may lead to early loosening of the implant (Pilliar et al., 1986; Engh et al., 1992; Jasty et al., 1997), and that cemented implants with inferior clinical results also display greater in vitro micromotion (Cristofolini et al., 2003).

As an in vitro model our study did not model biological processes. There was no bleeding in the canal during the procedure, which may have affected cement penetration. However, it has been shown experimentally that the intramedullary blood pressure did not significantly affect the depth of penetration in primary cemented THA (Majkowski et al., 1994). It has been suggested that early migration of the implant could be a result of a combination of postoperative consolidation of the graft (Giesen et al., 1999; Voor et al., 2000; Voor et al., 2004), shear failure (Brewster et al., 1999; Dunlop et al., 2003) and/or slippage at the host-bone interface (Frei et al., 2005a). Other mechanisms that have been proposed to affect longer-term implant migration in impaction allografting, including graft incorporation/fibrous invasion (Linder, 2000; Nelissen et al., 1995), cement fatigue (Masterson et al., 1997), and cancellization of the femoral canal (Frei et al., 2005b), could not be modeled in this experiment. The effect of these mechanisms on long-term subsidence of the implant in impaction allografting has not yet been determined. The importance of primary stability is emphasized by reports of significant subsidence in the early postoperative days. In clinical
studies using roentgen stereophotogrammetric analysis (RSA) some implants were seen to have subsided more than 1 mm within the first three months after operation (Nelissen et al., 2002; Ornstein et al., 2001). It was also noted that more than half of the subsidence observed at six weeks was usually seen within the first two weeks (Ornstein et al., 2000).

Our specimens represented class II bone defects. Most of the trabecular bone had been removed from the proximal femur, and the intramedullary canal was expanded. This type of bone loss is within the range commonly targeted by impaction allografting, but does not represent the most severe cases. As the migration of the implant may be proportional to the severity of the bone loss (Nelissen et al., 2002; Gokhale et al., 2005), we might see greater migration with a model of more severe bone loss.

Migration of implants previously seen in cadaveric studies of impaction allografting has varied greatly, with average distal migrations ranging between 12 µm (Chassin et al., 1997) and 1 mm (Bolder et al., 2004). There were many variables in these studies including the type of specimen, the magnitude and orientation of the loading, the number of loading cycles, and the techniques used to measure motion (Chassin et al., 1997; Bolder et al., 2004; Berzins et al., 1996; Hostner et al., 2001; Kligman et al., 2003; van Haaren et al., 2005). Comparison of these results with those of our pressure group shows that two other studies used a six degree of freedom motion measurement system similar to ours (Chassin et al., 1997; Berzins et al., 1996) and found similar results in all motion components. Berzins et al. used loads approximately twice as high as ours but only 50 load cycles, whereas Chassin et al. used only ten cycles, with approximately half our loads. Two other studies reported distal migration of an order of magnitude higher than ours, but one used RSA measurement with loads approximately twice as high as ours and 13 times more cycles (Hostner et al., 2001), and the other an extensometer measurement with similar loads but almost 200 times as many cycles (Cornu et al., 2003). Other studies have used the position of the actuator as their measure of migration, and have consistently reported greater migration by at least an order of magnitude (Malkani et al., 1996; Kligman et al., 2003; van Haaren et al., 2005). However, the position of the actuator does not provide an accurate measure of actual implant motion relative to the bone.
Our results indicate that following impaction allografting there is a substantial amount of cement penetration in the graft, and cement contact with the endosteum, in particular around the distal half of the implant. Eliminating cement pressurization during impaction allografting reduced the cement area and cement contact with the endosteal surface, but migration and micromotion of the implant were significantly increased. Distal migration, valgus/varus migration, and distal micromotion were significantly higher without pressure than with, and correlated with the average amount of cement contact with the endosteum and with the average cement area. It can be argued that some initial settling of the implant may be acceptable, provided it then becomes stable. Because our study applied a limited number of cycles which were roughly equivalent to one or two days of loading, the initial settling process was not observed entirely. It is possible that the micromotion would ultimately be similar between the two groups because of further compaction of the graft during implant migration. During the cycles applied, however, the micromotion of the implant in the no-pressure group did not decrease consistently with the increasing number of cycles applied, and did not tend to converge towards the same magnitude as those in the pressure group. Furthermore, the results of a clinical impaction allografting study indicate that migration during the first two weeks may be a good predictor of long-term migration (Nelissen et al., 2002). Therefore, the differences in the patterns of early migration observed between our pressure and no-pressure groups indicate that longer term stability of the implant could be compromised if the cement is not pressurized.

Previous research has demonstrated that the cement penetration in impaction allografting is affected by graft porosity (Frei et al., 2006). In our results, the lower porosity of the graft below the tip of the implant may explain the lower contact between the cement and the endosteum in that region due to a lower permeability of the graft in this region. However, the porosity of the graft was roughly uniform along the length of the implant, and the lower cement-endosteum contact in the proximal region is probably a result of the wider canal at that site. Our measurements of graft porosity at all levels were within the range previously reported in another in vitro study (Frei et al., 2004).

It is not clear how much cement is necessary for the structural support of the implant in impaction allografting. Without cement, the morsellized bone does not provide sufficient
structural support for the stem (Robinson et al., 2005). Some clinical studies have reported a link between excessive subsidence and the presence of zones where the cement mantle was less than 2 mm thick (Nelissen et al., 2002; Masterson et al., 1997). This indicates the importance of sufficient thickness of the cement mantle between the implant and the graft bed, without which the cement could be more susceptible to early fatigue failure (Masterson and Duncan, 1997). A recent in vitro study found that penetration of cement into the graft bed reaches the endosteal surface, and that the strength of the endosteal interface with graft/cement is proportional to the amount of cement contact (Frei et al., 2004; Frei et al., 2005a). In the present study, constructs with more than 50% of cement contact with the endosteum generally resulted in substantially lower distal migration and micromotion than did those with less contact. This indicates that the regions of cement endosteum contact are potentially critical to the primary stability of the implant. There may be a conflict between the biological and structural goals of impaction allografting. A biologically favourable construct is one with limited cement penetration, but the morsellized graft bed may not provide sufficient support for the implant without contact of the cement with the endosteum.

Attempts have been made to improve the mechanical properties of the morsellized graft bed by increasing the number of impactions (Bavadekar et al., 2001), rinsing the graft (Dunlop et al., 2003; Cornu et al., 2004), freeze-drying (Cornu et al., 2003) and/or irradiating the graft (Cornu et al., 2004; Butler et al., 2005), and by optimizing the size distribution of the graft particles (Dunlop et al., 2003). However, improvement of graft compaction will only be of clinical consequence if the implant is being supported largely by the graft bed. Future biomechanical studies should aim to determine the minimum graft packing necessary to support the implant without contact of the cement with the endosteum, how to achieve this level of packing consistently, and how to prevent the cement from reaching the endosteum. However, if the graft cannot provide sufficient support for the implant, efforts should be focused on how to control the cement penetration profile such that cement-endosteum contact occurs in regions not targeted for reconstitution of bone stock. The presence of cement at the endosteal surface in patients with impaction allografting has not yet been confirmed because published histological reports of biopsy and autopsy specimens used dehydrating solutions and embedding compounds that dissolve the bone cement (Linder, 2000; Ullmark and Linder, 1998; Ullmark and Obrant, 2002). The histological methods used in the present study did not dissolve the
cement. We found that the cement penetration at each level was most easily distinguished after each cross-section was mounted on a slide and ground to roughly 200 µm. Such biomechanical and retrieval studies could help determine whether cement contact with the endosteum is essential in preventing excessive migration in impaction allografting. Finally, surgeons should be aware that the potential for graft remodeling may be limited around the distal half of the implant, and that contact of the cement with the endosteum may be critically important for the initial stability of the implant in impaction allografting.
2.5 References


CHAPTER 3

THE EFFECT OF IMPACTION FORCE AND ALTERNATIVE COMPACTION
METHODS ON THE MECHANICAL CHARACTERISTICS OF
MORSELLIZED CANCELLOUS GRAFT

A version of this chapter has been published.
effect of impaction force and alternative compaction methods on the mechanical characteristics
395-405.
3.1 Introduction
Failure of total hip implants is often accompanied with problematic bone loss. The goal of femoral impaction allografting is to improve bone stock in patients with femoral deficiencies using impacted morsellized cancellous bone graft (MCB).

Clinical problems often reported with impaction allografting, however, include intra- and postoperative fractures (Knight and Helming, 2000; Fetzer et al., 2001; Ornstein et al., 2002; Schreurs et al., 2005) and high levels of implant migration (Masterson et al., 1997; Eldridge et al., 1997; van Biezen et al., 2000; Piccaluga et al., 2002). The mechanisms through which this migration occurs are not yet fully understood, but the MCB region might be critical because its stiffness is lower than that of the other materials in the reconstruction. Compressive stiffness between 3 and 135 MPa has been reported for impacted MCB (Giesen et al., 1999; Voor et al., 2000; Verdonschot et al., 2001; Bavadekar et al., 2001; Cornu et al., 2003a; Cornu et al., 2004; Voor et al., 2004; Fosse et al., 2004; Phillips et al., 2006b; Fosse et al., 2006) compared with 2 GPa, 17 GPa and 220 GPa for the cement, cortical bone, and stem, respectively (Mow and Huiskes, 2005). The role of the graft in the migration process is supported by the results of a clinical study, in which an apparent relationship was reported between migration and the density of the graft bed (Gokhale et al., 2005).

MCB is a biphasic material composed of bone particles and a fluid phase (marrow, fat and water). In addition to having a relatively low stiffness, impacted MCB exhibits viscoelastic-viscoplastic, i.e., time dependent, material behavior (Giesen et al., 1999; Phillips et al., 2006a). Under compressive stress, the load is carried initially in part by the fluid, and the fluid pressure dissipates over a short period (a few seconds) through fluid flow (Voor et al., 2000). Beyond this point, MCB continues to deform (Voor et al., 2000), indicating that the bone particles themselves behave in a viscoelastic fashion. This process of creep consolidation is believed to contribute to implant migration in impaction allografting (Giesen et al., 1999; Voor et al., 2000).

Particulate materials are susceptible to shear failures, which may also contribute to migration (Brewster et al., 1999; Ornstein et al., 2004). The shear strength ($\tau$) of MCB has been
described using the Mohr-Coulomb criterion: \( \tau = c + \sigma_n \tan \phi \), in which \( \sigma_n \) is the normal (perpendicular) stress applied on the shear failure plane, and \( c \) and \( \phi \) (the cohesion intercept and the friction angle, respectively) are constants for a given particulate material (Brewster et al., 1999; Dunlop et al., 2003; Tanabe et al., 1999). In soil mechanics, the shear strength of many particulate materials can be optimized by using a ‘well graded’ mix of particles, i.e., a wide range of particle sizes that allow maximum packing density (Craig, 1983). This, however, has not been shown to be consistently true for MCB (Dunlop et al., 2003). We suggest that, because MCB particles are highly deformable, the density of the graft bed may not depend only on the grading, but perhaps more importantly on the impaction force. Brewster et al. reported that the shear strength of dry MCB increased with increasing impaction energy, but the forces and energy levels used were not indicated (Brewster et al., 1999). We hypothesize that the shear strength of fresh frozen MCB increases with increasing impaction force, and that this strength increase is related to an increase in density of the graft bed.

Furthermore, because of the damping effect of the fluid phase (Voor et al., 2000) and the short duration (~5 ms) of an impaction impulse (Fosse et al., 2006), it can be presumed that only a portion of the impaction force is exerted on the graft particles, while the remainder is carried by fluid pressure. We therefore hypothesize that a slower compaction technique that allows sufficient time for fluid exudation and graft deformation can produce a denser, stiffer and stronger graft bed than are obtained with impaction by allowing a larger portion of the compaction force to be transferred to the bone particles.

Our first objective was to examine the relationship between the impaction force and the shear strength, compression stiffness, and creep behaviour of MCB over a range of impaction forces typical in impaction allografting. Our second objective was to examine the relationship between the above-mentioned mechanical characteristics and the density of impacted MCB. Finally, our third objective was to explore two alternative methods to graft impaction as a means to improve the mechanical properties of the graft bed compared with impaction at a given force level. We addressed our objectives with \textit{in vitro} tests on human MCB.
### 3.2 Methods

Thirty-nine human femoral heads were morsellized with a Lere bone mill (DePuy Orthopaedics, Inc.). Cortical bone from the femoral neck was removed prior to morsellization. The cartilage was also removed, as it has been demonstrated to decrease the stiffness of MCB (Bavadekar et al., 2001). The graft particle sizes obtained with this method ranged between 0.6 and 8 mm, with 50% of the particles (in weight) being finer than 2.4 mm. The particle size distribution, obtained using sieve analysis, is shown in Figure 3.1. The graft was pooled together to reduce variability and rinsed in saline, as this has been shown to improve its shear strength (Dunlop et al., 2003).

![Particle size distribution](image.png)

**Figure 3.1** Particle size distribution for the morsellized graft. The ordinate indicates the percentage by weight of particles smaller than the abscissa, e.g., 50% of the particles are smaller than 2.4 mm.

Graft compaction was done with an 18 mm diameter steel piston using a servohydraulic testing machine (Instron Model 8874, Instron, Canton, Massachusetts). The graft was compacted in a stainless steel cylinder, having a wall thickness of 6 mm, an inner diameter of 19 mm, and with 36 radial holes of 1 mm diameter to allow fluid exudation. The initial, unimpacted height of each specimen was approximately 35 mm (after light finger-packing). Compaction was done with one of the following compaction techniques: impaction, creep, and cyclic relaxation (Figure 3.2 and Table 3.1). The creep technique consisted of holding a constant compaction...
force of 300 N for 90 s, and the cyclic relaxation consisted of ten cycles of compressing the graft to 300 N, then holding the displacement constant for 10 s each. The impaction technique simulated 20 impactions of a hammer with force levels of 300 N, 600 N, and 900 N, which were chosen to represent low, moderate, and high impaction forces (Fosse et al., 2004). Graft impaction was simulated on a servohydraulic materials testing machine, for which the load input was chosen to match as closely as possible the desired force peaks and short duration of an impaction impulse, i.e., approximately 0.005 s (Fosse et al., 2004). A square load input with a frequency of 4 Hz – the highest frequency achievable by the testing machine – was used, which resulted in load impulses of 0.125 s. The square load input generated a load profile as shown in Appendix 3 (Figure A3.3). A pilot experiment showed that this method of graft impaction produced equivalent graft stiffness to that achieved when using a hammer for a given peak force and number of impactions, while allowing controllable and repeatable forces between specimens. Stiffness development was monitored during impaction, $E_{\text{imp}}$, as the stress amplitude divided by the natural strain amplitude during the loading phase of each impaction.

![Impaction, Creep, Cyclic Relaxation](image)

**Figure 3.2** Compaction techniques. Impaction (left): Peak compressive forces of 300, 600 and 900 N (1, 2, and 3 MPa) were used. Creep (center): a compressive force of 300 N was held for 90 s. Cyclic relaxation (right): a force of 300 N was applied ten times, holding displacement constant for 9 seconds after each loading.

**Table 3.1** Test matrix. Graft compaction techniques and number of specimens used for compression, shear, and density tests.

<table>
<thead>
<tr>
<th>Graft compaction technique</th>
<th>Compression tests</th>
<th>Shear tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaction 300 N (‘I300N’)</td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
<tr>
<td>600 N (‘I600N’)</td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
<tr>
<td>900 N (‘I900N’)</td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
<tr>
<td>Creep (‘C300N’)</td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
<tr>
<td>Cyclic Relaxation (‘R300N’)</td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal stress, $\sigma_n$ = 125 kPa</th>
<th>Normal stress, $\sigma_n$ = 250 kPa</th>
<th>Normal stress, $\sigma_n$ = 375 kPa</th>
<th>Density tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 6</td>
<td>N = 6</td>
<td>N = 6</td>
<td>N = 6</td>
</tr>
<tr>
<td>N = 6</td>
<td>N = 6</td>
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<td>N = 6</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

51
Following compaction, each specimen underwent either: compression testing, shear testing, or density measurement (Table 3.1 and Figure 3.3). Shear and compression tests were performed on the same testing machine as that used for compaction, which enabled us to regulate the time between compaction and testing. After compaction, the piston was lifted from the specimen surface and the graft was allowed to recoil for 60 s. This was done to simulate the recoil occurring during surgery in the time between the removal of the final impactor and the injection of the cement into the graft. One minute was chosen arbitrarily for the recoil, but most of the recoil is known to occur during the first 10 s (Ullmark and Nilsson, 1999). New graft was used for each specimen to ensure that the properties measured were not affected by previous testing.

**Figure 3.3** Compression tests (top) consisted of one hour creep tests. Shear tests (bottom) were performed at three normal stress levels, $\sigma_n$.

Compression tests (Figure 3.3, top) consisted of one hour creep tests, for which the set-up is shown in Appendix 3. After recoil, a seating load of 10 N (0.035 MPa) was applied and held for ten minutes – the position of the piston at this time was recorded and used to obtain the initial specimen height. A load of 320 N ($\sigma_o=1.1$ MPa) was then applied in a 1 s ramp and held for one hour. The initial compression stiffness, $E_i$, was defined as the slope of the stress-natural strain curve during the initial loading ramp, and the compression stiffness at one hour, $E_{1hr}$, was defined as the normal stress applied, $\sigma_o$, divided by the natural strain after one hour of creep, i.e., the inverse of creep compliance (Figure 3.4). Similarly, the initial strain, $\varepsilon_i$, was defined as the natural strain at the end of the initial loading ramp, and the creep constant, $C_{\varepsilon}$,
was defined as the slope of the strain versus log time curve during the one hour creep period (Voor et al., 2000), Figure 3.5. A nonparametric approach was taken for the statistical analyses of these data because the stiffness and strain variances were not homogeneous between all the groups (Levene’s tests). Spearman rank R correlations were used to determine the relationships between $E_i$, $E_{1hr}$, $\varepsilon_i$, and $C_\varepsilon$ and the impaction force, and these mechanical characteristics were compared between the three compaction techniques (impaction, creep, and cyclic relaxation) with a Kruskal Wallis tests.

Figure 3.4 Definition of initial compression stiffness, $E_i$, and stiffness after one hour creep, $E_{1hr}$, under an applied stress of 1.1 MPa.
Shear tests (Figure 3.3, bottom) were performed in a custom-built shear box (Appendix 3). The apparatus was designed to be mounted directly on the testing machine used to simulate graft compaction (Instron Model 8874, Instron, Canton, Massachusetts), such that the specimens did not need to be transferred, and potentially damaged, prior to shear testing. The shear box consisted of two 19 mm diameter stainless steel cylinders. The upper cylinder was fixed rigidly to the testing machine table with a custom rig, while the lower cylinder was mounted on a linear guide. During shear testing, the lower cylinder was displaced at a rate of 1.2 mm/min by an actuator (actuator: Instron Model A591-4, Instron, Canton, Massachusetts; load cell: Sensotec Model 75/C863-01, Honeywell, Columbus, Ohio) while the MCB was subjected simultaneously to a normal compressive stress by the testing machine. Three levels of normal compressive stress, $\sigma_n$, were used: 125, 250, and 375 kPa, similar in magnitude to previous studies (Brewster et al., 1999; Dunlop et al., 2003; Tanabe et al., 1999). During testing, shear stress, $\tau$, was defined as the shearing force divided by the area of intersection between the inside of the upper and lower cylinders (Equation 3.1).
\[
\tau(\delta) = \frac{F_{\text{shear}}}{(d/2)^2 \left[ 2 \cos^{-1}(\delta/d) - \sin(2 \cos^{-1}(\delta/d)) \right]}
\]  

(3.1)

where \( F_{\text{shear}} \) is the shearing force, \( d \) is the inner diameter of the cylinders, and \( \delta \) is the displacement of the lower cylinder relative to its initial position. This equation accounts for the reduction in specimen cross-sectional area in the shearing plane due to the shear displacement, \( \delta \).

Shear strength was defined as the shear stress at a displacement of 1 mm (approximately 5% of the cylinder diameter). For each compaction technique, a linear curve fit was obtained from the shear strength versus normal stress curves, such that the parameters of the Mohr-Coulomb failure envelope, \( c \) and \( \phi \), could be determined. Shear strength was compared between the impaction forces with a 2-way ANOVA (impaction force, normal stress). Similarly, the shear strength was compared between the creep compaction technique and impaction of the same force (300 N) with a 2-way ANOVA (compaction technique, normal stress). Student-Newman Keuls tests were used for post hoc analyses, and a significance level of 0.05 was used.

In addition to the specimens used for mechanical testing, six more specimens were compacted at each impaction force level (300, 600, and 900 N) in order to measure their density (Table 3.1). The graft specimens were impacted in a 3 mm thick polyurethane cylinder with an inner diameter of 19 mm, perforated with 18 radial 1 mm holes for fluid exudation during impaction. A single 2.3 mm slice located 10 mm from the bottom surface of the specimen was scanned using peripheral quantitative computed tomography, pQCT, (Norland/Stratec XCT 2000). The scan speed was 10 mm/s with an in-plane pixel size of 0.10 x 0.10 mm. All measurements were made by a single trained technician. The apparent bone density, \( \rho \), was measured with the Norland/Stratec XCT 5.50 software, using Contour mode 1 and adjusting the threshold such that the region of interest contained only the graft region (i.e., area inside the polyurethane cylinder). After scanning, the specimens were processed into slides for histological analysis. The top and bottom 5 mm of each of these graft specimens were removed with a diamond saw (Model 310 CP, Exakt Apparatebau). Each remaining cross-section, approximately 10 mm thick, was set in 10% buffered formalin for two days, and dehydrated in 70%, 95%, and twice in 100% ethanol for a day each. The ethanol was then evaporated at 60°C for two hours, after
which the cross-sections were embedded in resin (Buehler EpoThin). The middle cross-section of each block was mounted onto a slide, ground down to 200 µm, and stained with Alizarin Red S, such that the areas of bone appeared in red. In contrast, the areas of resin, which originally contained the fluid phase, appeared as white (Figure 3.6). The slides were placed on a light box to enhance the distinction between graft and void areas, and were photographed with a digital camera (resolution 3.2 Megapixels). The percentage of each cross section occupied by bone, ‘percentage bone’, was determined using the Image-Pro 4.5 (MediaCybernetics) image analysis software. The area of interest was defined as the area inside the polyurethane cylinder, and the ‘percentage bone’ was quantified as the percentage of this area occupied by bone (Figure 3.6, dark regions). Linear regression models were used to determine the percentage bone, $\%b$ (histology) and graft density, $\rho$ (pQCT) as a function of the impaction force, as well as to examine the relationship between graft density and percentage bone.

Figure 3.6 Histological measurement of graft density, quantified as the percentage of the specimen area occupied by bone (dark).

3.3 Results

The results of the creep compression tests, i.e., $E_i$, $E_{1hr}$, $\varepsilon_i$, and $C_e$ are shown for each group in Table 3.2. The graft compression stiffness, $E_i$ and $E_{1hr}$, correlated positively with the impaction force (both with $R_s=0.89$, $p<0.05$), whereas $\varepsilon_i$, and $C_e$ correlated negatively with the force ($R_s=-0.86$ and $R_s=-0.92$, respectively, with $p<0.05$). The median $E_{1hr}$ in the 600 N and 900 N
impaction groups were 64% and 93% higher, respectively, than in the 300 N impaction group. Similarly, the median creep constant, $C_\varepsilon$, was 56% and 63% lower in the 600N and 900N groups compared with the 300 N impaction group.

**Table 3.2 Results of the creep compression test.**

<table>
<thead>
<tr>
<th>Graft compaction technique</th>
<th>$E_i$ (MPa) Median (range)</th>
<th>$\varepsilon_i$ (%) Median (range)</th>
<th>$E_{ihr}$ (MPa) Median (range)</th>
<th>$C_\varepsilon$ (% / log time) Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaction 300 N ('I300N')</td>
<td>11.0 (9.5-11.5)</td>
<td>9.7 (9.0-10.9)</td>
<td>7.4 (6.6-7.7)</td>
<td>1.10 (1.02-1.25)</td>
</tr>
<tr>
<td>600 N ('I600N')</td>
<td>15.6 (12.9-17.8)</td>
<td>6.8 (6.0-8.0)</td>
<td>12.2 (10.4-13.7)</td>
<td>0.48 (0.44-0.53)</td>
</tr>
<tr>
<td>900 N ('I900N')</td>
<td>18.6 (16.5-22.6)</td>
<td>5.8 (4.7-6.6)</td>
<td>14.3 (12.5-16.6)</td>
<td>0.41 (0.37-0.46)</td>
</tr>
<tr>
<td>Creep ('C300N')</td>
<td>12.2 (11.6-12.6)$^a$</td>
<td>8.5 (8.2-8.7)$^a$</td>
<td>8.6 (8.3-8.9)$^a$</td>
<td>0.94 (0.84-1.01)$^b$</td>
</tr>
<tr>
<td>Cyclic Relaxation ('R300N')</td>
<td>11.9 (9.8-11.9)</td>
<td>9.4 (8.5-10.6)</td>
<td>7.4 (6.5-8.0)</td>
<td>1.22 (1.04-1.41)</td>
</tr>
</tbody>
</table>

$^a$ $p<0.01$ compared to Impaction 300 N  
$^b$ $p<0.05$ compared to Impaction 300 N

During shear testing, we did not observe a shear stress plateau when plotting shear stress versus shear displacement (Figure 3.7). By defining shear strength as the shear stress at a displacement of 1 mm (~5% of specimen diameter), we obtained the shear strength versus normal stress curves shown in Figure 3.8. From these results, the main effect of the impaction force on shear strength was significant ($p<0.001$). The average shear strength in the 600 N and 900 N impaction groups was 79% and 164% greater, respectively, than in the 300 N impaction group (Figure 3.8). Note that the shear strength increased with increasing normal stress ($p<0.0001$), and that there was no interaction effect between normal stress and impaction force. The lack of a shear stress plateau led us to use a more arbitrary shear strength definition; nevertheless, similar observations were made when comparing the shear strength results between the compaction groups regardless of the threshold displacement value used in the definition of shear strength (Table 3.3). The cohesion intercept, $c$, increased consistently with increasing impaction force, but friction angle, $\phi$, did not (Table 3.3).
Figure 3.7 Shear stress (black) versus shear displacement curve for a typical specimen. In grey is the same curve when the shear stress is derived with the initial specimen area, i.e., without accounting for the changing cross-sectional area.

Figure 3.8 Results of the shear tests - shear strength, $\tau_f$, versus normal stress, $\sigma_n$, for all impaction forces: 300 N (I300N), 600 N (I600N) and 900 N (I900N), and for the creep compaction method (C300N). Results in the C300N group were offset on the abscissa for clarity.
Table 3.3 Mohr-Coulomb parameters versus strength definition for three impaction forces: 300 N (I300N), 600 N (I600N) and 900 N (I900N), and for the creep compaction method (C300N). Also shown is the shear strength, $\tau_f$, (median and range) under a normal stress, $\sigma_n$, of 375 kPa.

<table>
<thead>
<tr>
<th>Shear strength definition</th>
<th>I300N</th>
<th>I600N</th>
<th>I900N</th>
<th>C300N</th>
</tr>
</thead>
<tbody>
<tr>
<td>c (kPa)</td>
<td>214</td>
<td>311</td>
<td>510</td>
<td>166</td>
</tr>
<tr>
<td>$\phi$ ($^\circ$)</td>
<td>15</td>
<td>28</td>
<td>29</td>
<td>18</td>
</tr>
<tr>
<td>$\tau_f$ (kPa)</td>
<td>288 (247-315)</td>
<td>485 (461-626)</td>
<td>724 (660-791)</td>
<td>310 (287-328)</td>
</tr>
<tr>
<td>at 1 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c (kPa)</td>
<td>247</td>
<td>394</td>
<td>633</td>
<td>303</td>
</tr>
<tr>
<td>$\phi$ ($^\circ$)</td>
<td>41</td>
<td>42</td>
<td>41</td>
<td>19</td>
</tr>
<tr>
<td>$\tau_f$ (kPa)</td>
<td>389 (358-462)</td>
<td>720 (695-832)</td>
<td>961 (866-1064)</td>
<td>459 (387-469)</td>
</tr>
<tr>
<td>at 2 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c (kPa)</td>
<td>410</td>
<td>579</td>
<td>648</td>
<td>424</td>
</tr>
<tr>
<td>$\phi$ ($^\circ$)</td>
<td>60</td>
<td>52</td>
<td>60</td>
<td>41</td>
</tr>
<tr>
<td>$\tau_f$ (kPa)</td>
<td>641 (588-797)</td>
<td>1044 (1022-1140)</td>
<td>1254 (1188-1478)</td>
<td>755 (620-817)</td>
</tr>
<tr>
<td>at 4 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The graft density, measured as apparent bone density, $\rho$ (pQCT) and as the percentage bone, $%b$ (histology) was found to correlate positively with the impaction force, $F$: $\rho = 0.197\cdot F + 217 \text{ mg/cm}^3$ ($R^2=0.84$, $p<0.0001$), $%b = 0.018\cdot F + 21.5\%$ ($R^2=0.60$, $p=0.0002$). The $\rho$ and $%b$ measurements were also correlated with each other: $\rho = 7.04\cdot %b + 108 \text{ mg/cm}^3$, ($R^2=0.58$, $p=0.0003$). Finally, the relationships between the graft density and the compressive stiffness as well as the creep constant are shown in Figures 3.9 and 3.10, respectively.
Figure 3.9 Post-impaction stiffness, $E_i$ (top) and $E_{1hr}$ (bottom) versus graft density for each force group. Shown are medians and ranges, and the median values were used for curve fitting. See Tables 3.2 and 3.4.
Figure 3.10 Creep constant during post-impaction creep compression versus graft density for each force group (medians and ranges, see Tables 3.2 and 3.4).

Table 3.4 Graft density and percentage bone as a function of impaction force. Medians (ranges).

<table>
<thead>
<tr>
<th>Impaction force</th>
<th>Graft density, $\rho$ (mg/cm$^3$)</th>
<th>Percentage bone, $%b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 N</td>
<td>272 (251-301)</td>
<td>27 (21-32)</td>
</tr>
<tr>
<td>600 N</td>
<td>342 (306-365)</td>
<td>31 (28-36)</td>
</tr>
<tr>
<td>900 N</td>
<td>385 (371-453)</td>
<td>38 (33-45)</td>
</tr>
</tbody>
</table>

The main effect of the compaction technique on the graft compression behaviour, $E_i$, $E_{1hr}$, $\varepsilon_i$, and $C_\varepsilon$ was statistically significant ($p<0.01$) but for practical purposes the differences in median values between the groups were small, Table 3.2. Compared to impaction, the creep technique resulted in a small increase in stiffness and a small decrease in $\varepsilon_i$ and $C_\varepsilon$, e.g., 16% higher median $E_{1hr}$, whereas the cyclic relaxation technique did not affect the compression behaviour. Similarly, the main effect of the compaction technique on shear strength was significant ($p<0.0001$, Figure 3.8) but the difference in average shear strength between the two groups is for practical purposes small. The creep compaction technique resulted in 14% greater shear strength, on average, compared with impaction at the same force - however, its effect on
the Mohr Coulomb coefficients was not clear as it varied as a function of the definition of shear strength used (Table 3.3).

Stiffness as measured during impaction, $E_{imp}$, increased with each impact (Figure 3.11). The $E_{imp}$ during the twentieth impact was proportional to the impaction force ($R_s=0.90$ p>0.05). The median $E_{imp}$ was 70.8 MPa (range 66.0-75.6 MPa), 78.6 MPa (71.6-84.2 MPa), and 87.0 MPa (84.6-96.8 MPa), in the 300 N, 600N and 900 N impaction groups, respectively. Finally, the stiffness of the impacted MCB, $E_i$ and $E_{1hr}$, were correlated with $E_{imp}$ at the twentieth impaction ($R_s=0.92$ for both, with p>0.05).

![Stiffness graph](image)

**Figure 3.11 Median stiffness of the graft during impaction, $E_{imp}$, and during subsequent creep test for all impaction forces.**

### 3.4 Discussion
Morsellized cancellous bone grafts exhibit viscoelastic-viscoplastic behaviour. In other words, MCB deforms under load in a way that is partly recoverable (elastic) and partly non-recoverable (plastic), in a process that is time-dependant (viscous). Simple confined compression and shear tests are useful in estimating the effect of surgical parameters on the mechanical performance of impacted MCB. However, it must be emphasized that viscoelastic-viscoplastic materials do not exhibit distinctive stiffness or shear strength properties, and that the apparent stiffness or shear strength measurement of such a material are sensitive to time-related testing parameters such as the rate and duration of loading. Moreover, MCB has been
described as a nonlinear viscoelastic material (Phillips et al., 2006a), indicating that its mechanical properties also depend on the stress applied. One must therefore be careful when comparing the results of MCB characterization studies.

A wide range of stiffness values have been reported for fresh frozen, impacted MCB: 3-135 MPa (Giesen et al., 1999; Voor et al., 2000; Verdonschot et al., 2001; Bavadekar et al., 2001; Cornu et al., 2003b; Cornu et al., 2004; Voor et al., 2004; Fosse et al., 2004; Phillips et al., 2006a; Phillips et al., 2006b; Fosse et al., 2006). This large range of results is likely due to variation in the test methods among the studies. Our post-impaction MCB stiffness under creep loading, $E_{1hr}$, ranged between 7 and 17 MPa – which is comparable to the results of other studies that have similarly measured stiffness in creep under a similar stress: 3-8 MPa (Voor et al., 2000; Voor et al., 2004; Fosse et al., 2004). Studies that measured stiffness immediately after impaction, without allowing the graft to recoil, consistently reported higher stiffness: 10-70 MPa (Phillips et al., 2006b; Fosse et al., 2006). Similarly, stiffness measured during a loading ramp ranged 40-70 MPa (Cornu et al., 2003a; Cornu et al., 2004) and during impaction or cyclic loading, 15-135 MPa (Verdonschot et al., 2001; Phillips et al., 2006b). Our stiffness measurements during the twentieth impaction, $E_{imp}$, 66-97 MPa, were within the range reported by others (Phillips et al., 2006b). Dynamic stiffness measurements, however, are influenced by the fluid phase, rendering the measurements sensitive to the loading rate and that of fluid dissipation, which is affected by the geometry and permeability of the graft and its environment. By characterizing MCB stiffness in creep, we were able to account for fluid effects and, therefore, to measure the response of the graft particles to the applied load. Finally, we believe that measuring stiffness post-impaction, and after having allowed the graft to recoil, provides a more clinically relevant measure of graft stiffness since recoil is unavoidable during surgery.

It has been demonstrated that MCB stiffness increases with the number of impactions (Bavadekar et al., 2001; Cornu et al., 2003a). In these studies, however, the impaction force was not reported. In the current study, $E_{imp}$ appeared to have reached a plateau within ten impactions at forces of 600 N and 900 N (2 and 3 MPa), whereas with a force of 300 N, $E_{imp}$ was still increasing beyond the first ten impactions (Figure 3.11). It did not appear, however, that further increase in stiffness would be achieved beyond 20 impactions. In another study, the
stiffness of bovine MCB was shown to increase with the number of impactions, or ‘cycles’, and increasing compacting force (Phillips et al., 2006b). Their specimens, however, were impacted in force increments, thus the effect of force was not isolated from that of the number of impactions – furthermore, no recoil was allowed prior to stiffness measurement, therefore it is not clear whether the effect of the force they observed would remain following the removal of the impaction tool. Another study demonstrated that the graft compression stiffness is proportional to the drop height of a slap hammer, and reported a correlation between MCB stiffness and density (Fosse et al., 2006). In their study, however, the impaction force was neither controlled nor reported specifically. Furthermore, their bone mineral density measurements appeared to have been taken following creep testing at 2.3 MPa and they reported using a correction factor, but it was not described. Our results agree that increasing the impaction force increases the post-impaction compressive stiffness of MCB, and demonstrate that this improvement is related to the graft density. Since our density measurements were taken after impaction without subjecting the specimens to further testing that may affect the density, we believe this provides a more clinically relevant measure of the MCB density at the time that the stem is cemented in place. Nonetheless, it is worth noting that the shear strength and stiffness of the graft bed may be affected by the endosteum roughness, and the fluid paths, which can be influenced by the absence of drainage holes in the femur, the varying canal geometry, and the size of the gap around the impactor. For this reason, the stiffness and shear strength measured in this study should be regarded as approximate values.

The stiffness of structural cancellous bone is known to be roughly proportional to the square (Hayes and Bouxein, 1997) or cube (Carter and Hayes, 1977) of its apparent density. The nature of the relationship between the stiffness and density of morsellized cancellous graft, however, is not known. A linear regression offered a reasonable fit to our stiffness versus apparent density data (Figure 3.9), but it is not clear whether this linear relationship would apply over a wider range of apparent graft density.

The correlation observed between the two density measurements, %b and ρ, was somewhat weak, i.e., R²=0.58. This may be explained by the following observations. The ρ and %b measurements were taken at approximately but not exactly the same location. Furthermore, while the pQCT measurements of ρ were obtained from three-dimensional voxels (0.1 mm x
0.1 mm x 2.3+/−0.2 mm), the histological measurements of %db were obtained from a single
two-dimensional cross section. Finally, a small swelling of the graft occurred during the
preparation of the histological slides, which may have led to a lower %db measurement, and this
swelling was not controllable between the specimens.

Based on the current results, the relationship between the compression properties of MCB and
its density can be described by the following equations, with:

- A: specimen cross sectional area
- \( H_o \): height of the graft specimen prior to impaction
- \( V_o \): specimen volume prior to impaction
- \( \rho_o \): graft apparent bone density prior to impaction
- \( H \): instantaneous specimen height during impaction
- \( V \): instantaneous specimen volume
- \( \rho \): instantaneous graft density
- \( \varepsilon_{N \text{ imp}} \): MCB strain during impaction (natural)

The natural compressive strain of the graft during impaction, \( \varepsilon_{N \text{ imp}} \) can be calculated as:

\[
\varepsilon_{N \text{ imp}} = \ln \left( \frac{H_o}{H} \right) \quad (3.2)
\]

During impaction, fluid flows out of the MCB, and conservation of mass of the graft particles
gives:

\[
\rho_o V_o = \rho V \quad (3.3)
\]

Because the cross sectional area is constant during the test:

\[
\frac{H}{H_o} = \frac{V}{V_o} \quad (3.4)
\]

From (2-4) we can estimate the instantaneous bone density of the MCB:

\[
\rho = \rho_o \varepsilon_{N \text{ imp}} \quad (3.5)
\]
We can estimate \( \rho_0 \) from our correlation results (graft density versus impaction force) as \( \rho \) resulting from an impaction force of zero, i.e., approximately 217 mg/cm\(^3\).

Under post-impaction compression loading, we observed that the initial stiffness, \( E_i \), of the impacted MCB (loading ramp to 1.1 MPa in 1 s) and the stiffness after one hour creep, \( E_{1hr} \), were proportional to the graft density achieved during impaction (Figure 3.9):

\[
E_i(\rho) = C_1 \cdot \rho + C_2
\]

and

\[
E_{1hr}(\rho) = C_3 \cdot \rho + C_4
\]

where \( C_1 \approx 0.068 \text{ MPa cm}^3/\text{mg} \), \( C_2 \approx -7.39 \text{ MPa} \), \( C_3 \approx 0.062 \text{ MPa cm}^3/\text{mg} \), and \( C_4 \approx -9.24 \text{ MPa} \).

Given the relationship in Equation 3.6 and the data shown in Figure 3.5, knowing the MCB density post-impaction, we can estimate the total creep strain, \( \varepsilon \), that will develop over time under a sustained confined compression stress, \( \sigma_o \):

\[
\varepsilon(t) \approx \varepsilon_i(\rho) + C_\varepsilon(\rho) \cdot \log t = \frac{\sigma_o}{E_i(\rho)} + C_\varepsilon(\rho) \cdot \log t \tag{3.8}
\]

Furthermore, from the results shown in Figure 3.10, with a compressive stress \( \sigma_o \) of 1.1 MPa, the creep constant of the MCB, \( \varepsilon_\sigma \), was related to the graft density as follows:

\[
C_\varepsilon(\rho) = D_1 e^{-D_2 \rho}
\]

where \( D_1 \approx 12.1 \), and \( D_2 \approx 0.009 \text{ cm}^3/\text{mg} \).

Finally, by combining Equations 3.6, 3.8 and 3.9, we can express the creep compression strain \( \varepsilon(t) \) as a function of the post-impaction graft density (Equation 3.10a) or its density before impaction, \( \rho_0 \), and total strain during impaction, \( \varepsilon_{N \text{ imp}} \) (Equation 3.10b):

\[
\varepsilon(t) = \frac{\sigma_o}{C_1 \rho + C_2} + D_1 e^{-(D_2 \rho)} \cdot \log t \tag{3.10a}
\]

\[
\varepsilon(t) = \frac{\sigma_o}{C_1 \rho_0 e^{\varepsilon_{N \text{ imp}}} + C_2} + D_1 e^{-(D_2 \rho_0 e^{\varepsilon_{N \text{ imp}}})} \cdot \log t \tag{3.10b}
\]
Equations 3.2-3.10 illustrate how the density achieved during compaction affects its stiffness and creep behaviour. Constitutive equations have been previously proposed to describe the time-dependent behaviour of MCB under compressive loading (Giesen et al., 1999), and the relationship between stiffness of MCB and the compressive stress to which it is subjected (Phillips et al., 2006a). In these studies, the graft was subjected to 23 and 750 cycles of preconditioning at high loads (2.3-3 MPa) prior to the stiffness measurement. Consequently, their specimens would have been of roughly uniform, high density. Our work expands on those findings by factoring in the effect of the graft density achieved during impaction. Further work, however, is required to determine if and how $C_\varepsilon$, $E_i$, and $E_{1hr}$ vary as a function of the compression stress, $\sigma_o$.

The creep technique brought some improvement in compression properties compared with impaction: e.g., 16% increase in $E_{1hr}$ (median values, Table 3.2). We can use the derived constitutive equations explain this finding. From Equation 3.7, we can estimate that for a 25% gain in $E_{1hr}$, we would need to achieve a graft density of approximately 298 mg/cm$^3$ (i.e., a compaction strain $\varepsilon_{N_{imp}}$ of 0.317, assuming an unimpacted density of 217 mg/cm$^3$). When extrapolating the strain-time data obtained during compaction with the creep technique, we estimate that to achieve such graft density, the 300 N compression load would have to be held for approximately 4 hours. This would not be practical in a clinical setting. Finally, the cyclic relaxation technique did not offer any benefit to the compressive properties of MCB.

A recent study reported that applying a small pressure to the graft bed following impaction can offer a considerable increase in stiffness compared with impaction alone (Lunde et al., 2008). The current study used considerably larger pressure and yet offered only a modest increase in graft stiffness compared with impaction. Nonetheless, further consideration may be warranted towards a technique that incorporates both impaction and a slow compression of the graft.

The shear strengths of MCB reported in the literature also vary greatly between studies. For example, under a normal stress of 350-370 kPa, shear strengths between 225 kPa (Dunlop et al., 2003) and 1700 kPa (Tanabe et al., 1999) have been reported. The current results are within the range of values seen in the literature. In contrast to what is often reported for hard particulate materials, no shear stress plateau was observed (Figure 3.7, black line). More
specifically, if we defined shear stress as the shearing force divided by the initial cross-sectional area, the shear stress would have reached a plateau after approximately 3 mm of shear displacement (Figure 3.7, grey line). This shear strength definition, however, would be inaccurate for a large displacement. We therefore accounted for the changing specimen cross-sectional area in our definition of shear stress, after which no shear stress plateau was observed even at a displacement of 9 mm (50% of specimen diameter). For this reason, we used a threshold displacement of 1 mm (5% of specimen diameter) in our definition of shear strength. This makes the definition of shear strength ambiguous and direct comparison with literature values difficult. It is not known what causes the lack of a shear stress plateau, but qualitative observations during the tests revealed a substantial amount of deformation and cohesiveness of the MCB particles – this behaviour is in sharp contrast to what is seen when a stiff particulate material such as sand or gravel is tested in shear. The lack of plateau may also be attributed partly to an increase in ‘true’ normal stress due to the decreasing cross-sectional area in the shear plane. This kind of error would have probably been much smaller with harder particles for which shear failure would have occurred at a smaller shear displacement.

Our results demonstrate that the shear strength of MCB is proportional to the impaction force. Because MCB particles are highly deformable, the ‘packing density’ may therefore depend more on the impaction force than on the particle size distribution. Finally, the creep technique offered a 14% average increase in shear strength compared with impaction.

Shear failure and creep consolidation of the graft bed are not the only mechanisms that are believed to influence implant migration in impaction allografting. Other mechanisms such as cement fatigue (Masterson et al., 1997), graft incorporation/fibrous invasion (Linder, 2000; Nelissen et al., 1995), and cancellization of the femoral canal (Frei et al., 2005b) are also suspected to play a role in implant stability, while previous studies also point to the importance of cement contact with the endosteum (Frei et al., 2005a; Albert et al., 2007). Nonetheless, clinical studies have shown that a substantial amount of subsidence develops in the early postoperative days: more than 1 mm subsidence was often observed within the first three months after surgery (Ornstein et al., 2001; Nelissen et al., 2002) and more than half of the subsidence observed at six weeks was seen typically within the first two weeks (Ornstein et al., 2000). Furthermore, a recent clinical study indicated that there appears to be relationship
between implant migration and the density of the graft bed (Gokhale et al., 2005). These observations point to the importance of adequate MCB compaction, and the resulting shear and compression properties.

A number of surgical parameters have been reported to affect graft properties. The following parameters were observed to affect the shear strength of MCB: rinsing the graft increased shear strength by 15-25% (Dunlop et al., 2003); controlling the graft particle size distribution affected shear strength by 8-14% (Dunlop et al., 2003); and using a Bioglass extender to optimize the particle size distribution increased shear strength by 7% (Brewster et al., 1999). Washing the graft with a detergent increased the compression stiffness by 5% (Voor et al., 2004), while combining washing, freeze-drying and irradiation increased graft stiffness by 17% when compared with fresh-frozen graft (Cornu et al., 2004). With increases of 14% in stiffness and 16% in shear strength, our proposed creep technique appears to offer a benefit comparable to other surgical parameters such as optimizing the particle size distribution. However, it is not yet clear whether this small increase in graft stiffness is of clinical relevance, and for this reason, we do not recommend changing the current technique of impaction.

A recent study investigated the potential benefit of vibration during graft compaction in a composite femur model of impaction allografting – on average, the use of vibration compacted 9% more graft (by weight) in the medullary canal compared with standard impaction, and this resulted in 28% less migration (Bolland et al., 2007). These results indicate that a small increase in graft density may have a large effect on implant stability. Other recent studies, however, have observed extensive cement contact with the endosteum after impaction allografting in a cadaver model (Frei et al., 2005a; Albert et al., 2007; Frei et al., 2004). This leads to the following questions. Does implant stability rely on a cement-endosteum interface rather than on the stiffness and strength of the graft bed? Alternatively, how dense must the graft bed be to adequately support the implant without cement-endosteum contact? We believe that it is essential to answer these two questions prior to proposing changes to the current graft impaction technique.

Within the range of forces used in impaction allografting, the impaction force has a substantial effect on the graft compression stiffness and shear strength. The current results point to the
importance of maximizing impaction forces – therefore it would be beneficial to reinforce the femur during surgery to minimize the risk of intraoperative fracture, especially when dealing with severe bone loss. A graft compaction method yielding greater strength and stiffness without increasing the compaction force could reduce the risk of fracture. Our ‘creep method’ resulted in a small increase in stiffness and shear strength compared with standard graft impaction; however it is not clear whether this would be clinically beneficial in impaction allografting.
3.5 References


CHAPTER 4

INFLUENCE OF CEMENT PROFILE AND GRAFT PROPERTIES ON STEM MIGRATION AND MICROMOTION

A FINITE ELEMENT STUDY

A version of this chapter has been accepted for publication.
4.1 Introduction

Implant loosening is the leading cause of femoral implant failure in total hip arthroplasty (THA) (Karrholm et al., 2007; Canadian Institute for Health Information, 2008; Bozic et al., 2009). Loosening is often accompanied by bone loss, which can pose a challenge during revision surgery (Engelbrecht et al., 1990; Chandler et al., 1994; Haddad and Duncan, 1999). Impaction allografting was introduced to address the problem of bone loss in revision THA, however, some concerns have been raised about the high incidences of femoral fractures (Knight and Helming, 2000; Fetzer et al., 2001; Schreurs et al., 2005) and excessive implant migration relative to bone (Meding et al., 1997; Eldridge et al., 1997; van Biezen et al., 2000; Robinson et al., 2002; Piccaluga et al., 2002). While implant migration may not necessarily lead to failure, excessive migration (>10 mm) increases the risk of thigh pain, dislocation and the need for re-revision – for this reason, excessive migration is often deemed a failure of the reconstruction (Meding et al., 1997; Eldridge et al., 1997; Masterson et al., 1997a; Robinson et al., 2002).

It has been suggested that early implant migration may be caused by: settling of the stem into the cement mantle (Malkani et al., 1996); postoperative compaction of the graft (Nilsson and Karrholm, 1996; Linder, 2000, Halliday et al. 2003); shear failures in the graft (Brewster et al., 1999; Dunlop et al., 2003; Halliday et al., 2003; Ornstein et al., 2004; Bolland et al., 2006; Bolland et al., 2007); and sliding of the graft at the endosteum (Ornstein et al., 2004; Frei et al., 2005a). In the long-term, other variables such as cement fatigue (Ornstein et al., 2004), femoral expansion due to ageing or interruption of vascular supply (Ornstein et al., 2004; Frei et al., 2005b), and remodeling of the bone graft (Franzen et al., 1995) may also contribute to migration. However, it is not known what effect these events and mechanisms have on long-term implant stability, nor is the wide range of migration seen in impaction allografting understood.

Morsellized cancellous bone graft has substantially lower stiffness compared to the other materials in an impaction allografting construct (Voor et al., 2004; Albert et al., 2008), and it may be susceptible to shear failure due to its particulate nature (Brewster et al., 1999). It is therefore believed that graft bed density plays a role in implant stability (Lind et al., 2002;
Cabanela et al., 2003; Pekkarinen et al., 2000; Morgan et al., 2004; Gokhale et al., 2005; Bolland et al., 2007). For this reason, numerous studies have focused on the mechanical characteristics of morsellized bone graft (Brodt et al., 1998; Brewster et al., 1999; Tanabe et al. 1999; Giesen et al., 1999; Voor et al., 2000; Schreurs et al., 2001; Bavadekar et al., 2001; Dunlop et al., 2003; Cornu et al., 2003; Voor et al., 2004; Cornu et al., 2004a; Cornu et al., 2004b; Fosse et al., 2004; Butler et al., 2005; Fosse et al., 2006; Phillips et al., 2006a; Phillips et al., 2006b; Albert et al., 2008). In impaction allografting, however, the graft bed is infiltrated in part with bone cement, and for this reason the role of the graft in the migration process may be more complex. In recent in vitro studies, high levels of cement penetration into the graft bed were observed after impaction allografting, resulting in substantial cement contact with the endosteum around the distal half of the stem (Frei et al., 2004; Albert et al., 2007). Stem migration was also found to increase with a decrease in amount of cement and cement-endosteum contact (Albert et al., 2007). The relative importance of graft bed density and cement penetration profile, however, is not known.

The first objective of this study was to determine the effects of graft density and cement penetration profile on the shear stresses at the endosteum interface. The second objective was to estimate the effects of four variables on stem migration and micromotion: graft density, cement penetration profile, and the status of the stem-cement and endosteum interfaces; i.e., bonded or sliding. The third objective was to estimate the relative contribution of each of the following mechanisms on implant motion: sliding at the stem-cement interface, shear deformation of the cement mantle layer, shear deformation of the graft and/or graft/cement composite region, and sliding at the endosteum interface – and how these four contributions vary as a function of the four study variables. These objectives were addressed using a finite element model, and the resulting migration and micromotion were validated against experimental in vitro results.

4.2 Methods
A finite element mesh of 2004 eight-noded axisymmetric elements was built using ANSYS 11.0 (ANSYS, Inc., Canonsburg, PA, USA) to simulate the proximal femur after impaction allografting. Four variables were incorporated into the model. The first variable was the cement
penetration profile; nine profiles were simulated, ranging from little cement penetration into the graft to extensive cement contact with the endosteum (Figure 4.1). The second variable was graft density, which was simulated by controlling the stiffness and shear strength of the graft and graft-cement composite regions to represent low, moderate, and high graft impaction forces. The last two variables were the status of the stem-cement and cement-endosteum interfaces; i.e., bonded or sliding. The effects of these parameters on implant motion were examined during cyclic loading corresponding to a walking cycle. A total of 90 simulations were conducted, and the simulations and post-processing were performed using Abaqus/Standard and Abaqus/CAE 6.6-1 (Abaqus Inc./Simulia Inc. Rhode Island, USA).

Figure 4.1 Geometries of the nine cement penetration profiles modeled. Profiles A-C: idealized constructs with uniform cement penetration that reached depths of 25%, 50%, and 75% of the graft bed width, respectively. Profiles D-I: constructs with 11%, 24%, 36%, 49%, 61% and 80% cement contact with the endosteal surface, respectively (the width-to-length aspect ratio was increased to facilitate viewing the cement profiles).

The distal 13 cm of a stem was modeled as an axisymmetric solid body with a total taper angle of 4.4°, i.e., the average between the taper angles in the frontal and lateral planes for a CPT stem (CPT 12/14 Hip System, Size 2, Zimmer Inc.). The femur was modeled as a tapered axisymmetric cylinder mimicking the dimensions of proximal human femurs with moderate bone loss and cortical thinning. The following morphometric features were chosen based on measurements from radiographs of twelve human femur specimens (six donors) on which impaction allografting had been performed: an inner diameter of 14 mm at stem tip level; an
endosteal taper angle of 2.4° from the axis of symmetry (total taper angle of 4.8°); and a cortical thickness of 5 mm at stem tip level and 2 mm at 13 cm above the stem tip. The top of the distal plug was located 38 mm distal from the stem tip.

Nine distinct profiles of cement penetration into the graft were simulated (Figure 4.1). In all profiles, a 2 mm thick layer of pure cement (cement mantle) was modeled adjacent to the stem, and a polyethylene centralizer was included at the stem tip. The remaining canal content consisted of areas of pure graft and of graft/cement composite, forming nine configurations, each representing a distinct cement penetration profile. Profiles A, B and C represented idealized constructs with uniform cement penetration that did not reach the endosteum, but reached a depth of 25%, 50%, and 75% of the graft bed width, respectively. In profiles D through I, the graft/cement composite region was in contact with 11%, 24%, 36%, 49%, 61% and 80% of the endosteum interface, respectively. The centers of the cement-endosteum contact regions were located 50 mm above the stem tip, to mimic cement profiles that were observed in previous in vitro studies, in which cement-endosteum contact was seen predominantly around the mid and distal stem (Albert et al., 2007; Frei et al., 2004).

The stem, cement and femur were modeled with linear elastic behaviour. The stem consisted of a CoCrMo alloy and was given a Young’s modulus, $E$, of 210 GPa (Hallab et al., 2004) and a Poisson’s ratio, $\nu$, of 0.3. The femoral cortex was assumed isotropic and assigned $E = 20$ GPa (Reilly and Burnstein, 1975) and $\nu = 0.28$ (Pidaparti and Vogt, 2002); and the bone cement $E = 2$ GPa (Kindt-Larsen et al., 1995) and $\nu = 0.37$ (Guild et al., 1994).

The graft was modeled with elasto-plastic behaviour. In tension and compression, the graft behaviour was assumed linear elastic, while in shear it was assumed linear elastic up the onset of failure where it exhibited plastic behaviour with a pressure-dependent Mohr-Coulomb shear failure envelope that was defined based on experimental data. The graft properties, shown in Table 4.1, represented low, moderate and high graft densities based on experimental data (Chapter 3). The Mohr-Coulomb cohesion and friction parameters were assumed constant for each graft density. The graft was assigned a Poisson’s ratio, $\nu_{\text{graft}}$, of 0.2 (Brodt et al., 1998).
Table 4.1 Graft properties used in the finite element model, representing low, moderate or high graft density.

<table>
<thead>
<tr>
<th>Graft impaction pressure (MPa)</th>
<th>Graft apparent density (mg/cm³)</th>
<th>Volume fraction of bone, f (%)</th>
<th>E_graft (MPa)</th>
<th>Mohr-Coulomb parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>272 (low)</td>
<td>27</td>
<td>7.4</td>
<td>214, 15</td>
</tr>
<tr>
<td>2</td>
<td>342 (moderate)</td>
<td>31</td>
<td>12.2</td>
<td>311, 28</td>
</tr>
<tr>
<td>3</td>
<td>385 (high)</td>
<td>38</td>
<td>14.3</td>
<td>510, 29</td>
</tr>
</tbody>
</table>

Values taken from (Albert et al., 2008).

The graft/cement composite region was assumed isotropic. Its modulus and Poisson’s ratio were estimated for each graft density level using Equations 4.1-4.4 (Halpin and Tsai, 1969; Halpin 1984). The volume fraction of graft in the composite regions, f, was estimated based on the percentage of bone observed experimentally in morsellized graft specimens for each graft density level (Chapter 3); these values are shown in Table 4.1. It was assumed that cement filled all of the spaces that were not occupied by bone in the graft/cement composite regions, such that the volume fraction of cement was equal to 1-f. From Equations 4.1-4.4, it was estimated that E_composite and ν_composite were 1289 MPa and 0.32, 1201 MPa and 0.32, and 1053 MPa and 0.31 for the low, moderate and high density level, respectively.

\[
E_{\text{composite}} = E_{\text{cement}} \left( \frac{1 + \zeta \eta f}{1 - \eta f} \right) \quad (4.1)
\]

with \( \eta = \left( \frac{E_{\text{graft}}}{E_{\text{cement}}} \right) - 1 \) \quad (4.2)

and \( \zeta \approx 2 + 40 f^{10} \) \quad (4.3)

\[
\nu_{\text{composite}} = f \nu_{\text{graft}} + (1 - f) \nu_{\text{cement}} \quad (4.4)
\]

The stem-cement interface was modeled as either bonded or as sliding with a Coulomb friction model and \( \mu = 0.3 \) (Nuno et al., 2002; Nuno et al., 2006). The graft-endosteum interface was modeled as sliding with \( \mu = 0.61 \) (Zhang et al., 1999), and the cement-endosteum interface was modeled as bonded or sliding with \( \mu = 0.61 \).
Loading was applied in two steps. In step 1, an axial force of 1646 N (14.5 MPa) was applied to the proximal cross section of the stem in the distal direction. In step 2, the force was reduced to 213 N (1.9 MPa). These two force levels were chosen to represent the minimum and maximum peak distal loads on the hip joint during walking for a 75 kg patient; i.e., 2.24 and 0.29 times body weight (Bergmann et al., 2001).

The shear stress was calculated at the endosteal interface, and the implant motion relative to the femur was calculated at the most proximal cross section. Migration was defined as the vertical position of the proximal section of the stem relative to the bone while it was loaded (step 1), minus its initial position. Micromotion was defined as the vertical stem position relative to the bone while loaded (step 1), minus its position after it was unloaded (step 2). Micromotion and migration (δ) were each decomposed into: motion at the stem-cement and endosteum interfaces (δ_{stem-cement} and δ_{endosteum}, respectively); motion as a result of shear deformation of the cement mantle (δ_{mantle}); and motion due to shear deformation of the graft and/or graft/cement composite regions (δ_{graft/composite}), see Appendix 4, Figure A4.2. In other words, the migration and micromotion were decomposed as:

\[ \delta = \delta_{stem-cement} + \delta_{mantle} + \delta_{graft/composite} + \delta_{endosteum} \]  

(4.5)

Migration and micromotion were validated against in vitro experimental data from Chapter 2.

4.3 Results

The cement penetration profile had a substantial effect on shear stresses at the endosteum (Figure 4.2). For profiles A-C, representing increasing uniform cement penetration into the graft, an average endosteum shear stress of 0.14 MPa was observed above the stem tip (Figure 4.2), where a gradual load transfer occurred from the stem to the femur. For these constructs, the endosteum shear stress peaked at 10 mm below the stem tip, where the load remaining on the distal stem was transferred sharply to the femur through the graft. For profiles D-I, representing increasing amounts of cement-endosteum contact, the load transfer occurred almost entirely through the cement-endosteum contact regions, where the average shear stress was 1.12, 0.52, 0.35, 0.26, 0.20, and 0.16 MPa, respectively. For these profiles, the shear stress was less than 0.05 MPa in the graft-endosteum interface regions.
Figure 4.2 Shear stress at endosteum interface for profiles A-C (top) and D-I (bottom). For profiles D-I, simulations in which the cement-endosteum contact region was bonded are shown in grey, and those in which the entire endosteum interface was sliding are shown in black.

For profiles A-C, where there was no cement-endosteum contact, the migration and micromotion were 578-3323 µm and 48-289 µm, respectively (Figure 4.3). For these profiles, the cement penetration depth (i.e., profile A, B, or C) had a substantial effect on the implant motion. For example, when comparing equivalent cases (i.e., having the same graft density and
status of the stem-cement interface), profile A resulted in much higher migration and micromotion (by 968-2071 µm and 102-199, respectively) than did profile C. For profiles A-C, a low graft density resulted in much greater migration and micromotion (by 552-1649 µm and 36-132 µm, respectively) than did a high graft density. Debonding of the stem-cement interface, however, had little effect on implant motion, increasing migration and micromotion by only 74-89 µm (2-11%) and 5-6 µm, respectively.

The motion results for profiles D-I, where there were varying amounts of cement-endosteum contact, are shown in Figure 4.4, together with the in vitro experimental results. For these profiles, migration and micromotion (5-356 µm and 4-37 µm, respectively) were much lower than for profiles A-C, and the motion decreased with increasing cement-endosteum contact. With profiles D-I, however, graft density had little effect on the implant motion – migration and micromotion differences of only 0-13 µm and 0-3 µm, respectively, were observed between the three graft density levels, with all other variables being equal. For these profiles, debonding of the stem-cement interface increased migration and micromotion by 80-170 µm and 4-7 µm, respectively.

A breakdown of the contributions of each material and interface to total migration and micromotion (Equation 4.5) is presented in Table 4.2 and Appendix 4. Most of the migration occurred at the interfaces. For all cement profiles and graft densities, slippage at the stem-cement interface accounted for 104-124 µm of the migration when this interface was defined as sliding. Slippage at the endosteum, however, was much more varied: it accounted for 0-2982 µm of the migration, and its contribution was largest when there was no cement-endosteum contact, in which case it decreased with increasing graft density. Shear deformation of the graft and graft/cement composite regions, however, accounted for only 42-262 µm (6-8%) of the migration for profiles A-C, and 1-24 µm of the migration for profiles D-I. For all profiles, micromotion occurred mainly within the graft and graft/cement composite regions and at the endosteum interface.
Figure 4.3 Implant migration (top) and micromotion (bottom) for cement penetration profiles A-C. The grey data points represent constructs in which the stem-cement interface was bonded, while the black points represent those in which this interface was sliding, i.e., debonded.
Figure 4.4 Implant migration (top) and micromotion (bottom) for profiles D-I. Simulation results are shown in black and grey, and experimental data are shown as white triangles (after 10 cycles of walking loads) and white squares (after 5000 cycles). Note that there are six migration data points in grey (cement-endosteum bonded) and six in black (cement-endosteum sliding) for each profile. These six points form two clusters: the top cluster represents constructs with a sliding stem-cement interface while the bottom one represents those with a bonded stem-cement interface. Each cluster contains three overlapping points, representing the three graft densities (low, moderate and high).
Table 4.2 Contribution of each material and interface to the distal implant motion relative to the bone. Micromotion (migration).

<table>
<thead>
<tr>
<th>Profile</th>
<th>Interfaces</th>
<th>( \delta_{\text{stem-cement ((\mu)m)}} )</th>
<th>( \delta_{\text{endosteum ((\mu)m)}} )</th>
<th>( \delta_{\text{mantle ((\mu)m)}} )</th>
<th>( \delta_{\text{graft/composite ((\mu)m)}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0-6 (0-130)</td>
<td>7-8 (1421-2982)</td>
<td>2 (2)</td>
<td>141-273 (127-262)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>0-6 (0-123)</td>
<td>4-5 (996-1994)</td>
<td>2 (2)</td>
<td>87-168 (82-159)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0-6 (0-120)</td>
<td>8-9 (537-1096)</td>
<td>2 (2)</td>
<td>38-74 (42-82)</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>0-3 (0-124)</td>
<td>5-26 (32-221)</td>
<td>0-1 (0-1)</td>
<td>3-29 (3-24)</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>0-3 (0-119)</td>
<td>6-16 (17-121)</td>
<td>0-1 (0-1)</td>
<td>2-19 (2-16)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>0-3 (0-116)</td>
<td>6-11 (12-83)</td>
<td>0-1 (0-1)</td>
<td>2-14 (2-12)</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>0-3 (0-115)</td>
<td>5-8 (8-56)</td>
<td>0-1 (0-1)</td>
<td>1-10 (1-10)</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>0-4 (0-117)</td>
<td>4-6 (5-48)</td>
<td>0-1 (0-1)</td>
<td>1-7 (1-8)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0-5 (0-114)</td>
<td>0-6 (0-35)</td>
<td>1-2 (0-1)</td>
<td>2-3 (2-3)</td>
<td></td>
</tr>
</tbody>
</table>

4.4 Discussion

A wide range of stem migration has been reported in impaction allografting patients, and the reason for this variability has not yet been determined. In this study, a finite element model was used to estimate the effects of cement penetration profile and graft density on implant motion after impaction allografting, and to identify key mechanisms responsible for early implant migration.

While graft density and the status of the stem-cement interface (bonded vs. sliding) had little effect on shear stresses at the endosteum, the cement penetration profile had a large effect. When there was cement-endosteum contact, very low stresses were observed in the graft regions and at the graft-endosteum interface, and virtually all load transfer to the femur occurred in the cement contact region (Figure 4.2, bottom). This is not surprising due to the higher stiffness of the cement compared to the graft. The average shear stress at the cement-endosteum interface was inversely proportional to the area of cement contact. Shear stresses were also found to peak at the distal and/or proximal edges of the cement-endosteum interface. In this finite element model the transitions between cement and graft contact regions with the endosteum were very sharp, which can have a large effect on local stresses while having a small effect on the overall migration and micromotion. For this reason these local stresses should be interpreted in a qualitative rather than quantitative manner. In all constructs in which there is cement-endosteum contact, the radial compressive stresses in the graft-cement composite were highest in the proximal region. When the cement-endosteum interface was
sliding the shear stress at this interface was proportional to the normal stress (due to friction), thus peaking proximally. When the cement-endosteum interface was bonded, however, shear stress concentrations occurred at both ends of the cement contact region due to a shear lag effect, a phenomenon that is well-known in adhesively bonded joints.

Although bone cement does not bond chemically with bone, the cement-bone interface exhibits some strength through mechanical interlocking (Race et al., 2007). In impaction allografting, the apparent shear strength of the endosteal interface was found to be proportional to the amount of cement contact at that surface (Frei et al., 2005a). In the studied range of cement content, an apparent cement-endosteum shear strength of 0.8 MPa (0.25 to 1.25 MPa), average (range), has been reported (Frei et al., 2005a). Assuming that shear stresses in excess of 0.25 and 0.8 MPa indicate ‘possible’ and ‘likely’ cement-endosteum debonding, respectively, we can conclude that debonding of the cement-endosteum interface would be likely for Profile D (12% cement contact), and possible for profiles E-H (24-61% contact), particularly in the proximal and distal regions. For profile I (80% contact), however, this interface is likely to remain ‘bonded’.

Migration and micromotion were highest in constructs in which the cement penetration front had not reached the endosteum. In these constructs, implant motion increased with decreasing graft density and increasing cement content. When there was cement-endosteum contact, however, implant motion was much lower and decreased with increasing contact. For these profiles, implant motion was not affected by graft density, which is not surprising because the load transfer occurred through the cement while the graft carried little load. Finally, migration was attributed primarily to slippage at the endosteum, and this mechanism was responsible for most of the variability between constructs. Conversely, while shear deformation of the graft contributed to micromotion, shear deformation and failures within the graft had little effect on migration.

A simplified geometry was used to facilitate the generation of multiple cement profiles. The model was axisymmetric and bending and/or torsional loading, which can increase implant motion, were not simulated. The loading was limited to one cycle and the model did not account for long-term processes such as creep and fatigue of the cement, and biological
processes such as graft incorporation or osteolysis, which could affect long term implant fixation. However, because a substantial part of the migration often occurs early after surgery; i.e., weeks to months (Nelissen et al., 2002; Ornstein et al., 2002), we incorporated the mechanisms of shear failure and compression of the graft, and slippage at the interfaces, which could induce early migration. Although the creep behaviour of the graft was not incorporated explicitly, creep was taken into account indirectly by using graft stiffness values equal to the inverse of the creep compliance (one hour under 1.1 MPa of confined compression) that were measured Chapter 3. A sensitivity analysis confirmed that the resulting stress and implant motion trends remained essentially the same when the graft was modeled as having half the graft stiffness (assuming further creep) or using shear failure parameters that were reported in another study (Dunlop et al., 2003). Nonetheless, despite the simplifying assumptions made in the model, there was reasonable agreement between model results and those of in vitro experiments. Migration and micromotion were in the same range as was measured experimentally, and in both cases the motion decreased with increasing cement-endosteum contact. In light of the simplifying assumptions made in this study, however, it should be noted that the trends observed are more important than the actual numerical results.

A sensitivity analysis was also performed to assess how the current findings would be affected by changes in $\nu_{\text{graft}}$ and the endosteum friction coefficient, $\mu_{\text{endosteum}}$. The actual values of these parameters are not known, and these are likely to vary within each construct. In this model, estimates for these parameters were taken from the literature. More specifically, $\nu_{\text{graft}}$ was assumed to be 0.2, a value obtained experimentally for unimpacted morsellized cancellous graft (Brodt et al., 1998). A $\mu_{\text{endosteum}}$ value of 0.61 was assumed, based on a value determined experimentally for a cancellous-cortical bone interface (Zhang et al., 1999). This value, however, was obtained for a smooth and dry surface, whereas the endosteum interface seen in impaction allografting is rougher and wet (with blood, fat and marrow). A sensitivity analysis was done, in which $\nu_{\text{graft}}$ and $\mu_{\text{endosteum}}$ were varied between 0.2-0.4 and 0.61-1.0, respectively. It was found that the migration results were affected by changes in $\nu_{\text{graft}}$ and $\mu_{\text{endosteum}}$, however, the trends observed in this study – i.e., the relative effects of cement content and graft density on migration, the important role played by the endosteum interface, and the small
contribution of shear failures in the graft bed – remained the same regardless of $v_{graft}$ and $\mu_{endosteum}$ (Appendix 4, Figures A4.12 and A4.13).

Previous research studies have been focused primarily on the graft rather than on the cement profile. Earlier findings have raised concerns about the risk of cement mantle fracture due to insufficient mantle thickness (Masterson et al., 1997a), which has prompted the re-design of impaction tools to allow for a wider gap between the stem and the graft bed. Over the last decade, however, very few studies have looked at the cement penetration profile (Frei et al., 2004; Frei et al., 2005a; Albert et al., 2007; Bolland et al., 2008). Clinically, it is difficult to distinguish the cement profile due to the radiographic similarity between the cement and the graft regions (Masterson 1997b; Robinson et al., 2002; Cabanela et al., 2003; Krupp et al., 2006). The use of cortical struts, wire meshes, and other hardware further obscures the radiographic observation of the graft and cement regions (Morgan et al., 2004). Moreover, in autopsy and biopsy studies, the cement was often dissolved during the histological process (Ling et al., 1993; Linder, 2000; Ullmark and Obrant, 2002). Most clinical reports, therefore, do not include cement mantle analysis. With limited research data concerning the cement penetration profile in impaction allografting, surgeons may overlook its relevance.

While the presence of cement at the endosteum can hinder new bone formation in the graft (Frei et al., 2005b), some cement-endosteum contact may be unavoidable during surgery, particularly around the distal half of the stem (Frei et al., 2004; Albert et al., 2007). The depth of cement penetration in the graft bed has been shown to be proportional to both the cement pressure applied and the permeability of the graft bed, the latter of which is inversely proportional to its density (Frei et al., 2006).

In a recent in-vitro study, the use of vibration and drainage holes in the impaction tool was found to improve stem stability in impaction allografting (Bolland et al., 2007), and this improvement was associated with an increase in graft density (Bolland et al., 2008). Contrary to other studies (Frei et al., 2004; Albert et al., 2007), the cement penetration profiles observed by Bolland et al. appeared to have little cement-endosteum contact. These differing morphological observations may be explained by differences in the impaction forces used. In one study (Bolland et al., 2007), the specimens were composite femurs with no cortical
thinning, enabling the use of very high impaction forces, 2.8-4.7 kN, and resulting in a very dense graft bed (65-95% bone). In the other studies, the specimens were human cadaveric femurs with simulated cortical thinning, enabling impaction forces of only 400-1200 N (Frei et al., 2004) and 200-300 N (Albert et al., 2007), and resulting in much lower graft densities (18-60% bone, Albert et al., 2007). The results of the current study concur with Bolland’s observation that implant migration decreased with increasing graft density, but only when there was no cement-endosteum contact. However, since the risk of fracture is greater in the presence of extensive bone loss, it may not be possible to achieve a sufficiently dense graft bed to prevent cement from reaching the endosteum when the bone loss is moderate or severe. A certain amount of cement contact with the endosteum may thus be unavoidable in severely deficient femurs. Nonetheless, the current results indicate that some cement contact (e.g., 12% or more) may be beneficial to stem stability, particularly if post-operative adhesion of the peripheral graft to the endosteum is not achieved early.

In conclusion, the cement penetration profile has a considerable effect on implant motion. Migration and micromotion decrease with increasing cement penetration into the graft bed, and some cement contact with the endosteum is beneficial for stability. Without cement-endosteum contact, implant motion increases with decreasing graft density, but the effect of graft density is negligible in constructs in which the cement profile reaches the endosteum. The results of this study emphasize that the cement penetration profile may have thus far been widely overlooked in studies of femoral impaction allografting. The results of this study also provide valuable insight into the mechanisms responsible for excessive implant migration in some impaction allografting patients. Slippage at the endosteum interface was a major contributor to implant migration and was responsible for most of the variability between constructs – this observation indicates that early adhesion of the peripheral graft to the endosteum may be critical to implant stability. Shear failures in the graft, on the other hand, played little role in implant migration.
4.5 References


CHAPTER 5

GENERAL DISCUSSION AND CONTRIBUTIONS
5.1 Discussion
Failure of femoral implants in THA is often accompanied by problematic bone loss in the proximal femur. Impaction allografting has the potential to restore bone stock in deficient femurs. However, femoral fractures are common with this procedure, as are high levels of implant subsidence which can cause thigh pain and hip dislocation. A number of mechanisms have been proposed to contribute to subsidence, but their relative impact on implant stability is not known. Much research has focused on improving the stiffness and shear strength of the graft, however, it is not known how much effect postoperative graft compression and shear failure have on implant subsidence. Moreover, in a recent in vitro study of impaction allografting, a substantial portion of the graft bed was found to be saturated with bone cement, and some cement was found to have reached the host bone. The consequence of such extensive cement penetration on implant stability has not been determined. This thesis examined the effects of cement profile and graft properties on initial stem stability in revision THA with impaction allografting. Key mechanisms that contribute to early implant subsidence were identified. The results of this study provide valuable information that will help surgeons, scientists, and engineers to develop strategies to minimize the risk of problematic subsidence in femoral impaction allografting.

5.1.1 Cement penetration profile
Limited information is available about the cement morphology within the graft bed in impaction allografting patients. As mentioned earlier, bone cement is not clearly distinguishable from the graft radiographically (Robinson et al., 2002; Krupp et al., 2006), and histological studies often use methods that dissolve the cement (Ling et al., 1993; Linder, 2000; Ullmark and Obrant, 2002). In this study, extensive cement-endosteum contact was seen around the distal half of the stem, and the same was true in a previous cadaveric femur study (Frei et al., 2004). In these two studies, the surgical procedures were performed by three surgeons using two different sets of graft impaction tools: X-change (Howmedica Inc, Rutherford, NJ, USA) and CPT (Zimmer Inc., Warsaw, IN, USA). Cement-endosteum contact was reported in two other in vitro studies (Berzins et al., 1996; Ohashi et al., 2009). While no clinical studies of femoral impaction allografting were found that mention cement-endosteum contact explicitly, published radiographs appear to confirm regions of cement contact with the
host bone in some patients. In personal communications with surgeons from Vancouver General Hospital, Dr. Bassam Masri and Dr. Clive Duncan, the surgeons were asked to describe the cement profiles in a selection of radiographs taken from the clinical literature – both surgeons agreed that cement-endosteum contact appeared to be present in some of the radiographs, usually around the distal half of the stem, but that no cement contact was apparent in others. The surgeons, however, cautioned that the true cement profiles could not be inferred definitively from the radiographs. Nonetheless, although the actual cement profile is essentially impossible to confirm in individual impaction allografting patients, a wide range of cement penetration appears to occur.

5.1.2 Effects of cement profile and graft density on initial implant subsidence

The results of the current study demonstrate that cement penetration profile has a sizeable effect on implant motion. In vitro stem subsidence correlated negatively with the amounts of cement in the construct and cement-endosteum contact (Chapter 2). These results were corroborated by those of the finite element model (Chapter 4), in which simulations without cement-endosteum contact resulted in substantially greater migration than did those with cement contact, and the implant motion decreased with increasing cement contact. Cement contact with host bone has not received much attention in the literature and could explain, at least in part, the variability in early implant subsidence seen between impaction allografting patients.

Achieving a dense graft bed during impaction is believed essential for initial stem stability (Franzen et al., 1995; Knight and Helming, 2000; Pekkarinen et al., 2000; Gore, 2002; Halliday et al., 2003; Morgan et al., 2004; Krupp et al., 2006). In a clinical study, subsidence was reported to correlate negatively with graft density around the stem tip (Gokhale et al., 2005). A relationship between subsidence and graft density was also reported in an in vitro study (Bolland et al., 2007; Bolland et al., 2008b). However, no such relationship was found in other clinical studies (Ornstein, 2002, Nelissen et al., 2002). These seemingly contradictory findings can be explained by the results of the current study, in which the relationship between graft density and subsidence was demonstrated to be dependent upon the cement penetration profile. Without cement-endosteum contact, implant motion decreases with increasing graft
density, however, graft density has little effect on implant motion in the presence of cement-endosteum contact (Chapter 4 and Figure 5.1). The apparent relationship between subsidence and graft density around the stem tip reported in Gokhale’s study indicates that their cohort of patients may have had minimal cement-endosteum contact, or that the appearance of dense graft may have been the result of extensive cement penetration in that region. The relationship between graft density and \textit{in vitro} migration observed by Bolland \textit{et al.} can be explained by an apparent lack of cement-endosteum contact in their specimens. In Bolland’s study, very high impaction forces were used, generating high graft densities that may not be achievable in many patients. Impaction allografting is commonly performed in patients with considerable femoral bone stock deficiencies, for whom the use of such high impaction forces is likely to result in iatrogenic fracture. Furthermore, because the depth of cement penetration in the graft increases with decreasing graft density (Frei \textit{et al.}, 2006), the likelihood of producing regions of cement-endosteum contact is probably very high in patients with moderate and extensive bone stock deficiencies. For this reason, the effect of cement profile on stem stability probably explains why graft density and the extent of bone stock deficiency have not been found to correlate consistently with subsidence (Meding \textit{et al.}, 1997; van Doorn \textit{et al.}, 2002; Nelissen \textit{et al.}, 2002; Ornstein, 2002; Halliday \textit{et al.}, 2003; Ornstein \textit{et al.}, 2004; Gokhale \textit{et al.}, 2005; Hassaballa \textit{et al.}, 2009).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure5_1.png}
\caption{Relationship between distal migration (left) and micromotion (right), and graft density after impaction allografting in cadaveric femurs (Chapter 2). Lines represent linear regressions.}
\end{figure}

In conclusion, the current study demonstrates that the risk of excessive subsidence is highest in constructs with low cement content and low graft density, and that achieving a dense graft bed is helpful for stability, but only when there is no cement-endosteum contact.
5.1.3 Subsidence mechanisms

The clinical literature reveals a wide range of implant subsidence after impaction allografting, and several attempts have been made to identify the clinical factors and the mechanisms that play a role in its development.

There is radiographic evidence that longitudinal cement fracture can cause excessive subsidence (Masterson and Duncan, 1997; Masterson et al., 1997a; Masterson et al., 1997b). Since these studies were published, graft impaction tools have been redesigned to address this problem by ensuring a thicker cement mantle. Nonetheless, high levels of subsidence have continued to occur in some patients (Nelissen et al., 2002; Gokhale et al., 2005; Deakin and Bannister, 2007; Sierra et al., 2008). Therefore, other mechanisms are likely to contribute to subsidence, namely: cement creep/settling of the stem within the cement, graft compression, shear failures within the graft, sliding at the endosteum interface, allograft resorption, and expansion of the femoral canal. The relative impact of each mechanism on stem subsidence is not known.

In most clinical studies, subsidence is measured from plain radiographs (e.g., Gie et al., 1993; Eldridge et al., 1997; Masterson et al., 1997a; Knight and Helming, 2000; Boldt et al., 2001; Gore, 2002; Halliday et al., 2003; Gokhale et al., 2005; Deakin and Bannister, 2007; Sierra et al., 2008; Hassaballa et al., 2009). With this method, subsidence less than 4 mm cannot be measured reliably (Brand et al., 1986), and the subsidence reported in impaction allografting patients is usually less than that. It is therefore no surprise that no clinical factors have yet been identified that correlate consistently with subsidence. A more accurate measurement of implant motion is obtained with roentgen stereophotogrammetric analysis (RSA). In RSA, two radiographs are taken simultaneously from different angles, allowing the calculation of the three-dimensional stem displacement relative to the femur by using implanted metal beads as reference points. The estimated error when measuring distal migration using RSA is 0.2-0.3 mm (Karrholm et al., 1999). However, as most centres do not have the necessary equipment, few RSA studies on impaction allografting patients have been published (Karrholm et al., 1999; Ornstein et al., 2000; van Doorn et al., 2002; Nelissen et al., 2002; Ornstein et al., 2003; Ornstein et al., 2004). Nonetheless, from these studies we have learned that a large part of the implant migration often develops early after surgery. For example, 0.4-2 mm can occur within
the first week, i.e., approximately half of that seen in the same patients at six months (Ornstein et al., 2000). We have also learned that unstable implants are often distinguishable from stable ones within the first three months (Nelissen et al., 2002; Ornstein et al., 2004). These reports therefore highlight the relevance of initial implant subsidence – and the mechanisms that affect it – on long-term stability.

Some settling of the stem within the cement is expected when using smooth-tapered stems in impaction allografting (Gie et al., 1993). The observation of high levels of subsidence in some patients (e.g., Eldridge et al., 1997; Meding et al., 1997), however, has led some surgeons to substitute the popular smooth-tapered stem designs with rough-collared ones (Leopold et al., 1999; Karrholm et al., 1999; Fetzer et al., 2001; de Roeck and Drabu, 2001; Boldt et al., 2001; Ullmark and Obrant, 2002; Ullmark et al., 2002; Piccaluga et al., 2002; van Kleunen et al., 2003; Sorensen et al., 2003; Krupp et al., 2006; Van Kleunen et al., 2006; Nich and Sedel, 2006; Ullmark et al., 2007). Migration reported with rough-collared stems has ranged between 0 and 8 mm (e.g., Boldt et al., 2001; Nich and Sedel, 2006), compared with 0 to 80 mm for smooth-tapered stems (e.g., Sierra et al., 2008). It is not clear whether rough stems are truly superior to smooth ones, because although very high subsidence can occur with smooth stems, the same stems are stable with less than 2 mm subsidence in many patients (Nelissen et al., 2002). These studies, however, support the assumption that settling of the stem within the cement accounts for some but not all of the subsidence observed clinically after impaction allografting. In our finite element simulations (Chapter 4), regardless of cement profile or graft density, sliding at the stem/cement interface accounted for roughly 100 µm (104 to 124 µm) of the implant migration when this interface was debonded (Appendix 4). This contribution represented 30-96% of total migration for profiles D-H, but only 4-17% of the large migration seen in profiles A-C. This mechanism therefore did not explain the wide range of migration observed. Finally, while our model did not incorporate cement creep, it was demonstrated in a previous finite element study that subsidence of polished stems due to creep in primary hip arthroplasty did not exceed 50 µm (Verdonschot and Huiskes, 1997). Therefore, creep of the cement does not appear to be a major contributor to stem subsidence in impaction allografting.

Slippage between graft particles due to shear stresses, i.e., the formation of shear failure planes in the graft bed, has also been speculated to contribute to subsidence (Ornstein et al., 2001;
Halliday et al., 2003; Ornstein et al., 2004; Bolland et al., 2007; Bolland et al., 2008b). The results of the current study, however, do not point to this mechanism as a major contributor. Instead, our results emphasize the importance of the endosteum interface in the development of subsidence. *In vitro* migration correlated negatively with the amount of cement at the endosteum (Table 2.5). In our finite element simulations, slippage at the endosteum accounted for a substantial portion of the implant migration, and this slippage decreased with increasing cement contact (Appendix 4). Without cement-endosteum contact, migration was almost entirely attributed to slippage at the endosteum interface, and this slippage decreased with increasing graft density (Figures A4.3 to A4.5). Hence, not only was the contribution of slippage at the endosteum substantial, it also accounted for a large portion of the migration variability between simulations. Slippage at the endosteum is accompanied by some radial and longitudinal compression of the graft bed due to the tapered and confined geometry of the intramedullary canal. Our model simulated creep deformation of the graft indirectly by using stiffness values equal to the inverse of the creep compliance obtained after one hour of loading. We can presume that any additional creep occurring postoperatively in the graft would further contribute to the amount of slippage at the endosteum interface. The portion of the implant migration that was attributed to shear deformation and slippage within the graft bed, on the other hand, was much smaller. In summary, for all graft densities and cement penetration profiles, migration was attributed primarily to slippage at the stem-cement and the endosteal interfaces (Figure 5.2), and the latter was responsible for most of the variability between constructs.
The small effect of shear failure within the graft upon subsidence is further confirmed when comparing the motion obtained by including, versus without including, graft shear failure in our finite element model. An additional simulation was performed that replicated one of the simulations from Chapter 4, but this time without defining a graft shear failure criterion. The resulting micromotion was unaffected by shear failures while the migration was only 6% lower than that obtained when the shear failure criterion was modeled (Figure 5.3). Shear failure in the graft bed, therefore, does not appear to be an important contributor to early subsidence.
Finally, we can use the knowledge gained in Chapter 4 to speculate about mechanisms that took place during implant migration in each cadaveric specimens in Chapter 2 (Figure 2.5). In Chapter 4, micromotion was found to result from shear deformation of the graft and cement regions and slippage at the endosteum, while large migrations were attributed primarily to
slippage at the endosteum. Three of the four specimens with the highest migration in Chapter 2 experienced decreasing micromotion as the implant migrated. In these three specimens, the migration and micromotion trends are consistent with the assumption that the large migration was attributed to slippage at the endosteum, which caused a stiffening of the graft as it became increasingly compressed. In the eight specimens with the lowest migration, however, the micromotion was stable – it did not increase or decrease during the simulated walking load cycles. In these specimens, the migration due to endosteal slippage appears to have been too small to have a pronounced effect on graft density or stiffness. Finally, only one specimen did not fit the abovementioned trends. In the specimen with the third highest migration (264 µm), micromotion actually increased during migration (from 31 to 42 µm), indicating that the graft did not become denser. Migration in this specimen may therefore have been attributed to mechanisms such as a gradual debonding of the stem cement interface and/or slippage between the distal plug and the femur rather than endosteal slippage.

In summary, the results of the current study indicate that early implant stability relies largely on the endosteum. Excessive implant migration may be avoided if early post-operative adhesion of the graft onto the endosteum surface is achieved. There is clinical evidence that early graft adhesion to the endosteum is possible after impaction allografting (Ullmark and Obrant, 2002; Leopold et al., 1999); however, this does not occur consistently (Ullmark et al., 2002; personal communications with Dr. Clive Duncan). Without graft adhesion to the endosteum, the presence of cement-endosteum contact may be necessary to prevent excessive migration, nonetheless compromising the potential for new bone formation. Our results further indicate that high levels of cement penetration into the graft may be unavoidable in some impaction allografting patients. A lesser extent of cement penetration may be obtained if a very dense graft bed is achieved, however, this may only be possible in less defective (i.e., stronger) femurs. In moderately or severely defective femurs, the higher risk of fracture may preclude the use of high impaction forces, and extensive cement penetration may be unavoidable in some regions. Thus, patients with less defective femurs may have a better potential for new bone formation than those with severe bone loss. Finally, the development of methods to ensure early graft adhesion to the endosteum would be useful in minimizing the risk of excessive migration.
5.1.4 Postoperative biological changes

The process of graft incorporation is difficult to evaluate clinically. There is no widely accepted guideline on how to infer graft incorporation from radiographs in femoral impaction allografting. Interpretation of the radiographic appearance of the graft bed is imprecise due to the difficulty in distinguishing the graft from the cement (Duncan et al., 1998; Mikhail et al., 1999; Lind et al., 2002). Furthermore, the presence of external hardware such as reinforcement wires, meshes, plates, or dense cortical graft struts that are often required to prevent or repair fractures only further obscures the appearance of the graft (Elting et al., 1995; van Biezen et al., 2000; Ullmark et al., 2002; Schreurs et al., 2005). Many clinical studies, for that matter, simply do not comment on the appearance of the graft bed (Eldridge et al., 1997; Masterson et al., 1997b; Pekkarinen et al., 2000; Knight and Helming, 2000; Ornstein et al., 2001; Fetzer et al., 2001; Ornstein et al., 2002; Gore, 2002; Atroshi et al., 2004; Ornstein et al., 2004; Mahoney et al., 2005; Sierra et al., 2008). Nonetheless, radiographic evidence of cortical repair and/or cancellous remodeling has been reported in some patients (Franzen et al., 1995; Elting et al., 1995; Flugsrud et al., 2000; Boldt et al., 2001; Deakin and Bannister, 2007), and changes that are consistent with graft incorporation, i.e., changes in radiopacity, have been noted in others (Meding et al., 1997; Leopold et al., 1999; Lind et al., 2002).

Histological studies have indeed revealed incorporation, at least in part, of the dead graft (Ling et al., 1993; Nelissen et al., 1995; Ullmark and Linder, 1998; Mikhail et al., 1999; Linder, 2000; Weidenhielm et al., 2001; Ullmark and Obrant, 2002). Early autopsy and biopsy case reports described three zones in the graft bed: an outer zone consisting of viable cortical bone, presumably regenerated from peripheral graft; a middle zone consisting of viable trabecular bone and cement; and an inner zone consisting of partly necrotic graft and cement, with occasional regions of fibrous tissue and viable bone (Ling et al., 1993; Nelissen et al., 1995; Mikhail et al., 1999). A larger study with 14 autopsy and biopsy specimens was later published that revealed that graft incorporation is highly variable (Linder, 2000). While one patient showed complete bony reconstitution, variable amounts of dead graft remained in the others even after eight years. Cortical healing, trabecular incorporation, and/or trabecular remodeling were observed only in some femurs. The author commented that the graft appeared to have been first invaded by fibrovascular tissue from the periphery, eventually embedding the graft particles, but that the vascular front did not always reach the cement surface, sometimes
leaving many millimeters of avascular dead graft adjacent to the cement. In another biopsy study, fibrous tissue invasion was observed as early as one month post-surgery, and many graft particles had layers of living bone at four months (Ullmark and Obrant, 2002). Finally, graft incorporation in the distal region was reported to be more extensive than in the proximal region in three autopsies performed after six months to three years (Ullmark and Linder, 1998; Weidenhielm et al., 2001; Ullmark and Obrant, 2002).

The appearance of the graft was also described during a few re-revision surgeries. During one re-revision performed three weeks after impaction allografting due to a fracture, the inner surface of the femur was said to have changed from “smooth” to having a “pronounced rough appearance, resulting from firmly attached small graft pieces” (Ullmark and Obrant, 2002). In three other re-revisions at three to six years, the graft was described as “bleeding and healed to the cortex” (Leopold et al., 1999), and as “soundly incorporated” (Deakin and Bannister, 2007). Nonetheless, this is certainly not always true. In one re-revision at five years, the graft was described as partly necrotic without ingrowth of fibrous tissue or bone in most areas (Ullmark et al., 2002). Moreover, in the few femoral impaction allografting patients who have been re-revised at Vancouver General Hospital, the graft bed was not found to have incorporated; it essentially disintegrated during the re-revision procedure (personal communication with Dr. Clive Duncan).

Some recent studies have used nuclear imaging methods to monitor blood flow and bone turnover after impaction allografting (Boldt et al., 2001; Sorensen et al., 2003; van Kleunen et al., 2003; Hisatome et al., 2004; Van Kleunen et al., 2006; Ullmark et al., 2007; Temmerman et al., 2008). These methods involve the injection of a radioactive blood tracer from which the emitted gamma rays are captured by cameras. Increases in blood flow and tracer uptake, indicating revascularization and graft incorporation, were observed in and around graft regions (Boldt et al., 2001; Sorensen et al., 2003; van Kleunen et al., 2003; Hisatome et al., 2004; Van Kleunen et al., 2006; Ullmark et al., 2007; Temmerman et al., 2008). In areas adjacent to the graft, the increase in blood flow and tracer uptake was seen within two weeks after surgery, indicating a swift onset of neovascularization and osteoblastic activity (Sorensen et al., 2003; Temmerman et al., 2008). The uptake was noted to decrease significantly within a year (Hisatome et al., 2004), however, at four to six years it remained elevated in the trochanters.
(Hisatome et al., 2004) and around the stem tip (Hisatome et al., 2004; Ullmark et al., 2007), indicating that remodeling was probably still incomplete in those regions.

In short, without invasive biopsies, clinical evaluation of the graft is difficult, and therefore the actual status of the graft incorporation remains unknown in most impaction allografting patients. However, these studies demonstrate collectively that graft incorporation is variable, usually incomplete, and often limited to the distal region and the periphery. Nonetheless, it is apparent that some peripheral graft incorporation can take place as early as within a few weeks.

The effect of the graft incorporation process on implant migration is not clear. Structural cortical grafts have been shown to lose strength during the early stages of their incorporation due to resorption-induced porosity (Enneking et al., 1975). Their density and strength eventually return to normal as new bone gradually forms. Cancellous structural grafts see a reverse effect gaining density as new bone apposes onto trabeculae, without experiencing initial resorption (Abbott et al., 1947; Burchardt, 1983). For morsellized cancellous graft, however, it is not known how the mechanical properties evolve during incorporation. Nonetheless, the biological changes occurring in the graft after surgery could be the cause of some implant subsidence. In an in vivo experiment in goats, cancellous graft particles implanted in a defect in the distal femur were subjected to loading through a piston, which was reported to have moved by 2 mm at two weeks in two out of four goats (Lamerigts et al., 2000). The same experiment was repeated in three femurs ex vivo, but no piston displacement was reported after 198,000 cycles of loading. Thus, biological changes in the graft may be significant enough to cause some implant subsidence. Furthermore, in addition to the changes occurring within the graft bed, the host bone can also experience changes postoperatively. Cancellization of the cortex has been observed following the implantation of graft particles and cement against the inner cortical surface of rat tibiae (Frei et al., 2005). It was suggested that the formation of pores in the cortex may be the result of impaired vascular circulation, and that some subsidence of the stem and cement/graft conglomerate relative to the host bone after impaction allografting may be caused by a widening of the femoral canal due to resorption of the host bone.
Although our in vitro and numerical studies did not model biological processes that take place in the graft post-surgery, our results indicate that postoperative bonding of the peripheral graft to the endosteum may be a critical factor to implant stability. As discussed earlier, in our finite element results, substantial migration occurred at the graft-endosteum interface. From the results presented in Appendix 4, we can estimate that if peripheral graft bonding to the endosteum is successful and prompt after surgery, the migration may be reduced by over 75% if there is no cement-endosteum contact. It has been demonstrated that fibrous invasion of the graft increases the unconfined compression strength of morsellized cancellous graft (Tagil and Aspenberg, 2001), as well as the shear strength of the graft/host-bone interface (Frei et al., 2005). From a mechanical viewpoint, this fibrous invasion may provide sufficient anchoring of the peripheral graft to prevent excessive subsidence. Nonetheless, unless the fibrous tissue is eventually replaced with new bone, it would likely be removed during any future re-revision.

Finally, the effects of cement profile and graft density on graft incorporation remain unknown. In a bone chamber model in the rat, impacted graft particles were found to yield less bone ingrowth than unimpacted ones (Tagil and Aspenberg, 1998); however, the effect of graft density on incorporation has not been confirmed in the impaction allografting graft bed. And although the presence of cement at the endosteal surface presents a mechanical advantage, it does not allow restoration of the host bone stock in those regions. Furthermore, it is not clear how the presence of cement-endosteum contact affects incorporation of the surrounding graft regions. The resulting reduction in micromotion may provide a more favourable environment for bone ingrowth in the graft regions; however, it is not clear how the resulting reduced loading in graft regions would affect the incorporation process. While loading of the graft appeared to promote its incorporation in a study in the rabbit tibia (Wang et al., 2000), no difference in density was seen between loaded and non-loaded grafts in the sheep (van der Donk et al., 2002).

5.1.5 Relevance of current work with respect to other in vitro studies
The results of the current study, which emphasize the role of the endosteum and the effect of the cement penetration profile on initial stem stability in impaction allografting, are valuable to future research studies. Factors such as fat or moisture content and graft irradiation have been shown to affect the stiffness and shear strength of cancellous graft particles (Voor et al., 2000;
Dunlop et al., 2003; Voor et al., 2004; Cornu et al., 2004; Butler et al., 2005). Based on the results of our structural tests (Chapter 2) and our finite element model (Chapter 4), however, changes in graft stiffness would only affect initial subsidence in the absence of cement-endosteum contact. Other in vitro studies have explored how initial stability would be affected if the graft particles were processed differently or replaced with other materials. It was reported that freeze-drying the graft (Cornu et al., 2003), replacing it with cortical particles (Kligman et al., 2003), and using calcium phosphate particles as graft extenders (Grimm et al., 2001; Blom et al., 2002; van Haaren et al., 2005; Fujishiro et al., 2005) or as graft substitutes (Munro et al., 2006) reduced in vitro subsidence. It was also reported that fusion of the proximal graft region produced a greater reduction in subsidence than did fusion of the distal graft, indicating that emphasis should be placed upon the proximal graft region during surgery (Heiner et al., 2008).

None of these studies, however, have factored in the cement penetration profile, which may have differed between the groups studied. For example, in the study examining the effect of graft fusion (Heiner et al., 2008), the fusion was simulated using epoxy, which may have hindered cement penetration compared to the clinical scenario. Therefore, in order to eliminate the possibility that a difference in cement content may be responsible for the observed effects, cement profiles must be examined. Other than the current study, only one in vitro study has considered the cement penetration profile. In that study, the use of vibration and drainage during graft compaction improved in vitro stability compared with traditional graft impaction (Bolland et al., 2007), and further investigation with microcomputed tomography revealed that the reduction in migration was attributed to differences in graft density rather than cement content (Bolland et al., 2008b).

### 5.1.6 Trends in impaction allografting research

In addition to problems of fracture and excessive subsidence, the risk of disease transfer is a significant concern with the use of allografts. Transplantation of bone tissue involves the risk of transmitting viruses such as human immunodeficiency virus (HIV), and hepatitis B and C (Yao et al., 2007), as well as various bacterial contaminants. In one study, as many as 22% of femoral heads donated to an Australian bone bank were found to be contaminated (Sommerville et al., 2000). The most common contaminants found in bone grafts are in the Staphylococcus family (Sommerville et al., 2000; James et al., 2004; van de Pol et al., 2007), which could lead to deep infection in the recipient (van de Pol et al., 2007).
In order to address the problems of disease transmission and graft availability, various synthetic materials have been studied in mechanical and/or biological environments representative of impaction allografting. These materials include bioglass (Fujishiro et al., 1997; Brewster et al., 1999) and calcium phosphate ceramics such as hydroxyapatite (Fujishiro et al., 1997; Voor et al., 2004; van Haaren et al., 2005; Fujishiro et al., 2005; Coathup et al., 2008) or hydroxyapatite combined with tricalcium phosphate (Grimm et al., 2001; Blom et al., 2002; Voor et al., 2004; Blom et al., 2005; Hannink et al., 2006; Arts et al., 2006a; Arts et al., 2006b; Hannink et al., 2007).

Calcium phosphate ceramic particles have shown promising results in in vivo studies. Fibrous ingrowth and new bone formation were seen in and around ceramic particles, whether these were used alone or as an extender to cancellous graft particles in bone chamber models (Arts et al., 2006b; Hannink et al., 2007). In one study, calcium phosphate granules smaller than 150 µm appeared to have resorbed within eight weeks in a rabbit model (Arts et al., 2006b). In a femoral impaction allografting model in sheep, the use of ceramic graft extender in one group yielded comparable postoperative outcomes (ground reaction forces, bone density and subsidence) to those of another group of sheep in which cancellous graft alone was used (Blom et al., 2005). In a similar sheep study, some new bone formation was observed whether 90% or 50% hydroxyapatite was added to the graft (Coathup et al., 2008).

From a mechanical viewpoint, adding small particles of bioglass to morsellized cancellous graft can increase its resistance to shear forces (Brewster et al., 1999). The use of calcium phosphate particles as a graft substitute or extender in impaction allografting reduced in vitro stem subsidence (Grimm et al., 2001; Blom et al., 2002; van Haaren et al., 2005; Fujishiro et al., 2005). Nonetheless, calcium phosphate particles are much stiffer than graft (Verdonschot et al., 2001; Voor et al., 2004), and the use of hard synthetic particles in impaction allografting can increase the risk of femoral fracture during impaction (van Haaren et al., 2005).

Three recent clinical studies have reported the use of calcium phosphate particles in femoral impaction allografting (Nich and Sedel, 2006; Fujishiro et al., 2008; Aulakh et al., 2009). The results have been encouraging. In all three studies, the hip score – which denotes pain and
function – improved in most patients. In one study, in which calcium phosphate particles were used as either extenders or substitutes, radiological evidence of cortical repair was noted in most patients (Nich and Sedel, 2006). In another study, when hydroxyapatite was added to the graft, the 13 year survival rate and function were reported to be comparable to that of patients in which graft alone was used (Aulakh et al., 2009). Nonetheless, the appearance of the graft and ceramic particles as noted during subsequent re-revisions varied. During re-revision surgeries, the synthetic particles were found to be partly integrated in two patients at 20 and 33 months (Nich and Sedel, 2006; Fujishiro et al., 2008), but mostly unincorporated in another patient revised 16 months (Fujishiro et al., 2008).

Over the last few years, a number of research studies have been aimed at enhancing the incorporation of cancellous graft particles through additives such as bone morphogenetic protein, bisphosphonate, and stem cells. The use of bone morphogenetic protein BMP-7 was found to increase the distance of bone ingrowth into the graft particles in a bone chamber model in the rat (Tagil et al., 2000). In later studies, however, BMP-7 did not enhance new bone formation in rabbit and goat models (Tagil et al., 2003; Hannink et al., 2006; Buma et al., 2008), and it was found to increase resorption during the early stages of graft incorporation in a sheep model (McGee et al., 2004). Finally, the use of BMP-7 did not appear to affect implant migration in a clinical study (Karrholm et al., 2007).

Bisphosphonate, a compound known to inactivate osteoclasts (bone-resorbing cells) has also been investigated as a graft additive (Jeppsson et al., 2003). However, while it was found to increase graft density, the use of bisphosphonate resulted in a shorter bone ingrowth distance than the use of BMP-7 alone. It was concluded that although the problems associated with the use of BMP-7 in impaction allografting may be solved by adding bisphosphonate, some of the benefits of BMP-7 would also be lost.

Bone marrow stromal cells (BMSCs) have also generated recent research interest in impaction allografting (Tilley et al., 2006; Bolland et al., 2006; Korda et al., 2008; Bolland et al., 2008a; Green et al., 2009). Similar to mesenchymal stem cells, BMSCs have the potential to differentiate into many types of specialized cells including osteoblasts (bone-laying cells), but they are harvested from bone marrow rather than embryos. BMSCs have been shown to
survive impaction (Bolland et al., 2006), and adding them to morsellized graft yielded greater new bone formation around a cementless stem in a sheep model than did the use of graft alone (Korda et al., 2008). In a study investigating the use of poly-lactic acid as a graft substitute, adding BMSCs increased vascularization and new bone formation in a subcutaneous model in mice (Bolland et al., 2008a). Their potential benefit in enhancing bone formation is further supported by a recent clinical study in which BMSCs were used successfully in two patients in conjunction with cancellous graft particles to repair femoral bone defects (Tilley et al., 2006). In those patients, postoperative radiographs revealed that the lesions were replaced by bone having a higher density than the surrounding bone. Finally, the use of bone marrow (without extracting the stromal cells) as a graft additive has also been investigated in a group of patients undergoing femoral and/or acetabular impaction allografting (Deakin and Bannister, 2007). The results were encouraging, with radiological signs of incorporation observed in most patients. Bone marrow and bone marrow stromal cells could therefore prove useful in enhancing graft incorporation in impaction allografting.

In conclusion, impaction allografting offers a unique potential to reverse problematic bone loss in hip arthroplasty. The success of this procedure, however, relies upon achieving adequate initial implant stability and graft incorporation. While its clinical results have varied in terms of both stability and graft incorporation, recent research aimed at finding solutions to these problems has generated valuable information. Mechanical studies such as those presented in this thesis provide orthopaedic surgeons and researchers with a growing understanding of the mechanisms that cause problematic implant subsidence, while biological studies are exploring promising strategies aimed at enhancing new bone formation. Moreover, the growing popularity of stem cells in medical research, as well as the recent lifting of a ban on embryonic stem cell studies in the United States, could lead to new methods for improving graft incorporation. Continuing research aimed at minimizing the risks of subsidence and incomplete graft remodeling is critical to improving the effectiveness of impaction allografting as a revision hip arthroplasty procedure.
5.2 Contributions

1. The relationship between initial implant subsidence and the cement penetration profile after femoral impaction allografting had not been determined previously. Constructs in which cement reached the endosteum were found to subside less than those with no cement-endosteum contact.

2. It has thus far been widely assumed that a dense graft bed is critical in ensuring initial stability. This study has demonstrated that this assumption is only true if the cement profile has not reached the host bone interface – thus, the cement profile was shown to play a dominant role over that of graft density on implant stability. This finding emphasizes the importance of taking the cement profile into consideration in any study aiming to optimize the properties of the graft bed in impaction allografting.

3. This study developed constitutive equations that describe how the morsellized cancellous graft material behaviour in compression and shear are affected by the graft bed density achieved during impaction. No other study had described this relationship. These constitutive equations can be useful in future finite element simulations or mathematical models aiming to study the structural behaviour of femoral impaction allografting constructs and other surgical applications where morsellized cancellous graft is used.

4. This thesis identified slippage at the endosteal interface as a major contributor to subsidence and to variability in subsidence between constructs. This information will be valuable in developing strategies to minimize the risk of excessive implant subsidence in impaction allografting.
5.3 Conclusions

1. In femurs with moderate or severe bone loss, impaction allografting with cement yielded extensive cement contact with the host bone, particularly around the distal half of the stem.

2. The cement penetration profile had a large effect on initial stem stability after femoral impaction allografting – micromotion and migration were correlated negatively with the amount of cement in the construct and with the amount of cement-endosteum contact.

3. Graft density, compression stiffness and shear strength were proportional to the impaction force used.

4. A slower graft compaction method that allowed more time for the fluid to exudate out of the graft bed resulted in increased graft density, stiffness, and shear strength, but these increases were small relative to the effect of increasing the impaction force.

5. The relationship between graft density and initial implant subsidence was dependent on the cement profile: in the absence of cement-endosteum contact, subsidence decreased with increasing graft density; however, density did not affect implant subsidence in the presence of cement-endosteum contact.

6. Initial subsidence was primarily attributed to slippage at the endosteum and stem-cement interfaces, and most of the variability in subsidence between constructs of varying cement penetration profiles and graft densities was the result of slippage at the endosteum.

7. Some cement contact with the endosteum (e.g., 10% or more) is advisable to reduce the risk of excessive implant subsidence.
5.4 Future Work

- The relationship between the degree of bone deficiency, the magnitude of impaction force that can be achieved without causing fracture, and the resulting graft density and cement penetration profile should be investigated in cadaveric femurs.

- Future autopsy and biopsy studies describing the cement penetration profile in impaction allografting patients would be useful. The histological method described in this thesis would be helpful in preserving the cement in the processing of histological slides.

- The relationship between graft incorporation and cement profile should be explored. The potential for new bone formation is compromised in regions where cement is present; however, the increased stability provided by the presence of cement-endosteum contact may be favourable in promoting new bone formation in the surrounding pure graft regions.

- The development of a non-invasive method that would enable surgeons to distinguish the cement penetration profile from the morsellized graft in impaction allografting patients would be valuable.

- Methods aiming at enhancing graft incorporation at the host-bone interface should be explored. For example, coating the endosteum with marrow stromal cells or stem cells prior to graft impaction may improve peripheral graft incorporation and reduce implant subsidence.

- The development of a method that would enable surgeons to control the cement penetration profile such that cement-endosteum contact occurs in regions that are not targeted for bone stock reconstitution could be helpful.

- Future research aimed at enhancing the mechanical characteristics of the graft region in order to improve implant stability should also consider the cement penetration profile, as the effects of these factors on implant stability are interdependent.
5.5 References


Knight, J.L. and Helming, C. (2000) Collarless polished tapered impaction grafting of the femur during revision total hip arthroplasty: pitfalls of the surgical technique and follow-up in


Tilley, S., Bolland, B.J., Partridge, K., New, A.M., Latham, J.M., Dunlop, D.G., and Oreffo,


APPENDIX 1

MECHANICAL TESTING SET-UPS
A1.1 Simulation of hip joint loading
Prior to structural testing of the implanted cadaveric femurs (Chapter 2), each specimen was potted distally at 13° of adduction and 0° of flexion (Figure A1.1). The implant was used as a reference for alignment rather than the femurs themselves to eliminate inter-specimen variability due to differences in femoral shaft curvature. The reference axis of the implant was defined by a 2.5 inch bold fastened into a thread hole on the proximal surface of the implant. Specimen alignment was achieved using two laser levels projecting the desired specimen angles in the sagittal plane and frontal plane.

Figure A1.1 Specimen potting schematics. Specimen alignment was achieved using two laser levels projecting the desired angles, shown as bold black lines, in the sagittal plane (vertical) and frontal plane (θ=13°). (Right) Custom-built pot, mounted onto a linear guide.

The application of the hip joint contact loads on the cadaveric femur specimens was done with a biaxial servohydraulic testing machine (Figure 2.1). A linear actuator force, F, of -955.5 ± 735.0 N, and a rotary actuator moment, M, of -5.88 ± 8.32 Nm (Figure A1.2) generated the desired craniocaudal and anteroposterior forces, which were described in Chapter 2. The
direction of the rotary moment was adjusted between left and right specimens, such that the largest peak anteroposterior force was consistently in the posterior direction.

![Graph showing actuator force and moment for one cycle of simulated walking loads.](image)

**Figure A1.2** Actuator force and moment for one cycle of simulated walking loads. Black line: Actuator force, in compression. Grey lines: Actuator moment for right specimens (solid) and left specimens (dashed).

An attempt was made to also simulate stair climbing loads, with the same hip contact load as walking in the frontal plane but with a higher anteroposterior load of 0.6 times body-weight. However, the higher torsional loading caused fracture of the first two specimens tested (Figure A1.3). The fractures were initiated between the tip of the implant and the potting level, indicating excessive stress concentration in this region. For this reason, the remaining specimens were not subjected to stair climbing loads.
A1.2 Measurement of implant motion

A motion measurement system was custom-designed for this study to measure the implant motion relative to the bone. The system consisted of a *stem reference triangle*, which was rigidly attached to the stem, and a *femur reference frame*, through which six linear variable differential transformers (GCD-121-250, Shaevitz Sensors, Hampton, Virginia) were rigidly attached to the femur (Figure A1.4).
Figure A1.4 Custom-built motion measurement system components.

The stem reference triangle was attached to a pin, which was fitted into a 5 mm square hole that was machined 5 cm below the implant shoulder on the lateral side by electrical discharge (Figure A1.5). After the stem was implanted in the femur, an 8 mm diameter hole was drilled through the femur, guided by a custom-built steel hole-finder, to expose the hole in the implant (Figure A1.5, left). Prior to the surgical procedures, the hole in the implant was sealed with a small piece of cellophane tape to prevent bone cement from filling the hole during the surgical procedure. After drilling of the femur, the square hole was cleaned with acetone and a 5 mm square pin was glued into it with cyanoacrylate (Figure A1.5, right). The pin was allowed to set in place for at least two hours. The stem reference triangle was then attached to the pin with a set screw and the distance between the triangle’s reference coordinate system (Figure A1.8) and the implant surface, $d_{\text{triangle}}$, was measured. The junction between the triangle and the pin was strengthened with a drop of polymethyl methacrylate (Lecoset, LECO Corp, St Joseph Michigan).
To ensure a consistent positioning of femur reference frame relative to the stem reference triangle, the frame was temporarily bolted onto to the triangle through a spacer (Figure A1.4). The femur reference frame was mounted onto the femur as described in Chapter 2, after which the frame was detached from the stem reference triangle and the spacer was removed. At this point, the frame remained attached rigidly to the femur and the triangle to the stem. The potted specimen was mounted on a linear guide and transferred to the servohydraulic testing machine (Figure A1.6). The sensors were attached to the frame in their respective locations and their positions were adjusted to give initial readings of 0 V, such that their output remained well within their calibrated range, i.e., +/- 1.7 V (Figure A1.7), during testing. To verify that the motion measurement assembly components were rigidly fixed to the stem and femur, the reference frame and triangle were tapped gently, ensuring that the sensor readings returned to zero.
The motion of the stem relative to the femur was obtained from the sensor voltages using equations A1.1 to A1.5. First, the LVDT voltages \((V_1, V_2, V_3, V_4, V_5, V_6)\) were converted into sensor displacements \((w_1, v_2, w_3, u_4, w_5, v_6)\):

\[
\begin{bmatrix}
w_1 \\
v_2 \\
w_3 \\
u_4 \\
w_5 \\
v_6
\end{bmatrix} = \begin{bmatrix}
C_1 & C_2 & C_3 & C_4 & C_5 & C_6
\end{bmatrix} \begin{bmatrix}
V_1 \\
V_2 \\
V_3 \\
V_4 \\
V_5 \\
V_6
\end{bmatrix}
\]

Equation A1.1

where \(C_i\) were the LVDT calibration coefficients obtained experimentally by calibrating each sensor with a dial gauge micrometer, i.e., the slopes of the micrometer displacement vs. LVDT voltage curves: \(C_1 = 642.7561 \ \mu m/V, \ C_2 = 648.8754 \ \mu m/V, \ C_3 = 653.5494 \ \mu m/V, \ C_4 = 648.1879 \ \mu m/V, \ C_5 = 640.1567 \ \mu m/V, \ C_6 = 646.5890 \ \mu m/V\) (Figure A1.7).
Figure A1.7 Calibration of each motion sensor against a micron-precision dial gauge.
The three-dimensional displacement of the stem reference triangle relative to the femur reference frame \((x_t, y_t, z_t, \theta_{xt}, \theta_{yt}, \theta_{zt})\) was then obtained from the sensor displacements through the following geometrical relationship (Figure A1.8):

$$
\begin{bmatrix}
  w_1 \\
  v_2 \\
  w_3 \\
  u_4 \\
  w_5 \\
  v_6 
\end{bmatrix}
= 
\begin{bmatrix}
  0 & 0 & 1 & 0 & R_1 & 0 \\
  0 & 1 & 0 & 0 & 0 & -R_2 \\
  0 & 0 & 1 & R_1 & 0 & 0 \\
  1 & 0 & 0 & 0 & 0 & 0 \\
  0 & 0 & 1 & 0 & -R_1 & 0 \\
  0 & 1 & 0 & 0 & 0 & R_2 
\end{bmatrix}
\begin{bmatrix}
  x_t \\
  y_t \\
  z_t \\
  \theta_{xt} \\
  \theta_{yt} \\
  \theta_{zt} 
\end{bmatrix}
$$

Equation A1.2

where \(R_1 = 55.0\) mm and \(R_2 = 60.0\) mm.

Figure A1.8 Coordinate system of stem and that of the stem reference triangle.

The three-dimensional displacement of the stem relative to the femur reference frame \((x_s, y_s, z_s, \theta_{xs}, \theta_{ys}, \theta_{zs})\) was obtained from that of the stem reference triangle, based on the previously measured distance between the stem surface and the origin of the triangle coordinate system, \(d_{\text{triangle}}\):
Finally, the stem motion measurements were transformed to an anatomical coordinate system (Figure A1.9), using Equations A1.4 for right femurs, and A1.5 for the left ones.

Figure A1.9. Illustration of the anatomical coordinate system used to describe three-dimensional implant motion.
\[
\begin{aligned}
\{ \text{posterior translation} & \} \\
\text{lateral translation} & \\
\{ \text{distal translation} & \} \\
\text{valgus rotation} & \\
\text{flexion} & \\
\text{retroversion} & \\
\} = \\
\begin{bmatrix}
-x_s \\
y_s \\
-z_s \\
\theta x_s \\
-\theta y_s \\
-\theta z_s
\end{bmatrix}
\]
\text{Equation A1.5}

The motion measurement from each sensor was validated against a dial gauge micrometer, and a maximum error of 2.2 \(\mu m\) was found (Table A1.1).

Table A1.1 Validation of each motion sensor against a dial gauge micrometer.

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Note: Values are rounded to the nearest tenth of a micro meter. (\text{LVDT})
The accuracy of the motion measurement system was also evaluated along the three translational axes by mounting the femur reference frame onto an over-reamed composite femur and subjecting the stem to motion relative to the femur along each axis. The servohydraulic testing machine was used to generate implant motion along the z-axis, and an x-y table was used to generate motion along the x and y axes. The motion measurements were validated against a micron-precision dial gauge and maximum errors of 5.8 µm, 2.4 µm and 2.7 µm were found along the x, y, and z axes, respectively (Table A1.2).

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Table A1.2 Validation of motion measurement system against dial gauge micrometer.
APPENDIX 2

HISTOMORPHOMETRIC ANALYSIS METHODS
**A2.1 Preparation of histology slides**

Prior to cross-sectioning, the remaining soft tissue was removed as much as possible with a scalpel, pliers and sand paper. The stem was removed by tapping it proximally with a hammer, and the stem-shaped canal was filled with polymethyl methacrylate (Lecoset, Leco Corp.) mixed with green or blue food colorant (not red).

The specimen was aligned and mounted on the diamond saw table (model 310 CP, Exakt Apparatebau, Norderstedt, Germany), and a permanent marker was used to make a small mark on the outside of femur, indicating the proximal side of each cross section. This mark will later be dissolved during ethanol dehydration, but it was useful initially for shape matching the cross sections - the proximal cross-sections were easy to match given their taper, but the distal ones would have been less obvious without a mark. The specimen was cut into 6 mm thick cross sections.

The cross-sections were shape-matched and labeled, while being careful not to damage the fragile graft bed surfaces. Starting at the first proximal cross-section where the entire stem area was present, the cross-sections were labeled: e.g., 1065L-3: donor identification number 1065, left femur, third slide from the most proximal cross-section, etc. The cross-section label was marked on the distal surface of each cross-section with a pencil, on either cortical bone or cement.

Alternating cross-sections were prepared used for histomorphometric analysis. The cross-sections were set in formalin and dehydrated in ethanol solutions as described in Chapter 2. The total duration of the dehydration process was four days – any longer than that was found to cause some swelling and dissolution of the bone cement.

After dehydration, the cross sections were dried in an oven at 60°C for one hour, and allowed to cool down for a few minutes. The dried cross-sections were placed proximal surface down in plastic moulds and embedded in resin (Buehler EpoThin, Lake Bluff, Illinois). The resin (powder) was mixed with the hardener (liquid) with the appropriate ratio as instructed by the manufacturer until it was uniform, after which it was poured over the cross-sections. Each cross-section was lifted and lowered with tweezers to dislodge the larger air bubbles, and
placed in a vacuum chamber. A vacuum of 25 in. Hg was applied, held for a couple of minutes, and released slowly, i.e., at a rate of approximately 0.5 in.Hg/s. The cross section was lifted and lowered again with tweezers to dislodge the newly appeared air bubbles. The vacuum process was repeated until no air bubbles remained and the cross-section was thoroughly embedded in resin. The specimens were labeled again, this time with pencil on a small piece of paper which was inserted in the resin facing away from the cross-section, along the mould wall. The moulds were covered with a lid to protect from dust or debris, and the resin was allowed to set overnight.

The resin-impregnated cross-sections were processed into histology slides by trained technicians (Jesse Chen and Caron Fournier). One slide was obtained from the proximal surface of each cross-section, and it was ground to a thickness of 200 µm.

**A2.2 Calcium staining of histology slides**

Stain preparation:
- Mix together the following in a beaker:
  - 2 g alizarin red S dye (powder)
  - 100ml distilled water
- Insert a pH meter.
- Slowly add/mix 0.5% ammonium hydroxide.
- Stop when pH reaches between 4.1 and 4.3.

Slide staining procedure:
- Rinse slide with distilled water
- Immerse slide in Alizarin red stain solution
- Rinse gently with distilled water
- Set aside to air dry
A2.3 Slide photography for histomorphometric analysis

Figure A2.1 Slide photography set-up for histomorphometric analysis. (Top) Set-up for measurement of cement contact with endosteum and cement area. (Bottom) Set-up for measurement of graft porosity.
APPENDIX 3

GRAFT SHEAR AND COMPRESSION TESTING
The custom-built shear and compression testing apparatuses used for the graft characterization experiments (Chapter 3) are shown in Figures A3.1 and A3.2.

Figure A3.1 Compression testing apparatus. Schematics of compression testing assembly on the servohydraulic testing machine (left). Mould with drainage holes (right).

Figure A3.2 Shear testing apparatus. Schematics (left) and photograph (right) of shear testing assembly on the servohydraulic testing machine.
Figure A3.3 Forces applied during simulated impaction for (top) low, (middle) moderate, and (bottom) high impaction forces.
APPENDIX 4

FINITE ELEMENT ANALYSIS MESH AND STEM MOTION RESULTS
A4.1 Finite element mesh: (left) intact, and (right) under load. Note that the displacements were amplified by a factor of two for this illustration.
Figure A4.2 Migration and micromotion decomposed into motion occurring at the stem-cement and endosteum interfaces ($\delta_{\text{stem-cement}}$ and $\delta_{\text{endosteum}}$, respectively); motion as a result of shear deformation of the cement mantle ($\delta_{\text{mantle}}$); and motion due to shear deformation of the graft and/or graft/cement composite regions ($\delta_{\text{graft/composite}}$).
Figure A4.3 Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for femoral impaction allografting constructs with no cement-endosteum contact, but having 25% cement penetration into the graft bed (Profile A).
Figure A4.4 Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with no cement-endosteum contact, but having 50% cement penetration into the graft bed (Profile B).
Figure A4.5  Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with no cement-endosteum contact, but having 75% cement penetration into the graft bed (Profile C).
Profile D

Figure A4.6  Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with 11% cement-endosteum contact (Profile D).
Figure A4.7 Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with 24% cement-endosteum contact (Profile E).
Figure A4.8 Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with 36% cement-endosteum contact (Profile F).
Figure A4.9  Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with 49% cement-endosteum contact (Profile G).
Figure A4.10 Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with 61% cement-endosteum contact (Profile H).
Figure A4.11 Implant migration (top) and micromotion (bottom) predicted with the FE model (Chapter 4), for constructs with 80% cement-endosteum contact (Profile I).
Figure A4.12  Sensitivity analysis – effect of endosteum friction coefficient, \( \mu_{\text{endosteum}} \), for profile B (top) and profile E (bottom). Shown are the results for constructs where the stem-cement interface was sliding.
Figure A4.13  Sensitivity analysis – effect of graft Poisson’s ratio, $\nu_{\text{graft}}$, for profile B (top) and profile E (bottom). Shown are the results for constructs where the stem-cement interface was sliding.
APPENDIX 5

UBC RESEARCH ETHICS BOARD CERTIFICATES OF APPROVAL
(H03-70359) C03-0359 - Restoration of bone stock in revision total hip replacement with impaction allografting:

<table>
<thead>
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<th>Principal Investigator (PI):</th>
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<td>Thomas R. Oxland</td>
<td>UBC</td>
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# Certificate of Expedited Approval: Renewal

**Clinical Research Ethics Board Official Notification**

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<td>Orthopaedics</td>
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**Institution(s) Where Research Will Be Carried Out**

Vancouver Coastal Health Authority

**Co-Investigators**

Albert, Carolyne, ; Fernlund, Goran, Materials Engineering

**Sponsoring Agencies**

Canadian Institutes of Health Research

**Title:**

Restoration of bone stock in revision total hip replacement with impaction allografting: Morphology and structural stability

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**Certification:**

In respect of clinical trials:

1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 6 of the Food and Drug Regulations.

2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.

3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

The CREB approval for renewal of this study expires one year from the date of renewal.

---

Approval of the Clinical Research Ethics Board by one of:

Dr. Gail Bellward, Chair
Dr. James McCormack, Associate Chair
Dr. Alain Gagnon, Associate Chair
The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL WITH AMENDMENTS TO THE STUDY

PRINCIPAL INVESTIGATOR: Tom R. Oxland

DEPARTMENT: UBC CREB NUMBER: 405-70359

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

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Other locations where the research will be conducted:

W3

CO-INVESTIGATOR(S):

Carolyn I. Albert
Clive P. Duncan
Bassam A. Masri
Goran H. Peltlund

SPONSORING AGENCIES:

Canadian Institutes of Health Research - "Restoration of bone stock in revision total hip replacement with impaction allografting: Morphology and structural stability" - "Morphology & the Structural Stability of Hip Implants in Impaction Allografting"

PROJECT TITLE:

Restoration of bone stock in revision total hip replacement with impaction allografting: Morphology and structural stability

The current UBC CREB approval for this study expires: September 20, 2007

AMENDMENT(S):

Addition of Primary Contact and Co-Investigators, Addition of Research Site and Grant

AMENDMENT APPROVAL DATE: September 15, 2006

CERTIFICATION:

In respect of clinical trials:

1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.

2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.

3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

Approval of the Clinical Research Ethics Board by one of:

Dr. Gail Bellward, Chair
Dr. James McCormack, Associate Chair
Dr. John Russell, Associate Chair

Dr. Caron Strahlendorf, Associate Chair
adduction: action by which the femur is drawn towards the body axis
anteroposterior: along an axis directed from the front towards the back of the body
arthroplasty: joint replacement surgery
aseptic: without infection
cancellous bone: part of a bone having a porous structure
cement mantle: region surrounding a cemented femoral stem that is occupied by cement; in this thesis, cement mantle refers to the region of pure cement surrounding the stem that does not include the regions of cement-graft composite
cortex (femoral): the outer layer of a bone, in this case the cortical shell making up femoral canal
cortical bone: parts of a bone having a dense non-porous structure
craniocaudal: along an axis directed from the head towards the feet
diaphysis: the shaft of a long bone, in this case the femur
distal: situated away from the point of attachment; e.g., distal femur is the part of the femur that is located towards the knee, therefore distal stem migration refers to the migration of the stem towards the knee
endosteum: membrane lining the medullary cavity of a bone; in this thesis endosteum is used to refer to the inner surface of the femoral canal (adjective: endosteal)
condyle (femoral): rounded prominence at the distal end of the femur
flexion/extension: rotation of the stem relative to the femur in the median plane, i.e., the plane that divides the body into left and right halves; see illustration in Appendix 1
histomorphometric analysis: quantitative study of the microscopic structure of a tissue; in this case femurs and/or graft specimens
iatrogenic fracture: fracture that is caused by the surgical procedure
in vitro: in an artificial environment outside a living organism; e.g., in cadaveric or artificial femurs (antonym: in vivo)
in vivo: within a living organism; e.g., inside a living animal
incorporation (of bone graft): process by which the graft becomes a viable part of the bone into or onto which it was implanted; i.e., the host femur
initial stability (of the stem): describes the initial postoperative resistance to subsidence of the stem within the bone construct (synonym: primary stability)
instability (of the hip): partial or complete joint dislocation
intramedullary canal: canal that is located inside a bone, in this case the femur
lateral: located away from the median plane, i.e., the plane that divides the body into left and right halves; see illustration in Appendix 1
lytic defect: bone defect caused by osteolysis; i.e., degeneration of bone tissue through disease
medial: situated towards the median plane (antonym: lateral)
mediolateral: along an axis directed from the medial side towards the lateral side
medullary cavity: marrow cavity inside the shaft of a long bone
metaphysis: proximal femur
morphology: study of structure or shape of a living thing such as an organ; in this case the femur-implant construct (adjective: morphological)
morsellized cancellous bone (MCB): cancellous bone graft that has been morsellized into particles with a bone mill
neo-medullary canal: intramedullary canal that has been re-shaped surgically
periosteal surface: fibrous outer layer of a bone, to which muscles attach
posterior: situated towards the back (antonym: anterior)
prophylactic: preventive; e.g., aiming to prevent fracture
proximal: situated towards the point of attachment; e.g., proximal femur is the part of the femur that is located towards the hip
proximodistal: along the long axis of the femur, directed towards the knee
radiolucent: almost entirely invisible in radiographs
remodeling (of the graft): formation of an oriented trabecular structure within the graft that has adapted to the directions of loading
retroversion/anteversion: rotation of the stem relative to the femur in the transverse plane, i.e., about the long axis of the femur; see illustration in Appendix 1
stem: femoral implant; these terms have been used interchangeably throughout this thesis
subsidence (of the stem): non-reversible gradual stem displacement relative to the femur (synonym: migration)
trabecular bone: see cancellous bone
valgus/varus rotation: rotation of the stem relative to the femur in the coronal plane; i.e., the plane that divides the body into front and back halves; see illustration in Appendix 1