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Stochastic failure modelling of total hip replacement

Pavel E. Galibarov, BSc, MSc

A thesis submitted to the University of Dublin in partial fulfilment
of the requirements for the degree of
Doctor in Philosophy

Supervisors:

Dr. Alexander B. Lennon

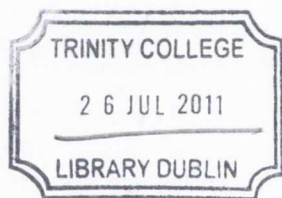
Prof. Patrick J. Prendergast

Trinity Centre for Bioengineering

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Summary

Failure of total hip replacement (THR) can be a highly variable phenomenon. Many factors of a different nature may affect the outcome of this operation, e.g. loads occurring in the joint, patient geometry, implant design, genetic factors, etc. Building a predictive model for failure of a THR is a technically challenging task requiring the incorporation of many uncertainties and modelling failure long-term processes.

In this work a stochastic numerical framework was developed to predict aseptic loosening of the femoral component, which remains one of the main reasons for the failure of THR. To enable the development of the stochastic framework two technologies were created. First, a fully automated method to reconstruct proximal femur geometry from planar X-rays, based on contour extraction of the femur and warping a generic surface model, was developed. It was capable of reconstructing proximal femur geometries with an average surface distance error not exceeding 3.8 mm, which stands in line with other existing methods to reconstruct femur from medical images. Additionally, an FE analysis of strain dependency on the geometric error was performed. It was shown that the error level of the reconstructed geometries does not dramatically change the strains. Secondly, a fully automated technique to mesh a surgical plan, i.e. an implant placed in the patient femur, was developed. This technique was based on morphing a pre-generated generic mesh employing parameterization of the meshed surfaces. An FE solver was employed to warp the internal structure of the generic mesh. The method produced good quality meshes in a rapid and fully automated manner. These techniques enabled the creation of the stochastic framework for modelling failure of total hip replacement. An FE-based approach for modelling aseptic loosening due to the damage accumulation scenario was employed as a basis for the stochastic framework. A Re-

sponse Surface Methodology was utilized as an approximation to perform large trial Monte Carlo simulations. This surface was generated based on predicted values for a deterministic training set. Implant migrations was used as an indicator of revision risk.

Two potential applications were chosen to demonstrate the capability of the framework. These applications used patient morphology, implant design and surgical position as explanatory variables. First, a patient-specific study was performed. Three implants were placed into a publicly available CAD model (reference positions), then 6 deviations (rotations) were applied. This deterministic training set of aseptic loosening simulations allowed construction of response surfaces, which were further used to generate the stochastic set. Secondly, a population-based study was undertaken. For this study, the training set was extended to another 2 patient morphologies with similar implant positions. The difference between the two studies was that different random variables were chosen and, thus, allowed the answering of different research questions.

Analysis of the predicted values indicated that the varus/valgus angle of the implant was the most strongly correlated factor with implant migration, hence revision risk. Reference positions generated according to templating procedure did not necessarily produce the best result. However, using a training set of templated position plus deviations, it was also impossible to discriminate the implant performance with statistical significance. The stochastic approach was necessary to enable the statistical discrimination of different factors. Furthermore, an implant performance analysis carried out on a single femur would give a false prediction compared to a sample of femora from a population. Finally, based on a single femur predicted rankings for implant performance were different from the rankings received using population-based scenario. Thus, a stochastic approach to investigation is very important and strongly recommended for the failure modelling of joint replacements.

This framework is a powerful tool for hypothesis testing in the mechanics of joint replacements and has a large range of potential applications, e.g. patient-specific pre-operative planning and population-based device testing.

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Chapter 1

Introduction

1.1 Failure and variability

Mechanical failure can be a highly variable phenomenon. Reliability of a system, which consists of several parts, depends on mechanical strength of its components, which, in turn, are subject to failure. The mechanical strength of materials depends on microstructural defects, e.g. porosity, shrinkage cavities, surface defects, etc., introduced during the manufacturing process [4]. Variability of failure has long been recognized by engineers. For example, Leonardo da Vinci carried out repetitive tensile experiments on iron wire to investigate its strength with respect to the length and observed that there was a scatter in the results, i.e. the fracture event had a statistical nature (see Hertzberg [4]). Materials have different mechanical strengths due to different nature and microstructure. For instance, fatigue strength of steel and cement are very different, and can even vary considerably in the same family of material, e.g. cements with different mixing techniques. Murphy and Prendergast [5] investigated fatigue failure of bone cement for two different preparations of cement: vacuum-mixed and hand-mixed. Considerable variability in the number of cycles required to fail for the vacuum-mixed bone cement was observed (See Fig. 1.1). However, variability is not limited to material factors. Variability in environmental conditions, e.g. loads occurring in a system, can affect a failure scenario as well. Thus, predicting failure of a mechanical system is a very complex task, which requires understanding and accounting for variability from many case-specific factors.

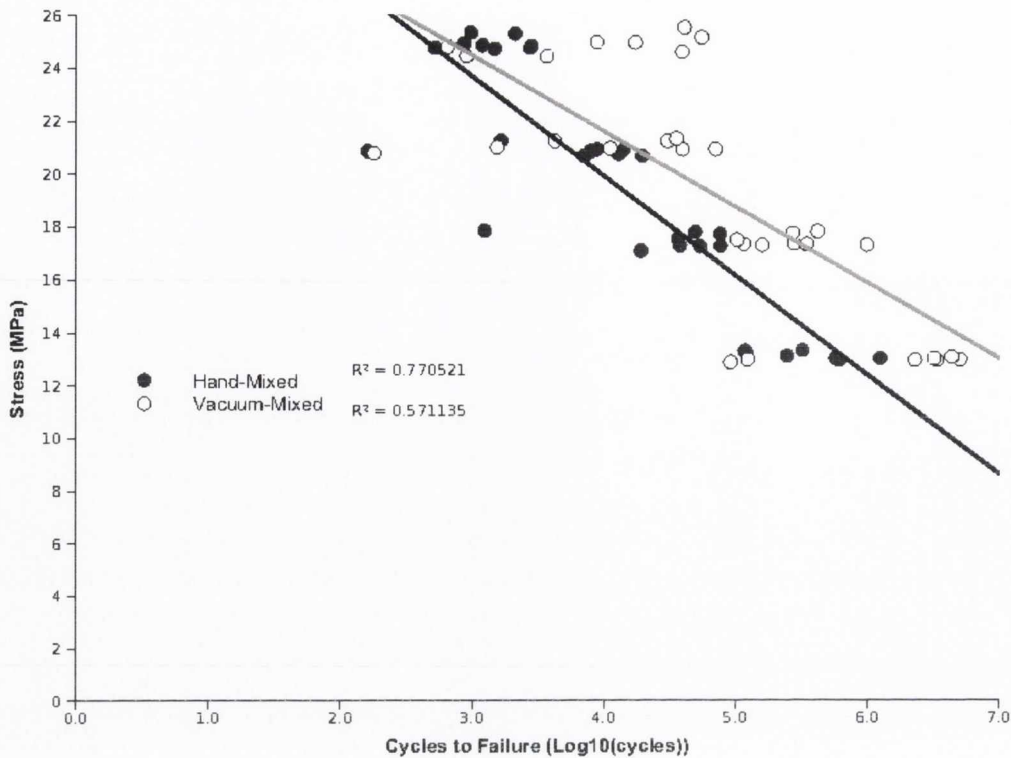


Figure 1.1: Variability in the number of cycles required to fail for vacuum-mixed and hand-mixed bone cement. (Courtesy of Dr. Bruce Murphy)

1.2 Designing for variability

Modern advances in mathematics and engineering together with state-of-the-art computer technologies enable engineers to solve complex failure modelling tasks and produce very precise predictions for a variety of problems. That, in turn, enables cost reduction for device production and increases life-cycle of the product. However, the number of possible scenarios and variables used to describe a modelled process can be extensive. Sometimes behaviour of certain factors is not well known and it is difficult to define a range of possible values for a particular parameter. How can one design a valid predictive model for such system? The answer to this question is to account for the variability of the scenarios and factors influencing device or structure service-life during the design process.

1.2.1 Deterministic approach

A common practise for failure modelling and designing in general is to calculate a set of deterministic predictions. Normally, several known possible failure scenarios

are considered and common criteria for component failure are chosen, e.g. limits for stresses, strains, damage, displacements, etc. A set of input parameters (input vector) chosen by an engineer is then used to compute a corresponding outcome vector. Normally there are two types of input vectors to be tested for a particular component: extreme and normal values. Extreme values mean excessive stresses, strains, displacements, etc., that most likely will be sufficient to induce failure. If computed output vectors show that the component resists extreme conditions and does not undergo further failure, it is considered safe. Otherwise it undergoes a process of redesigning such as reinforcement or use of stronger materials to ensure that the component meets design criteria.

This approach works well if a small number of uncertainties affect the outcome and it is feasible to model such a process. However, in a model with very large complexity dimension it is impossible to account for all required input vectors. Often input vectors chosen by an engineer are not optimal and might not need to be tested at all. Alternatively, the testing procedure may be very time consuming so that modelling all possible input vectors becomes prohibitive. Stochastic approaches to failure modelling may be used to overcome these difficulties.

1.2.2 Stochastic approach

In stochastic modelling a probabilistic density function (*pdf*) is introduced to describe distributions of input parameters and their combinations. A number of vectors are generated using the *pdf* and then the outcome is evaluated on this set of input parameters. An advantage of this technique is that, once the *pdf* is defined, further evaluation is independent of human choice and, therefore, is more objective. Furthermore, for a large number of input parameters this approach often better describes behaviour of the system using a smaller number of samples to be evaluated.

Monte-Carlo simulation is a common technique to perform stochastic simulations. It is based on repeated random trials of the phenomenon using a chosen function. It is normally performed until a trend in the results becomes obvious, i.e. the solution converges. Different sampling strategies may be utilized to carry

out this kind of simulation. Sequential, random, systematic, convenience, size-based and other sampling techniques are available.

Stochastic methods are well suited to modelling failure of complex models as they can reveal problems that are not visible to experienced engineers.

1.2.3 Difficulties for Monte Carlo modelling

Monte Carlo simulation is a very popular approach due to its ability to handle large numbers of variables. However, a number of issues restrict this method from being applied widely. Firstly, for an increase in the number of variables to be taken into account, the number of samples needed to evaluate performance of the method grows exponentially. For example, if a Latin Hypercube sampling strategy is used with 4 divisions for 2 variable factors, the number of samples will be equal to 24, for 3 variables it would be 576, and so on. A second problem arises from this potential for large numbers of trials. If the process of evaluating a response from the deterministic function is quick, then a high trial count is not a problem. However, often an individual trial evaluation/simulation might take several days or months. Thus, this technique is not well suited for performing a large number of simulations in such cases. The following section suggests possible solution strategies to overcome this problem.

1.2.4 Solution strategies for reducing trials

Design of Experiment(DoE) [6] techniques may be used to tackle the problem of increasing sample numbers. These techniques are based on the following principles:

Blocking - allows grouping of factors, thus, reducing the dimension of complexity for a certain task, ignoring irrelevant variation.

Orthogonality - this principle suggests that it is possible to find an orthogonal basis in vectors which represent the sample field.

Factorial Design - proposes to perform multiple evaluations of the method, in order, to reveal independent and dependent factors affecting the outcome.

Utilization of these principles helps to minimize the number of samples needed to achieve convergence of Monte Carlo simulations and reduce total time of the experiment.

Response Surface Methodology(RSM) [7] is a numerical technique to optimize experiments. It explores the relationship between a set of factors that describe a model being tested. A very simple example of this technique is a surface in 3D space for which x and y are the factors to be investigated and z is the response variable. An approximation of the 3D surface can be built using discrete values of x and y , and then this representation might help to locate extrema. Approximate response values can be computed for another discrete set of input variables without calculating the actual surface function, but using linear or quadratic approximations.

The application of this technique may significantly reduce experiment time as there is no need to carry out a full-scale deterministic simulation. A large number of simulations can be performed in orders of magnitude less time than is required for individual sample point simulations (e.g. seconds rather than days or weeks).

Advanced Mean Value(AMV) [8] techniques are based on utilizing a Taylor series approximation of the function/method to be tested. It is built on mean values of uncertainties used in an initial step of the Monte-Carlo simulations. Linear and quadratic elements are used to construct the approximation via Taylor series. Computing original deterministic outcomes for intermediate points and adjusting the Taylor series may increase accuracy of this approximation. This technique can also be used in combination with other strategies, e.g. RSM, to further reduce the number of trials needed to achieve realistic predictions.

1.3 Failure of Total Hip Replacement

Total Hip Replacement or Arthroplasty (THR/THA) is a commonly performed operation in orthopaedic surgery in which a diseased hip joint is replaced by a prosthetic implant. These replacements are conducted in order to relieve pain caused by conditions such as osteoarthritis and rheumatoid arthritis, which affect the articulating components of the hip joint, namely the acetabulum and the femoral head (Fig. 1.2).

During typical THR surgery the femoral head is removed, acetabulum is reamed and acetabular components then inserted. After that the femur is reamed, and the femoral part of the prosthesis is implanted, with or without cement fixation. Successful operation means that a patient is able to live with the replaced joint for the rest of their life or an acceptable period of time without signs of pain, any other symptoms, or major inconveniences. If a patient reports to be suffering from sufficient pain after primary operation, revision surgery takes place.

1.3.1 Hip replacement failure mechanism

Pain may occur in THR patients due to the following reported reasons — mechanical (aseptic) loosening($\sim 75\%$), infection($\sim 8\%$), dislocation($\sim 7.5\%$), periprosthetic fractures($\sim 6\%$), etc [9]. Modern surgical techniques have decreased infection considerably and aseptic loosening is now considered to be the major reason for failure of THR [10].

Aseptic loosening happens due to degradation of the components keeping the replaced joint together. Bone tissues weaken, resorb with time, implant materials wear, cement cracks, etc. Two possible scenarios for aseptic loosening (Fig. 1.3) have been proposed [11]: (i) a particulate reaction scenario — wear particles migrate to the bone interfaces and induce osteolysis, which can result in the formation of a soft-tissue layer, and (ii) a cement damage accumulation scenario — when damage (in the form of microcracks) accumulates in the cement mantle and at the prosthesis-cement interface, gradually causing the prosthesis to loosen. The first scenario can be minimised by using modern biocompatible bearing materials. However, a strategy to improve results for the second scenario is less clear given the variable performance strength of bone cement. Due to increased loading of the cement or increased wear particle production, these scenarios may interact by introducing additional stresses and resorption in the replaced joint [1].

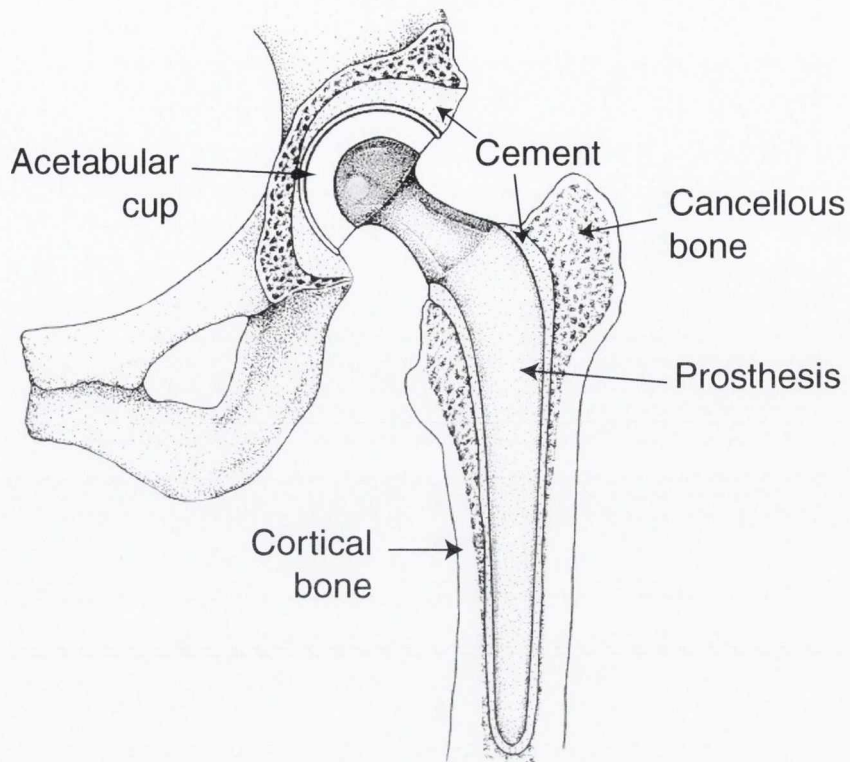


Figure 1.2: Schematic of a total hip replacement (adapted from [1])

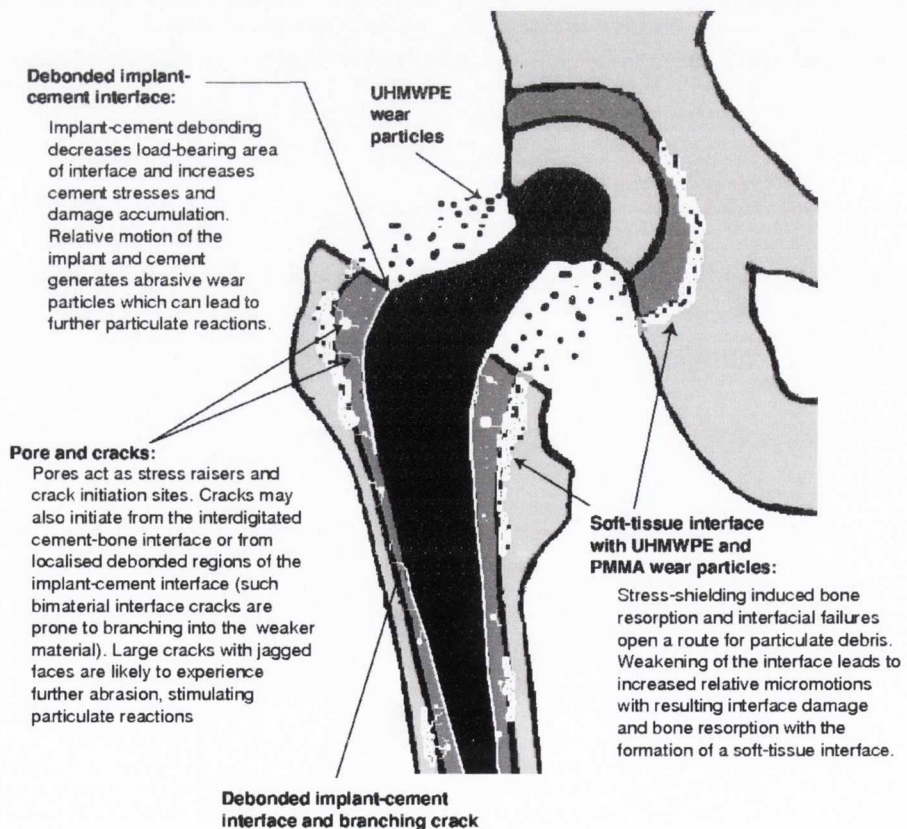


Figure 1.3: Illustration of instances and interaction of damage accumulation and particulate reaction failure scenarios (adapted from Lennon [1])

1.3.2 Sources of variability in total hip replacement

Due to a large number of patient-specific factors the failure of total hip replacement can vary considerably. Differences in patient-specific bone morphology can be large [12] and since femur shape affects load distribution, which is likely to affect outcome, a single femur model is insufficient for capturing population variability. Furthermore, bone morphology can be affected by diseases. Individual patients' everyday activities [13] introduce unpredictable joint loading patterns. Each activity is based on actions of a group of several muscles. For instance, walking involves the following set of muscles: quadriceps, adductors, gastrocnemius, hamstrings, and soleus [14]. In turn, morphology and strength of these muscles vary from patient to patient. Accounting for different activities requires an individual simulation for each activity. Increasing life span of elderly patients for cemented THR and application of uncemented THR and hip resurfacing surgeries to younger patients make it difficult to anticipate the typical activity profile experienced by prostheses [15, 2]. Also, nutrition [16], gender [17] and genetic [18] factors indirectly influence the bone properties and their maintenance rates. Furthermore, there is a large variability in designs of THR components. For instance, it has been observed that different implant designs can have both different survival rates as well as variability in their survival rates (See Fig. 1.4).

As previously mentioned, a large variability is observed in the fatigue strength of cements (Fig. 1.1). The variety of cement materials and mixing procedures make this variability even larger. Analogously, implant component materials, metals and polyethylene, are subject to fatigue and wear failure. Furthermore, a position of the implant chosen by a surgeon defines another source of uncertainty.

Thus, failure modelling of total hip replacement in a real patient is a very challenging task. However, a system that can account for this variability could be used for pre-operative planning, to investigate limitations on movements/activities, form post-operative recommendations on a patient-specific basis, and for development of implant designs capable of matching wide ranges of patients.

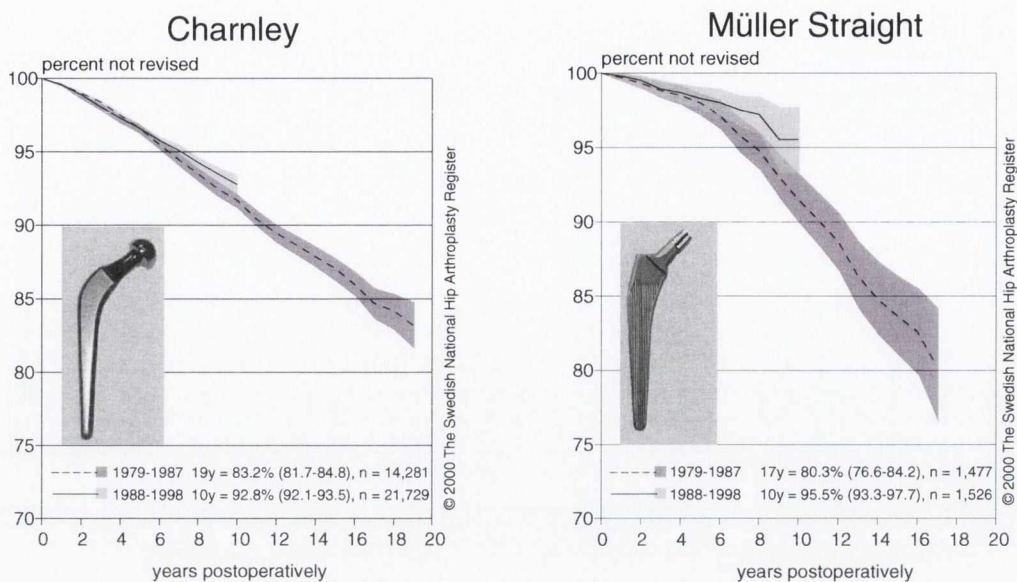


Figure 1.4: Survival data for Charnley and Müller Straight Prostheses (Figures adapted from Lennon [1], data from Swedish Hip Register [2])

1.3.3 Difficulties for modelling joint replacement behaviour

Long-term prediction of implant behaviour is a challenging task of a multidisciplinary nature. A realistic biomechanical model can serve a role as the basis for pre-operative patient-specific simulations. The Finite Element Method (FEM) has proved to be a very effective tool to model various mechanical processes and has been commonly used to model human and animal joints as a system of deformable solid bodies [19, 20]. Therefore, a realistic FE model could serve the purpose of modelling THR pre-operatively. Building such a model can be subdivided into several steps: (i) reconstructing patient geometry; (ii) generating a mesh; (iii) assigning material properties, and (iv) defining realistic initial and boundary conditions. While each of these steps have their own difficulties, the first two have historically been strong barriers to finite element modelling of joint replacement behaviour.

Geometry reconstruction

Modern advances in medical imaging provide an opportunity to create a very precise geometrical model of a patient's organ. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are widely used for acquisition of patient-specific anatomic data. CT imaging creates a three-dimensional image of an organ by pro-

ducing multiple X-ray images rotated about a certain axis. Robustness against digital noise generated by soft tissues makes the CT technique well suited to acquisition of hard, calcified parts of the human body such as bones. Very often CT images are adopted for 3D geometry reconstruction of bones for scientific purposes [21, 22]. MRI on the other hand is mostly used for imaging of soft tissues like brain, liver, heart, muscle tissues, etc. Although, CT enables creation of accurate 3D models, CT equipment is often expensive and not available for mass use; also, there are medical limitations on using this type of acquisition frequently on patients due to an increased radiation dose compared to traditional X-ray imaging. A 3D reconstruction technique that could use the much more common planar radiographs routinely used for pre-operative planning could overcome some of the difficulties faced by CT-based approaches. However, the question then arises whether a 3D model reconstructed using such an approach would be accurate enough to model failure of an implant in a replaced joint?

Mesh generation

The finite element method is a numerical technique to solve partial differential equations by subdividing the problem domain into smaller regions (meshing) and solving an approximated form of the differential equations for each region. Each case-specific scenario requires its own unique FE mesh due to specific combination of an individual patient's bone geometry with different implant designs, as well as desired positions of the implant within the bone. Generally, meshing of irregular geometric shapes, such as bones, is difficult, time consuming, and can become an obstacle for performing large numbers of case-specific simulations. Therefore, a robust, rapid, and automated method for generating case-specific FE meshes would bring patient-specific finite element simulations a step closer to widespread adoption.

1.4 Proposed framework for simulating joint replacement failure

An FE-based simulation framework (Fig. 1.5) is proposed to carry out joint replacement failure investigations with high numbers of random variables. For a single case, a patient-specific geometry needs to be generated from a source of geometric data, e.g. a medical image obtained from a picture archiving and communication system (PACS). Next, a surgeon or a computational algorithm will select an appropriate implant and position it within the patient's bone. Once all the geometric components are positioned, they need to be meshed for the next step. An FE-based failure simulation for this particular case incorporating patient-specific mesh and boundary conditions, cement fatigue, creep and bone adaptation algorithms, etc. needs to be performed to understand whether the requested scenario fails or not. Multiple scenarios can be similarly processed to generate a Monte-Carlo-style simulation system, which, in turn, will enable multivariate analysis of case-specific factors. Sample size reduction techniques, e.g. Response Surface methods, can be incorporated to decrease the time needed to achieve realistic predictions.

1.5 Objectives and outline of thesis

This work aims to create a framework for failure modelling of cemented THR utilizing a probabilistic FE-based approach. The main requirement for the framework is to be able to incorporate patient-specific bone morphologies, implant geometry and position, cement fatigue and creep, and other variable case-specific factors. It needs to be capable of being applied to both patient-specific and inter-patient population samples. It should be possible to employ individual methods developed within this study as a toolkit for modelling total hip replacement or other intramedullary joint replacements. The influence of major variable input parameters on a mechanical failure scenario such as patient-specific geometry, position of the implant within the bone, and implant size need to be investigated.

This framework should be capable of answering many research questions rele-

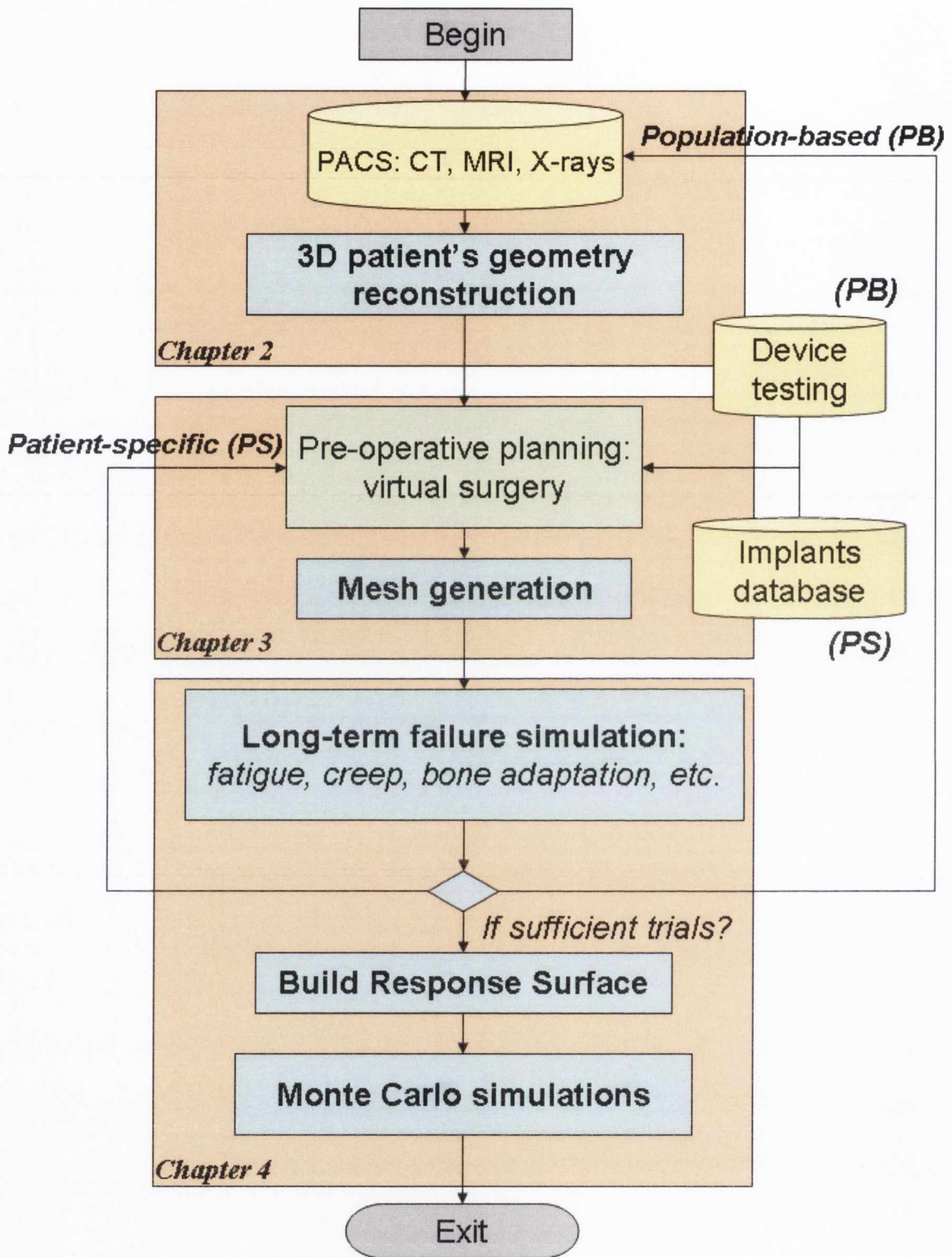


Figure 1.5: Probabilistic failure modelling scheme for THR. An automated approach to reconstruct femur geometries from medical images is described in Chapter 2. An automated mesh generation technique is proposed in Chapter 3. A stochastic failure modelling framework enabled by these methods (Chapters 2-3) is described in Chapter 4. Two hypothetical applications were used to test the framework (PS and PB).

vant to joint replacement performance. For example, what are the most important factors governing revision risk for a specific patient — implant selection or surgical technique? Can a single femur be used to test performance of implant designs? What are the most relevant factors to be focused on in a device testing application — implant positions or femur dimensions? Can a particular prosthesis design be reliable across a population sample?

Only by including sufficient sources of variability can it be expected to predict the probable performance envelope of joint replacement prostheses. Furthermore, such a stochastic approach is more likely to capture non-intuitive combinations of input parameters than a single or small set of deterministic simulations. This thesis aims to demonstrate the potential of a stochastic approach to investigate cemented hip replacement failure. This is achieved by first developing methods to overcome some of the technical barriers (automated 3D femur reconstruction from planar radiographs (*Chapter 2*) and automated meshing of surgical plans (*Chapter 3*) to implementing the proposed stochastic framework (*Chapter 4*).

Chapter 2

Patient-specific 3D geometry reconstruction

2.1 Introduction

Modern procedures of medical treatment often involve analysis of a patient's organ using medical images. Imaging techniques that are commonly used in hospitals and research centres are CT, MRI, ultrasound, and conventional radiography. Each of the techniques has its own field of application, specifications, advantages and disadvantages. For example, CT and radiographs are normally used for imaging calcified parts of the body, e.g. bones, whilst MRI and ultrasound are better for monitoring softer tissues. Volumetric imaging techniques (CT, μ CT, MRI, 3D ultrasound) have proved to be very useful for researchers who are particularly interested in morphology of anatomical structures. However, volumetric medical images are not always available for research and clinical use. Often just planar radiographs are used for preoperative planning and templating due to their low cost and for radiation safety reasons [23]. In this situation it is possible to use Roentgen images to create a surface model of a patient's body part by warping an existing surface model into the required sizes. However, due to the lack of 3D data, accuracy of the reconstructed geometry is lower than from that created using volumetric data.

Conventional 3D reconstruction begins with a stack of 2D images (slices) with a prescribed spacing between each slice. Reconstruction of the 3D model from the

image data consists of several steps, e.g.:

- (i) Image processing — enhance initial image prior to the procedure of extracting an object's contours. Image processing methods are also capable of revealing an object's contours without user intervention, which can reduce time of the subsequent steps.
- (ii) Image segmentation — segment 2D and 3D images into several regions using a set of rules. If an object's surface is not required then the 3D image can be converted directly into a 3D model using voxels. Volume ray casting [24] algorithms based on voxel intensities can be applied to visualize the object and direct conversion to voxel finite element model can be used to perform stress analysis [25].
- (iii) Surface extraction — extract object outlines from medical images.
 - a) One way of surface extraction is to create isosurfaces based on analysis of voxel intensities, e.g. the Marching Cubes algorithm [26]. Closest voxels with a specified Hounsfield [27] value are connected into polygons to organize a 3D surface.
 - b) Alternatively, 2D contours for each image in the stack are extracted and then all the contours are swept into a single surface. For instance, Couteau *et al.* [28] took CT scans from a cadaveric specimen, obtained femur contours using edge detection techniques and saved as 2D images, then *Patran Software* (MSC Software, Los Angeles, CA, USA) was used to construct a 3D model. Similar workflow has been used by many researchers [29, 21, 22].

Many open-source and commercial software packages are available for solving these tasks in an automated and semi-automated manner, e.g. *Slicer* (Harvard Medical School, Boston, MA, USA), *3D Doctor* (Able Software, Lexington, MA, USA), *Amira* (Visage Imaging Inc., Richmond, Australia), etc.

In cases when detailed volumetric data is not available, it is possible to reconstruct surfaces based on low-quality 3D images using statistical shape models (SSM).

Barratt *et al.* [30] proposed a technique to register a mean statistical femur model to ultrasound(US) image space. Generated models were compared to corresponding CT-based models. Results were favourable compared to other existing techniques (average error of 3.1 mm compared with a range of 2.94-6.88 mm [31, 32]). Heimann *et al.* [33] reviewed several SSM applications applied to the femur, e.g. Fleute *et al.* [34]. Sparse CT images (reduced number of slices taken) combined with SSM can be used to reconstruct patient-specific geometries [35, 34]. A study by Shim *et al.* [35] showed that root mean square errors for reconstructed geometry varied between 0.3 and 2.53 mm (subject to the number of slices).

An alternative approach is to use conventional 2D greyscale images which do not explicitly contain 3D information, e.g. X-rays, to generate an inverse transform from the projection that created the planar image. An experienced person looking at these images may notice position of typical anatomical landmarks and estimate orientation of the shape being reconstructed. As only a single or small number of images may be available, extra knowledge about the shape to be reconstructed is required to create a 3D surface. Most methods within this approach differ in their assumptions and/or the algorithm that apply this knowledge to bridging the gap between 2D projection to 3D volume. Le Bras *et al.* [36] proposed an approach based on low-dose biplanar radiographs and non-stereo corresponding contours(NSCC). They reported a mean distance error of 0.7 mm and a double root mean square error was 20 mm. An alternative method based on SSM was proposed by Zheng *et al.* [37]. They reported average errors of approximately 1mm. Langton *et al.* [38] based their method on a projection of 3D DXA image and General Procrustes Analysis to find selected landmarks. Thin plate splines were applied to warp a template model. However, these techniques have a common disadvantage - tests and error assessments were carried out just *in vitro*, i.e. using isolated cadaveric femora. Therefore, these methods do not account for the difficulty of acquiring X-rays in several planes *in vivo*, e.g. overlapping of pelvis and proximal femur on X-ray, and, thus, have to be further tested in realistic pre-operative conditions.

An automated method for generation of geometry from a single planar radio-

graph would undoubtedly be of use in a large number of patient-specific modelling tasks. The current study aims to develop a technique to generate extracortical geometry of a patient's femur from a pre-operative 2D X-ray in an automated manner. Since the lack of 3D data on a planar X-ray will most likely introduce errors to the final geometry, a comparison with more accurate techniques, such as CT-based reconstruction, needs to be performed. Finally, a conclusion must be made as to the suitability of these geometries for patient-specific modelling. In particular, the influence of geometric precision on mechanical responses, such as strain prediction in a finite element analysis, is evaluated.

2.2 Methods

The following strategy was adopted to solve the task of the generation of extracortical femur geometry from planar radiographs (see Fig. 2.1):(i) dimensional information, such as femur contours, is extracted from a planar radiograph, and (ii) the most similar model from a library of generic models is selected, and (iii) this model is then warped to fit the patient's bone.

2.2.1 Femur contour extraction algorithm

To extract contours of the femur on an X-ray image the following steps are taken: (i) the radiograph is enhanced, by removing noise, to preferably highlight just the contours of the bone, (ii) anatomical landmarks are found to construct an initial contour, and (iii) the contour is transformed using an Active Shape algorithm [39] to fit the femur.

X-ray image enhancement. Digital pelvic anterior-posterior (AP) X-rays with known magnification factor are used to reconstruct patient geometries. Often only the proximal femur is visible on pre-operative X-rays. Thus, the present technique targets the proximal part of an individual femur. The algorithm assumes a left femur as an input. If reconstruction of a right femur is required the X-ray is reflected and then reflection of the reconstructed 3D model is later performed to return to the right hand side.

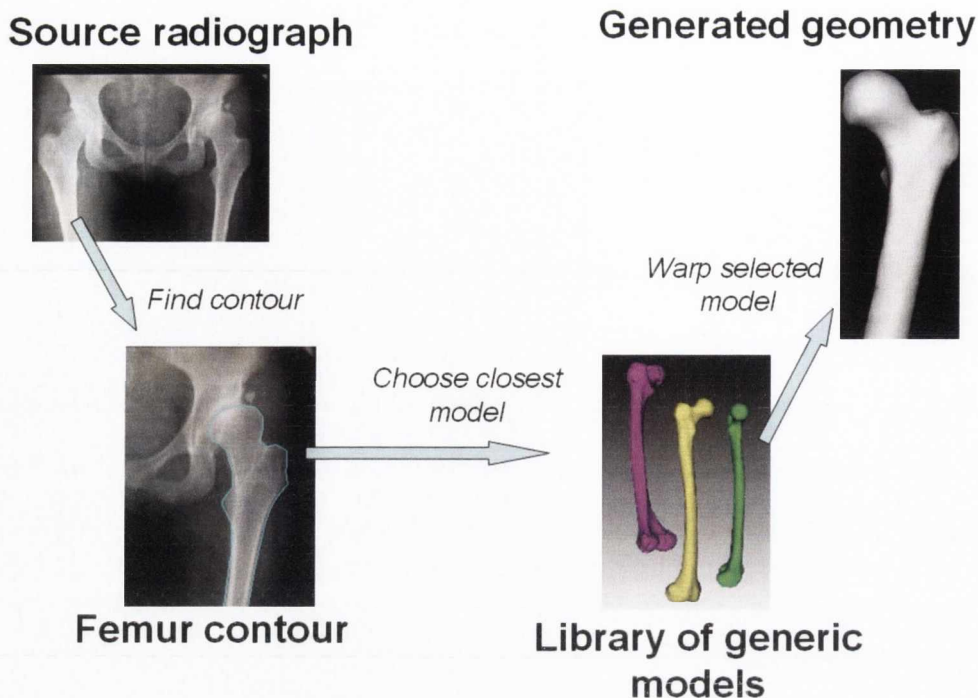


Figure 2.1: Method scheme for 3D femur reconstruction from planar radiograph

First, noise is removed and pixel intensities are enhanced to improve object recognition and produce less errors. This is an important procedure to reconstruct precise geometry and can significantly simplify the task of finding the contour of a femur on an X-ray. Next, functions of the Image Processing toolbox of Matlab (The MathWorks, Inc., Natick, MA,US) are used to enhance the radiograph. First, adaptive contrast enhancement algorithms are applied to adjust initial contrast and brightness. An adaptive low-pass noise-removal filter based on Wiener's method [40] is used to eliminate noise. Edge-detection methods are utilized to convert the image into a black and white binary image containing bone contours. A combination of Sobel's method [40] and vertical and horizontal gradients are then applied and the resulting binary image is processed using morphological operations — isolated pixels are removed and small objects are connected. This scheme extracts parts of the extracortical femur borders, which are used to construct a femur's contour (see Fig. 2.2).

Anatomical landmarks. Analysis of the binary image is performed to locate femur boundaries. Knowledge of femur anatomy, size, and image orientation is used for making a decision on which landmarks to use for recognition of femur borders.

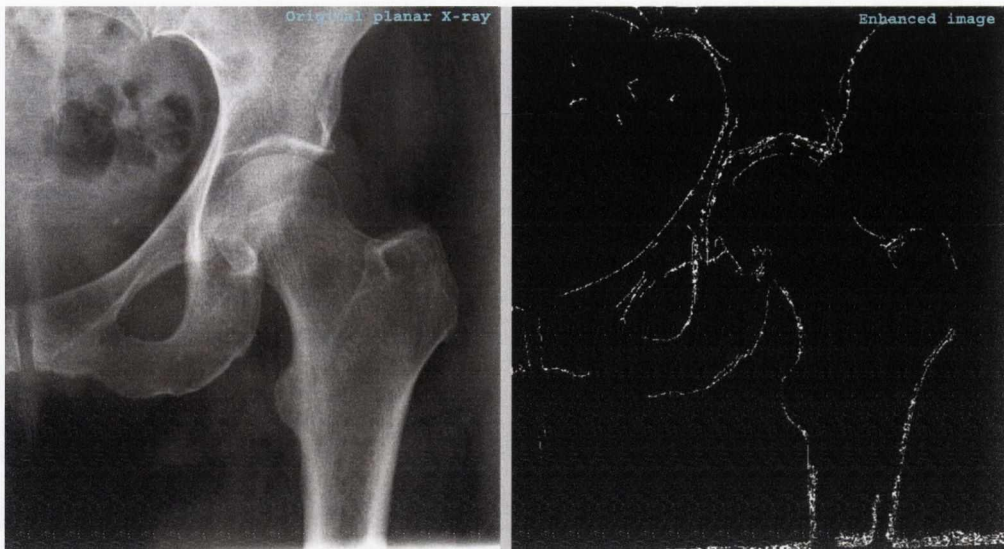


Figure 2.2: Image enhancement: (left) original radiograph; (right) corresponding enhanced image

Distal borders of the femur are used as a starting point for contour reconstruction due to the ease of identification. The greater trochanter can be identified as the most lateral point on the pelvic radiograph. Next, the most distal point of the femur is located on the femoral head. As the latter is overlapped by the acetabulum on a 2D radiograph, segmentation of the femoral head is difficult. However, boundaries of the femoral head remain the most circular parts of the edges extracted from the original X-ray. Taking this knowledge into account along with distributions of human femur measurements [3], it is possible to locate these boundaries (See Fig. 2.3).

A horizontal ray-tracing algorithm from right and left side is applied to the bottom half of the image. Distance between pairs of points found on medial and lateral sides of the femur are measured. According to the table of distributions by Noble *et al.* [12], the minimum extracortical width of a femur is 20.5 mm (H) and maximum canal width at lesser trochanter area + 20 mm is 63 mm (D) (Fig. 2.4). All points within this range are selected and used to calculate least squares lines (baselines) for each side. Then distances between the calculated lines and candidate points are measured again; outliers introduced by noise and imaging artefacts are eliminated.

Neighbourhood pixel analysis is performed using the most proximal points of medial and lateral candidate sets - clockwise on the medial side and counterclockwise on

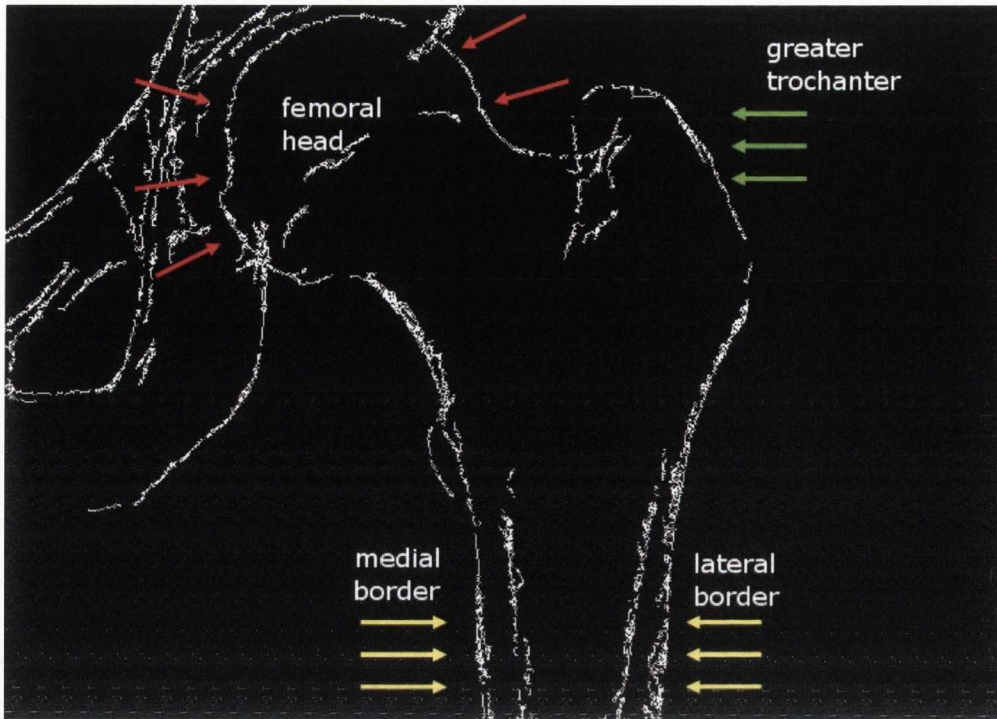


Figure 2.3: Femur landmarks: (yellow) distal extracortical borders; (green) greater trochanter; (red) femoral head boundaries

the lateral side; initial positions for search are located on the lateral-medial axis. The radius of the neighbourhood search is not specified but limited by the image sizes. Thus, analysis of the lateral side produces a lateral border for the femur and acetabulum and similarly for the medial femur border. After that all image pixels outside the borders are eliminated because they do not contain required points of the contour. The lateral femur border is used to locate the greater trochanter, which is defined by the most laterally distant point from the least squares line fitted into the lateral border points.

A cropped binary image is used to find contours of the femoral head. It was suggested by Sugano [3] that a best prediction of the head centre should be based on the midpoint of the femoral neck isthmus. When it is not available the position of the head centre can be estimated from the height of the femoral neck saddle and the distance from the medullary axis to the medial cortex at the 30% level (Fig. 2.4). Using this information along with the known position of the greater trochanter and the distribution of femoral measurements reported by Noble *et al.* [12] an approximate bounding box for the femoral head centre is calculated. This region defines a smaller image containing boundaries of the femoral head. A Hough transform is

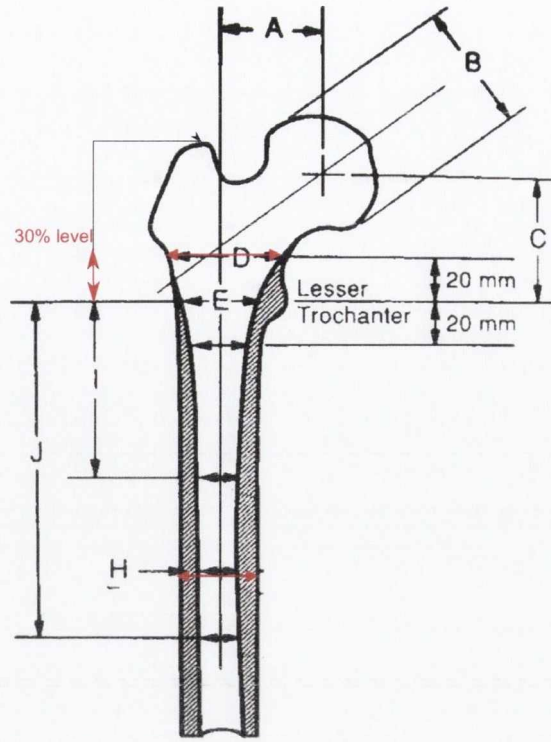


Figure 2.4: Schematic femur: (red) lesser trochanter +20 mm level (D) and minimum extracortical thickness at isthmus(H), and 30% level described in Sugano *et al.* [3] (adopted from Noble *et al.* 1988)

applied to calculate the most probable location of the circle on this image [41]. Pixels of the original image within the resulting circle are restored in the cropped image. All pixels outside of the top and left half of the circle are set to be black since they do not belong to the contour.

Active snakes algorithm. The remaining segments of the extracortical contour are extracted using an Active Contour algorithm. This is a technique to find/segment objects presented in images. It is an iterative process where a closed curve (snake) representing the contour of the object is changed to fit its boundaries. The rule for curve change is based on image pixel intensities.

Nowadays two types of active contour models are commonly used: *parametric active contours* [42] and *geometric active contours* [43]. For the current study, focus was on parametric active contours. Parametric active contours synthesize parametric curves within the image domain and allow them to move toward desired features, usually edges. Typically, the curves are drawn toward the edges by potential forces, which are defined to be the negative gradient of a potential function. Additional

forces, such as pressure forces, together with the potential forces comprise the external forces. There are also internal forces designed to hold the curve together (elastic forces) and to keep it from bending too much (bending forces) [39]. The parametric curve, $\chi(s)$, for a snake is:

$$\chi(s) = \{x(s), y(s)\}, s \in [0, 1], \quad (2.1)$$

where s is a perimeter-related parameter and $x(s)$ and $y(s)$ are the corresponding point coordinates on the curve. For each step, energy of the contour curve is calculated using the following equation:

$$E_{as} = \int_0^1 \frac{1}{2} (\alpha |\chi'(s)|^2 + \beta |\chi''(s)|^2) + E_{ext}(\chi(s)) ds \quad (2.2)$$

- where α, β are tension and rigidity parameters respectively and E_{ext} is the energy of external forces.

An implementation of the gradient vector flow (GVF) field “snake” algorithm was selected to find femur contours in this study. For this implementation potential forces are replaced by the intensity-based gradient vector field, which minimises the energy functional from Eq. 2.1. This implementation was chosen for the following reasons: a precise initial contour may be used, the initial contour may intersect boundaries of the femur, and the GVF “snake” proved to be more suitable for “U”-shaped boundaries (i.e. GVF works better on concavities, and human femur contours contain several cavities — e.g. femoral neck saddle and regions around the greater and lesser trochanter). A convex hull based on apparent contours extracted from cortex borders and femoral head circle is calculated and is used as an initial approximation for the “snake” algorithm. Parts of the contour found in the previous steps and considered to be accurate are used to improve the accuracy of this initial contour and reduce the number of iterations. At least 40 iterations are required to fill the concavities. Further iterations would improve the shape, however, increasing the number of iterations increases total time of the procedure. Therefore, to speed up the process, previously located parts of the femur are utilised to compose the final femur

contour. Selection of tension and rigidity parameters from Eq. 2.2 was performed empirically. Following parameters are used for the analysis: $\alpha = 1$, $\beta = 0.3$, and regularization parameter μ mentioned in [39] is equal to 0.22. Figure 2.5 shows the process of active contour evolution with growth of iteration number. The final contour is then constructed from the distal extracortical contour calculated in the landmark extraction step (up to the greater trochanter on the lateral side) combined with head, neck and greater trochanter contours calculated using the active snake algorithm.

2.2.2 Selecting the closest matching generic model to the extracted contour

To proceed, the extracted femur contour is used to find the closest model in a library of generic models. A number of publicly available femur models from online repositories, such as Biomedtown, were used to create the library of generic models: (i) the Standardized Femur [44] - a 3D surface model of extracortical femur with medullary canal, (ii) a model of a later generation composite femur [45] (Pacific Research Labs, Vashion Island, WA), (iii) VAKHUM femur — right and left femora [46], and (iv) a femur model from the Visible Human dataset [47]. According to Noble *et al.* [12], human femur length varies between 353 mm and 557 mm. Furthermore, femoral length correlates well with femoral head diameter and femoral neck length, which also correlate well with each other. Therefore, all models were scaled to have an average length of 447.07 mm. Right femora were reflected and the reflection flag was stored.

First, the models and contour need to be aligned in the same manner to identify the closest one. Then rotations and sizes are found from the extracted contour by comparing the contour to silhouettes of scaled and rotated generic models. A least squares line (using distal extracortical borders up to the lesser trochanter) corresponding to the centre line of the medullary canal is computed for the contour and 3D models. Then a second line is built using the femoral head and neck (middle of the isthmus connected with the femoral head centre). The contour and 3D models

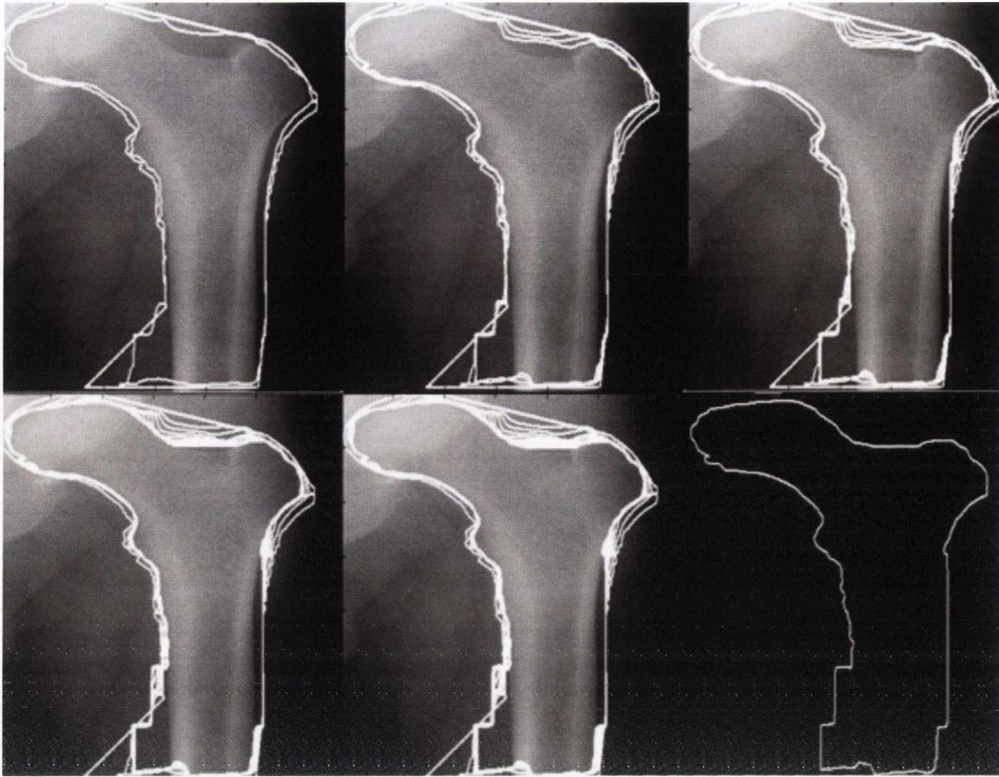


Figure 2.5: Active snake iterations: (top row) 5, 15, 40; (bottom row) 50, 75, last step (Note that images are scaled down vertically)

are translated to have the intersection point of these lines in the coordinate system origin and then rotated such that the femoral shaft centre line aligns with the vertical direction of the image/the Z axis of the coordinate system. However, the computed lines do not necessarily intersect for the 3D models. All 3D models are transformed to align the Z axis with the femoral shaft line and then rotated to make the femoral neck axis parallel to the XZ plane, then the projected line is used instead and the origin of the coordinate system is readjusted (Fig. 2.6).

The next step in finding the best fit generic model is to account for different sizes and rotations of femora. Taking into account cross-correlations of femur dimensions, all aligned models are scaled according to the ratio between patient's femoral head diameter and average femoral head diameter (46.59 mm) [12]. To account for the rotation of a patient's femur during X-ray acquisition, all models are rotated from the initial position described in the previous paragraph from -15 to +15 degrees with a step of 3 degrees. At each of these increments evaluation of similarity between the femur contour and generic model is carried out. First, a virtual radiograph

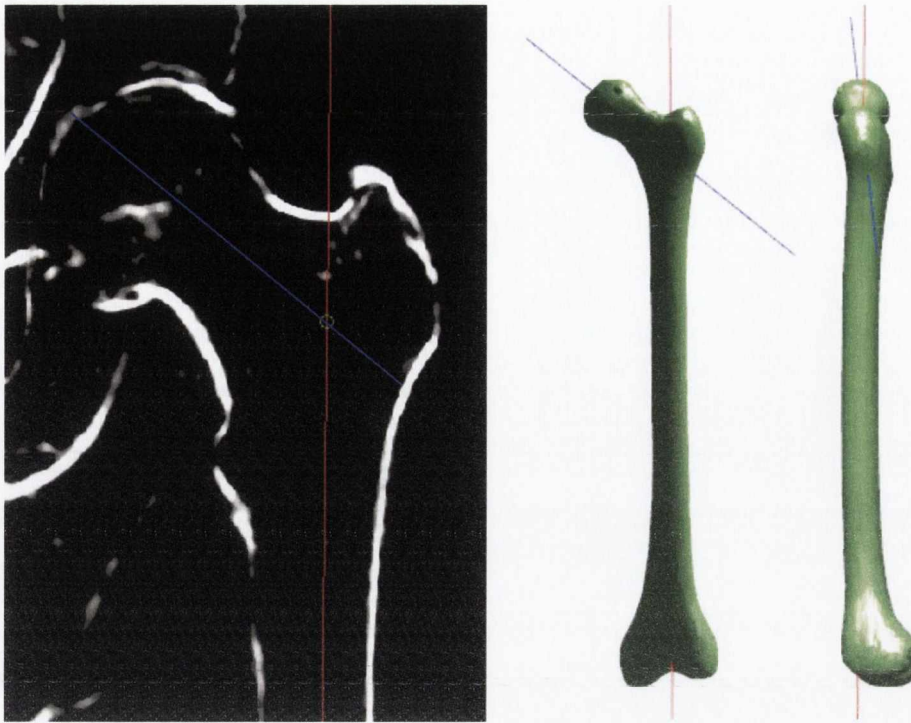


Figure 2.6: Contour alignment lines: (red) femoral shaft axis; (blue) femoral neck axis

acquisition procedure is performed, i.e. rectangular projection on the XZ plane is calculated for a particular model, position and scale. Then the projection contour and patient's contour are bounded within the same limits and a black and white picture is created (Fig. 2.7). Similarity between these images is then calculated using a 2D correlation coefficient, which is used as a likelihood metric of two contours. Using the above procedure on each model and each position of generic model gives a number, the similarity metric. The correlation coefficient for two entities varies between -1, when entities are inverted, and 1, when entities are similar. Therefore, a

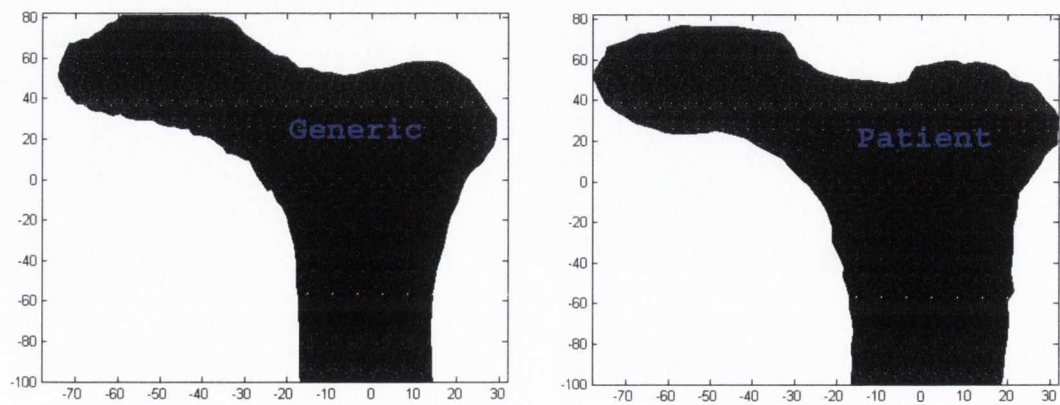


Figure 2.7: Contour comparison: (left) generic model; (right) patient's femur (Note that images are scaled down vertically)

largest absolute value would correspond to the closest model in the library of generic models. Figure 2.8 shows how three different scales of the same model affect the result.

2.2.3 Warping the generic model

Femoral neck

Having selected a generic model and aligned it with the extracted contour, the next step is to morph the generic model to fit the patient's contour. The scaling procedure in the previous section provides a reasonably close approximation of the periosteal sizes of femur parts. However, according to Noble *et al.* [12], femoral neck shaft angle does not correlate very well with periosteal dimensions. Also, Barratt [30] observed that variation of femur shape has two principal modes lined to the following dimensions: femur length and femoral neck angle. Thus, a first step for warping the generic model is to change the angle of the femoral neck shaft. For each generic model, vertices of the model that belong to the femoral head and neck were bounded by an ellipsoid with its centre on the femoral neck axis (centre point of the ellipsoid and radii were stored with the model). The same scaling and rotation transform from the previous section is applied to the centre point so it remains the bounding ellipsoid for the scaled and rotated model (Fig. 2.9). Femoral neck angle is measured between the projection of the femoral neck axis and femoral shaft axis of the generic model. Axes computed from the contour are used to calculate target

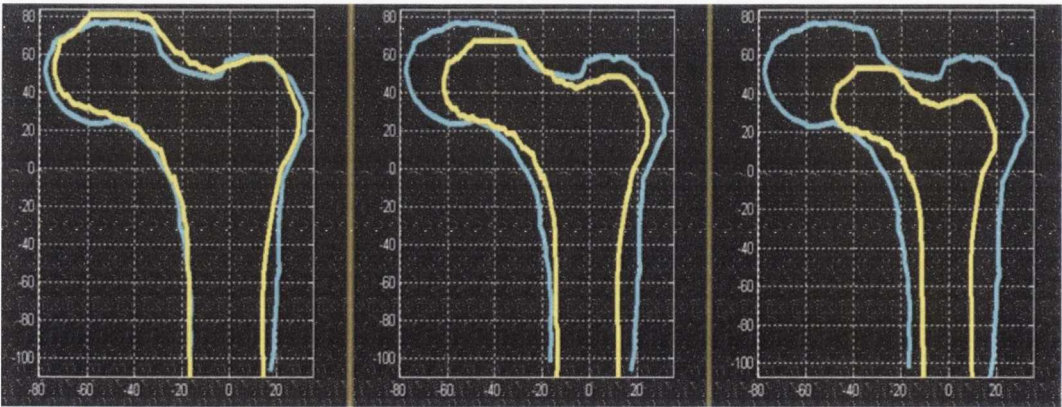


Figure 2.8: Correlation coefficients for 2 contours: (left) maximum scale ($R = 0.899$); (middle) average scale ($R = 0.7838$); (right) minimum scale ($R = 0.6388$)

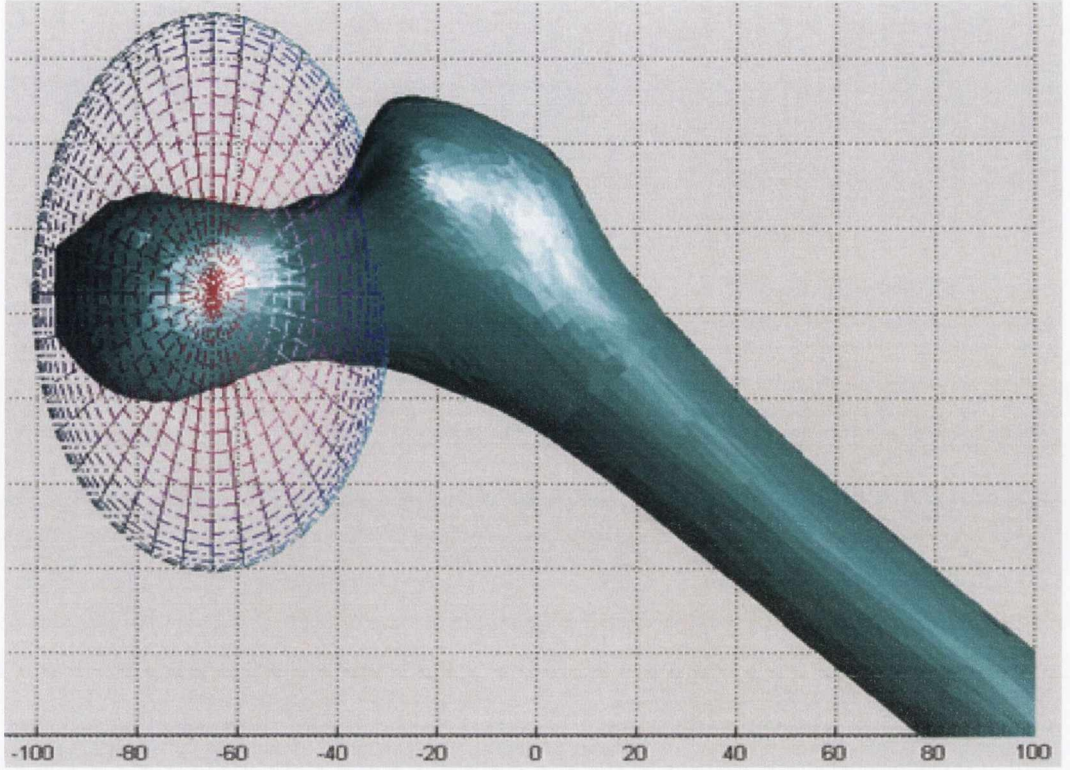


Figure 2.9: An ellipsoid bounding femoral neck and head for one of the generic models

angle. Then all points within the ellipsoid are rotated about the Y axis using the difference between computed angles. Displacements between original points and target points are applied to the model. This procedure can introduce artificially long distances between connected vertices (Fig. 2.10, top, left). To prevent this, a smoothing transform is applied to a belt of points (Fig. 2.10, right). This belt is defined by a parameter $\alpha \in [0, 1]$, which describes a fraction of the ellipsoid radius containing the point ($\alpha = 0$ refers to the centre of the ellipsoid). Each belt point is then moved using displacement values multiplied by the following coefficient, based on α :

$$\tau(p, \nu) = \begin{cases} \frac{1}{\sqrt{2\pi \frac{(1-\nu)}{2}}} \exp -\frac{(p - \frac{1-\nu}{2})^2}{\gamma}, & p \in [\nu, \nu + \frac{(1-\nu)}{2}] \\ 1 - \frac{1}{\sqrt{2\pi \frac{(1-\nu)}{2}}} \exp -\frac{(p - \frac{1-\nu}{2})^2}{\gamma}, & p \in [\nu + \frac{(1-\nu)}{2}, 1] \end{cases}, \quad (2.3)$$

where p is a relative distance to the centre of ellipsoid, ν is a parameter describing thickness of smoothing layer, γ is a parameter defining behaviour of the smoothing method and was empirically found to be best at a value of 0.2.

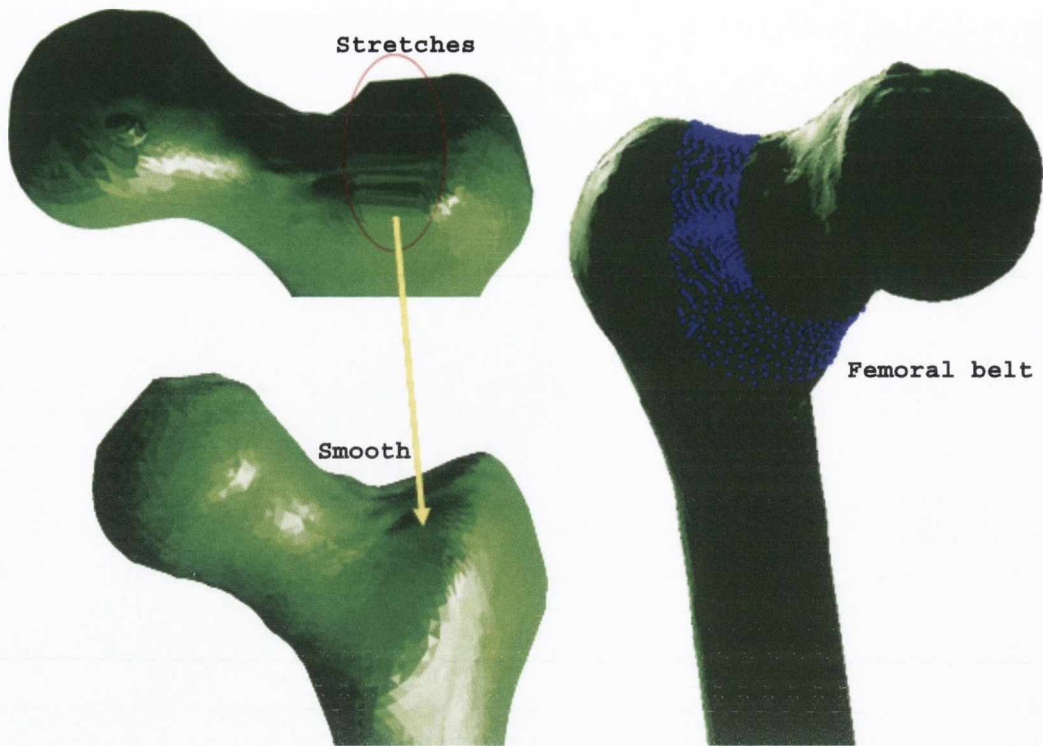


Figure 2.10: Head rotation smoothing: (top, left) large displacements; (bottom, left) smooth; (right) smoothing belt ($\nu = 0.5$)

Distal femur

The next step is to warp the rest of the femur from the greater trochanter distally. This portion of the femur can be represented by a tubular surface with central line aligned to the Z axis. First, the femur contour is split by a number of planes normal to the central line with a desired step. For each section, maximum and minimum horizontal coordinates are found. Similarly, the aligned 3D model is cut by the same amount of planes and boundary coordinates in the X direction are then calculated. A closed 2D figure for each plane is defined by two half-ellipses with horizontal radii calculated as $R_{right} = R_P/R_M$ and $R_{left} = R'_P/R'_M$; vertical radii are equal and found using $R_{AP} = \frac{R_{right} + R_{left}}{2}$ (Fig. 2.11). Further, for each point on the surface of the generic model, an angular parameter is assigned, ϕ , representing an angle about the Z axis. According to this angle, it is possible to locate a point on the scaling “ellipse” which defines a scale for radial displacement of the point. A loop through all the cuts is then performed for each point. Displacements for each point are found taking into account two closest cutting planes and corresponding scaling ellipses. A linear approximation of the scaling factor is computed for required displacements

based on distance of the point from planes and scaling factors on each plane. Finally, a smoothing scheme similar to Eq. 2.3 is used to smooth displacement at the proximal and distal parts of the scaled model.

2.2.4 Validation tests

It is very important to understand whether the algorithm works and the models reconstructed using the current approach are suitable to perform realistic patient-specific analysis as planar radiographs do not directly provide 3D information to reconstruct a femur. This section describes some validation techniques to measure error level of the generated surface models and its impact on patient-specific FE analysis.

Robustness test

A set of radiographs, total of thirty two images, were selected from a dataset provided by the Adelaide & Meath Hospital, Tallaght, Dublin, Ireland. All thirty two radiographs were selected to fulfill the following requirements: (i) presence of the proximal femur and the pelvis (typical pelvic X-ray), (ii) absence of any non-anatomical objects, and (iii) femur visibility, i.e. images where the femur was not visible for any reason (contrast problem, position, etc.) were rejected. These thirty two radiographs were utilised to test the proposed algorithm.

Self-reconstruction test

A first step to validate accuracy of the proposed method is to compare results from a reconstruction to measurements from the original geometry used for the reconstruction. Two tests were carried out for self-reconstruction validation. First, one of the generic models was utilised to produce a “virtual” radiograph, it was projected to the XZ plane of the reference coordinate system. The contour of the figure was calculated manually, introducing a minor error, and used to reconstruct the femur. Then a surface model was generated using all the generic models in the library. For the second test, one of the generic models was excluded from the library

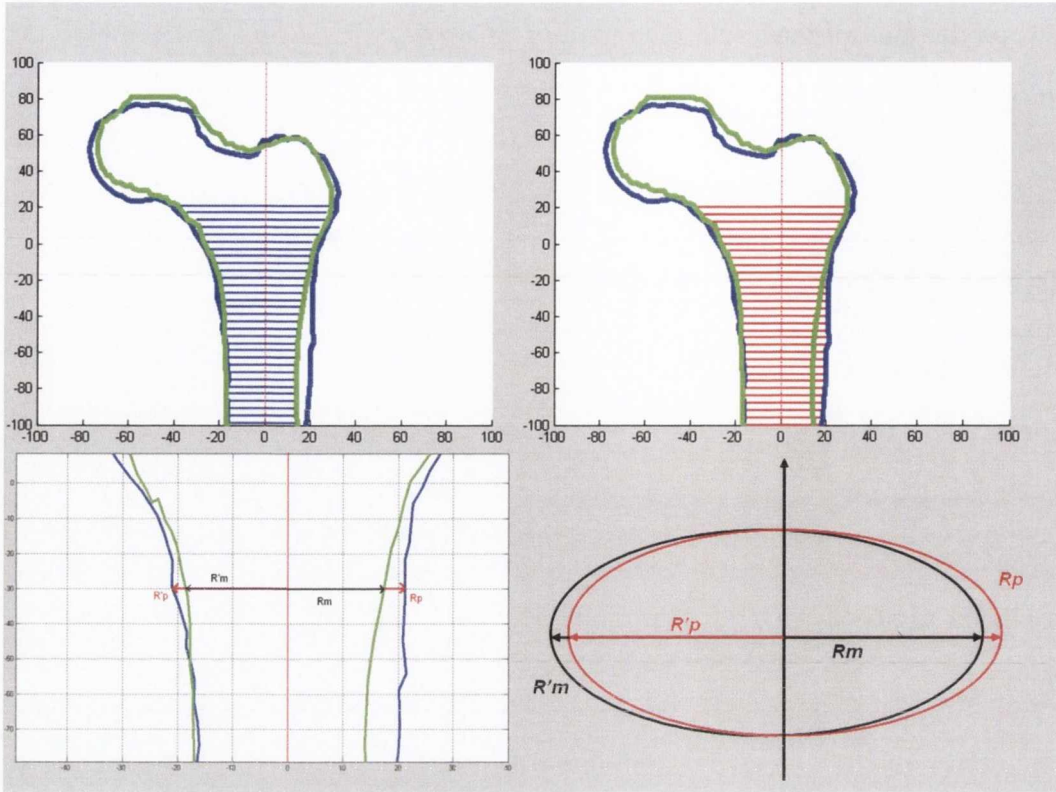


Figure 2.11: Warping scheme for distal femur: (top row) cuts for patient's contour and generic model; (bottom row) scaling "ellipse"

to test the behaviour of the algorithm with a lower number of generic models. The excluded generic model was used to create a "virtual" radiograph. A surface was reconstructed using the remaining generic models.

For each point of the created geometry, a distance to the original surface was calculated using the formula:

$$d(\bar{p}) = \min_{\forall T \in S_t} \text{dist}(\bar{p}, T), \quad (2.4)$$

where T is a single facet of the target surface, S_t .

Comparison to CT-based models

Computed Tomography is considered to be a reliable source of volumetric data and often CT-based models are used as control samples to evaluate morphological accuracy [30]. A dataset of corresponding CT scans and radiographs was provided by the Adelaide & Meath Hospital, Tallaght, Dublin, Ireland. Four matched pairs of pelvic CT scans (512×512 , 30–70 slices, 3mm spacing) and planar radiographs

(2136×1760 , magnification factor of 5) were used to create 3D geometries. The stereolithography (STL) [48] file format is widely used to store surface models reconstructed from medical images due to the simplicity of surface representation via a connected collection of triangles (facets). Each CT scan was processed using a semi-automatic scheme to extract contours of femora and STL models were generated using *Slicer* (Harvard Medical School, Boston, MA, USA). Then the reconstruction algorithm proposed in this work was also used to create corresponding right and left femora for each patient. Models were aligned using an Iterative Closest Point approach and distance maps were computed using Eq. 2.4. Geometry for the proximal femur down to lesser trochanter with a variable offset was present on CT scans. Thus, comparison of the models was carried out only on the available parts of the geometry.

Impact of accuracy on finite element analysis

In order to evaluate influence of geometrical accuracy on FEA a scheme originally proposed by Viceconti *et al.* [49] and later used by Ramos and Simões [50], was adopted to construct several FE models with varying degrees of error.

- (i) a CT-reconstructed femur model — this model was considered to contain no error, and, therefore, was used as a reference point to analyse strain distributions (reference model).
- (ii) A surface model was reconstructed using the proposed algorithm — this model was created using an X-ray corresponding to the CT scan generated by the developed reconstruction algorithm (reconstructed model).
- (iii) Extrapolated surface model — this model was an extrapolation of the previous two. For each point on the reconstructed model a minimum distance to the reference surface was computed, then it was shifted by the same value from the reference surface in a normal direction.

These models were meshed using a mapping scheme such that the same number of nodes and elements was kept and approximate positions of the nodes were

preserved. To perform sensitivity analysis intermediate models were created using linear interpolation between the reference, reconstructed, and extrapolated models, i.e. for each new model nodal coordinates were interpolated between the aforementioned models. Corresponding error values were calculated for each model. Nine interpolated/extrapolated models were subjected to FE analysis.

Each proximal femur was restrained at the isthmus point and joint and gluteus maximus forces (1976 N and 1240 N, respectively), were applied at expected positions on the surface of the bone. Values for Young's modulus and Poisson's ratio were taken equal to 14,200 MPa and 0.3 respectively. Linear-elastic analysis was performed using Abaqus (SIMULIA, Providence, RI, USA). For each mesh, principal strains on the surface of the bone were recorded at ten virtual gauges on medial and lateral sides and then used to compare strain distributions between models. Locations of the gauges to measure principal strains were selected arbitrarily on the first model due to the different lengths of the femora and mapped to analogous locations on the target models along with all other surface nodes.

2.3 Results

2.3.1 Geometry reconstruction

Robustness: Application of the technique to the dataset of thirty two radiographs from the Adelaide & Meath Hospital, Tallaght, Dublin, Ireland showed its robustness as it managed to process all images and did not fail to generate first contours and then geometries. An average runtime of the method was ~ 5 minutes using Matlab (The MathWorks, Inc., Natick, MA, US) on a computer with Intel Pentium(R) 4 CPU with 3 GHz frequency. Approximately 90% of the runtime was consumed by the "snake" algorithm. Models were saved using ASCII STL file format.

Self-reconstruction: Measured mean surface distance for the self-reconstructed model using the full generic library was equal to 0.48 mm with standard deviation of 0.001 mm. The largest errors (~ 4 mm) were observed in the femoral neck saddle and femoral head regions — a minor error was introduced by

the manual procedure of choosing the contour points. For the model reconstructed without one generic model, the measured mean distance error was 1.44 mm with standard deviation of 0.02 mm. The largest errors for the reconstructed femur were located around the lesser trochanter and the greater trochanter regions (see Fig. 2.12).

CT vs X-rays: For the four matching CT-X-ray pairs, reconstructed femora mean distance error varied from 2.57 mm to 3.28 mm with the standard deviation varying between 0.02 and 0.06 mm (see Table. 2.1). The most problematic region was the femoral head ($\sim 16\text{mm}$) 2.13. If the problematic femoral head was removed (as would be the case for a joint replacement application) the mean distance value dropped by approximately $\sim 0.5\text{mm}$; in this case the highest error region was around the greater trochanter area ($\sim 8\text{mm}$).

2.3.2 FEA results

Maximum and mean surface errors ranged from 0.4365–11.6557 mm and 0.0475–2.8755 mm respectively for an error factor (linear interpolation/extrapolation coefficient) of 0–2 (See Table 2.2), where 0 is the original model, 1 is the reconstructed model, and 2 corresponds to the extrapolated model. The largest mean surface error (Table 2.2, bold) stands in line with measured mean distance errors shown in Table 2.1. Principal strain measurements for gauges on medial and lateral side showed increasing error for octahedral shear strain with increasing geometric error (Fig. 2.14). Furthermore, Figure 2.14 shows that the growth of strain was almost linear in all cases. Average errors for maximum, middle and minimum principal strain components for the reconstructed model were 30.228 ± 38.916 , 13.593 ± 15.137 , and



Figure 2.12: Mean errors, mm (text) and peak errors (red contours) for self-reconstructed case from the full LGM (left) and generic model from the LGM reconstructed without corresponding geometry

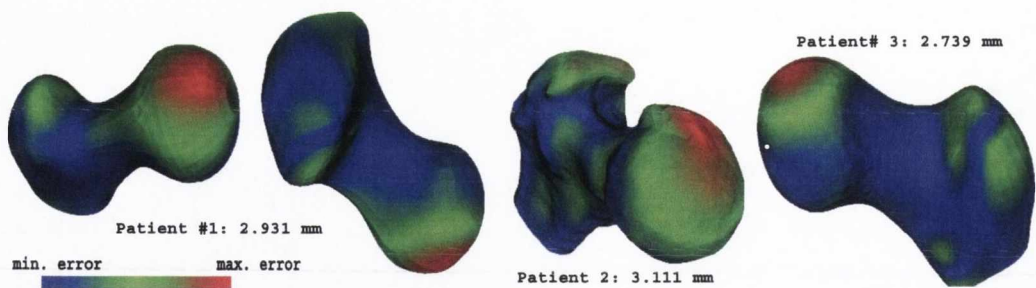


Figure 2.13: Mean surface errors (text) and peak distance errors (red) for CT-X-ray comparison: Patient #1, Patient #2, and Patient #3, Table 2.1

Table 2.1: Mean surface errors between CT- and radiograph-based models (mm)

Patient ID	Right Femur	Left Femur
Patient#1	3.2825 ± 0.04	2.931 ± 0.03
Patient#2	2.573 ± 0.02	3.111 ± 0.03
Patient#3	3.743 ± 0.06	2.739 ± 0.04
Patient#4	3.101 ± 0.03	2.876 ± 0.04

Table 2.2: Surface distance between tested models and reference model (mm): d_{max} is a maximum observed error on the surface, d_{mean} — a mean surface error, and ef is a linear interpolation/extrapolation coefficient, representing the error factor for a particular model; Underlined value — mean error in the least accurate model

Model#:	1	2	3	4	5	6	7	8	9
d_{max}	0.437	1.456	2.913	4.370	5.827	7.284	8.741	10.198	11.656
d_{mean}	0.048	0.370	0.727	1.085	1.443	1.801	2.159	2.517	<u>2.876</u>
ef	0	0.25	0.5	0.75	1	1.25	1.5	1.75	2

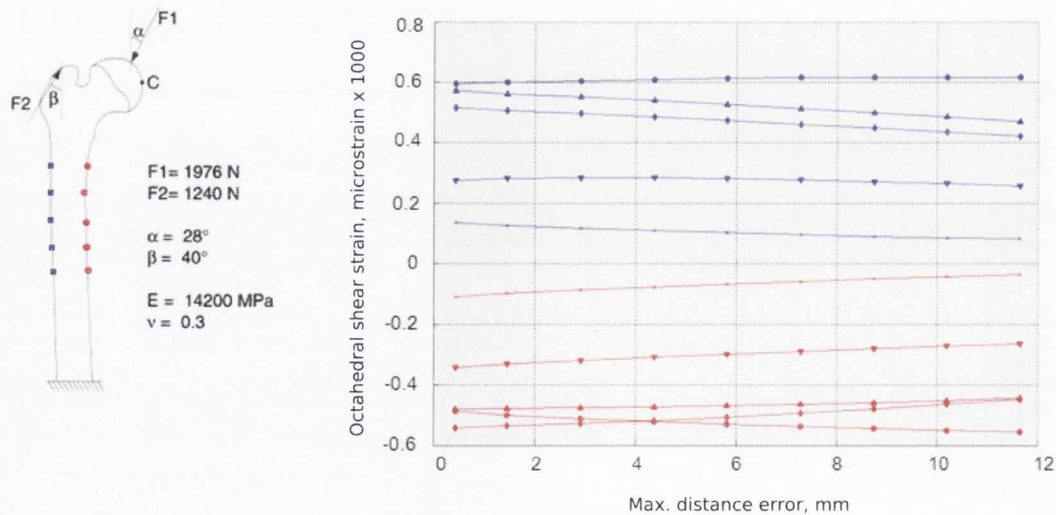


Figure 2.14: (left) schematic explanation of loading and gauge measurement; (right) octahedral shear strain at gauges: strain level, $\mu\epsilon \times 10^{-3}$, vs maximum surface distance to reference model, mm

Table 2.3: Principal strain field differences for reconstructed and extrapolated vs. reference models, $\mu\epsilon$

Statistics	Max. Principal ϵ	Mid. Principal ϵ	Min. Principal ϵ
<i>Reconstructed Model($ef = 1$)</i>			
Maximum	714.210	385.618	1734.530
Mean	30.228	13.593	32.981
SD	38.916	15.137	46.013
<i>Extrapolated Model($ef = 2$)</i>			
Maximum	1408.660	682.778	2854.190
Mean	55.917	24.982	61.076
SD	72.479	27.739	84.332

$32.981 \pm 46.013 \mu\epsilon$ respectively. For the extrapolated model similar values were 55.917 ± 72.479 , 24.982 ± 27.739 , and $61.076 \pm 84.332 \mu\epsilon$ 2.3. A comparison of the principal strains in the reference, reconstructed, and extrapolated models shows that change in strain level was relatively small and strain values for the majority of elements were within mean and standard deviation range; this was further confirmed by computing strain error histograms for the reconstructed and extrapolated models (Fig. 2.15). Examination of contour plots of strain error (Fig. 2.16) show greatest error on lateral and medial sides of the distal part of the femur. Similar to the previous results, proportional growth of deformations was observed with increasing geometric error.

2.4 Discussion

Successful application of the proposed technique to thirty two planar pelvic radiographs showed that it is robust, rapid and does not require user intervention, i.e. fully automated. Models reconstructed from corresponding CT scans and planar X-rays consistently contained a mean distance error less than 3.7 mm. Peak errors were most often in the femoral head and the greater trochanter regions (Fig. 2.13). Additionally, one can notice the error values for the second self-reconstruction test and CT *vs.* X-rays differ by a factor of 2. Investigation of the influence of geometric error on predictions of strain revealed an almost linear relationship between predicted strain error and reconstructed geometry error, with relatively low strain error predicted for models reconstructed using the proposed technique.

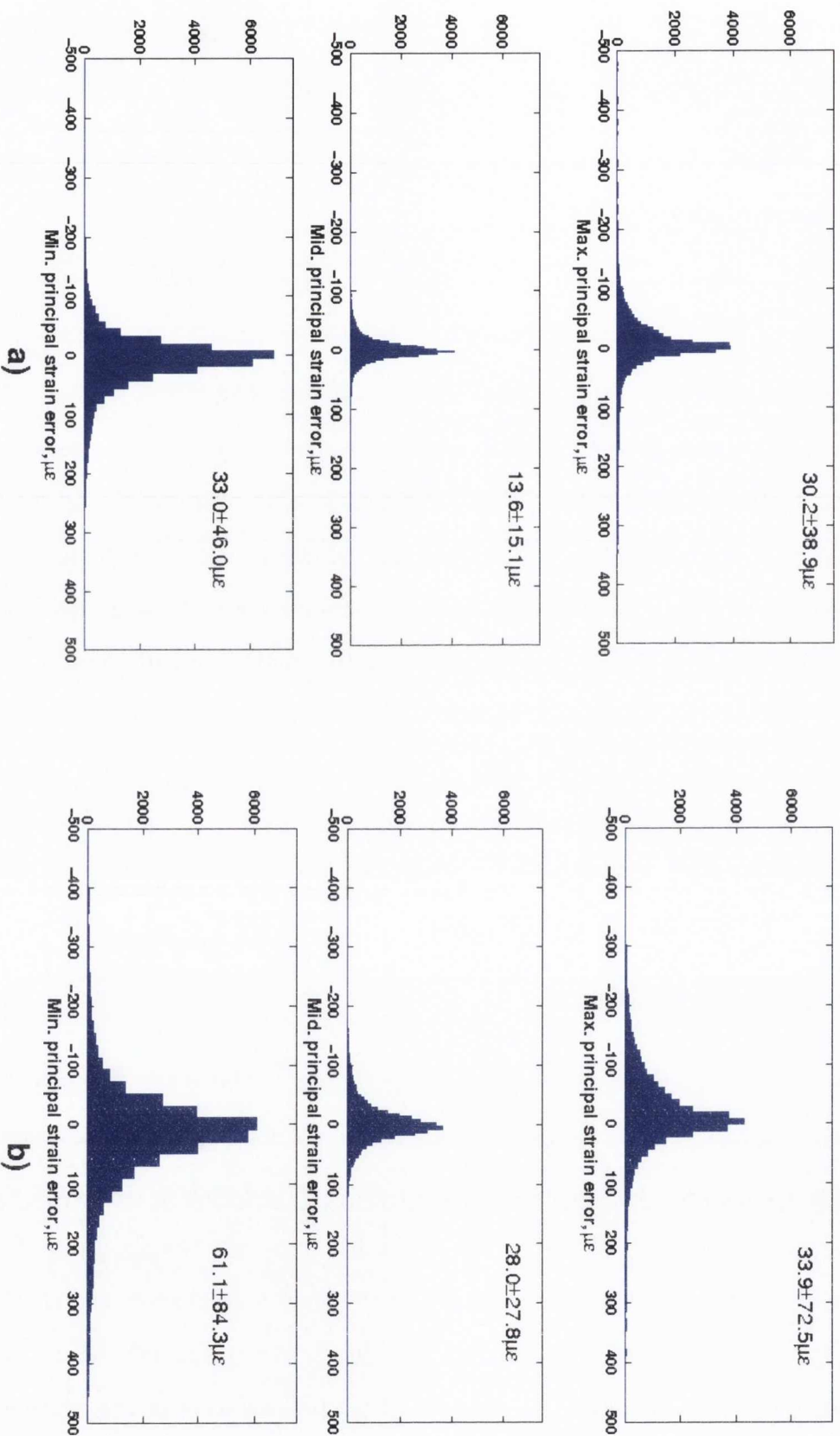


Figure 2.15: Error strain field histograms: a) reconstructed model; b) extrapolated; Text — absolute values of mean error, $\mu\epsilon$

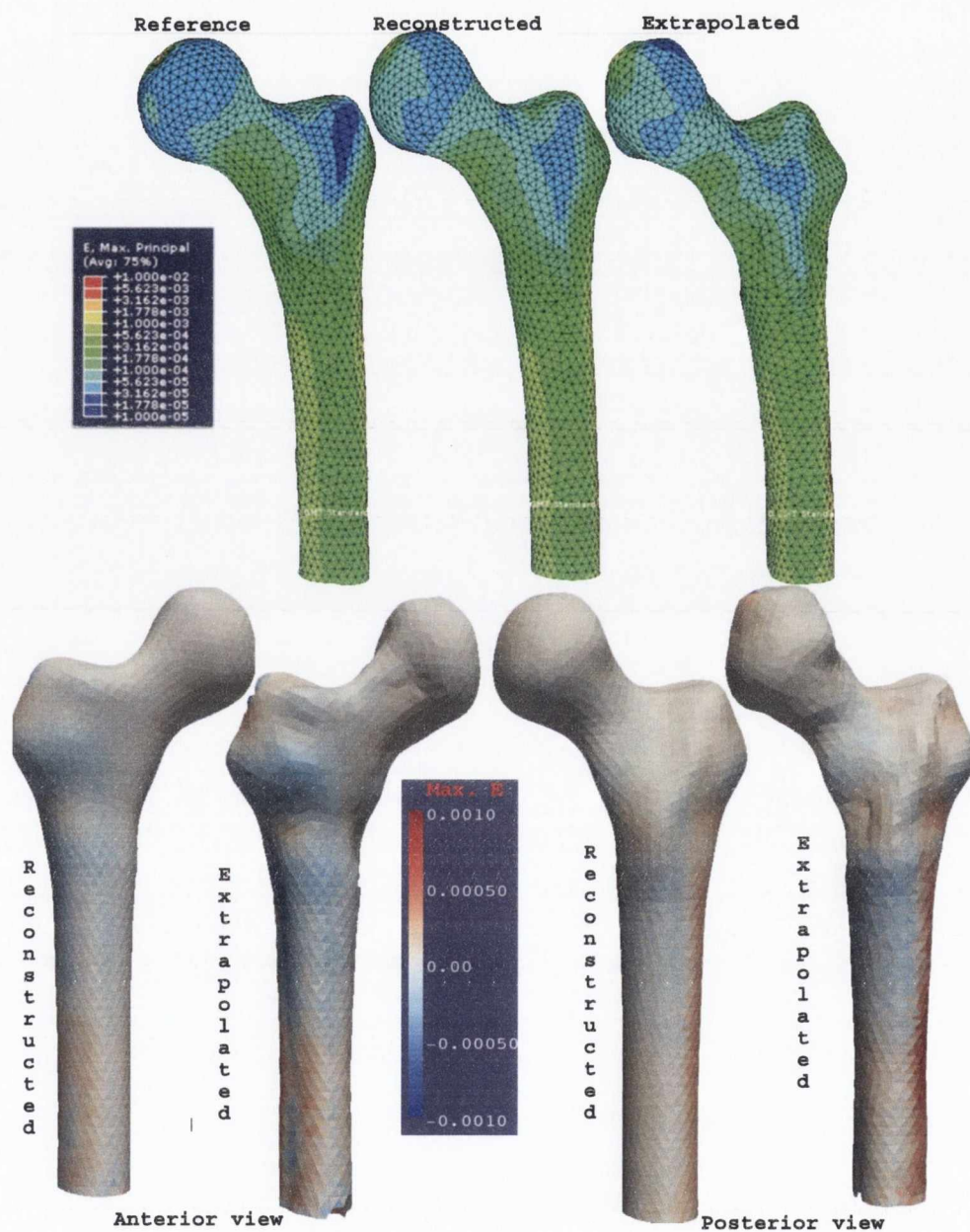


Figure 2.16: Strain and strain error contours: (top row) strains contours in reference, reconstructed, and extrapolated models; (bottom row) strain errors in reconstructed and extrapolated models

Results of the present study showed that the technique developed to automatically generate surface models from planar images was suitable to perform the task. An evaluation of the accuracy was carried out and showed that average surface distance error was equal to 3.04 mm; this stands in line with error magnitudes computed using other techniques, which were within the following range – 0.7-6.88 mm [30, 31, 32, 37, 36, 38]. However, an advantage of the current method is that it utilises a single planar radiograph to generate a surface model whilst for most of the other methods at least two or more radiographs were required. Another advantage of the technique is that it is fully automated and able to generate surface models rapidly. This can be used to process large amounts of X-rays to measure anatomical variations in proximal femur shape as well as pre-operative planning simulations.

Investigation of the influence of geometric error on mechanical strain in loaded bone showed that strain error growth is proportional to the surface error magnitude as expected. It also showed that change in precision up to the level of generated models does not change strain level dramatically (see Table 2.3, Fig. 2.15). Therefore, these models may be used to carry out patient-specific analysis with an estimate of the likely error when CT geometry is not available.

Possible limitations of this method are low-quality radiographs (e.g. if an uncalibrated X-ray machine was used to acquire images), artefacts generated by presence of metallic and other objects which may mislead the contour recognition technique. Also, femur shapes which are not covered by the adopted size distribution may lead to an increased geometric error - e.g. high-grade dysplastic femora or extreme dimensions for ethnicities/genders that were unlikely covered by the distribution table proposed by Noble *et al.* [12]. Furthermore, this technique does not allow reconstruction of the intramedullary canal of the femur as planar radiographs do not allow identification of intramedullary borders. Moreover, planar pelvic radiographs do not capture the 3-dimensional morphology of the greater trochanter region, in particular, the attachment location of the piriformis muscle, very well. Therefore, the current technique could be improved for reconstruction of this region. From the the surface error distributions of the matched CT-X-ray pairs, one notices that

the femoral head was a source of inaccuracy for the reconstructed geometry. If the femoral head was removed and distances were measured again, error magnitude decreased from 3.04 mm to 2.31 mm. Analysing visual results in Zheng *et al.* [37] and Barratt *et al.* [30] it is possible to notice similar problems. This may happen for various reasons, one of which is an insufficient resolution of either the CT image, e.g. large spacing in coronal plane, used to generate the reference model or the X-ray image. However, these surfaces may still be used for such applications as pre-operative patient-specific simulations of total hip replacements where the femoral head is being removed and replaced by an implant. Furthermore, for the current investigation only the most proximal part of the femur was used to validate the accuracy against the CT scans — it is expected that this region contains the largest errors from the reconstruction procedure, thus, making the erroneous part proportionally large compared to other investigations. For the FEA test, relatively simple boundary conditions and homogeneous material properties were used to perform the analyses. More accurate application of physiological loads may be required, e.g. better distributed muscle load (a patch instead of one node), a larger number of muscles and activities, and also realistic mechanical properties of the bone can improve the test. In spite of these limitations, this study shows that a patient-specific surface model can be reconstructed from a planar radiograph image when volumetric data is not available, and the geometry reconstructed can be used in a number of orthopaedic applications.

2.5 Conclusions

An automated method to create 3D surface models from planar radiographs was developed. This method proved to be fully automated, rapid and robust on a given set of radiographs. Measured mean surface distance error values were low and within ranges of similar studies. An advantage of the method compared to other existing techniques is that it requires less input data to perform the surface reconstruction task and is fully automated. Mechanical simulations of loaded bone with different levels of accuracy showed that an error in predicted strain fields grows proportion-

ally to the error level in geometric precision. In conclusion, models generated by the proposed technique are deemed acceptable to perform realistic patient-specific simulations when 3D data sources are unavailable.

Chapter 3

Automated method for patient-specific hexahedral mesh generation

3.1 Introduction

Recent advances in computer simulation have enabled engineers to predict the behaviour of objects and systems of widely different nature — e.g. from mechanical components to parts of the human body. Computer simulation has proven particularly useful for orthopaedic applications where it has been applied to areas such as pre-clinical evaluation of devices [51], pre-operative planning systems [52, 53], and biomaterials testing [54]. Potential benefits of computer simulation of biomechanical systems include decreasing the reliance on animals and humans for pre-clinical trials and simulating the outcomes of pre-operative plans to support surgical decision making. One of the bottlenecks in creating a pre-operative simulation system is the difficulty in generating patient-specific finite element models in a rapid and automated manner. Widespread adoption of computer simulation for such applications can only be achieved when reliable patient-specific meshes can be generated rapidly and with minimal human interaction.

Several studies have proposed automated and semi-automated approaches to generate subject-specific surface models of femurs from medical images (CT, MRI,

X-ray) [45, 55, 56, 57]. Due to the complex nature of generated geometries, meshing these models in an automated manner is a very challenging task. Implementations of tetrahedral and hybrid meshing schemes are commonly used for this purpose [58, 59, 60, 61]. However, using tetrahedral element meshes has some disadvantages. Linear tetrahedron elements produce larger errors in displacements in tasks where shear elastic-plastic deformations are dominant [62]. Moreover, when meshing a configuration consisting of several objects, e.g. a bone-implant system, linear tetrahedral elements may result in a jagged surface representation of the implant-tissue interface if too coarse a mesh is used (Fig. 3.1). Hexahedral meshes can often be smoother for an equivalent mesh density and therefore are preferable for solving contact problems and frictional debonding (Fig. 3.1). Furthermore, linear tetrahedra are considered to be too stiff and may produce inaccurate results [63].

Quadratic tetrahedra overcome many of the problems encountered with linear elements [64]; however, they are more sensitive to poor element shape, which may lead to inaccuracies and instability while modelling highly nonlinear material or geometric phenomena. Also, quadratic elements contain a larger number of degrees of freedom, which make them computationally more expensive than linear tetrahedral and hexahedra. Eight-noded hexahedra are considered a good alternative in many cases as they provide similar accuracy to quadratic tetrahedra, and can even out-perform them in some problems [62]. It has been shown that computational cost of models meshed using these elements is similar to one meshed with quadratic tetrahedral elements [65]. Quadratic hexahedra are considered to be even more robust but are more computationally expensive [63]. These factors have resulted in an ongoing demand for hexahedral meshes in many industrial applications.

It is possible to generate all-hexahedral FE meshes directly from volumetric medical images, e.g. CT, MRI. Keyak *et al.* [25] proposed an automated technique to generate cube-shaped element FE meshes from CT scans. However, surface representation of these voxel meshes is poor and, thus, not suitable for modelling of interfaces. Several automated methods for generating all-hexahedral meshes from 3D geometries have been developed [66, 67, 68, 66, 69, 70, 71, 67]. The Whisker-

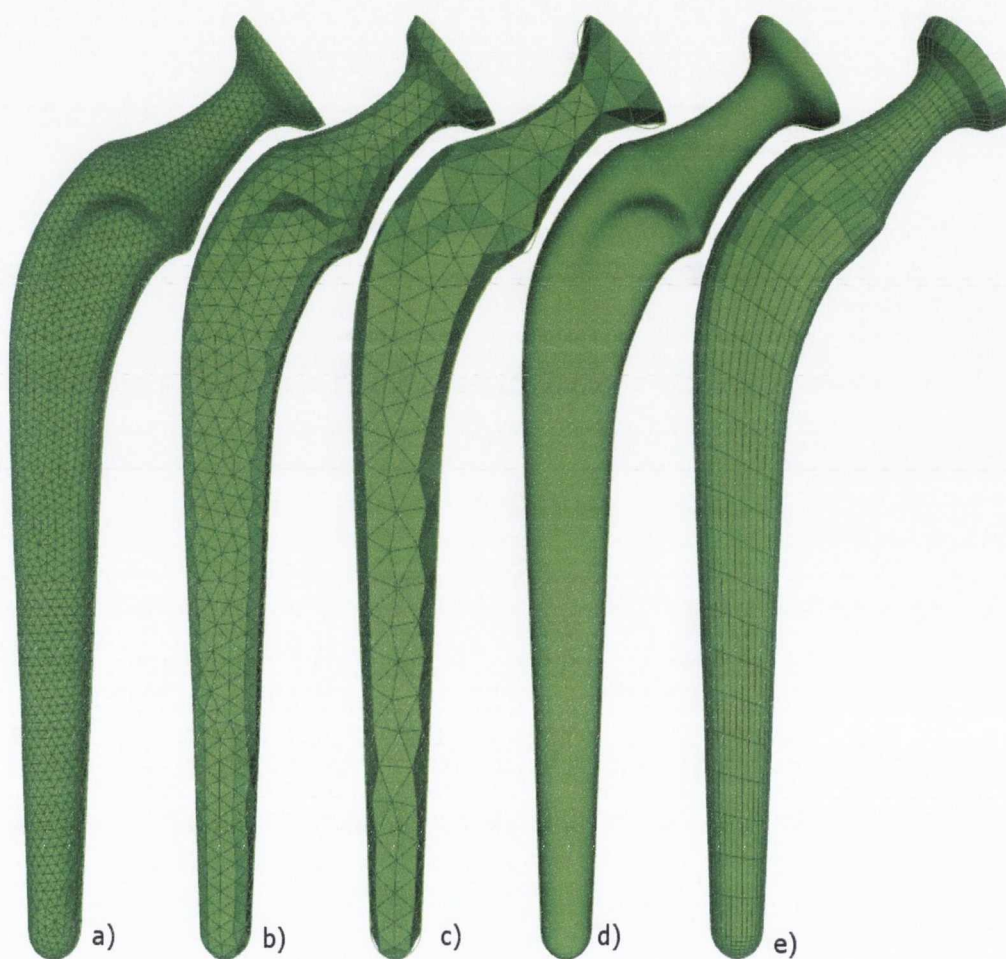


Figure 3.1: Example of different meshing schemes: tetrahedra-meshed implants [different element size level: 1.5 mm (a), 3 mm (b), 6 mm (c)], original CAD model (d), and hexahedra-meshed implant (e)

weaving algorithm [69] starts from a quadrilateral surface mesh and advances into the solid, constructing hexahedral elements based on dual entities. Grid-projection based algorithms [72, 66] provide the flexibility to generate a conforming mesh (i.e. one which shares nodes at interfaces) for a system of objects. This is possible due to the nature of the algorithm: first, a grid containing the object being meshed is generated, and then the free nodes are projected to the faces of the object using a set of rules. Alternatively, Couteau *et al.* [70] proposed an approach to morph an existing source mesh using octree-splines into a target shape. This approach is capable of generating smooth surfaces. However, it is not widely available and needs to be modified to be applicable to a system of objects. Similar morphing approaches were proposed by Baldwin *et al.* [71] and Bah *et al.* [73] (tetrahedral mesh) using different morphing methods. Grosland *et al.* [67] developed a semi-automated platform to mesh anatomic objects with all-hexahedral meshes based on surface parameterization; however, it requires manual assignment of the blocks to be meshed. In summary, there are several methods capable of meshing patient-specific shapes; however, some are oriented for meshing a single object or meshing a system of bodies independently, i.e. resulting meshes may not be coherent. Matching nodes on master and slave surfaces allows selection of larger number of contact algorithms, which can improve efficiency of the modelling. Thus, there is a need for a fully automated method to generate high quality meshes for systems of highly irregular objects in a controllable way (e.g. with node-to-node correspondence).

This study proposes an automated technique to mesh a complex irregular geometry consisting of a patient's femur and an implant. It provides flexibility to preserve important mesh features, such as: desired element type, a smooth surface representation of the prosthesis interface (See Fig. 3.1,e), predefined node- and element-sets, and controllable mesh densities at chosen locations.

3.2 Methods

A C++ class based on the Visualization Toolkit (Kitware Inc., NY, USA) was created in order to generate finite element (FE) meshes in an automated manner.

The eight-noded hexahedron was chosen as the target element type because of its robustness and as well as being a strong test of the algorithm's performance because of the difficulty in generating all-hexahedral meshes. The method is based on parameterization of exterior surfaces of the generic mesh and target 3D model. Parameterization approaches enable morphing of a 3D object into another object of similar morphology and have been widely adopted for such tasks [74]. A generic mesh of an implant and an artificial femur are transformed using a displacement controlled finite element analysis to fit the geometry of the patient and position of the prosthesis selected by an operator (Fig. 3.2). For these purposes the generic femur mesh was parameterized using 2 parameters. In order to minimize displacements, the composite generic mesh is rigidly transformed such that the surface of the implant mesh within the generic femur would coincide with the surface of the prosthesis positioned by the operator. Using the aforementioned parameters, target nodes on the extra-cortical surface of the patient's femur are then found while the surface of the implant is constrained to keep node-to-node correspondence with the interior surface of the femur mesh. Warping is performed by means of solving a displacement controlled finite element analysis using the commercial software Abaqus (Dassault Systemes Simulia Corp., Providence, RI, USA). Mesh smoothing is performed on the resulting mesh using the Mesh Quality Improvement Toolkit [75]. The following sections describe the main steps of the algorithm in more detail.

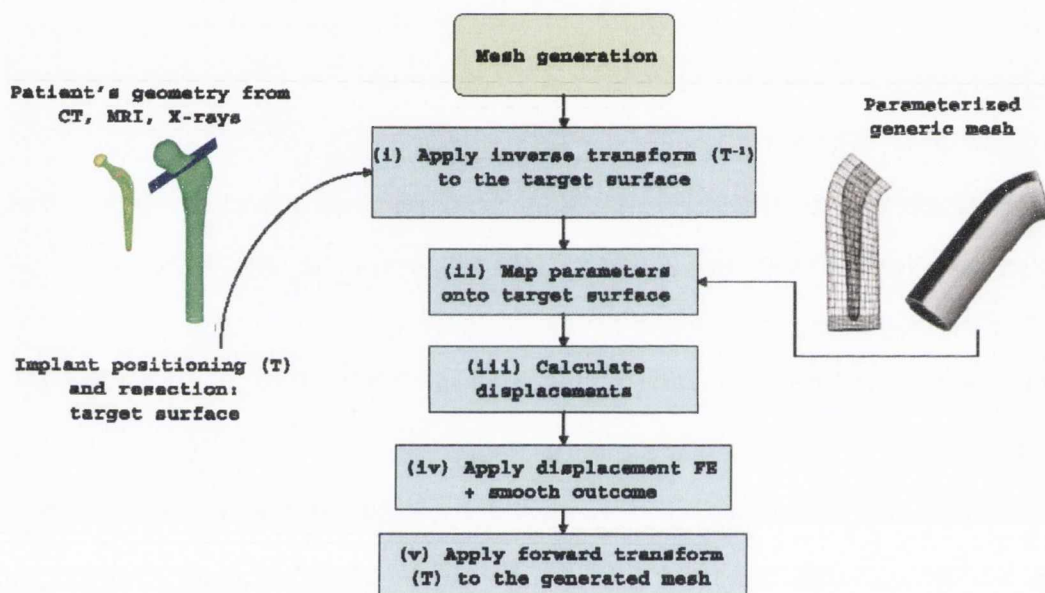


Figure 3.2: Mesh generation scheme: the implant is positioned by an operator, the femur resected, and the extracortical surface used to create the mesh using previously generated and parameterized generic mesh

3.2.1 Generic mesh

Generic meshes were created using Cubit (Sandia National Laboratories, New Mexico, Albuquerque). Existing 3D CAD models of three flanged Charnley prostheses (standard, extra-heavy and long-neck) were used to calculate curves following the middle of the stem when moving from proximal to distal. Medial and lateral curves (CAD implant models) were meshed using the same number of nodes. Segments connecting corresponding nodes were built. For each segment a middle point was computed. A set of mid-points then was connected into a curve, the mid-curve. For each implant an ellipse with 22 mm greater radius and 16.5 mm lesser radius was swept along the generated mid-curve to create the generic bone geometry. These swept geometries were resected below the tip of the implant and at the collar (Fig. 3.3). All-hexahedral meshes were then generated for the implants and the artificial bone.

Four nodesets were defined for the external nodes of each generic mesh for the parameterization and warping procedures: extracortical surface, top surface, bottom surface, and implant surface (See 3.3,(b,c,d,e)). These nodesets are used to define boundary conditions in the displacement controlled FE simulation.

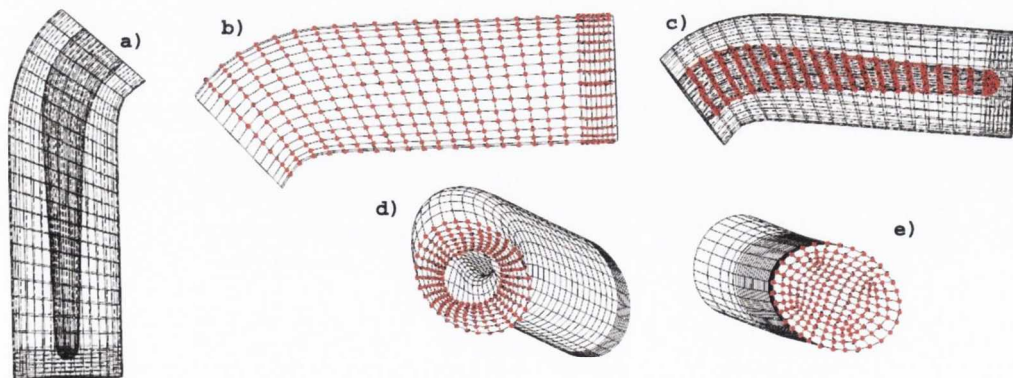


Figure 3.3: Generic mesh for standard Charnley: (a) artificial femur geometry with the implant inside meshed using hexes, (b) extracortical nodeset, (c) implant surface nodeset, (d) top surface nodeset, and (e) bottom surface nodeset

3.2.2 Generic mesh parameterization

Extracortical surface

To parameterize the extra-cortical surface of the generic mesh, 2 parameters specific to this surface were introduced. For each node on the extra-cortical surface, it is possible to build a plane which would pass through an intersection line of the planes used to resect the artificial femur. Therefore, the first parameter, t_1 , is defined by:

$$t_1 = \frac{\alpha_{node} - \alpha_{bottom}}{\alpha_{top} - \alpha_{bottom}} \quad (3.1)$$

where α_{node} is an angle between the bottom plane and a node plane and $\alpha_{top} - \alpha_{bottom}$ is the maximum possible angle (Fig. 3.4).

To calculate the second parameter, a contour of the generic mesh located on a node plane is calculated. This contour is a planar ellipse with respect to the centre of mass. Therefore, a ray from the centre of mass to the parameterized curve and a reference ray can define an angle, ranging from 0 to 2π depending on the orientation of the chosen ray. The reference ray is given by a vector parallel to one of the unit vectors. Hence, the second parameter, t_2 , is described by:

$$t_2 = \frac{\beta}{2\pi} \quad (3.2)$$

where β is an angle between the reference ray and a ray through the node (Fig. 3.5).

Top and bottom surfaces

These two surfaces are both planar and convex. Consequently, a first parameter for both of them is defined in a similar manner as parameter t_2 for the extracortical surface nodeset (Fig. 3.6(a,b)).

The second parameter is calculated using radial distance from the mass centre

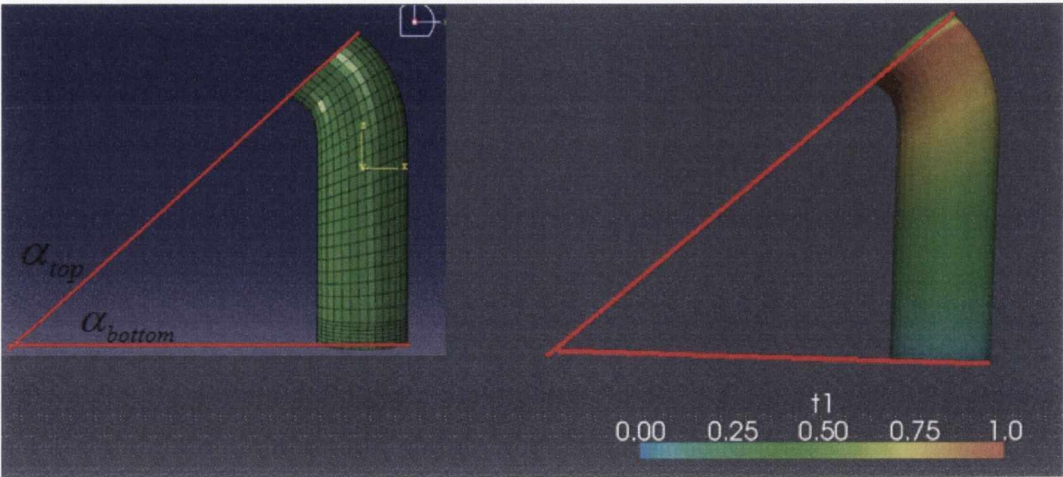


Figure 3.4: t_1 parameter for extracortical surface: (left) top and bottom planes, (right) parameterized surface

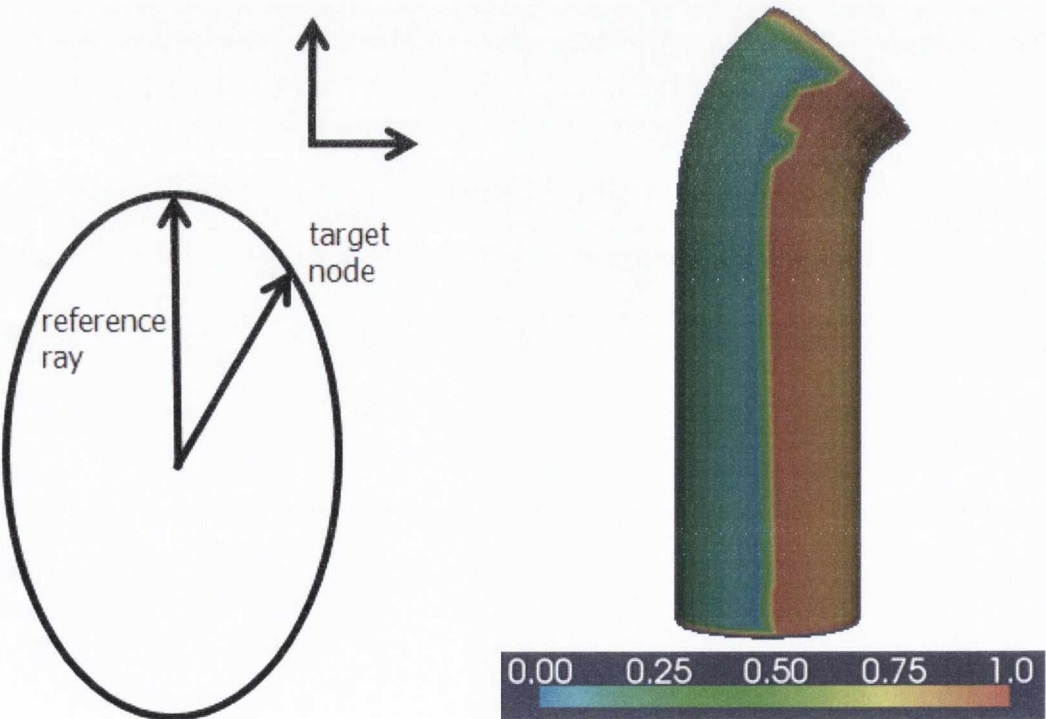


Figure 3.5: t_2 parameter for extracortical surface: (left) schematic explanation, (right) parameterized surface

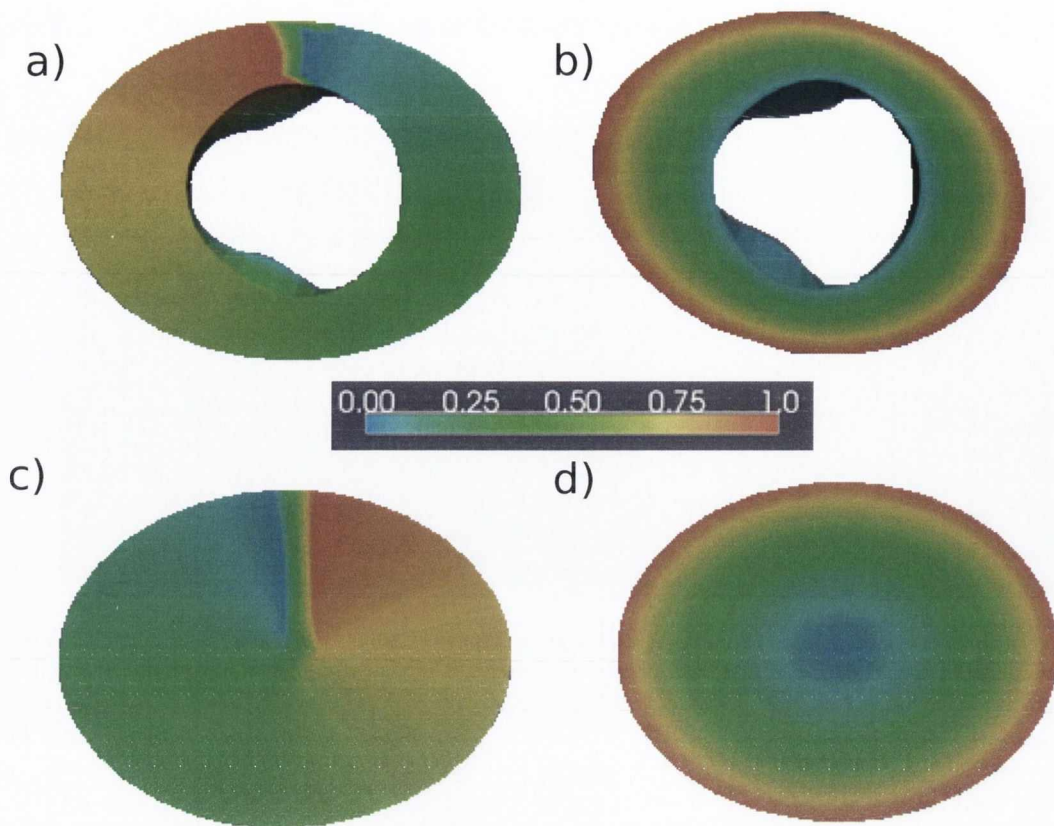


Figure 3.6: t_1 parameter for top (a) and bottom (c) surfaces, t_2 parameter for top (b) and bottom (d) surfaces

to the node. In case of the top surface, it is a proportion defined by Eq. 3.3:

$$\acute{a}_2 = \frac{R_{node} - R_{inner}}{R_{outer} - R_{inner}}, \quad (3.3)$$

where R_{node} is a radial distance from the mass centre to the node, R_{inner} is a radial distance from the mass centre to the implant curve and R_{outer} to the extracortical curve. For the bottom surface R_{inner} is constant and equals to 0 (Fig. 3.6(c,d)).

3.2.3 Parameterization of target surface model

The input for the mesh warping procedure is a surface which represents the patient's proximal femur resected at the isthmus region and at the neck/greater trochanter region as selected by an operator. The prosthesis must also be positioned within this geometry. This can be achieved using existing computer assisted pre-operative planning systems. As mentioned earlier, the entire system must be rigidly transformed to minimize final displacements so that the prosthesis coincides with the

generic prosthesis mesh.

To set up a displacement controlled FE simulation, target points need to be found for the nodes on external surfaces of the generic mesh. Parameters calculated in the previous section are used to locate destination nodes. The reverse parameterization procedure is applied to compute the displacements required for warping.

Extracortical surface

Planes which were used to resect the patient's femur define a maximum possible angle similar to the parameterization procedure. Using parameter t_1 a plane containing a target point can be built. This plane contains a 2D contour of the patient's femur. Mass centre is calculated for this contour. A ray which starts at the mass centre and makes an angle β (calculated from parameter t_2) with the reference ray (Fig. 3.5) hits the contour at the required point.

Top and bottom surfaces

Similar to the parameterization procedure, the mass centre of the outer curve is calculated for the bottom surface, a ray corresponding to angle β calculated from t_1 defines a point on the outer curve. The target point will be located on the resulting segment, i.e. mass centre to a point on the curve. A proportional parameter t_2 is used to define distance on the segment from the mass centre.

For the top surface the approach for finding target points is slightly different. Instead of calculating the mass centre of an outer curve, the positioned implant is cut using the planar top surface; this is needed because this surface does not necessarily coincide with the plane of the implant's collar. Then the mass centre of the resulting contour is calculated. A ray fired from this mass centre using angle β intersects the implant curve and also the outer curve. Proportional parameter t_2 gives the location of the target point on the segment defined by the intersection of the ray with the implant and outer curves.

3.2.4 FE morphing

An Abaqus input file is generated for the warping procedure with a boundary section containing X, Y and Z displacements for each node of the parameterized surfaces. The implant surface is rigidly constrained and, therefore, no contact algorithm was employed as the surface mesh remains the same. Two element layers are defined for the surface elements forming the extracortical and implant surfaces respectively. Two types of material properties are assigned to this model. Young's modulus of 13,000 MPa is assigned to the surface element layers mentioned above, and the rest of the elements have Young's modulus of 10,000 MPa. Such an assignment prevents sensitive surface elements from collapsing due to the movement of the mesh. Poisson's ratio is constant for the entire model and equals 0.3. Magnitudes for mechanical moduli were chosen to provide desired constant element density in the resulting mesh. Displacements are requested in the output section of the file. Once the input file has been generated an automated script calls Abaqus to solve this FE problem. The resulting file contains computed displacements for every node of the generic mesh and these displacements are used to update the mesh.

3.2.5 Mesh smoothing scheme

A C++ based program is called after mesh generation to smooth the mesh. Mesquite (Mesh Quality Improvement [75]) was utilized to implement the smoothing algorithm. The nodesets defined previously (Fig. 3.3) are used to define surfaces in the generated mesh — the extracortical surface is smoothed using a Winslow smoothing scheme [76], then the bottom and top surfaces are processed using a Mean Ratio scheme [77], after that the entire femur mesh is smoothed using a volumetric Mean Ratio smoothing algorithm [77].

3.2.6 Tests

Robustness

In order to demonstrate the capabilities and verify the robustness of the mesh generation technique, a number of cases for three femora were meshed. Each set consisted of three flanged Charnley prostheses in seven positions per prosthesis. Generic femur meshes for the following prostheses were developed: standard flanged 40 Charnley (F40), extra-heavy flanged 40 Charnley (F40EH), and long-neck long-stem flanged 40 Charnley (LNLS). Three publicly available CAD femur models from the Living Human Digital Library (www.biomedtown.org — the Standardized Femur [44], the third generation femur [78], and the Visible Human femur [79]) were used to perform virtual surgeries. For each combination of the femur and prosthesis, seven meshes were generated — a reference position and six deviations. The reference position of the implant was achieved by placing the implant according to standard templating procedure. Six deviations were rotations (1° or smaller, subject to the size of the femur) about the following axes: anterior-posterior, proximal-distal, and medial-lateral. Total number of meshing scenarios was 63 (3 femora, 3 implants, 7 positions).

For each generated combination, mesh quality assessment was performed on the resected femur mesh; this was not needed for the implant mesh as it remains the same and subject to the initial state. Metrics chosen to analyze the mesh quality were: scaled Jacobian, hexahedron shape, and skew metrics [80]. All these metrics are based on calculation of a Jacobian matrix for each element of the mesh. In turn, the ‘Jacobian’ matrix (Eq. 3.4) and its determinant α_k are computed for each k^{th} node of the element [80].

$$J_k(x_k, y_k, z_k) = (-1^k) \times \begin{pmatrix} x_{k+1} - x_k & x_{k+2} - x_k & x_{k+3} - x_k \\ y_{k+1} - y_k & y_{k+2} - y_k & y_{k+3} - y_k \\ z_{k+1} - z_k & z_{k+2} - z_k & z_{k+3} - z_k \end{pmatrix} \quad (3.4)$$

Eight additional symmetric matrices (the ‘metric’ tensors) are computed by form-

ing combinations $J_k^T J_k$. Let $\lambda_{ij}^k, i, j = 1, 2, 3$, be the ij^{th} component of the k^{th} metric tensor. The shape metric f_{shape} can be described:

$$f_{shape} = \frac{24}{\sum_{k=0}^7 (\lambda_{11}^k + \lambda_{22}^k + \lambda_{33}^k) / (\alpha_k^{2/3})}, \quad (3.5)$$

where f_{shape} equals to 1 in case of the cube shape, and 0 if the hexahedron is degenerate. And the skew metric is defined by Eq. 3.6:

$$f_{skew} = \frac{8}{\sum_{k=0}^7 ((\sqrt{\lambda_{11}^k \lambda_{22}^k \lambda_{33}^k}) / (\alpha_k))^{2/3}}, \quad (3.6)$$

where f_{skew} is 1 when the hexahedron is a right parallelepiped, and 0 when it is degenerate.

Finally, scaled Jacobian is the minimum Jacobian divided by the lengths of the 3 edge vectors.

Comparison to existing morphing techniques

An attempt was made to generate an all-hex mesh by morphing the generic mesh of the standard Charnley implant into a prepared CAD model (a reference implant position in the Standardized Femur) using a mesh morphing algorithm available in Cubit. Meshing time was recorded and compared to the current technique. A ‘‘Copy/Morph’’ meshing scheme [81] was used; reference entities were the top surface of the generic mesh and the curve defined by intersection of the implant and the surface.

3.3 Results

The proposed algorithm successfully meshed 61 out of 63 scenarios. An average time to parameterize the target surface was approximately 2 seconds for the generic mesh with ~ 6400 elements. An average time to solve the displacement controlled linear-elastic FE task (~ 7566 nodes, ~ 6400 elements) was 33.5 seconds, of which, actual analysis took ~ 19 seconds on Intel(R), Pentium 4 CPU, 3.00 GHz with 1Gb

RAM. Smoothing time varied from less than a second to maximum allowed time (20 minutes). Smoothing time reached the maximum value when a thin wall was observed in the proximal extracortical regions (see Fig. 3.7). Element quality of the generated models were within acceptable limits for the majority of elements with only a few below the minimum threshold (Table 3.1 + Fig. 3.8)

The technique failed to mesh the following scenarios: anterior deviation from the reference position (the Standardized Femur + LNLS) and posterior deviation (the Visible Human femur + F40) (see Fig. 3.7). Minimum value of J_{scaled} for the generated meshes was observed in the Standardized Femur + LNLS implant, varus deviation.

Cubit failed to warp the hexahedral generic mesh according to the desired surgical plan. It successfully meshed exterior surfaces with quadrilaterals: top, bottom and extracortical, but not the implant surface. The implant surface became distorted and the mesh was not usable. The total time taken to generate this mesh was more than 30 minutes.

3.4 Discussion

The proposed technique was robust and produced good quality meshes with few, if any, poorly shaped elements. It was successfully applied to 61 out of 63 scenarios. An average hexahedral element quality, measured using scaled Jacobian, was 0.7446 ± 0.1730 and minimum value was 0.1099. An automated mesh generation toolkit (Cubit) failed to mesh a similar scenario.

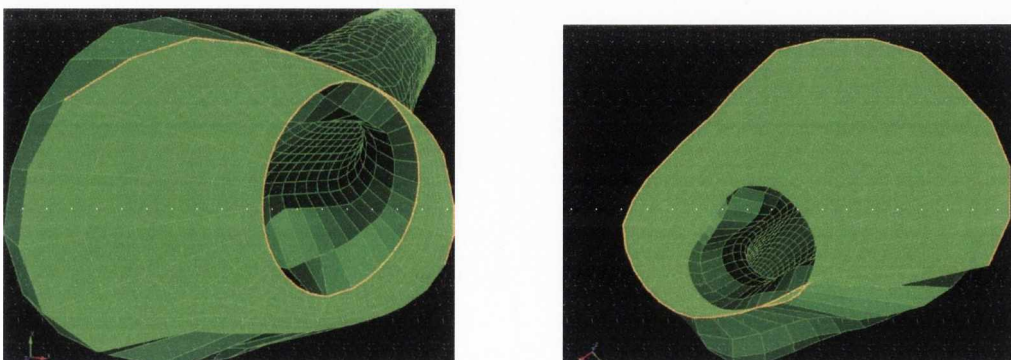


Figure 3.7: Failed scenarios: thin wall and curve intersections

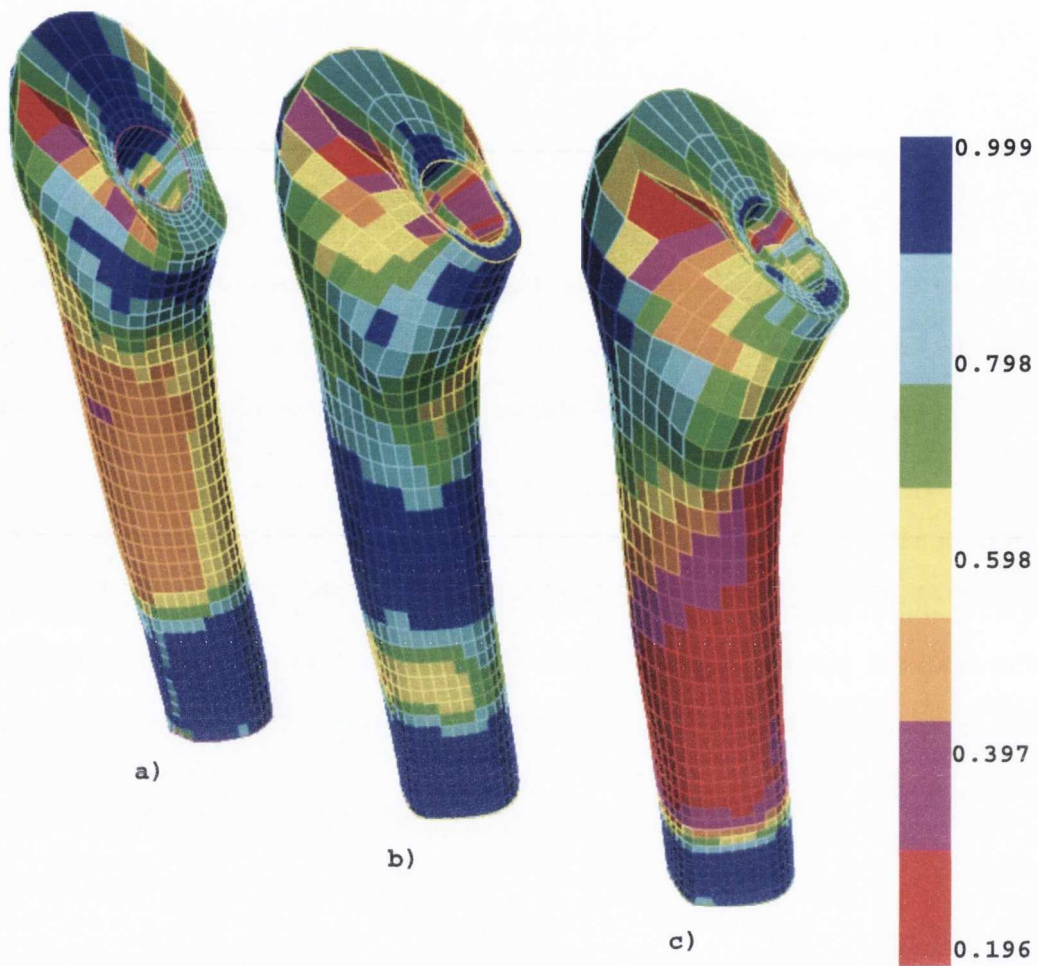


Figure 3.8: Generated meshes for 3rd generation composite femur: (a) F40, (b) F40EH, and (c) LNLS. All prostheses are in a reference position. Scaled Jacobian is represented by the colours. Only 1 element was below 0.2 threshold value.

Table 3.1: Overall element quality statistics on generated meshes: mean, standard deviation and minimum

Metric	J_{scaled}	f_{shape}	f_{skew}
$\bar{x}$	0.7446	0.5664	0.4633
σ	0.1730	0.1850	0.2433
min	0.1099	0.0094	0.0020

Investigation of the failed scenarios revealed that the curves defining the top surface (the implant and the outer curve) were intersecting or a very thin layer was observed (Fig. 3.7). It was impossible to mesh such scenarios using an all-hexahedral strategy; however, these can be described as unrealistic, i.e. such scenarios are not likely to occur during a real joint replacement procedure. Furthermore, cases where thin walls were observed normally had lowest quality metrics as expected. A similar finding (increased number of elements violating quality criteria) can be observed in Bah *et al.*, Figure 2,a [73]. Therefore, this technique is limited to good initial geometry, i.e. the implant stem should intersect just the top surface and be separated from the extracortical surface by a layer, allowing introduction of a few radial elements (the cortical bone). Extended data on the quality of generated meshes is available in Appendix A. Another limitation is that this technique was tailored specially for the task of meshing a femoral implantation scenario. However, possible modifications of this technique to be applicable to a different scenario are intuitive.

One of the main advantages of the current technique is that it is independent of element type choice, i.e. a tetrahedral, hybrid or any other element type can be used to create a generic mesh, the only requirement is to use a corresponding smoothing scheme. Another advantage is that this technique is fully automated and does not require manual intervention. Moreover, this method is insensitive to poor input surfaces, i.e. it will connect closest vertices on the surface to generate a final mesh. Furthermore, this method managed to handle flanged geometry of Charnley prostheses, which includes tangential surfaces and irregularities, which typically become obstacles in the task of all-hexahedral mesh generation. Application of the method to different types of implant (e.g. Exeter, roundback Charnley, Muller Straight, etc) can potentially produce meshes of better quality.

The method itself and its modifications are applicable in a large range of problem-specific applications, e.g. population-based device testing using FEA or patient-specific pre-operative planning, where a family of similar FE meshes is required. Additionally, a similar approach could be used to generate FE meshes of other

joints with intramedullary implants, for instance in the upper extremity, and other systems with a nested configuration. Furthermore, parameterization schemes used in this study can be used in a variety of tasks. For instance, an FE mesh of blood vessels can be easily generated using a similar approach — inner and outer surfaces need to be parameterized and then warped using an FE scheme.

Selecting a better combination of smoothing schemes and warping methods can improve the quality of the generated mesh, reduce the overall time for mesh generation and overcome some limitations. For instance, different type of morphing approaches can be applied for the warping part of this algorithm instead of or combined with FEA, for instance, octree-splines [70], thin-plate splines [82], non-uniform rational B-splines (NURBS) [83], analytical and landmark-based transforms [84], spline combinations [85], etc. The thin wall limitation can be solved by introduction of an additional generic mesh with lower numbers of radial elements or an alternative mesh topology in the problematic region. However, additional investigations are needed to estimate applicability of this method to other types of FE elements. Also, performance of generated meshes needs to be verified against alternative approaches.

To summarize, this method indicates that an approach to generate problem-specific FE models based on manually tailored generic meshes can produce high-quality meshes, be easily modified for a particular task, and be fully automated.

3.5 Conclusion

An automated method to generate case-specific FE meshes for an implant within a proximal femur was developed. This method proved to be fully automated, rapid, and robust on a given set of surgical scenarios. The lowest scaled Jacobian value was 0.1099 and overall quality can be described as $J_{scaled} = 0.7446 \pm 0.1730$. Minor limitations do not allow this method to mesh geometries with extremely thin walls, which are not likely to appear in real applications in any case. However, in general, this method performed well and is applicable in a wide range of patient-specific applications. Modifications of the method can potentially be applied to more complex objects.

Chapter 4

Probabilistic FE method for analysis of case-specific factors

4.1 Introduction

Probabilistic approaches to model failure in many engineering applications are becoming more common. In fact, in some engineering fields, such as biomechanics, where experimental investigation is expensive or unfeasible, a probabilistic approach may significantly reduce cost and enable pre-production evaluation, e.g. mechanical testing of orthopaedic devices [86, 87]. However, developing a framework for probabilistic failure analysis requires incorporation of many complex processes and coverage of a wide range of input parameters, some of which may not be intuitive. Each process within such a framework can be a complex task to implement in itself. Traditionally, to perform a probabilistic analysis researchers try to expand existing deterministic schemes to account for a variety of input values, i.e. varying load magnitudes, mechanical moduli, etc [88]. However, it is difficult to include the geometric variance of an implant and bone along with human-dependent factors, e.g. an implant positioning in a surgical theatre, in such schemes. A framework, which allows for geometric variance would, therefore, undoubtedly be of use for many tasks in biomechanical research.

Several studies have used probabilistic methods to investigate joint replacement performance. For example, Dopico-Gonzalez *et al.* [88] reviewed a number of prob-

abilistic approaches to model cemented and uncemented THR, and also total knee replacement (TKR). An approach to handle variability of knee implant positions was proposed by Laz *et al.* [87] using Monte Carlo simulations in combination with an Advanced Mean Value method (AMV). However, this study did not account for variability of patient geometry and implant design. Perez *et al.* [89] analyzed influence of the design of four different implants on debonding processes in THR using a stochastic approach based on a cumulative damage predictive B-model. Similar to the previous study, this investigation did not account for variability of patient geometry; furthermore, implant positions were not investigated. A simplified 2D FE model of a cemented THR (implant positions) combined with a Response Surface method (RSM) was adopted by Bah and Browne [90]. Monte Carlo simulations were used by Viceconti *et al.* [91], who investigated influence of the host bone size (rigid scaling), along with traditional parameters, on the primary stability of uncemented hip replacements. Dopico-Gonzalez *et al.*, in three different studies, looked at the variability in mechanical moduli of the stem and bone, as well as load magnitude and direction by means of Monte Carlo simulations with different sampling strategies [88]; similar parameters plus anteversion of the prosthesis [92]; and variable positions of 2 different implants (Proxima and long-stem IPS) in 3 different femora [93]. However, the first two models did not include inter-patient bone geometry variability and difference in implant designs. Although the third study used several femora and 2 implants, only implant position and loading related parameters were treated as random variables.

Realistic simulation of biomechanical models can be computationally expensive. For instance, Dopico-Gonzalez *et al.* [88] reported that their Monte Carlo simulations based on a linear-elastic FE analysis took 1 hour 37 minutes for 1,000 samples, 3 days for 10,000 simulations, and so on. Viceconti *et al.* [91] performed 1,005 simulations and the required time was approximately 350 hours (P4 CPU, 2GHz). The computational time can grow dramatically with the addition of non-linearities to the simulated model. Furthermore, investigation of the behaviour of a complex time-dependent failure scenario, such as aseptic loosening in THR, relies on repetitive

subsimulations to mimic long time periods of patient activity. This restricts the applicability of many failure modelling algorithms even more. Thus, issues related to computational time need to be resolved if realistic simulation of the performance envelope of medical devices is to be achieved.

This chapter addresses the problem of developing a probabilistic framework to model failure due to aseptic loosening in total hip replacement. Response Surface Methods are used to enable Monte Carlo simulations incorporating variability in both patient-specific and inter-patient factors. Particular attention is given to simulating variability in *patient-specific geometry*, *prosthesis design*, and *implantation position*. The framework also allows inclusion of traditional parameters, such as body weight, load magnitudes and directions, material properties, etc. The latter however have been widely investigated before, and, thus, this study focuses on the former variables to demonstrate capability of the framework. The potential of the technology is demonstrated using two scenarios: (i) a patient-specific pre-operative analysis, and (ii) a population-based implant performance comparison.

4.2 Methods

4.2.1 Failure model for aseptic loosening

A Finite Element (FE) model was chosen to be the basis for modelling failure of THR. It has been shown by Lennon *et al.* [94] that predictive long-term FE simulations based on mechanical failure of bone cement in a replaced joint can be used to assess risk of revision due to aseptic loosening. The predictive capability of this technique was confirmed by means of a retrospective study. This failure modelling scheme was adopted as part of the present framework. A brief explanation of the deterministic aseptic loosening algorithm developed by Lennon *et al.* [94] is given as background.

In order to simulate aseptic loosening in THR a bone cement damage accumulation scenario [1] was employed. Bone cement behaviour was simulated by computing creep deformation and fatigue damage accumulation. Creep growth was calculated

using a Maxwell creep model [95]. Damage accumulation calculation was based on an anisotropic continuum damage mechanics formulation [96]. Additionally, interfacial fatigue was modelled using an adaptation of a shear fatigue model proposed by Perez *et al.* [97] to include tensile fatigue. Loading is repeated over time and high stresses in the cement and at the prosthesis interface induce microcracks, creep deformation, and interfacial debonding, causing degradation of the material properties which, in turn, results in prosthesis migration over time.

All simulations were carried out using MSC.Marc (MSC Software, Inc., USA) on a high-performance computer (SGI Altix 350, 32×1.5 GHz Itanium 2 CPU, 128 GB RAM, Linux 2.4 kernel). Python scripts were utilized to set up FE models in a semi-automated manner and Fortran user-subroutines implemented the aseptic loosening algorithm (courtesy of Dr. Alexander B. Lennon). Case-specific FE meshes were obtained using an automated mesh generation technique previously developed (Chapter 3). Material properties were considered to be constant and the following mechanical moduli were assigned: stainless steel ($E = 210$ GPa, $\nu = 0.33$) — implant, bone cement ($E = 2.28$ GPa, $\nu = 0.3$), cortical bone (longitudinal elastic modulus 17 GPa, transverse — 11.5 GPa, longitudinal shear modulus of 3.3 GPa, longitudinal transverse Poisson's ratio of 0.46 and transverse component of 0.58) [98]. Cancellous bone was assumed to have an apparent isotropic modulus of 1.5 GPa and Poisson's ratio of 0.33 [94]. Cement material properties were assigned to integration points based on results of a ray-tracing test with a superimposed surface mesh of the cement mantle [99]. The cement mantle was assumed to be slightly larger than the stem of an inserted implant and have a space about 10 mm distally from the prosthesis tip. Simplified muscle loads [100] were applied to simulate both walking and stair-climbing for a duration of 1 year on a per-week basis, i.e. 52 weeks for each activity. For each week two steps, walking and stairclimbing, of FE analysis were performed. For each activity the system was loaded to reach the maximum muscle-induced forces, allowed to creep, and then all of the loads were removed (see Fig. 4.1, a). The cement fatigue was modelled as a quasi-static process.

For a particular patient muscle (gluteus maximus, vastus medialis, vastus lat-

eralis) attachment locations were identified by performing a landmark transform. The Muscle Standardized Femur [101] was used as a source of muscle attachment patches. Each muscle was characterized as a centroid of the muscle attachment patch. Then these points were located on the patient's femur surface using the *vtkLandmarkTransformFilter* C++ class available within the Visualisation Toolkit (VTK) (Kitware Inc., NY, USA). The muscle loads were distributed to several closest nodes on the surface of the target mesh. The femur was restrained at the isthmus point. The joint load was applied to a node found on the surface of the implant head mesh. All load magnitudes were proportional to the patient body weight [100], which was assumed to be constant for all patients and was equal to 70 kg. Probability of failure, similar to Lennon *et al.* [94], was assumed to be proportional to migrations of the implant due to the walking and stair-climbing activities, e.g. end of the implant migration curves for each activity were taken as the numeric description of the failure (see Fig. 4.1, b).

4.2.2 Probabilistic scheme

In order to perform stochastic simulations explanatory and response variables need to be defined. For this study, case-specific scenarios were defined by combinations of patient geometry, implant choice and implant position. Only the proximal part of the femur was used for this study and patient geometry was described by three values: medial-lateral width of the femur at the isthmus (W_i , Fig. 4.2(a)), medial-lateral width at the lesser trochanter area (W_{lt} , Fig. 4.2 (a)), and the distal border of isthmus (L_i , Fig. 4.2 (a)). Implant design was described quantitatively as the implant head offset (L_{offset}), stem cross section diameter (D_{cs}), femoral neck angle (α_{neck}) and length of the stem (L_{stem}) (Fig. 4.2,(b)). CAD models created by means of reverse engineering were measured to obtain these parameters.

Implant position was defined as a deviation from a reference position achieved by means of standard templating in the medullary canal. For the deviations, the tip of the implant was restrained at one node and rotations were applied about anterior-posterior (AP) — α , medial-lateral (ML) — β , and proximal-distal axes (PD) — γ .

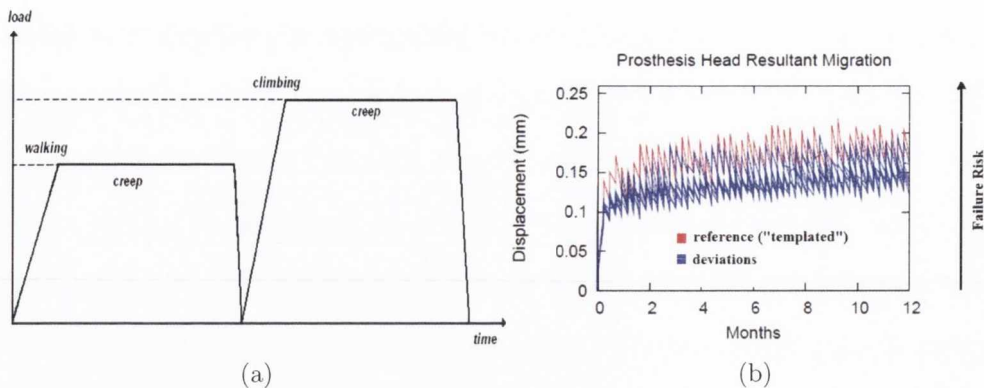


Figure 4.1: a) Scheme of modelling weekly physical activities: walking and stair-climbing; b) Schematic explanation of migration curves: (red) a migration curve for the reference position, (blue) migration curves for the deviations. Each curves contains 52 weeks of a specific physical activity. Each peak represents migration of the implant tip at the end of week.

Anterior-posterior, proximal-distal and medial-lateral components of the prosthesis migration due to aseptic loosening were used as response variables. In the Cartesian coordinate system these rotations were defined by rotations about X, Y and Z axes with respect to the tip of the implant (Fig. 4.3).

Thus, a single deterministic simulation can be described by the following function:

$$F_{deterministic} : \vec{r}_i, \vec{d}_i, \vec{d}_b \rightarrow \vec{dr}_i^w, \vec{dr}_i^s, \quad (4.1)$$

where subscript i relates to the implant, b to the patient's bone, superscripts w and s to the walking and stair-climbing activities respectively, $\vec{r}$ — defines a deviation vector of the implant, $\vec{d}$ — dimension vector, and $\vec{dr}$ — migration vectors. Regression analysis of explanatory variables was performed to determine the most relevant ones with respect to the construction of response surfaces.

Response Surface

A Response Surface methodology analyses behaviour of the response variables with respect to the explanatory variable field. The simplest example of a Response Surface is a function of two parameters which defines a 3D surface (see Fig. 4.4). Typically, minimum, maximum and ridge analyses of such a surface are used to optimize an experiment design. In the current study a second degree polynomial

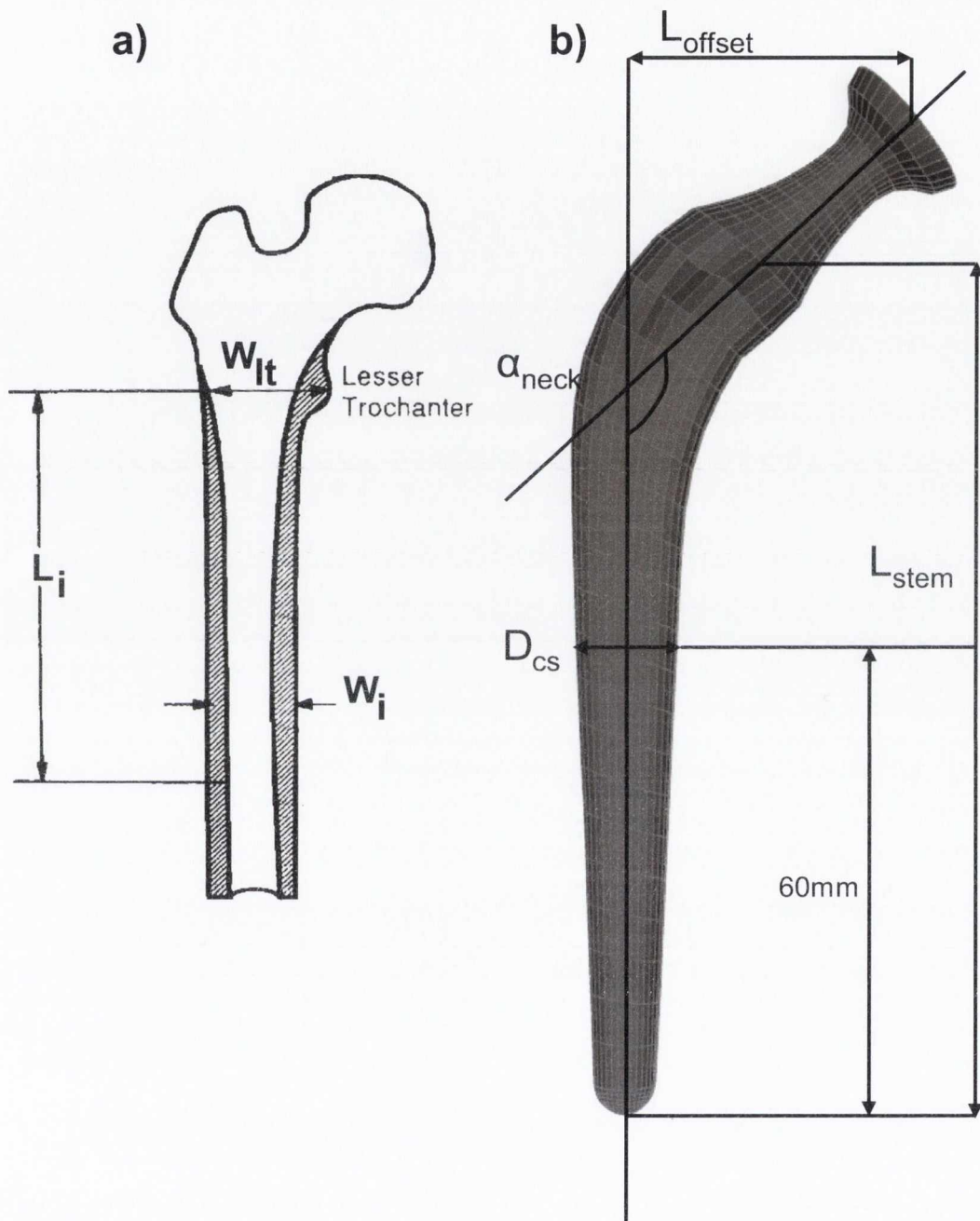


Figure 4.2: Schematic description of explanatory variables used in this study. (a) femur parameters: W_i , width at the isthmus, and W_{lt} , width at the lesser trochanter, and distal border of the isthmus, L_i ; (b) implant neck angle, α_{neck} , stem length and cross-section diameter (tip+60mm), L_{stem} and D_{cs} respectively, and implant head offset, L_{offset}

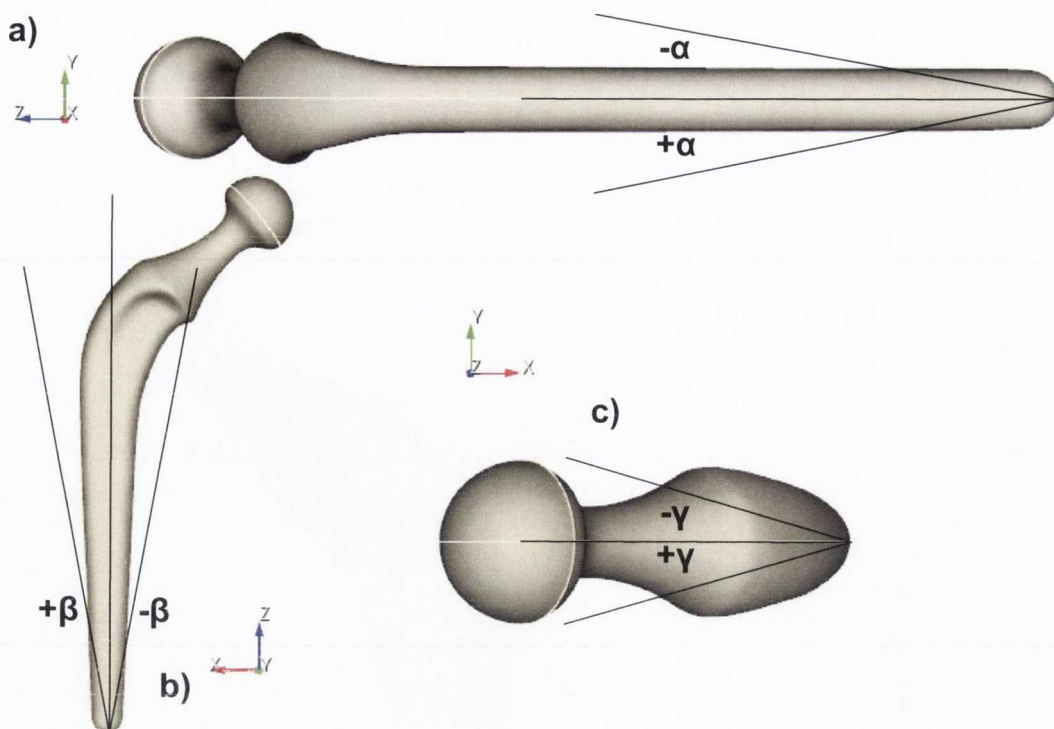


Figure 4.3: Schematic explanation of rotations used to describe variability of implant position. (a) rotation about Y axis, ML; (b) rotation about Z axis, PD; and (c) rotation about X axis, AP

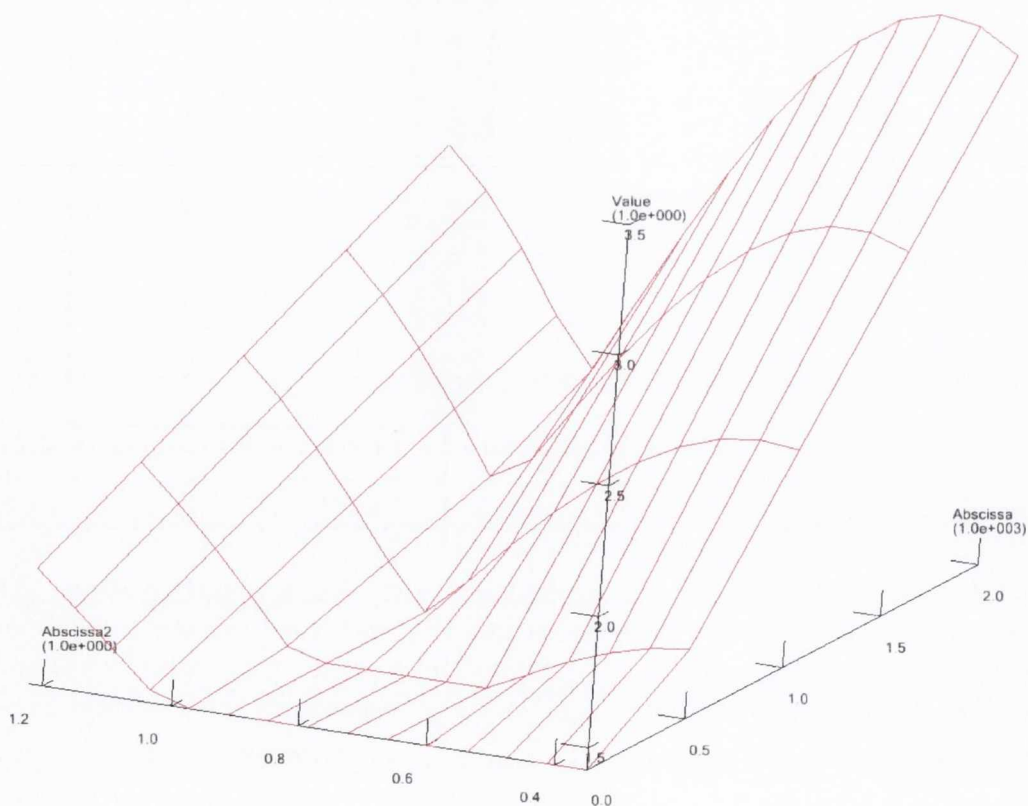


Figure 4.4: An example of Response Surface: abscissas - explanatory variables, value - response

was used for definition of the Response Surface [7]. Thus, in this study the response surface was assumed to be a quadratic approximation of the relationship between explanatory variables and a particular response. Numerical evaluation of the deterministic response surface functions allowed reduction of simulation solution times significantly. These surfaces were defined as follows:

$$y_r = b_0 + \mathbf{x}^T \mathbf{b} + \mathbf{x}^T \mathbf{B} \mathbf{x}, \quad (4.2)$$

$$\text{where } \mathbf{x} = \begin{bmatrix} \vec{r}_i \\ \vec{d}_i \\ \vec{d}_b \end{bmatrix} \text{ — vector of explanatory variables, } \mathbf{b} = \begin{bmatrix} b_1 \\ b_2 \\ \vdots \\ b_n \end{bmatrix} \text{ — coefficients}$$

$$\text{of the linear regression, and } \mathbf{B} = \begin{bmatrix} b_{11} & \frac{b_{12}}{2} & \cdots & \frac{b_{1n}}{2} \\ \frac{b_{21}}{2} & b_{22} & \cdots & \frac{b_{2n}}{2} \\ & & \ddots & \\ \frac{b_{n1}}{2} & \frac{b_{n2}}{2} & \cdots & b_{nn} \end{bmatrix} \text{ — quadratic coefficients}$$

for a particular surface. These coefficients were computed in Matlab (The Math-Works, Inc., Natick, MA,US).

4.2.3 Monte Carlo simulations

Monte Carlo simulation was performed by evaluating the function defined by Eq. 4.1 for a randomly generated set of explanatory parameters. Response surfaces describing relationships between these parameters and migration components were implemented in Matlab as quadratic functions of the explanatory variables with coefficients computed using a training set of full-scale finite element failure simulations. Thus, evaluation of the aforementioned function was achieved by means of a simple substitution of the generated parameters. Implant and position related parameters were assumed to be independent and uniformly distributed in a given range. A uniform distribution was chosen for these parameters because probability of every implantation scenario was assumed to be equal. Patient-specific parameters typically have a normal distribution (see Noble *et al.* [12]), however, for this study a

small number of femur geometries, representing a relatively various range, were used so the distribution was considered to be uniform between minimum and maximum values of femur dimensions obtained from the models. Table 4.1 describes the ranges of explanatory variables used in the study.

Normally, to ensure reliability of the results, Monte Carlo trials are performed repetitively until a stable solution is observed. In the present study, mean resultant migrations due to walking and stair-climbing of the implant tip were used as indicators of the converged solution.

4.2.4 Patient-specific study

The previously described methodology was applied to two different tasks to verify applicability of the framework. First, a hypothetical pre-operative planning task was investigated. An imaginary patient was subjected to a set of virtual THR surgeries. To simulate geometry of the patient, one of the publicly available femora, namely, the third generation composite femur model [78], was used. Variability of possible surgery scenarios was simulated by implanting three different prostheses (Standard Charnley (F40), Extra-Heavy Charnley (F40EH), and Long-neck long-stem Charnley (LNLS), quantified by the previously defined parameters — L_{offset} , L_{stem} , D_{cs} , and α_{neck}) according to the standard templating procedure (initial positions) and several deviations. Rotation about the tip of the implant about AP, ML, and PD axes were applied to simulate surgeon-dependent variability (3 parameters — α, β, γ). Thus, 21 predictive FE-based failure simulations (3 implants, 7 positions each) were carried out. Each set of input parameters was related to two migration vectors as mentioned before (Eq. 4.1). This enabled construction of 6 predictive response surfaces as functions of the 7 aforementioned variables, which were further used in a large trial Monte Carlo simulation to generate a population of hypothetical positions, implant choices/designs and corresponding outcomes. Sensitivity analysis based on Pearson correlation coefficient [102] by means of Matlab and generalized linear regression model [103] was performed on the resulting dataset. Nine additional deterministic simulations were carried out to compare predicted values with

Table 4.1: Value ranges for explanatory variables used for Monte Carlo simulations. Uniform distribution of implant and position related parameters is assumed. Normal distribution was used for patient-specific parameters.

Variable	Distribution	Description	min	max
W_i	Uniform	femur width (isthmus), mm	26.0	32.3
W_{lt}	Uniform	femur width (lesser trochanter), mm	43.0	47.0
L_i	Uniform	distal isthmus border, mm	127.3	143.4
L_{offset}	Uniform	implant head offset, mm	40.0	50.0
α_{neck}	Uniform	implant neck angle, degrees	138°	155°
D_{cs}	Uniform	stem cross-section (tip+60), mm	13.75	17.0
L_{stem}	Uniform	stem length (collar-tip), mm	122.5	126.0
α	Uniform	rotation about AP axis	-1	1
β	Uniform	rotation about ML axis	-1	1
γ	Uniform	rotation about PD axis	-1	1

the predictions of corresponding response surface Monte Carlo trials: 3 combinations of simultaneous change of parameters ($+\beta + \alpha$, $+\beta - \alpha$, and $+\beta + \gamma$), and 6 intermediate deviations ($\pm\alpha/2$, $\pm\beta/2$, and $\pm\gamma/2$).

4.2.5 Population-based study

In the second example, a population-based performance investigation was carried out for each implant type. For this purpose, the training set of predictive failure simulations from the previous section was extended by introducing a population factor, i.e. two extra femora — the standardized femur [44] and the Visible Human femur [79] were added. For each additional femur, similar implant positioning procedures were performed, increasing the total number of deterministic failure simulations to 63 (3 femora, 3 implants, 7 positions). For each implant type, response surfaces were generated based on the position parameters (α, β, γ) and femur-specific parameters (W_i, W_{lt}, L_i). Six predictive response surfaces were constructed as quadratic functions of the aforementioned variables. Monte Carlo simulations were carried out using the constructed response surfaces. For each prosthesis, its performance was

assessed by analysing mean resultant migrations (one-way Anova). Similar to the patient-specific study, a sensitivity analysis was carried out using Pearson's correlation coefficient [102] and generalized linear regression model [103]. Results of the deterministic training set were compared to the stochastic simulations.

4.3 Results

4.3.1 Patient-specific study

Each deterministic failure simulation from the previously described training set was solved in approximately 48 hours on average. Results are shown in Table 4.2. Twenty thousand Monte Carlo trials using a desktop computer (Intel Pentium(R) 4 CPU, 3.00 GHz, 1.00 GB RAM) were performed in 3 seconds. The total Monte Carlo simulation time for a single scenario was smaller than an individual deterministic aseptic loosening FE simulation time by a factor of approximately 10^9 . Convergence of mean values for aforementioned migration types was observed after approximately 10,000 simulations without employing optimization strategies (Fig. 4.5, a). Furthermore, both types of migrations were distributed normally with mean values of 0.167 ± 0.023 mm and 0.198 ± 0.019 mm for walking and stair-climbing respectively (Fig. 4.5 b).

Implant performance

Mean migration values for each implant in case of walking were as follows: F40 — 0.166 ± 0.024 mm, F40EH — 0.141 ± 0.022 mm, and 0.176 ± 0.032 mm for LNLS. For stairclimbing these values were: F40 — 0.201 ± 0.017 mm, F40EH — 0.165 ± 0.013 mm, and 0.211 ± 0.024 mm for LNLS. Analysis of migrations for the F40EH implant showed that the initial position had largest migrations (Fig. 4.6). In the case of LNLS, the original position had lower migrations than any of the deviations (Fig. 4.7). For the stochastic approach, mean values in case of walking for each implant were as follows: F40 — 0.166 ± 0.020 mm, F40 EH — 0.140 ± 0.013 mm, and LNLS — 0.175 ± 0.023 mm. For the stair-climbing migrations values were:

Table 4.2: Results of deterministic simulations: mig^W , mig^S (mm) — resultant migration due to the walking and stair-climbing respectively, α ($X,^\circ$), β ($Y,^\circ$), γ ($Z,^\circ$), L_{offset} (mm), and D_{cs} (mm) — input parameters; Bold — minimum and maximum migrations.

Implant	mig^W	mig^S	α	β	γ	L_{offset}	D_{cs}
F40	0.189	0.211	0	0	0	40	13.75
F40	0.179	0.207	0.5	0	0	40	13.75
F40	0.162	0.208	-0.5	0	0	40	13.75
F40	0.122	0.171	0	1	0	40	13.75
F40	0.163	0.188	0	-1	0	40	13.75
F40	0.155	0.200	0	0	1	40	13.75
F40	0.192	0.221	0	0	-1	40	13.75
F40EH	0.169	0.187	0	0	0	40	17.02
F40EH	0.115	0.155	1	0	0	40	17.02
F40EH	0.154	0.154	-1	0	0	40	17.02
F40EH	0.145	0.150	0	1	0	40	17.02
F40EH	0.164	0.163	0	-1	0	40	17.02
F40EH	0.119	0.175	0	0	1	40	17.02
F40EH	0.124	0.173	0	0	-1	40	17.02
LNLS	0.128	0.220	0	0	0	50	16.14
LNLS	0.182	0.249	1	0	0	50	16.14
LNLS	0.193	0.213	-1	0	0	50	16.14
LNLS	0.153	0.225	0	1	0	50	16.14
LNLS	0.230	0.174	0	-1	0	50	16.14
LNLS	0.174	0.202	0	0	1	50	16.14
LNLS	0.175	0.193	0	0	-1	50	16.14

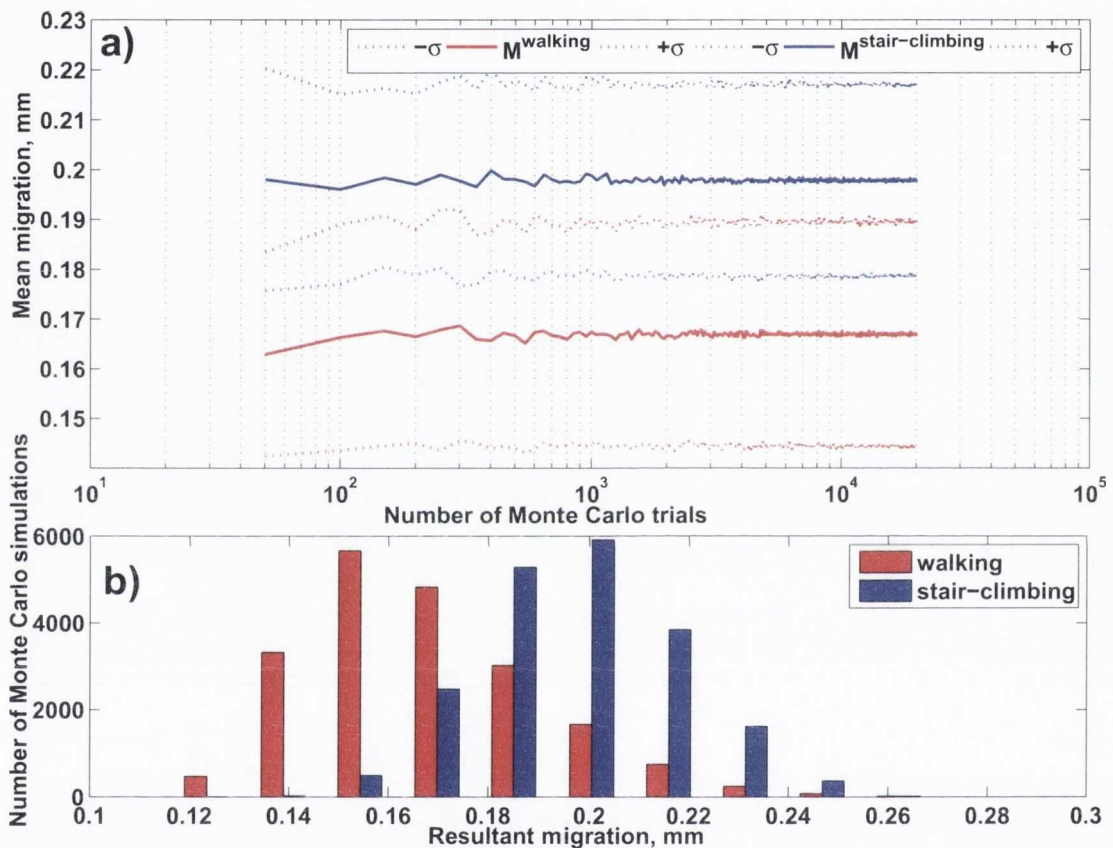


Figure 4.5: Resultant implant migrations vs number of trials: a) Stable behaviour of mean migrations observed after approximately 10,000 trials; b) Resultant migration histograms. $M^{walking}$ — implant migration due to walking, $M^{stair-climbing}$ — implant migration due to stair-climbing, σ — corresponding standard deviation

0.197 ± 0.012 mm, 0.163 ± 0.009 mm, and 0.209 ± 0.020 mm, for F40, F40EH and LNLS respectively.

No significant difference between mean values of walking migrations was observed at $p = 0.05$ level when the deterministic training set of simulations was analysed, i.e. it was not possible to discriminate between implants (Fig. 4.8, a). For the stair-climbing migrations, only the F40EH implant had a significantly lower mean value at $p=0.05$ level compared to the F40 and LNLS implants, which, in turn, were not significantly different between each other (Fig. 4.8, b).

For the stochastic approach, all mean values for both walking and stair-climbing were significantly different at $p < 0.0005$ level. (Fig. 4.8, a,b). F40EH showed minimum mean migrations for both activities, whilst F40 showed the second lowest mean values and LNLS had the largest migrations (Fig. 4.8, a,b).

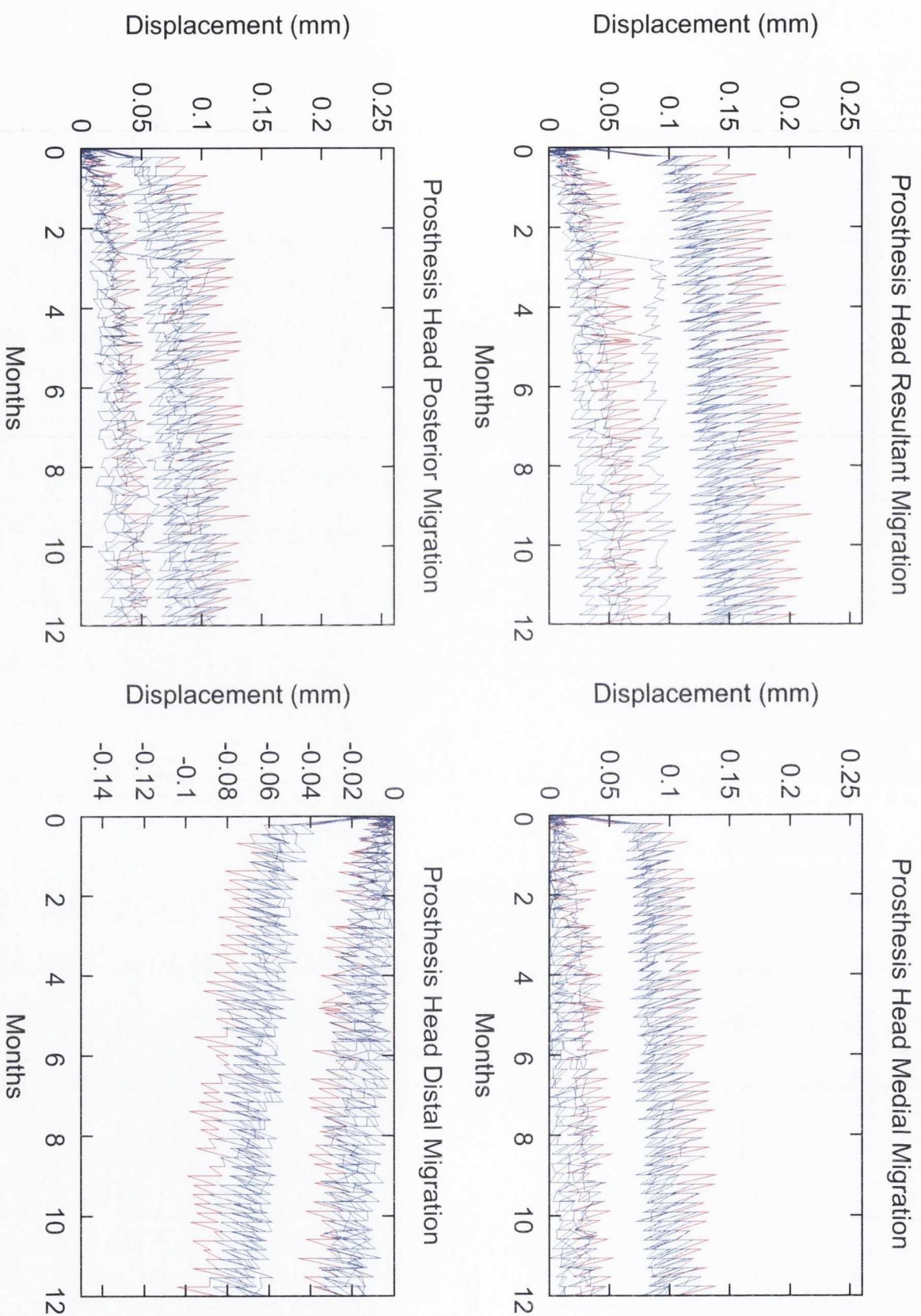


Figure 4.6: Predicted implant migration curves from the deterministic FE simulations (F40EH, walking (bottom set) and stair-climbing (top set), 7 deterministic simulations): (red) initial position; (blue) deviations; (note that the higher migration the larger revision risk)

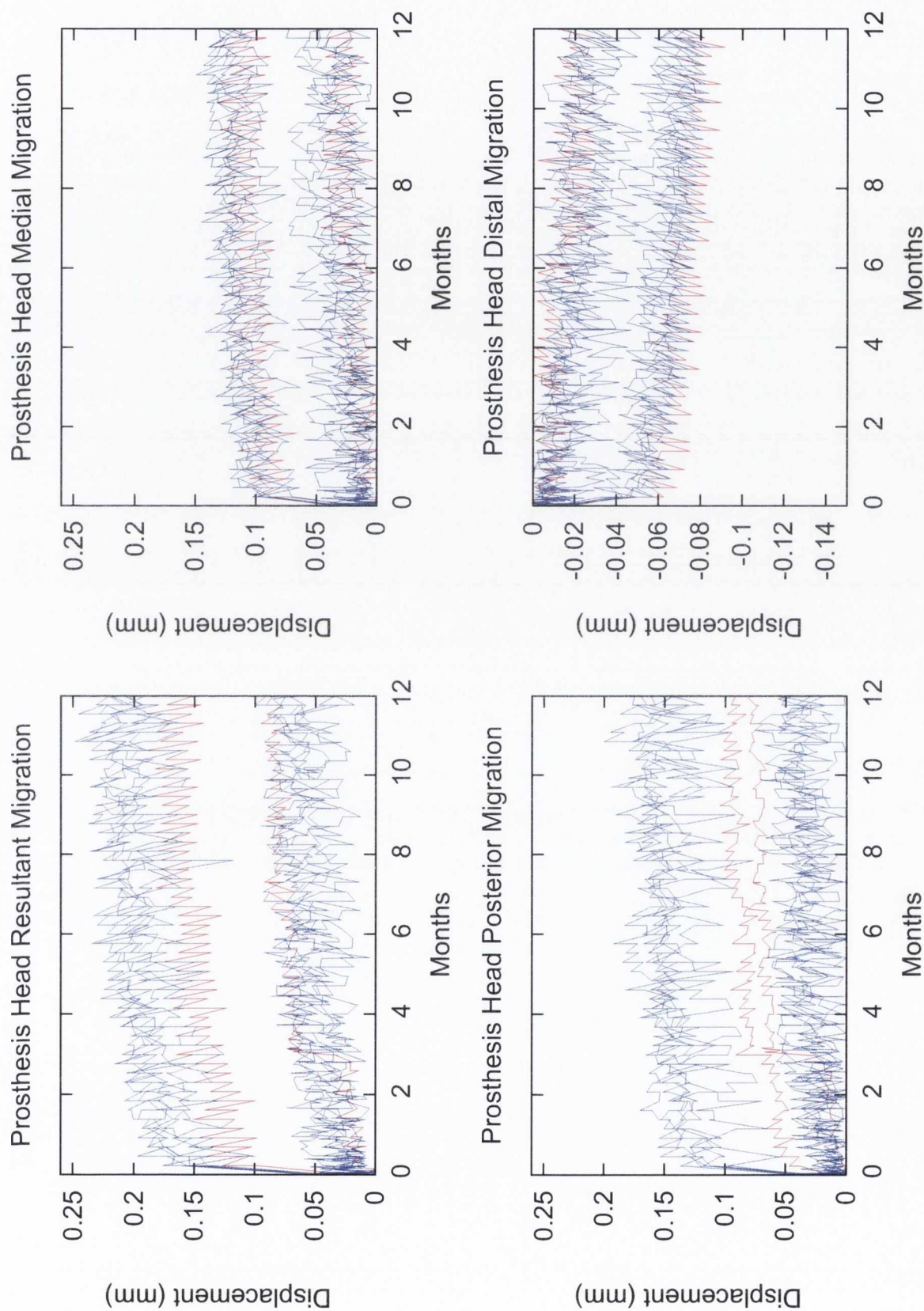


Figure 4.7: Predicted implant migration curves from the deterministic FE simulations (LNLs, walking (bottom set) and stair-climbing (top set), 7 deterministic simulations): (red) initial position; (blue) deviations; (note that the higher migration the larger revision risk)

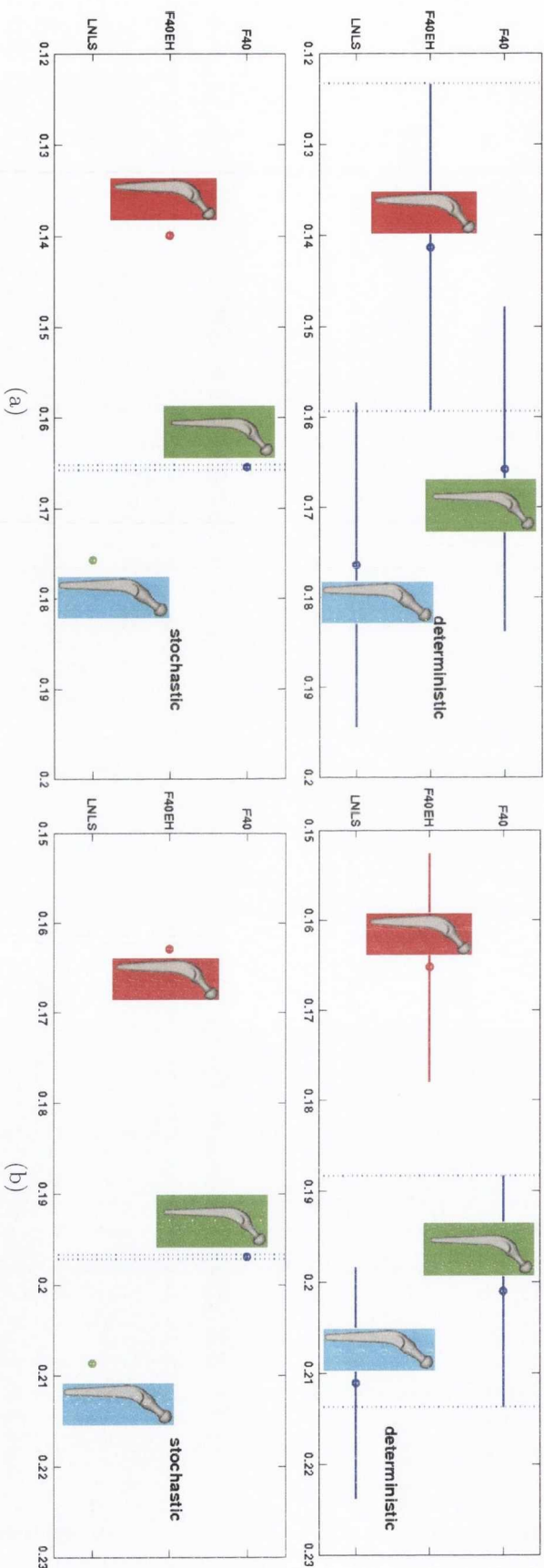


Figure 4.8: Walking (a) and stair-climbing (b) results of patient-specific study: mean implant migrations (mm) and confidence intervals. Confidence intervals in case of deterministic approach may overlap and this is not likely for the stochastic approach. Colour codes for the implants: (red) F40EH (Extraheavy Charney), (green) F40 (Standard Charney), and (blue) LNLS (Long neck long stem Charney)

Sensitivity analysis

Analysis of the input parameters showed that L_{offset} correlated as $R^2 = 1.0$ with α_{neck} and L_{stem} , i.e. it was possible to express L_{offset} as a linear function of the latter. Therefore, the next results are shown for L_{offset} and D_{cs} . The most sensitive explanatory variable, described using correlation coefficient and linear regression slope, in case of deterministic simulations and walking migrations was β (-0.4264/-0.0227). For the stair-climbing activities the most sensitive were D_{cs} (0.5039/0.0028). For the stochastic study 10,000 Monte Carlo trials were subjected to the sensitivity analysis. The most sensitive factor was β (-0.7311/-0.0288) for the walking migration; and for the stair-climbing migration the most sensitive parameters were L_{offset} and D_{cs} (0.5367/0.0058 and -0.5292/-0.0041) (Table 4.3, Fig. 4.9). Although the linear regression slope suggests a slightly different ranking, the larger slope did not always result in larger correlation and, therefore, can be misleading. In addition, it should be specified that the slope measure is dependent on measurement units.

Prediction validation

Comparison of the migration results predicted using the deterministic approach (FE simulation) and RSM showed that for the case of intermediate deviations the mean prediction error was 0.019 mm for walking activity, and 0.007 mm for stair-climbing activity. When combinations of parameters were used to compute the migrations the mean values of errors were larger: 0.029 mm for walking and 0.035 mm for stair-climbing activity (Table 4.4).

4.3.2 Population-based study

Implant performance

Predicted mean implant migrations for walking from the deterministic simulations were ranked from the smallest to the largest as follows: F40, F40EH, and LNLS (Table 4.5). Similar rankings were observed for all other cases: deterministic/stochastic, walking/stair-climbing (Table 4.5).

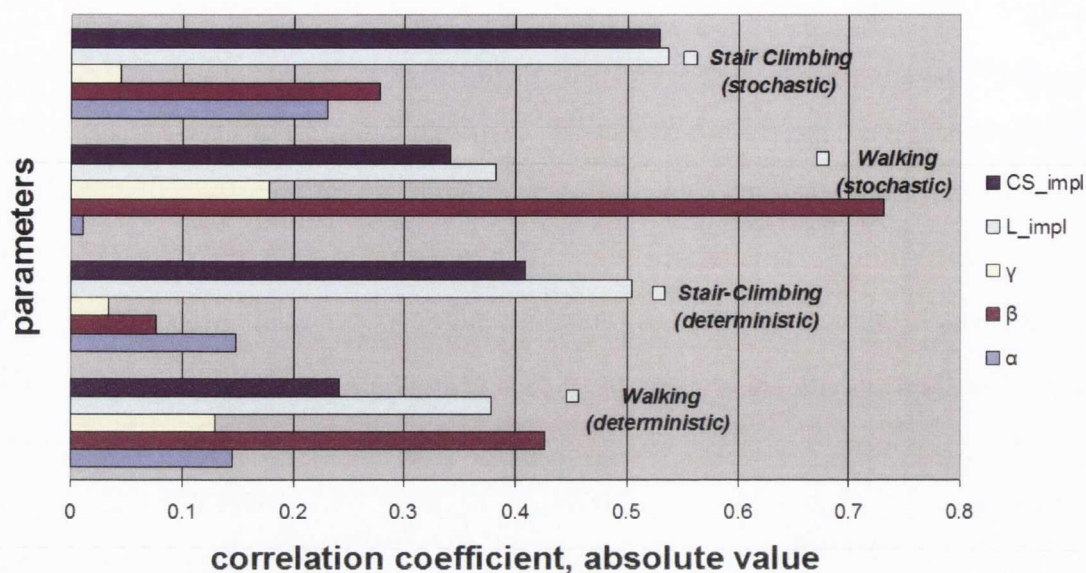


Figure 4.9: Sensitivity of parameters for patient-specific study described as absolute values of correlation coefficients

Table 4.3: Sensitivity analysis for patient-specific study: correlation coefficient, linear regression slope — D/W: deterministic approach, walking migration; D/S: deterministic approach, stair-climbing migration; S/W: — stochastic approach, walking; S/S: stochastic approach, stair-climbing migration. Bold font — large correlation coefficient values.

Variable/Case	D/W	D/S	S/W	S/S
<i>Correlation coefficient</i>				
α	-0.1462	0.1482	0.0115	0.2307
β	-0.4264	0.0757	-0.7311	0.2781
γ	-0.1298	-0.0341	-0.1783	-0.0443
L_{offset}	0.3779	0.5039	0.3827	0.5367
D_{cs}	-0.2415	-0.4092	-0.3417	-0.5292
<i>Linear regression</i>				
α	-0.0090	0.0084	0.0016	0.0078
β	-0.0227	0.0037	-0.0287	0.0090
γ	-0.0069	-0.0017	-0.0070	-0.0016
L_{offset}	0.0022	0.0028	0.0047	0.0058
D_{cs}	-0.0067	-0.0099	-0.0030	-0.0041

Table 4.4: Comparison of predicted migrations, mm: Det — predicted migration using deterministic approach, RS — Response Surface predicted, δ — difference between deterministic and RS approach; Walk — walking acitivity, SC — stair-climbing activity. Bold fonts: two largest differences in predictions

Model	Det.Walk	RS.Walk	δ .Walk	Det.SC	RS.SC	δ .SC
$+\alpha/2$	0.1766	0.1674	0.0091	0.2203	0.2076	0.0127
$-\alpha/2$	0.1820	0.1610	0.0210	0.2034	0.2015	0.0020
$+\beta/2$	0.1858	0.1573	0.0285	0.2028	0.2032	-0.0005
$-\beta/2$	0.1859	0.1712	0.0147	0.2128	0.2008	0.0120
$+\gamma/2$	0.1857	0.1593	0.0264	0.2145	0.2042	0.0103
$-\gamma/2$	0.1837	0.1683	0.0154	0.2102	0.2040	0.0063
$+\beta + \alpha$	0.1927	0.1612	0.0315	0.2195	0.2010	0.0184
$+\beta - \alpha$	0.1320	0.1530	-0.0210	0.2285	0.1894	0.0392
$+\beta + \gamma$	0.1982	0.1627	0.0355	0.2396	0.1923	0.0473

Table 4.5: Implant perfomance described using mean migration values (population-based study), mm

Description/Implant	F40	F40EH	LNLS
Mean migration, walking, <i>deterministic</i>	0.1200	0.1483	0.1543
Mean migration, walking, <i>stochastic</i>	0.1075	0.1404	0.1419
σ , <i>deterministic</i>	0.0437	0.0442	0.0469
σ , <i>stochastic</i>	0.0249	0.0427	0.0478
Mean migration, stair-climbing, <i>deterministic</i>	0.1421	0.1865	0.2104
Mean migration, stair-climbing, <i>stochastic</i>	0.1400	0.1672	0.2117
σ , <i>deterministic</i>	0.0546	0.0323	0.0476
σ , <i>stochastic</i>	0.0486	0.0331	0.0555

Mean walking migration for the F40 implant was significantly different from mean walking migration for the LNLS, however, significant difference from the F40EH was not predicted at $p = 0.05$ level (Fig. 4.10,a). Furthermore, there was no significant difference between mean values of F40EH and LNLS prostheses. Mean stair-climbing migration of the F40 was significantly smaller than both the F40EH and LNLS, which, in turn, were not different from each other at $p = 0.05$ level (Fig. 4.10,b). For the stochastic approach, significant difference in mean migrations at $p < 0.0005$ level was only observed between the F40 and other implants, however, not between F40EH and LNLS (Fig. 4.10,a). All mean migrations were significantly different from each other at $p < 0.0005$ level for the stair-climbing activity (Fig. 4.10,b).

Sensitivity study

For the deterministic training set the most sensitive correlation coefficient-based parameter was the femoral width variable W_{lt} (-0.2030 for walking and -0.3012 for stair-climbing)(Table. 4.6). For the stochastic set these were L_i (0.4488 walking and 0.4672 stair-climbing) and W_{lt} (-0.4783 for the climbing activity)(Table. 4.6, Fig. 4.11).

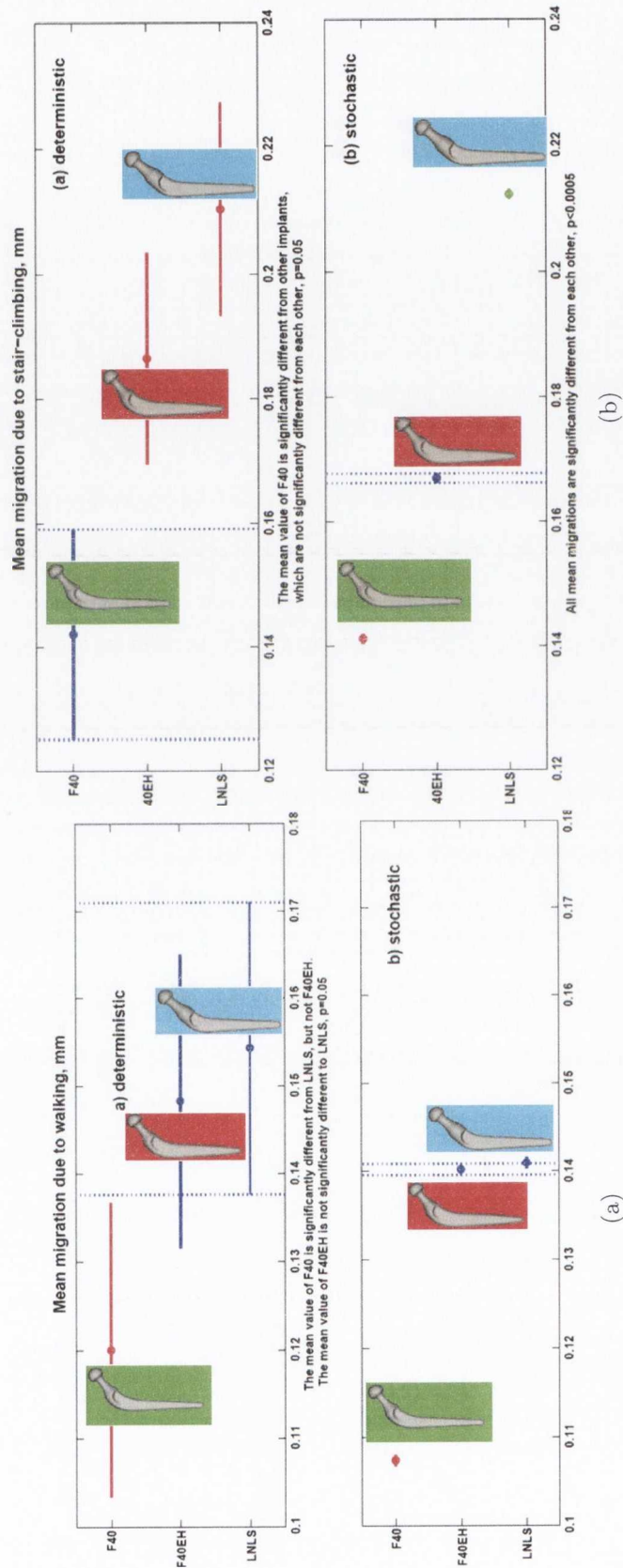


Figure 4.10: Walking (a) and stair-climbing (b) results of population-based study: mean implant migrations (mm) and confidence intervals. Confidence intervals in case of deterministic approach may overlap and this is not likely for the stochastic approach. Colour codes for the implants: (red) F40EH (Extraheavy Charnley), (green) F40 (Standard Charnley), and (blue) LNLS (Long neck long stem Charnley)

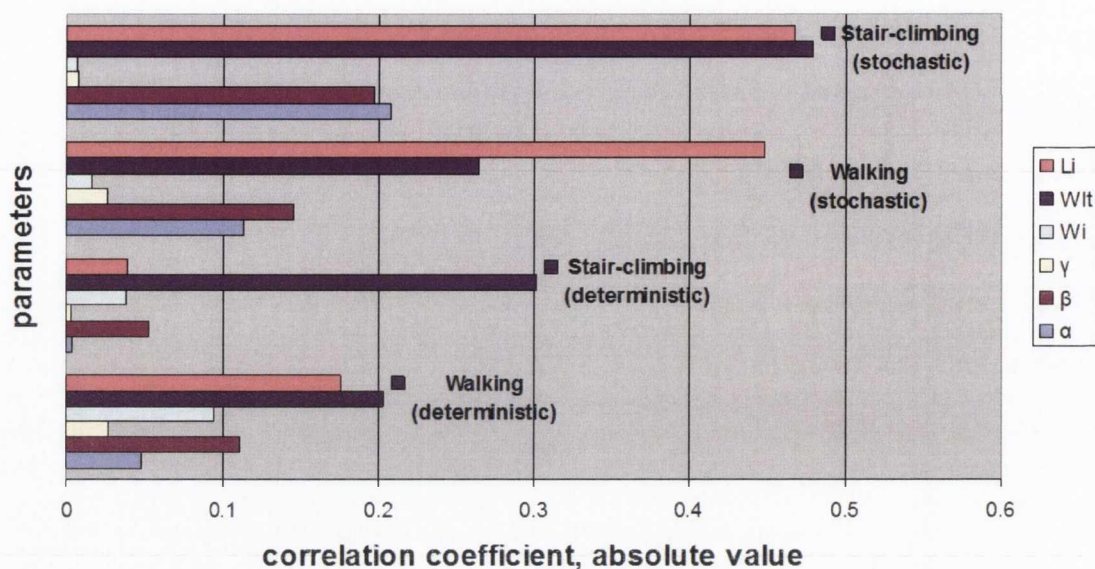


Figure 4.11: Sensitivity of parameters for population-based study described as absolute values of correlation coefficients

Table 4.6: Sensitivity analysis for population-based study: correlation coefficient, linear regression coefficient — D/W: deterministic approach, walking migration; D/S: deterministic approach, stair-climbing migration; S/W: — stochastic approach, walking; S/S: stochastic approach, stair-climbing migration

Variable/Case	D/W	D/S	S/W	S/S
<i>Correlation coefficient</i>				
α	-0.0474	-0.0036	0.1127	0.2075
β	-0.1112	0.0524	-0.1455	0.1980
γ	-0.0263	0.0030	0.0256	0.0076
W_i	0.0950	-0.0377	-0.0160	0.0060
W_{lt}	-0.2030	-0.3012	-0.2643	-0.4783
L_i	0.1752	0.0382	0.4488	0.4672
<i>Linear regression coefficient</i>				
α	-0.0027	0.0029	0.0074	0.0179
β	-0.0096	0.0052	-0.0094	0.0170
γ	-0.0023	0.0003	0.0021	0.0013
W_i	-0.0163	-0.0238	-0.0002	0.0016
W_{lt}	-0.0218	-0.0220	-0.0082	-0.0152
L_i	0.0120	0.0139	0.0037	0.0060

4.3.3 Deterministic vs stochastic

Firstly, a difference between mean values computed by the deterministic and stochastic simulations was predicted. Typically, the deterministic approach tends to predict higher values with the only exception, in the case of stair-climbing activity of the LNLS implant (population-based study)(Table 4.2, Table 4.5). Secondly, correlation coefficients in case of the stochastic simulations were larger, i.e. sensitivity of the parameters was stronger. The most important explanatory variables did not change between deterministic and stochastic approaches. When the deterministic FE simulations were carried out on a single femur — ranking of the implants (small to large) were F40EH, F40, and LNLS. However, when more femur models were used to simulate a population sample — the predicted ranks were F40, F40EH, and LNLS.

4.4 Discussion

The aim of this work was to develop a stochastic failure model of femoral component loosening incorporating such uncertainties as patient geometry, implant design and surgical technique. This was achieved by utilizing an automated mesh generation technique and simulating 63 case-specific scenarios (3 patients, 3 implants, 7 positions) to obtain a training set for the construction of a stochastic predictive model. Patient-specific pre-operative planning and a population-based comparison of implant performance were performed to demonstrate and test the capabilities of the framework.

For this study several simplifications were inherited from Lennon *et al.* [94]. These simplifications motivated investigation of the following sources of variability: patient's geometry, implant design and prosthesis placement. The list of assumptions based on the mechanical factors was as follows:

- 1) Material properties of each tissue type (cortical and cancellous bone, and marrow) were assumed to be homogeneous and constant. No microstructure was taken into account. No bone remodelling processes were included to allow

adaptation to the altered tissue loading arising post-implantation. The same material properties were used across different patients. However, it is possible to use patient-specific material properties obtained from medical images [25, 21]. Furthermore, bone remodelling algorithms could be incorporated in future (see Scanell [104]); however, their inclusion will require enlargement of the training set due to the increase in parameters.

- 2) Only aseptic loosening due to a cement damage accumulation failure scenario was investigated. Bone cement damage accumulation, although computed, was not used for the probabilistic analysis. A possible future work is to take into account a particulate reaction scenario and/or investigate stress shielding effects, e.g. bone remodelling as mentioned previously.
- 3) Physical activity was simulated as a certain number of walking and stair-climbing loading cycles. However, typical activity of a patient is also subject to variability. Questionnaires, such as WOMAC or UCLA scores, could be utilized to improve this modelling aspect for patient-specific studies. Datasets on daily activity (e.g. Morlock *et al.* [105]) could also be used to develop a stochastic activity model.
- 4) An ideal shape of cement mantle was assumed. No defects were taken into account. Homogeneous material properties were assumed. Size and position was assumed to be slightly larger than the implant in the reference position. A stochastic approach, for instance, similar to Lennon [1], to simulate variability of bone cement damage could be employed to improve this modelling aspect. Moreover, variability of cement mantle sizes, shapes, and positions could also be investigated.

In addition to assumptions related to the mechanical simulations, there were also several assumptions for the probabilistic part of the framework:

- (i) Approximation of the migration prediction was based on quadratic functions and a small number of the deterministic simulations, i.e. 3 femur shapes, 3 implants, and 3 positions for each rotation (reference and 2 deviations).

A more precise polynomial or another analytical function could be used for the approximation of implant migration if a larger number of deterministic simulations were performed. Also, the predictive capability of the response surface would improve with enlargement of the training set. For instance, a more representative population of femora could affect the conclusions made for the population-based study. The efficacy of the approximation was assessed by simulating additional possible scenarios and computing a corresponding prediction using RSM. The predictions were more reliable for the individual parameter deviations than for the combined deviation of pairs of parameters. This was due to the fact that combinations of parameters were not used for the construction of the Response Surfaces. Thus, the next step is to increase the number of deterministic simulations and construct more reliable Response Surfaces.

- (ii) Explanatory variables were selected arbitrarily according to the author's experience and judgement. Selection of explanatory variables should be more systematic and based on a statistical analysis performed on the modelled entity. For instance, an implant design can be described by a larger number of variables than presented in this study; however, only a subset of them describe the unique nature of a given design (as it has been shown for the example of D_{cs} , L_{offset} , α_{neck} , and L_{stem} in the patient-specific study). Such relationships can be revealed by performing principle component analysis (PCA) of the implant dimensions. Also, implant positions can be described by a larger number of variables than the 3 rotations used in this study, i.e. a full affine transform can be used as a variable in this case.
- (iii) Ranges of explanatory variables were obtained by measuring available CAD models. It is possible to define ranges of variables from the literature, e.g. femur dimensions could be taken from Noble *et al.* [12], if a custom implant is being designed for a patient there are patient-specific limitations on its dimensions. Moreover, with inclusion of realistic ranges for explanatory variables realistic probability distribution functions need to be utilized as well, i.e. not

all the variables are distributed uniformly.

- (iv) Furthermore, the framework cannot be considered fully tested unless a Monte Carlo simulations using full-scale FE trials rather than response surface functions were undertaken.

Although, this FE-based framework has been tested using the aforementioned assumptions, it is not limited to their inclusion; i.e. it is possible to include previously developed bone adaptation algorithms [106], add more parameters taken from other stochastic investigations [88, 91, 107], e.g. loads, their locations and directions, apply patient-specific material properties [28], and so on. Moreover, it does not require invention of new core algorithms needed to perform probabilistic analysis. For instance, material properties can be extracted from CT/DEXA scans and mapped onto the generated mesh automatically [28, 25, 108]. Furthermore, this framework could serve as a basis for fully automated assessment of implant performance. It allows investigation of several failure modes at the same time, i.e. it possible to perform stress analysis, compute damage accumulation, use bone remodelling rules, etc. Probably, the main advantage of this framework is the speed with which it can characterize a certain scenario. This framework can be used in many failure-related applications to investigate the most important factors and potentially support or decline a decision taken pre-operatively or while designing a new implant. Another strong side of this framework is that it allows inclusion of a large number of random variables and, therefore, is more likely to highlight true behaviour and risks of a certain surgical plan.

Predictions of the patient-specific study showed that a position of the implant achieved by the standard templating procedure does not necessarily provide the lowest implant migration (Fig. 4.6). Furthermore, 21 patient-specific deterministic simulations do not fully describe the probable performance envelope of a particular implant. Thus, reliance on results of a single or small number of simulations can be misleading. Furthermore, it was not always possible to discriminate the implant with lowest migrations based on the deterministic simulations. However, it was possible to make statistically significant conclusions using the stochastic analysis —

which predicted that the extra-heavy Charnley (F40EH) had the lowest migrations in the patient-specific study, and the standard Charnley was the least migrating in case of population-based investigation.

Sensitivity analysis of input parameters showed that medial-lateral rotation was one of the strongest factors affecting implant migration throughout the study (Table 4.3, Table 4.6). In case of patient-specific study implant dimension were important factors as well. The corresponding linear regression coefficient was negative, i.e. an implant rotation into varus positions results in higher migrations. These results correspond well to the retrospective study by Devit *et al.* [109], who showed that varus positioning of Charnley implants had lower survival rates compared to neutral (second worst) and valgus (best) positions. Dopico-Gonzalez *et al.* [93] highlighted that peak bone stresses were sensitive to medial-lateral displacements of the implant, varus-valgus rotation had a strong influence on strains and implant migration as well (uncemented hip replacement). Ong *et al.* [110] investigated the effect of varus/valgus implant rotation in Hip Resurfacing Arthroplasty and showed that extreme varus and valgus rotations of the implant may have a negative effect on the outcome. Given the differences in these studies combined with the predictions of this investigation, it seems likely that medial-lateral positioning of the implant plays an important role in the success of THR; it is, therefore, a good candidate to include in future investigations. Furthermore, the population-based study predicted that, independently of selected approach, size of the host bone had an effect on implant migrations. Moreover, negative coefficients of the linear regression suggest that patients with larger bones are less susceptible to high implant migration. Moreover, implant migrations due to the stair-climbing activity were more indicative of a difference in implant behaviours — therefore, stair-climbing could be a better predictor of implant failure and is a critical activity to include into the failure modelling scheme. Similar conclusions were made by Viceconti *et al.* [91]: the larger host bones had a lower rate of micromotion and that stair-climbing is a very important activity to include into a predictive model.

4.5 Conclusions

A stochastic framework capable of incorporating patient femur geometry, implant design and surgical technique was developed. Two hypothetical studies were carried out to demonstrate capability of the framework to investigate different phenomena. Application of the framework to a patient-specific analysis predicted that the most sensitive parameter in this case was medial-lateral rotation of the implant; however, implant sizes were important as well. Furthermore, when the implant was tilted in the medial direction the migration level increased. For the population-based study, the femoral dimensions were important factors: with increase of the femur width at the lesser trochanter level, the migration levels decreased. Sensitivity analysis revealed that for the deterministic approach the correlation coefficients between random variables and implant migration were weaker than compared to the stochastic case. Also, the deterministic approach did not allow statistical discrimination of the implant with the lowest migration; however, this was possible with the stochastic simulation. A stochastic approach to failure modelling has a number of advantages relative to the deterministic one, which can be summarized as that it allows better understanding of failure phenomena in THR.

Chapter 5

General Discussion

5.1 Achievements

This work set out to create a stochastic framework for failure modelling of THR using FEA to investigate, and better understand, reasons for THR failure by incorporating different sources of variability. To achieve this goal the following enabling methods were necessary.

First, a technique that enables reconstruction of patient-specific proximal femur geometries based on minimum available data, i.e. a planar X-ray image, was developed. This technique is important because it opens up the possibility of large scale retrospective testing since planar X-rays are more routinely taken pre-operatively than other imaging modalities. The goal of this part of the thesis was achieved — the method, based on warping of a generic surface model using a femur contour from an X-ray, was developed and then validated on corresponding pairs of planar pelvic radiographs and pelvic CT scans. This method is fully automated and rapid. The technique was capable of reconstructing femur geometries with an average surface error not exceeding 3.8 mm. The largest error consistently appeared in the region of the femoral head (similar to Zheng *et al.* [37] and Barratt *et al.* [30]). However, for modelling THR this part of the femur is typically removed and, therefore, accuracy of the head geometry is less relevant. The reported accuracy level compares well to a number of existing methods for reconstructing patient-specific geometries from medical images (0.7-6.88 mm [30, 31, 32, 37, 36, 38]). Additionally, the effect of the

reconstruction error on strain distribution in a loaded femur was investigated using FE analysis. This suggested that the error in strain prediction is proportional to the mean surface error of the reconstructed model. Moreover, it was shown that the reconstruction error of the method does not change the strain level dramatically and, therefore, the generated models could be employed as an approximation when a model of higher precision, e.g. CT-reconstructed femur, is not available. This technique can be employed for many different applications. For example, it could be used as a tool to build a model of patient variability. Alternatively, a large number of radiographs can be processed to analyse bone morphology across a population.

Secondly, an automated method to generate meshes of a surgical plan was required as a pre-requisite for further failure modelling using FEA. Generation of patient-specific meshes is a challenging and time consuming task and often becomes a barrier to a thorough analysis of various clinical phenomena, e.g. failure of joint replacements. This task was achieved by developing a method based on warping of a pre-generated mesh according to the surgical plan (patient's geometry and positioned implant). Mesh warping is performed using a combination of a mesh parameterization procedure, a displacement controlled FE analysis, and mesh smoothing algorithms. In order to verify the meshing capability of the developed technique, it was applied to a set of hypothetical scenarios using all-hexahedral generic meshes. Good quality case-specific meshes were successfully generated in a rapid and fully automated manner. An advantage of the developed technique is that it is element-type independent and can be applied to other intramedullary joint replacements. Minor limitations do not allow this technique to be applied to all possible surgical plans (very thin walls and intersecting curves); however, it is applicable to nearly all valid surgical scenarios.

Thirdly, the preceding two applications enabled the development of a failure modelling scheme that allows incorporation of different sources of variability, such as bone and implant geometry, implant positions, etc. Several studies have looked at the variability of geometric case-specific factors [88, 92, 93, 91, 87, 111, 112]. However, one or two parameters were investigated at once. For example, Dopico-

Gonzalez *et al.* looked at the positions of the implant [88], but not its design or patient geometry. Dopico-Gonzalez *et al.* [93] also looked at different implants and their positions in 3 different patients — however, implant shapes and patient geometry did not vary, i.e. these factors were fixed. Moreover, most of the studies did not investigate long-term revision risks. This study is the first time a stochastic approach has been applied to investigation of all main geometric factors — bone geometry, implant geometry and position, at the same time as investigating long-term revision risk. This framework was developed in two parts: (i) deterministic, and (ii) stochastic. The requirement for the deterministic part was to be able to predict a failure risk. Due to the mechanical nature of the problem, i.e. bone cement damage accumulation is one of the main problems of long-term THR endurance [11], an FE-based approach proposed by Lennon *et al.* [94] was employed. For the stochastic part, a Response Surface Methodology was used to enable rapid large trial Monte Carlo simulations.

5.2 Limitations and validity of framework

5.2.1 Technical

A number of simplifications for both deterministic and stochastic parts were assumed. A thorough list of limitations was previously described. However, it is important to highlight the following aspects of this modelling scheme. The main limitation of the probabilistic part is that further investigation is needed to assess and refine the response surface functions. Preliminary results showed that the deterministic training set needs to be extended by a combination of input parameters and a larger number of trials (Section 4.3.1). However, the full-scale finite element based aseptic loosening simulations, which are needed for thorough analysis and understanding of the response surface, are computationally expensive (typically approximately 2 days for an individual simulation of 1 year of activity). To address this problem the following optimization steps need to be taken: (i) an efficient sampling strategy or a combination of sample size reduction techniques needs to be employed

(AMV, RSM, etc.); (ii) a more efficient risk predictor must be found, which can highlight risks using smaller time frames, e.g. 2 months instead of 1 year of physical activities; and (iii) overall performance improvement, e.g. parallel computing, etc.

5.2.2 Philosophical

All the conclusions made in this study at this stage are based on hypothetical samples of variables and assumed conditions and, therefore, need to be further tested to be considered clinically relevant. Viceconti *et al.* [113] and Prendergast *et al.* [114] underlined that it is impossible to achieve a completely validated numerical model. However, there are a number of guidelines that could improve reliability of the THR failure model based on the presented framework. For example, Viceconti *et al.* [113] proposed that a numerical model needs to satisfy the following criteria to be considered clinically valid:

- a) Model selection — there should be a clear reason why a numerical model is well suited to particular study.
- b) Verification of the model — mesh dependency, particular analysis type, and other aspects need to be analysed/justified.
- c) A full sensitivity analysis — to show how uncertainties affect the results.
- d) Inter-subject variability.
- e) Validation against controlled *in vitro* experiments — this level of validation should be considered mandatory.
- f) Risk-benefit analysis — should be performed on a model validated using the previous steps.
- g) Retrospective studies — a good clinical test.
- h) Prospective studies — one of the most reliable methods to validate a model; however, often unfeasible.

The framework proposed in this thesis (based on a model, validated using a retrospective study [94]) allows performance of sensitivity studies as it was shown in both patient-specific and population-based cases and to include inter-subject variability modelling aspects. Hence, it satisfies several of the aforementioned criteria. Furthermore, a possible validation for the failure modelling framework would be to perform the same retrospective study by Lennon *et al.* [94], including uncertainties present in these models, e.g. cement mantle and implant positions, and repeat or, possibly, improve the predictions. It also allows validation against *in vitro* experiments — thus, it should be possible to apply this technology to simulate experimental tests such as those performed by McCormack *et al.* [115], Maher *et al.* [116], Lennon *et al.* [117], etc. Furthermore, many intuitive improvements can be employed to make this framework more reliable, e.g. include variability of loading, mechanical properties of the bone, etc.

5.3 Research questions

Surgical technique

Another goal of the thesis was to demonstrate the potential of the framework to investigate THR failure and answer stated research questions. Patient-specific and population-based studies were carried out for this purpose. Based on the quantitative results of the patient-specific study it was possible to answer the first research question. The sensitivity analysis predicted that surgical technique, namely varus-valgus rotation of the implant, had the strongest influence on implant migration, which is associated with revision risk. A linear regression coefficient for this factor was negative, meaning that an implant rotation into varus positions leads to higher migrations. These results correspond well to the retrospective study by Devitt *et al.* [109], who showed that varus position of the implant had a lower survival rate compared to neutral (second worst) and valgus (best) positions. Dopico-Gonzalez *et al.* [93] showed that peak bone stresses were sensitive to medial-lateral displacements of the implant, as well as to rotation in the medial-lateral plane (uncemented

hip replacement). Ong *et al.* [110] showed that varus/valgus implant rotation has an effect on the outcome of Hip Resurfacing Arthroplasty and showed that extreme varus and valgus rotations of the implant may have a negative effect on the outcome. Kobayashi *et al.* [118] reported that an exaggerated valgus alignment of the stem correlated positively with survivorship of the femoral component in case of low-friction THR. Although, there were substantial differences in these investigations it seems likely that medial-lateral positioning of the implant, i.e. surgical technique, plays an important role in the success of THR.

Implant selection

The patient-specific study also showed that although surgical technique was very important, the implant dimensions also affected revision risk, i.e. corresponding correlation coefficients used to assess the sensitivity were second strongest. Of these measures, the head offset had the strongest correlation with migration. Positive sensitivity suggested that smaller offsets lead to smaller migrations. However, the available range selected for the offset explanatory variable was based on measurements of the available CAD models, which only had 2 levels (40 and 50 mm), and therefore, does not include smaller offsets. Moreover, the head offset changes the moment arms of the joint load, which may also contribute to the predicted behaviour for varus-valgus positioning. Normally a hip surgeon tries to restore the femoral head offset [119], and does not tend to consider offsets that do not recreate this measure. Kleeman *et al.* [120] investigated the role of implant head offset on peak stresses in the cement mantle and predicted increase of stress level with increase of the offset — this finding correlates with results of this study. In addition to head offset, it was shown that the implant type, and hence overall geometry, affects the migration ranking for all implants. Thus, extra-heavy Charnley (F40EH) had the lowest migrations for the patient-specific study, followed by standard Charnley (F40) and then long-neck long-stem Charnley (LNLS), whilst for the population-based study F40 was predicted to migrate least, followed by F40EH and then LNLS. However, it is important to keep in mind the limitations, such as an incomplete representation

of the femur population, which may affect these conclusions.

Influence of patient-specific parameters

As it was shown in the previous section difference in shape and size of the implant can lead to different rankings of the mean migrations. A similar result was also predicted for the femur, which was the primary patient-specific factor in this study. This implies that a single femur cannot be used for device testing as it does not describe the potential variability of femur morphology in a population. An interesting result was that the F40 did not perform well in a particular patient, but used in a population sample had the lowest overall migration rates. Please note, that again, the assumptions made in this study may affect the conclusions. However, despite of the limitations, this illustrates the danger of using only a single femur geometry to pre-clinically test implant performance. The most significant factor was width of the femur in medial-lateral direction. Based on the negative linear regression coefficient it is possible to conclude that with increase of the host bone width the risk of revision surgery decreases — a similar result was predicted by Viceconti *et al.* [91] for uncemented THR. Furthermore, Kobayashi *et al.* [121] observed that the flare index was an important factor for the success of THR — this parameter is also related to the width at the lesser trochanter area, and thus, indirectly, confirms importance of the parameter. However, this conclusion needs to be further investigated as the sizes of the implant and cement mantle were not taken into account along with other limitations.

Deterministic vs Stochastic

In Chapter 4 it was shown that the sensitivity analyses applied to the stochastic sets of results produced larger correlation coefficients and, therefore, allowed stronger conclusions compared to the deterministic results. Furthermore, it was also shown that an aseptic loosening simulation for the reference position of the F40EH prosthesis predicted worse migration than many of the deviations (Fig. 4.6). Therefore, it is very strongly recommended not to use a single FE simulation for

predicting THR failure. It is also likely that a single simulation would not describe a highly variable phenomenon in general. Furthermore, although the extended set of FE simulations for each implant predicted ranges of responses, it was not possible to make statistically significant conclusions based on their results — however, the proposed stochastic approach was capable of statistically distinguishing different factors. Also, convergence of the mean value for implant migrations was observed after approximately 10,000 trials (without employing optimization strategies) — this indicates that a potentially large number of simulations may be required to produce reliable predictions. Furthermore, the stochastic approach is more likely to predict more realistic variation as it provides an unbiased selection of the input.

5.4 Value of the framework

Numerical modelling, in general, is an important and powerful approach to failure modelling of joint replacements. A validated numerical model enables reduction of pre-clinical evaluation cost/times and can reduce numbers of, or even avoid, animal trials [122, 113]. The range of potential applications of the presented stochastic framework is very wide. It includes a patient-specific pre-operative planning system, decision support tools, a population-based device testing scheme, and can be utilized as a part of the implant design process, e.g. an iterative process with assessment of implant performance. However, probably the most valuable use of this framework would be in a hypothesis testing tool, i.e. it proved to be capable of investigating research questions involving such uncertainties as patient geometry, implant design, and implant position. Prendergast [122] stated that biomechanics, as any other science, develops by an iterative testing of basic hypotheses, which leads to acceptance or rejection. Hence, such a framework could assist in the development of biomechanical theories of joint replacement failure. Furthermore, this framework can be seen as a tool to rapidly give an insight on a problem and assess whether a detailed analysis is required. It has been shown using several examples that the proposed technology can be employed to investigate the effect of uncertainties on risk of failure in THR. It can also be intuitively extended/modified to other joint

replacement operations. Although it is important to keep in mind limitations and that this methodology should be tested against both experimental models and clinical data [113, 114], the potential benefits of using the stochastic framework were clearly demonstrated in this work.

Chapter 6

Conclusions

A stochastic framework for modelling failure due to aseptic loosening of THR was developed. The development required the author to create the following enabling technologies: firstly, an automated method to reconstruct proximal femur geometries from medical images, in particular, planar radiographs, secondly, an automated mesh generation technique capable of producing good quality mesh for a surgical plan, and, finally, an FE-based failure modelling scheme for prediction of revision risk due to aseptic loosening. Successful application of this methodology to patient-specific and population-based studies suggested the following conclusions:

- a) Combining automated geometric reconstruction from planar X-rays with automated mesh generation and an aseptic loosening algorithm enabled development of a stochastic framework for predicting the probable performance envelope of a THR femoral prosthesis on a patient-specific basis
- b) A preliminary adaptation of the framework demonstrated that it is also capable of investigating implant behaviour within a population.
- c) With regard to surgical positioning, it was predicted that varus/valgus positioning of the implant has the strongest influence on the revision risk of the THR.
- d) Consideration of implant selection showed that the framework has potential for:
 - Matching an implant to a given patient.

- Choosing an implant that performs well in a wide range of patients.
- e) Regarding implant geometry:
- Larger implant head offsets tend to increase migrations rates.
 - Implant designs need to be tested using a population sample of bone morphologies as an inferior implant can be mistakenly identified as more reliable based on a low number of bone geometry samples.
- f) Bone morphology plays an important role in the risk revision assessment, particularly, increase in the width of the femur at the lesser trochanter region may decrease implant migration.
- h) A deterministic approach can lead to false conclusions and is unable to give a high fidelity prediction compared to the stochastic approach.
- g) Finally, this framework is well suited for development of patient-specific, population-based, and other variability-prone applications; for instance, patient-specific pre-operative planning, population-based device testing, iterative implant design procedure, and a scientific hypothesis testing tool.

Chapter 7

Future Work

- a) Full-scale Monte Carlo simulations need to be carried out to further test validity of the framework. This would involve selection of a different failure criterion, capable of predicting risk, based on shorter time periods, e.g. inducible displacements, cement damage, or possibly combinations of the factors. Furthermore, response surface nature and minimum requirements for good predictions need to be identified.
- b) Secondly, a retrospective study similar to Lennon *et al.* [94] needs to be carried out. Uncertainties related to the implant and cement positioning, as well as bone properties can be included. Possibly, the dataset of cases needs to be extended to allow more reliable conclusions. Alternatively, a comparison of other implants can be done with more publicly available information on their performance, e.g. Lubinus SPII vs Müller [123, 2].
- c) Thirdly, a number of possible improvements to the framework can be made: (i) include variability of the material properties and muscle loads, which were important in other studies [88, 91], etc.; (ii) increase number of failure scenarios, for instance, include particulate wear scenario; (iii) run a larger number of FE simulations to increase the deterministic training set; etc.

List of attended international conferences and publications

Galibarov, P.E., Lennon, A.B., Prendergast, P.J., Automated X-ray analysis for patient-specific 3D femur model generation and classification for pre-operative planning, in: Proceedings of the 15th Annual Symposium on Computational Methods in Orthopaedic Biomechanics, pre-ORS 2007, February, 10, 2007, San Diego, California, United States

Galibarov, P.E., Lennon, A.B., Prendergast, P.J., Automated generation of 3D bone models from planar X-ray images for patient-specific finite element modeling applications, in: editor(s) JMRS Tavares, RM Natal Jorge, book chapter in Computational Modelling of Objects Represented in Images, London, Taylor & Francis Group, 2007, pp. 191 - 195.

Galibarov, P.E., Lennon, A.B., Prendergast, P.J., Patient-specific finite element models based on radiographs for pre-operative planning, in: Proceedings of the 2007 Summer Workshop of the European Society of Biomechanics, Finite Element Modelling in Biomechanics and Mechanobiology, Trinity College Dublin, 26-28 August 2007, edited by Lennon, A.B., Prendergast, P.J., Trinity Centre for Bioengineering, Trinity College Dublin, Ireland

Galibarov, P.E., Lennon, A.B., Prendergast, P.J., Assessing the influence of bone properties and anatomical accuracy on computational prediction of revision risk of cemented hip prosthesis, in: Proceedings of the 17th Annual Meeting of the European Orthopaedic Research Society, April, 24-26, 2008, Madrid, Spain

Galibarov, P.E., Lennon, A.B., and Prendergast, P.J., Retrospective evaluation of an automated method for generating patient-specific FE femur models, in: Pro-

ceedings of the 16th Congress of European Society of Biomechanics, ESB2008, July, 6-9, 2008, Lucerne, Switzerland

Galibarov, P.E., Lennon, A.B., and Prendergast, P.J., Quantitative assessment of a technique for patient-specific geometry from planar radiographs., in: Proceedings of the 4th European Congress For Medical and Biomedical Engineering 2008, "Engineering for Health", FCCC Antwerp, November, 23-27, 2008, International Federation for Medical and Biomedical Engineering, Antwerp, Belgium

Galibarov, P.E., Prendergast, P.J., and Lennon, A.B., Simulating variable performance of joint replacements in patient-specific and population-based scenarios, in: Proceedings to the 9th International Symposium, Computer Methods in Biomechanics and Biomedical Engineering, CMBBE2010, February, 24-27, 2010, Valencia, Spain

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Appendix A

Mesh quality

Table A.1: The standardized femur + F40 implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	8.563e-001	1.229e-001	2.024e-001	9.993e-001
X+	J_{scaled}	8.493e-001	1.332e-001	2.629e-001	9.994e-001
X-	J_{scaled}	8.569e-001	1.241e-001	1.268e-001	9.993e-001
Y+	J_{scaled}	8.463e-001	1.308e-001	2.432e-001	9.993e-001
Y-	J_{scaled}	8.572e-001	1.204e-001	2.697e-001	9.993e-001
Z+	J_{scaled}	8.545e-001	1.247e-001	2.676e-001	9.994e-001
Z-	J_{scaled}	8.549e-001	1.238e-001	2.555e-001	9.993e-001
00	f_{shape}	5.425e-001	1.759e-001	9.826e-002	9.380e-001
X+	f_{shape}	5.403e-001	1.793e-001	1.084e-001	9.376e-001
X-	f_{shape}	5.425e-001	1.744e-001	8.514e-002	9.371e-001
Y+	f_{shape}	5.421e-001	1.778e-001	1.124e-001	9.371e-001
Y-	f_{shape}	5.422e-001	1.758e-001	1.881e-001	9.395e-001
Z+	f_{shape}	5.425e-001	1.763e-001	1.535e-001	9.377e-001
Z-	f_{shape}	5.426e-001	1.762e-001	1.364e-001	9.386e-001
00	f_{skew}	3.162e-001	1.923e-001	1.561e-002	8.170e-001
X+	f_{skew}	3.228e-001	1.992e-001	1.176e-002	8.352e-001
X-	f_{skew}	3.142e-001	1.914e-001	5.874e-003	8.938e-001
Y+	f_{skew}	3.243e-001	1.944e-001	5.750e-003	8.407e-001
Y-	f_{skew}	3.185e-001	1.942e-001	1.375e-002	8.219e-001
Z+	f_{skew}	3.177e-001	1.944e-001	1.019e-002	8.217e-001
Z-	f_{skew}	3.174e-001	1.930e-001	1.547e-002	8.302e-001

Table A.2: The standardized femur + F40EH implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	7.439e-001	1.835e-001	1.656e-001	9.997e-001
X+	J_{scaled}	7.385e-001	1.908e-001	1.463e-001	9.997e-001
X-	J_{scaled}	7.456e-001	1.823e-001	1.145e-001	9.997e-001
Y+	J_{scaled}	7.305e-001	1.872e-001	1.268e-001	9.997e-001
Y-	J_{scaled}	7.490e-001	1.897e-001	2.127e-001	9.997e-001
Z+	J_{scaled}	7.439e-001	1.838e-001	1.779e-001	9.997e-001
Z-	J_{scaled}	7.429e-001	1.842e-001	1.515e-001	9.997e-001
00	f_{shape}	5.723e-001	2.139e-001	4.209e-002	9.547e-001
X+	f_{shape}	5.705e-001	2.171e-001	4.341e-002	9.548e-001
X-	f_{shape}	5.726e-001	2.133e-001	2.423e-002	9.546e-001
Y+	f_{shape}	5.702e-001	2.137e-001	9.373e-003	9.522e-001
Y-	f_{shape}	5.714e-001	2.168e-001	4.860e-002	9.572e-001
Z+	f_{shape}	5.722e-001	2.141e-001	4.770e-002	9.550e-001
Z-	f_{shape}	5.721e-001	2.141e-001	3.621e-002	9.545e-001
00	f_{skew}	4.745e-001	2.736e-001	3.981e-003	9.113e-001
X+	f_{skew}	4.763e-001	2.760e-001	4.468e-003	9.468e-001
X-	f_{skew}	4.737e-001	2.731e-001	3.780e-003	9.472e-001
Y+	f_{skew}	4.908e-001	2.793e-001	5.054e-003	9.437e-001
Y-	f_{skew}	4.620e-001	2.724e-001	4.043e-003	9.428e-001
Z+	f_{skew}	4.748e-001	2.742e-001	4.905e-003	9.155e-001
Z-	f_{skew}	4.747e-001	2.732e-001	4.034e-003	9.243e-001

Table A.3: The standardized femur + LNLS implant, X+ failed to mesh due to very thin layers

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	5.487e-001	2.444e-001	0.1795e-001	9.99e-001
X-	J_{scaled}	5.588e-001	2.514e-001	0.1337e-001	9.99e-001
Y+	J_{scaled}	5.463e-001	2.548e-001	0.1044e-001	9.99e-001
Y-	J_{scaled}	5.641e-001	2.555e-001	0.1629e-001	9.99e-001
Z+	J_{scaled}	5.549e-001	2.537e-001	0.1377e-001	9.99e-001
Z-	J_{scaled}	5.557e-001	2.541e-001	0.1400e-001	9.99e-001
00	f_{shape}	4.861e-001	2.013e-001	7.325e-002	9.932e-001
X-	f_{shape}	4.941e-001	2.025e-001	5.183e-002	9.931e-001
Y+	f_{shape}	4.893e-001	2.067e-001	1.274e-001	9.940e-001
Y-	f_{shape}	4.958e-001	2.059e-001	6.710e-002	9.926e-001
Z+	f_{shape}	4.924e-001	2.054e-001	7.880e-002	9.931e-001
Z-	f_{shape}	4.928e-001	2.049e-001	6.928e-002	9.932e-001
00	f_{skew}	6.742e-001	2.879e-001	2.446e-002	9.778e-001
X-	f_{skew}	6.638e-001	2.903e-001	9.841e-003	9.765e-001
Y+	f_{skew}	6.703e-001	2.874e-001	2.440e-002	9.765e-001
Y-	f_{skew}	6.546e-001	2.937e-001	2.446e-002	9.768e-001
Z+	f_{skew}	6.649e-001	2.906e-001	2.461e-002	9.756e-001
Z-	f_{skew}	6.635e-001	2.911e-001	1.702e-002	9.756e-001

Table A.4: The composite femur 3rd generation + F40 implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	6.388e-001	2.273e-001	1.959e-001	9.990e-001
X+	J_{scaled}	6.385e-001	2.240e-001	1.647e-001	9.995e-001
X-	J_{scaled}	6.319e-001	2.331e-001	2.098e-001	9.986e-001
Y+	J_{scaled}	6.303e-001	2.308e-001	1.765e-001	9.990e-001
Y-	J_{scaled}	6.420e-001	2.240e-001	2.087e-001	9.990e-001
Z+	J_{scaled}	6.366e-001	2.273e-001	2.107e-001	9.991e-001
Z-	J_{scaled}	6.357e-001	2.262e-001	1.858e-001	9.990e-001
00	f_{shape}	5.144e-001	1.854e-001	1.540e-001	9.791e-001
X+	f_{shape}	5.145e-001	1.827e-001	1.417e-001	9.778e-001
X-	f_{shape}	5.110e-001	1.902e-001	1.551e-001	9.818e-001
Y+	f_{shape}	5.107e-001	1.878e-001	1.541e-001	9.780e-001
Y-	f_{shape}	5.154e-001	1.836e-001	1.535e-001	9.792e-001
Z+	f_{shape}	5.133e-001	1.869e-001	1.505e-001	9.797e-001
Z-	f_{shape}	5.133e-001	1.841e-001	1.544e-001	9.780e-001
00	f_{skew}	5.955e-001	2.892e-001	6.695e-003	9.685e-001
X+	f_{skew}	5.990e-001	2.852e-001	3.226e-003	9.691e-001
X-	f_{skew}	5.959e-001	2.903e-001	1.626e-002	9.679e-001
Y+	f_{skew}	5.999e-001	2.890e-001	6.650e-003	9.692e-001
Y-	f_{skew}	5.957e-001	2.872e-001	7.525e-003	9.690e-001
Z+	f_{skew}	5.957e-001	2.891e-001	7.648e-003	9.690e-001
Z-	f_{skew}	5.984e-001	2.875e-001	6.542e-003	9.688e-001

Table A.5: The composite femur 3rd generation + F40EH implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	8.669e-001	1.206e-001	2.473e-001	9.981e-001
X+	J_{scaled}	8.583e-001	1.341e-001	1.910e-001	9.985e-001
X-	J_{scaled}	8.691e-001	1.182e-001	1.921e-001	9.979e-001
Y+	J_{scaled}	8.679e-001	1.208e-001	2.371e-001	9.981e-001
Y-	J_{scaled}	8.708e-001	1.173e-001	2.339e-001	9.981e-001
Z+	J_{scaled}	8.666e-001	1.207e-001	2.540e-001	9.985e-001
Z-	J_{scaled}	8.493e-001	1.104e-001	2.244e-001	9.981e-001
00	f_{shape}	6.079e-001	1.626e-001	1.373e-002	9.690e-001
X+	f_{shape}	6.048e-001	1.686e-001	4.110e-002	9.665e-001
X-	f_{shape}	6.083e-001	1.623e-001	3.939e-002	9.695e-001
Y+	f_{shape}	6.099e-001	1.607e-001	5.546e-002	9.685e-001
Y-	f_{shape}	6.063e-001	1.656e-001	3.337e-002	9.701e-001
Z+	f_{shape}	6.078e-001	1.628e-001	6.361e-002	9.665e-001
Z-	f_{shape}	6.071e-001	1.461e-001	7.468e-002	9.454e-001
00	f_{skew}	2.996e-001	1.817e-001	5.647e-003	8.717e-001
X+	f_{skew}	3.065e-001	1.897e-001	1.587e-002	9.457e-001
X-	f_{skew}	2.982e-001	1.797e-001	4.958e-003	8.898e-001
Y+	f_{skew}	2.980e-001	1.814e-001	5.676e-003	8.445e-001
Y-	f_{skew}	2.937e-001	1.794e-001	2.013e-003	8.440e-001
Z+	f_{skew}	3.002e-001	1.822e-001	1.216e-002	8.506e-001
Z-	f_{skew}	3.492e-001	1.890e-001	4.035e-003	8.573e-001

Table A.6: The composite femur 3rd generation + LNLS implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	7.559e-001	1.616e-001	2.900e-001	9.992e-001
X+	J_{scaled}	7.451e-001	1.705e-001	2.445e-001	9.988e-001
X-	J_{scaled}	7.443e-001	1.675e-001	2.888e-001	9.992e-001
Y+	J_{scaled}	7.569e-001	1.611e-001	1.818e-001	9.990e-001
Y-	J_{scaled}	7.344e-001	1.741e-001	2.279e-001	9.990e-001
Z+	J_{scaled}	7.498e-001	1.642e-001	2.744e-001	9.990e-001
Z-	J_{scaled}	7.476e-001	1.662e-001	2.900e-001	9.988e-001
00	f_{shape}	6.011e-001	1.601e-001	1.630e-001	9.399e-001
X+	f_{shape}	5.986e-001	1.649e-001	8.996e-002	9.380e-001
X-	f_{shape}	5.982e-001	1.639e-001	1.960e-001	9.407e-001
Y+	f_{shape}	6.034e-001	1.604e-001	1.276e-001	9.363e-001
Y-	f_{shape}	5.947e-001	1.654e-001	1.327e-001	9.425e-001
Z+	f_{shape}	6.007e-001	1.615e-001	1.893e-001	9.389e-001
Z-	f_{shape}	5.998e-001	1.621e-001	1.387e-001	9.402e-001
00	f_{skew}	4.767e-001	2.618e-001	1.068e-002	8.828e-001
X+	f_{skew}	4.831e-001	2.625e-001	2.490e-003	9.171e-001
X-	f_{skew}	4.895e-001	2.646e-001	1.278e-002	8.966e-001
Y+	f_{skew}	4.733e-001	2.591e-001	1.138e-002	8.903e-001
Y-	f_{skew}	5.003e-001	2.683e-001	9.167e-003	9.092e-001
Z+	f_{skew}	4.840e-001	2.627e-001	1.241e-002	8.968e-001
Z-	f_{skew}	4.859e-001	2.633e-001	2.006e-003	9.023e-001

Table A.7: The Visible human femur + F40 implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	7.398e-001	1.648e-001	1.855e-001	9.994e-001
X+	J_{scaled}	7.160e-001	1.966e-001	1.172e-001	9.989e-001
Y+	J_{scaled}	7.419e-001	1.615e-001	7.993e-002	9.994e-001
Y-	J_{scaled}	7.261e-001	1.838e-001	2.452e-001	9.994e-001
Z+	J_{scaled}	7.359e-001	1.680e-001	1.953e-001	9.991e-001
Z-	J_{scaled}	7.398e-001	1.653e-001	1.766e-001	9.991e-001
00	f_{shape}	5.720e-001	1.795e-001	1.624e-001	9.761e-001
X+	f_{shape}	5.625e-001	1.932e-001	1.413e-001	9.778e-001
Y+	f_{shape}	5.721e-001	1.772e-001	5.442e-002	9.772e-001
Y-	f_{shape}	5.663e-001	1.900e-001	1.764e-001	9.777e-001
Z+	f_{shape}	5.708e-001	1.810e-001	1.471e-001	9.761e-001
Z-	f_{shape}	5.716e-001	1.793e-001	1.799e-001	9.790e-001
00	f_{skew}	5.012e-001	2.507e-001	9.943e-003	9.157e-001
X+	f_{skew}	5.107e-001	2.577e-001	1.204e-002	9.334e-001
Y+	f_{skew}	5.057e-001	2.506e-001	1.072e-002	9.449e-001
Y-	f_{skew}	5.020e-001	2.572e-001	1.174e-002	9.332e-001
Z+	f_{skew}	5.039e-001	2.528e-001	8.963e-003	9.227e-001
Z-	f_{skew}	5.007e-001	2.512e-001	9.644e-003	9.207e-001

Table A.8: The Visible Human femur + F40EH implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	8.805e-001	1.027e-001	3.381e-001	9.996e-001
X+	J_{scaled}	8.758e-001	1.104e-001	3.219e-001	9.996e-001
X-	J_{scaled}	8.858e-001	9.492e-002	3.276e-001	9.996e-001
Y+	J_{scaled}	8.906e-001	9.237e-002	3.129e-001	9.996e-001
Y-	J_{scaled}	8.679e-001	1.170e-001	2.741e-001	9.996e-001
Z+	J_{scaled}	8.803e-001	1.028e-001	3.203e-001	9.996e-001
Z-	J_{scaled}	8.825e-001	1.000e-001	3.484e-001	9.996e-001
00	f_{shape}	6.316e-001	1.858e-001	1.155e-001	9.751e-001
X+	f_{shape}	6.293e-001	1.893e-001	9.347e-002	9.749e-001
X-	f_{shape}	6.333e-001	1.832e-001	1.350e-001	9.750e-001
Y+	f_{shape}	6.342e-001	1.820e-001	1.329e-001	9.757e-001
Y-	f_{shape}	6.283e-001	1.914e-001	6.393e-002	9.736e-001
Z+	f_{shape}	6.315e-001	1.862e-001	1.203e-001	9.749e-001
Z-	f_{shape}	6.318e-001	1.852e-001	1.105e-001	9.748e-001
00	f_{skew}	2.851e-001	1.647e-001	5.834e-003	7.786e-001
X+	f_{skew}	2.906e-001	1.703e-001	6.356e-003	8.191e-001
X-	f_{skew}	2.780e-001	1.580e-001	5.012e-003	7.877e-001
Y+	f_{skew}	2.728e-001	1.567e-001	5.455e-003	7.948e-001
Y-	f_{skew}	2.985e-001	1.756e-001	5.047e-003	8.283e-001
Z+	f_{skew}	2.848e-001	1.642e-001	6.315e-003	7.733e-001
Z-	f_{skew}	2.831e-001	1.632e-001	4.788e-003	7.800e-001

Table A.9: The Visible Human femur + LNLS implant

Model	Function Name	Average	Std. Dev.	Minimum	Maximum
00	J_{scaled}	6.607e-001	2.128e-001	2.353e-001	9.993e-001
X+	J_{scaled}	6.555e-001	2.164e-001	2.491e-001	9.993e-001
X-	J_{scaled}	6.645e-001	2.108e-001	2.019e-001	9.993e-001
Y+	J_{scaled}	6.666e-001	2.108e-001	2.153e-001	9.994e-001
Y-	J_{scaled}	6.499e-001	2.190e-001	1.925e-001	9.993e-001
Z+	J_{scaled}	6.612e-001	2.131e-001	2.444e-001	9.993e-001
Z-	J_{scaled}	6.617e-001	2.126e-001	2.281e-001	9.993e-001
00	f_{shape}	5.611e-001	1.919e-001	1.676e-001	9.950e-001
X+	f_{shape}	5.585e-001	1.954e-001	1.403e-001	9.948e-001
X-	f_{shape}	5.628e-001	1.898e-001	1.472e-001	9.951e-001
Y+	f_{shape}	5.626e-001	1.909e-001	1.455e-001	9.947e-001
Y-	f_{shape}	5.578e-001	1.954e-001	1.634e-001	9.951e-001
Z+	f_{shape}	5.613e-001	1.919e-001	1.696e-001	9.950e-001
Z-	f_{shape}	5.613e-001	1.917e-001	1.627e-001	9.950e-001
00	f_{skew}	5.679e-001	2.858e-001	4.106e-003	9.362e-001
X+	f_{skew}	5.696e-001	2.855e-001	3.762e-003	9.344e-001
X-	f_{skew}	5.662e-001	2.867e-001	4.288e-003	9.377e-001
Y+	f_{skew}	5.625e-001	2.846e-001	3.296e-003	9.396e-001
Y-	f_{skew}	5.746e-001	2.865e-001	4.080e-003	9.446e-001
Z+	f_{skew}	5.670e-001	2.864e-001	4.247e-003	9.363e-001
Z-	f_{skew}	5.669e-001	2.860e-001	3.203e-003	9.359e-001