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Introduction and motivation
1.1 Aseptic prosthesis loosening: the clinical problem

Human life expectancy has increased dramatically over the past century [World Health Organization, 2014], which manifests in a quickly growing population of elderly people across the whole world. As humans live longer, more people suffer from painful hip or knee joints resulting from degenerative age-related diseases such as osteoarthritis and rheumatoid arthritis [Kurtz et al., 2011, Kurtz et al., 2005, Merx et al., 2003]. The hip joint, being a relatively simple ball and socket, was the first joint for which, in the first half of the twentieth century, an artificial replacement was developed to address the clinical problems of its deterioration [Charnley, 1961]. Hip arthroplasty, the procedure whereby the diseased joint is surgically replaced with an artificial joint, is today considered one of the most successful surgical interventions in existence [Gomez and Morcuende, 2005]. Literally millions of people world-wide already live with artificial hip implants, with approximately 1 million additional hip replacement operations carried out annually.

Despite hip arthroplasty’s overwhelming success, some implanted prostheses fail prematurely. A hip prosthesis could, and in principle should, last for more than 20 years. Despite this goal, approximately 10% of hip prostheses fail within ten years of placement [Thillemann et al., 2010]. When a prosthesis fails, the standard approach is to replace it surgically with a new prosthesis in what is called a revision procedure. Advances in materials and technique have led to improved implant designs, yet the last decades have seen a slowly decreasing trend in the age at which patients receive their first prosthesis. Younger patients tend to lead more active lifestyles and live longer, increasing the probability of eventually needing revision. These factors combine in such a way that the rate at which prostheses are revised have remained stable over recent years [Kurtz et al., 2005]. Regardless of whether significant improvement in prosthesis durability could be implemented today, the millions of already-implanted hip prostheses will result in hundreds of thousands of prostheses failing over the coming decades.

A hip prosthesis may fail for one of several reasons, yet there is one clearly predominant cause for their long-term failure: aseptic loosening caused by peri-prosthetic osteolysis [Harris, 2001]. The Swedish Hip Arthroplasty Register and Dutch Arthroplasty Register attribute approximately 70% of revisions to aseptic loosening [Garellick et al., 2011, Swe, 2013, Dut, 2013].

The term "osteolysis" refers to a process in which bone is broken down. Specifically, osteolysis is the active breakdown and resorption of bone during a cascade of cytokine release by macrophages and activation of both osteoclasts
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and osteoblasts. Osteolysis may act as a normal biological process of the human body. Peri-prosthetic osteolysis, however, refers to a specific pathological process. A local inflammatory reaction is caused by wear products of an implant, and is also mediated by the genotype of the patient. In other words, people with a pro-inflammatory genotype may be more susceptible. Periprosthetic osteolysis is characterized by the resorption of bone around the prosthesis with subsequent formation of soft fibrous interface tissue in its place. The mechanism by which periprosthetic osteolysis occurs is complex, but the implication for implant stability is straightforward: the layer of interface tissue offers little mechanical stability and allows the prosthesis to move relative to the surrounding bone. Aseptic osteolysis is an insidious problem as it is asymptomatic at first and typically progresses [Agarwal, 2004]; eventually osteolysis manifests in hip dysfunction and pain. Osteolysis can however be detected before it reaches a symptomatic or disabling level. The standard method for early detection is by searching for radiolucent regions in X-ray radiographs. If osteolysis is suspected, its extent can be further quantified in three dimensions using either Computer Tomography (CT) or Magnetic Resonance (MR) [Cahir et al., 2007, Cahir and Toms, 2009]. It has been shown that aseptic loosening may, however, be measured or predicted at a much earlier stage. Early three-dimensional sub-millimetre prosthesis migration may be detected using the RSA stereographic X-ray technique, and correlates with later and more severe aseptic prosthesis loosening [Nieuwenhuijse et al., 2012, Pijls et al., 2012].

It is our belief that timely detection and appropriate treatment of osteolysis may eventually postpone or even eliminate the need for replacement of the affected hip prosthesis. Although the osteolytic process is generally self-propagating and accelerated by the presence of increasing amounts of fibrous interface tissue [Park et al., 2004, Purdue et al., 2007], some authors have even hinted at reversal of the periprosthetic osteolytic area [Talmo et al., 2006]. For routine treatment of periprosthetic osteolysis to become a practical reality, however, new technologies and techniques are needed.

1.2 Existing options for treating aseptic hip prosthesis loosening

Prosthesis loosening is normally treated with open revision surgery where the loose prosthesis is replaced with a new one. The peri-prosthetic bone defects are either filled with a bigger metal implant or with allograft bone impaction and a new implant [Nelissen et al., 1995]. This surgery is demanding, and
may be prohibitively risky for older patients suffering from poor health. Alternatives to revision surgery either consist of conservative treatment (i.e. management of pain, without treating the cause), or new and experimental techniques such as the one to which this thesis pertains.

This thesis focuses on a relatively new and experimental treatment option where the aseptically loosening prosthesis is stabilised by injecting bone cement into the periprosthetic lytic zones surrounding the prosthesis. This method was first pioneered by [de Poorter et al., 2008a] and has since been adopted as an experimental treatment of last resort, also at other academic hospitals [Raaijmaakers and Mulier, 2010]. De Poorter et al. examined gene-directed enzyme therapy to selectively kill the peri-prosthetic interface tissue prior to percutaneous cement injection. With or without prior gene directed enzyme therapy, percutaneous cement injection has so far only been used to treat patients who do not qualify for traditional revision surgery. The mean age at the index operation, when a hip prosthesis is first placed, is 68 years in the Netherlands [Dut, 2013]. When loosening occurs 15–20 years after the initial treatment, patients are at an advanced age with generally more comorbidity and additional surgical risks. The median patient age in a relevant clinical trial was observed to exceed 80 years [de Poorter et al., 2008a]. Compared to traditional revision, a minimally invasive percutaneous procedure requires shorter hospital stay and can be performed at lower cost. The efficacy of this treatment is not believed to yet be comparable to that of traditional prosthesis replacement. However, the inherent advantage of less invasiveness that results in less patient morbidity gives this approach the potential of being applied to a wider population of patients suffering from aseptic loosening.

1.3 A new integrated planning and treatment approach

The work of this thesis forms part of a larger research project at our institution which aims to develop minimally invasive prosthesis refixation to reach its full potential. The envisaged goal is a multi-faceted and integrated diagnostic, planning and execution workflow that relies on medical imaging, planning and guidance software. Together with new purpose-designed surgical instruments this should lead to safe and effective prosthesis refixation. Our envisaged integrated approach is illustrated schematically in Figure 1.1.

The goal of the image processing component is to analyse radiographic images of a patient’s hip. Image analysis allows each patient’s unique anatomy to be identified and digitally encoded. The three dimensional distribution of
material in the periprosthetic region is determined—specifically bone and fibrous interface tissue, existing bone cement and the 3D position of the metal prosthesis. Technologies applicable to this step include automated image segmentation and tissue classification.

The modelling-and-simulation component uses the output of the image processing step to simulate the mechanical stability of the patient’s hip prosthesis. Modelling allows different treatment options to be evaluated. Primary among these choices is the desired location of cement to be percutaneously injected, as this may strongly determine the longevity and effectiveness of refixation. Technologies applicable to this step include three dimensional mesh building and finite element modelling.

**Figure 1.1** – A schematic illustration of an integrated approach to minimally invasive hip prosthesis refixation.
During the planning step, the outputs of the preceding steps are presented to a medical professional. Medical images and simulation results are visualized so that the professional may decide on a suitable approach for treating the patient. Technical and/or treatment decisions may be based on the planning software’s output. Technical decisions may include the way in which the fluoroscopic imager should be oriented to best view the procedure. Treatment decisions may include the amount of cement that should be injected, and the choice of where to inject the stabilizing cement. Technologies applicable to this step include volume rendering, non-linear optimization, data visualization and interaction techniques.

The larger project to which this thesis belongs also set out to develop new surgical tools. These tools will facilitate and/or enable new ways of removing periprosthetic interface tissue and of stabilizing cement to be injected. Technologies applicable to this step may include miniaturized steerable instruments that make use of plasma coblation or water-jet cutting [Kraaij et al., 2012, den Dunnen et al., 2013].

1.4 Contributions

In this thesis we examine how computer software can be used to assist a minimally invasive cement injection procedure intended to stabilize an aseptically loose hip prosthesis. We develop several algorithms and proof-of-concept software tools that can aid in the analysis of a patient’s aseptically loose hip. Our software may one day be used by a surgeon to plan a minimally invasive cement injection procedure, to guide him/her in its execution and allow insight into the achieved outcome. Software is developed on the assumption that a pre-operative CT image volume of the affected hip will be available, and dovetails with the existing treatment workflow for such patients.

We develop new tissue segmentation techniques for determining the tissue distribution adjacent to an aseptically loose (hip) prosthesis. Our approach focuses on automated methods that are able to deal with CT images affected by metal-induced image artefacts.

We improve upon an existing particle-based meshing algorithm that converts a three dimensional (3D) multi-tissue segmented image volume into a tetrahedral mesh. We show that a mesh can be made sparser than was previously possible, without sacrificing its geometric accuracy. This is important as a mesh with a tractable number of elements may be used to perform finite element simulations of a prosthesis’s stability.
Lastly, we develop a software preoperative planning system for fluoroscopy-guided minimally invasive cement injection. This system allows a simulated fluoroscopic snapshots to be made that can guide a surgeon as a patient-specific step-by-step per-operative roadmap. Our software can also estimate the percutaneously injected cement volume that reached the intended cement injection targets—information that would otherwise not be quantitatively known to a treating physician.

This thesis illustrates our techniques when they are applied to the femoral side of a hip with aseptic prosthesis loosening. We propose that all of our software and techniques may easily be adapted to be applicable to a loose acetabular component, or in fact to any loosened orthopaedic implant.

1.5 Structure of this thesis

The ordering of chapters in this thesis is aligned with the diagnosis-and-planning workflow illustrated in Figure 1.1. First we discuss imaging, then image analysis, followed by model-building and finally pre-operative planning and per-operative guidance.

We start in Chapter 2 by investigating whether manual delineation of peri-prosthetic lesions is feasible, and the extent to which metal-induced image artefacts interfere with this delineation. We then examine whether delineation is improved by standard techniques for metal artefact reduction.

Armed with the knowledge gained in the preceding chapter, we retrospectively examine CTs of patients that were treated via minimally invasive cement injection. In Chapter 3 we measure lesion and cement volumes in post-operative CTs of two patient groups. Both groups had aseptically loose hip prostheses that were treated by minimally invasive cement injection at the LUMC in Leiden.

In Chapter 4 we again look at the quality of CT images obtained in peri-prosthetic regions—specifically whether their image intensities are directly suitable for deriving mechanical properties in finite element models.

In Chapters 5 and 6 we develop supervised machine learning pipelines that can automatically segment the peri-prosthetic region in a CT image volume of the hip. These pipelines are based on voxel classification and simultaneously incorporates metal artefact reduction and unprocessed image data, gaining advantages from both. With the addition of a multi-label graph cut algorithm that enforces smoothness and geometrical containment relationships, tissue segmentation of a high resolution CT volume is performed on a standard desktop computer.
In Chapter 7 we address the issue of creating 3D finite element meshes from a segmented multi-material tissue map. Our algorithm attempts the creation of a conformal multi-material output mesh that has fewer elements and/or lower geometric approximation errors than comparable Delaunay-triangulation-based methods.

In Chapter 8 we describe HipRFX, a software preoperative planning system for fluoroscopy-guided minimally invasive cement injection. We report the results of a cadaver experiment where HipRFX could be used in a realistic pre-clinical setting to estimate injected cement volumes.

In Chapter 9 we conclude our work with a discussion and elaborate on possible future developments.