Patient-Specific Quantitative Analysis of Bone Fracture Fixations: Evaluation of Clinical Application

Thesis submitted for the degree of "Doctor of Philosophy"

By

Eran Peleg

Submitted to the Senate of the Hebrew University of Jerusalem
6/2009
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This work was carried out under the supervision of:

1. Prof. Aharony Lev-Tov

2. Prof. Meir Liebergall
Abstract

When assessing a fracture, an orthopedic surgeon has to integrate multiple factors before deciding on the optimal treatment plan. These include patient-factors, surgeon-specific factors, hospital-specific factors and mainly fracture-specific factors such as bone quality, number of fragments and fracture classification.

Existing computer-aided preoperative planning software provide a 2D environment for visualization, measurement, and implant selection and positioning tools that assist in preplanning, however, none provide the ability to perform biomechanical evaluation of the broken bone and or the different fixation devices.

In this study, we present a new preplanning and analysis workflow with a purpose to address patient specific needs regarding fracture care. The workflow provides clinically relevant biomechanical information which is important for the preplanning phase, intra-operative execution and for post operative evaluation and treatment. The workflow enables preplanning of fracture reduction, implant positioning and choosing the implant. We chose to focus on proximal femoral neck fractures (perchoanteric) because of their high prevalence and the vast clinical knowledge available regarding this issue.

The main challenge when constructing such a workflow is its ability to present relatively low sensitivity to uncertainties in model input variables. This is a prerequisite, in addition to other requirements put forth by the clinicians, which all together create a clinically relevant technological tool.

The workflow presented in this study, implements maximal principle strain ratio (SR) as the primary field-output variable. The SR field-output variable was acquired by employing a comparative analysis algorithm developed in house, enabling computation and presentation of stress shielded and over strained patterns that
develop in the fractured/fixated bone relative to the natural intact bone before its failure.

The motivation for the use of the SR field-output variable is its ability to present results in an intuitive manner for the clinicians while damping the errors that arise from uncertainties in model input variables. This is particularly important when coping with uncertainties in density based elasticity relationships.

The first phase of this study presents sensitivity tests carried out with one specific patient model and two types of fixative solutions. Uncertainties in model input variables were examined for their influence on outcome. Controlled input parameters such as implant positioning were also examined. The second phase was a retrospective study in which the whole workflow was carried out for five different authentic cases enabling examination of a patient-specific approach in a modeling process.

The proposed SR based method was found to be in-sensitive to uncertainties in model inputs such as density-based elasticity relationship. Response to implant positioning, specifically the location of the slide screw in the femur head, complied with known clinical outcomes. The workflow exhibited patient-specific results according to fracture configuration, bone morphology and anatomy.

The outcome of this study is a novel patient specific methodology which may support clinical decision making in the field of fracture care, taking biomechanical considerations as a key factor. In addition, the process and tools developed may assist in additional clinical oriented subjects such as training and inquiry of failure mechanisms. Additional development is needed in order to create a full seamless workflow enabling reduction in labor time. Further research is required with larger population and fracture types.
To conclude, the workflow has the potential to improve patient outcome
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Introduction

1.1 Background

Choosing and executing an optimal treatment plan for skeletal fractures in clinical practice is a complex procedure, requiring simultaneous consideration of patient, surgeon, hospital, and fracture-specific factors. Treatment decisions are often qualitative, based on general guidelines and experience/training of the orthopedic surgeons, and therefore, treatment plans for similar medical cases can vary widely among orthopedists despite the use of standard fracture classification and treatment algorithms (Audige et al, 2004)

Despite its potential to assist in quantifying fracture fixation and thus in improve patient outcome, computational patient-specific modeling for selection and planning of fracture treatments is limited at present. Current preoperative planning is not routinely used. when performed: usually it consists of digital implant templating on two dimensional X-ray images, and include angle and distance measurements and position planning. Finite element analysis (FEA) of fracture fixation models derived from computed tomography (CT) scans of individuals holds great potential to provide quantitative patient-specific analysis and evaluation tools but currently its not used in clinical practice.

Indeed, many studies of patient specific FEA based on CT data sets have been reported in the literature over the last two decades, but still, the medical community as well as the orthopedic community, has not been "enthusiastic" to adopt this technology. Patient specific modeling is regarded as a time consuming process with little affect on patient treatment and outcome.
In this study we present a new approach in which patient specific modeling and FEA may be implemented in a clinical environment involving trauma care. Sensitivity tests were carried out in order to assess robustness to uncontrolled model input variables on one hand and response to controlled modeling variables on the other.

Initially, we decided to focus on proximal femur fractures analyzing both the pattern of the fracture and different fixations methods. Specifically we used CT data sets of pertrochanteric fractures simple and multi fragmentary fractures. It was decided to focus on this type of fractures since they are very common, they impose significant economic burden on the society and because of the vast knowledge and literature about these fractures.

1.2 Literature review

Patient specific model creation

During the past 25 years extensive work has been reported regarding the improvement, validation and atomizing patient specific finite element modeling from quantitative CT data sets. The basic steps required for constructing a patient specific model include: surface extraction of the desired bone region, creating a volumetric mesh and assigning density based isotropic material properties to each element by translating the average Hounsfield unit to bone density (apparent or ash) and then computing bone elasticity of the certain element by using one of the known density based elasticity relationships (Carter et al., 1977; Keller, 1994; Helgason et al, 2007; Morgan et al, 2000; Wirtz et al, 2000). Keyak et al, introduced and validated a voxel based mesh method. (Keyak, et al., 1990; Keyak et al, 1993).

In this technique each brick element comprising the mesh is related to a voxel created by the CT data set. The main advantage of the voxel based technique is high
automation, the disadvantage is the unsmooth bone surface creating inaccuracies especially when surface stresses are of interest. (Viceconti et al, 1998)

Other automated mesh generation techniques require an additional semi-manual step in order to extract surface geometry (Viceconti et al, 2004). This step is usually performed by segmentation of CT slices and then, after possessing a surface mesh, creating a volumetric mesh. Material properties are assigned to the elements by first calculating the average HU of each element (Taddei et al, 2004; Zannoni et al, 1998) and then calculating density based elasticity as described before. The different techniques of automated mesh generation and material property assignment have been evaluated for their accuracy (Schileo et al, 2007; Taddei et al, 2004; Taddei et al, 2006; Taddei, Cristofolini et al 2006;Viceconti et al, 1998; Viceconti et al, 2004).

Clinical applications of patient specific FE modeling

Naturally, failure prediction at static loading condition is one example of a possible clinical use that has been reported (Cody et al, 1999; Keyak et al., 1998; Keyak and Rossi, 2000; Keyak et al., 2001; Testi et al., 2004) These studies focused on the ability of patient specific finite element models to predict proximal femur fracture failure. Different failure criterions were assessed and validated against in vitro models. All studies mentioned above used whole bone models of the proximal femur. Failure predictions of total hip implants have also been reported. Of main concern was the implant-bone interface reaction (Stolk et al, 2002; Reggiani et al, 2007) and implant loosening as a result of stress shielding (Anderson et al, 1999; Garcia et al, 2002; Huiskes et al, 1987; Pawlikowski et al, 2003; Rietbergen et al, 1993; Weinans et al, 2000)
Proximal femur fractures and fixations

The failure of fixation of peritrochantenic femoral neck fractures is of major concern to patients and the health care systems. Many clinical studies have been carried out in order to determine whether one fixation device has an advantage over the other (for example intra-medullar versus extra-medullar) moreover studies looked for parameters that can be used in order to predict failure of treatment with different implants (Adams et al, 2001; Baumgaertner et al, 1995; Baumgaertner et al, 1998; Cleveland et al., 1959; Hardy et al, 1999; Harrington et al, 2002; Haynes et al, 1997; Saudan et al, 2002; Walton et al, 2007) After reviewing the literature we could not define any specific implant that has been found to be significantly favorable over the other concerning stable pertochanteric fractures. There a re several classifications for femoral neck fracture. In this research we used that of the Orthopedic Trauma Association (OTA-AO/OTA) and in particular we refer to fractures that are classified as 31-A1 and 31-A2 fractures. Among the different failures reported cut out of the sliding screw has been strongly correlated with slide screw positioning (Baumgaertner, 1995) (Davis, 1990) but not with implant type. Finite element studies have dealt with fixation of femur neck fracture fixation but not on a patient specific basis (Seral et al, 2004; Sowmianarayanan et al, 2008)

To the best of our knowledge, no attempt has been made to evaluate patient specific finite element modeling as a pre-operative planning tool or as a post-operative evaluation and treatment tool for femur neck fracture fixations in a clinical environment, neither has it been implemented in massive retrospective studies. The clinical experience and importance of these fractures makes them a good alternative to begin with.
1.3 Method overview and planned workflow

Figure 1 describes a general workflow for a patient specific preplanning or for retrospective evaluation in a clinical environment.

![Diagram of workflow](image)

Figure 1 – A general patient specific modeling workflow to be employed in a clinical environment. A CT scan is a prerequisite for any modeling procedure. If the process is to be used as a preplanning tool, than the modeling and analysis steps are to be carried out before the surgical procedure (black line arrows and text boxes). If the process is carried out retrospectively (dotted arrows and text boxes), than results can be used for post-operative evaluation.

Detailed and good quality CT scan data of the affected region is crucial for the analysis. Although it may be regarded as a draw back for planned proposed procedures since usually femoral neck surgery is carried out without the need of a CT scan, this technology is currently used in most hospitals, including for diagnostic orthopaedic problem such as hip fractures. A three dimensional model of the fractured bone is generated from the CT data with available tools such as semi-automatic segmentation. Than the fracture is virtually reduced and the implants are positioned according to the surgeon preferences. The virtual fracture reduction and implant positioning are carried out by a clinician. For standard cases, the modeling stage may be sufficient for further treatment. If biomechanical analysis is required, the model data is imported into a finite element analysis environment and results are analyzed as part of a decision making process.
There are several situations where it is reasonable to first carry out a known surgical procedure and perform the modeling and analysis retrospectively; 1) the procedure is straightforward but there is a need for post-operative evaluation for further treatment and 2) clinical studies. In these scenarios the modeling and analysis would be carried out parallel to patient treatment (dotted text boxes in figure 1).

Different techniques, algorithms and tools may comprise a modeling and analysis methodological workflow. If such a workflow is to be adapted into a clinical environment, the following conditions are to be met; 1) Generality - ability to provide well-conditioned meshes for all bones, independently from their geometric complexity, 2) Robustness - thr. ability to generate a mesh of almost every data set (Viceconti, M., 2004) and 3) Clinical relevance - the added value to patient treatment must be significant relative to the effort required for completing such a workflow.

In this study, the new approach and technique presented emphasize the relevance of biomechanical information which is essential for the optimal solution for specific fracture care. Sensitivity tests were carried out in order to assess the effects of un-controlled and controlled parameters.

1.4 Novel aspects

General concept

The most common field-output variables for finite element analysis are stress (von-Mises) and strain. Specifically strains calculated by numerical simulations can be validated in-vitro with use of strain gauges. However, from the clinical point of view, there are a few limitations for the use of these field-output variables; 1) Stresses and strains are sensitive to the value of Young-modulus. This means that any change in choice of density based elasticity relationship would strongly influence field-output results (Weinans et al, 2000; Schileo et al, 2007). Moreover stresses and strains are
not intuitive from a clinicians’ point of view thus it is difficult to derive significant clinical information.

In this study, we present the use of maximal principal strain ratio (SR) as a preferred field-output variable.

The SR variable expresses the ratio between the maximal principle strains evolving in an element in the virtually reduced and fixated bone to that evolving in the same specific intact bone. The result is a dimensionless indicator expressing the degree of stress shielding (if SR<1) or over stressed regions.

The use of a dimensionless strain based variable withholds a few advantages;

- Numerical - sensitivity to unknown parameters such as load and density-based elasticity relationships is reduced (Weinans et al, 2000).
- Simplicity - it can be easily implemented in an automated subject-specific FE model maintaining the highest possible degree of automation (Schileo et al, 2007).
- Physiological - Adaptive elasticity theory states that the rate of adaptation is coupled to the difference between the equilibrium (intact bone) and the actual strain states (fixated bone) (Cowin and Hart., 1985). Adaptive elasticity has been validated in-vivo (Anderson et al., 1999; Cowin and Hart., 1985), and in finite element studies (Garcia et al, 2002; Gefen, 2002; Huiskes et al, 1987; Pawlikowski et al, 2003; Rietbergen, 1993; Ruimerman, 2005).
- Failure criteria – maximal principal strain has been proved to be a better predictor for fracture than Von Mises stress and max principal stress (Schileo et al, 2008). In addition, yield strain was found to be independent on elasticity values and orientation (Bayraktar et al., 2004; Ford et al, 1996; Bayraktar, 2004) (Ford and Keaveny, 1996).
In the proposed workflow (figure 1), the analysis stage includes two finite element simulations both creating maximal principal strain values; one of the fixated bone (fractured bone with implants) and one for the same specific virtually intact bone (virtually fused fracture surfaces without implants). This enables to present a comparative biomechanical analysis between the fixated bone relative to its natural state before fracture occurred without the need to construct an intact model from the non-broken opposite side bone which may be asymmetric in anatomy and pathology. The comparative biomechanical analysis was implemented with an in-house developed algorithm and software. The end result is a model presenting SR patterns which are much more intuitive to clinicians and present relevant clinical information. The sequence of the workflow is compatible with a clinical environment workflow in which a patient arrives with a fractured bone and there are no healthy control or any bone available for biomechanical analysis.

*Sensitivity tests*

Sensitivity tests are usually performed to investigate how uncertainties in model input influence the analysis results (Viceconti, 2005). Certainly, the workflow suggested, would be used for comparing one fracture fixation solution against the other (fixation device, fixation placement etc), because of this, sensitivity tests were performed for the whole workflow and for two fixation devices using the same affected bone. The sensitivity analysis assessed the ability to compare two fixative solutions for different model inputs such as density-based elasticity relationship, implant material etc.
Sensitivity to implant positioning, specifically sliding-screw positioning in femur head, was performed and results were compared to known results of clinical studies.

Patient specific response

The workflow was carried out for five different real patients’ CT scans presenting different types of fracture classifications, with different anatomy and morphology. Performing such a workflow, using this patient's data, represent a patient-specific approach.

1.5 Goals of research

The main goal of this research was to construct a new workflow and to evaluate the use of patient-specific modeling and biomechanical analysis in the clinical environment in the preoperative preplanning phase, and in the post-operative evaluation phase or for retrospective analysis of the treatment. Specifically we tested the hypothesis that; 1) The use of the SR field-output variable presents a potential as an intuitive, less sensitive and more clinically useful indicator, 2) the workflow has the potential to be clinically relevant meaning that the added value to patient outcome is substantial relative to the effort required and 3) the choice of a fixative solution is patient specific and that a patient-specific biomechanical analysis is desired.

1.6 Thesis organization

In general, this research had three stages: preliminary tests and developments, extensive sensitivity tests with one specific model and the analysis of five cases (one cadaver and four patients). The methods and results chapters follow this chronological order.
Methods

2.1 Preliminary mechanical tests with cadavers

The methodology was initially assessed with cadaver specimens. Cadaveric studies are routinely used in any biomechanical clinical orthopedic evaluations, and refereed as "gold standard". In this study, they were needed in order examine the capabilities and improve the tools used in the study. It was also important to determine whether it is suitable to implement a simplified linear approach and what are the limits of the linear region. It was not less important to better understand failure mechanism of the mechanical construct. It was not in the scope of this study to perform experimental validation of pre and post operational principal strains. A validation study was performed by Peterson et al (Peterson et al, 2009) for a straight cemented prosthesis.

Three fresh femurs were harvested from cadavers within 24 hours of the beginning of the perfusion procedure. This ensured minimal effects of the preservation protocol on the bone's mechanical properties (Wingerter et al, 2006). The femurs were then cleaned of soft tissues and a AO/OTA 31-A1 extra-articular femoral neck fracture was introduced with a disk (Fig 2a). The bone fragments were scanned together in a Philips Brilliance 64ME CT machine at the Hadassah University Medical Center, Jerusalem, Israel. Each CT dataset had approximately 300 slices, with a slice thickness of 1mm and pixel area of 0.195×0.195mm². Following the CT scan, the femoral neck fractures were fixated with a Richards® 135° DHS following a standard orthopaedic surgical technique (Fig 2b). The femurs were then covered with a humid cloth and frozen at -20°C.
Figure 2 – Preparations for the human cadaver study
(a) A 31-A1 extra-articular fracture introduced with a disk. (b) the femurs were fixated with a Richards® 135° DHS as performed in a standard orthopedic surgical technique.
In order to examine the performance and failure mechanism of the fixated femur under quasistatic axial loading, a uniaxial compression test was carried out using an Instron 5544 uniaxial testing machine (Fig 3). Specifically, the femur was positioned upside down with the femoral head placed in a brass cup, and the distal end of the shaft was placed in a metallic cylinder and tightened with screws. Positioning the distal end of the femur shaft exactly above the femur head ensured minimal external bending moments. Deflection values of the actuator in contact with the distal end of the femur and the axial force applied by the actuator were recorded.
2.2 Convergence tests

A CT data set of an intact third generation saw-bone (Sawbones® Europe AB, Malmö, Sweden) was used for this section. A surface mesh was constructed by semi-automatic segmentation with AmiraDev 4.0. (Amira, Mercury computer systems) A rigid pin shaped implant pierced the femur head (Fig. 4). For the same model 10 different quality grids were created. The average element size was 4.17 mm for the coarse mesh and 2.135 mm for the finest mesh. The grids were exported to the ABAQUS finite element software package (ABAQUS SIMULA, Rising Sun Mills, Providence RI, USA). In all of the simulations the density elasticity relationship was $E = 6950\rho^{1.49}$ (Morgan et al, 2003) which has been found to correlate well in validation studies (Schileo et al, 2007). The load and boundary conditions were identical for all grids. For each model, two analyses were carried out: with the implant and without the implant. The average SR was calculated for the proximal region, which includes the screw bone interface and for the distal region which is not pierced by an implant. Maximum displacement was also measured for each grid.

![Figure 4- A grid quality test model. A grid created from a CT data set of a third generation sawbone. Nine other grids with varying grid qualities (mesh density) were created from the same CT data set](image-url)
2.2 Model generation

The proposed methodology for a future clinical workflow is summarized in the flowchart provided in Fig. 5.

Figure 5 – The planned workflow.
The Planned workflow is comprised of four main steps: CT scan, model generation which includes fracture reduction and implant positioning, comparative finite element analysis and evaluation of different solutions.
The input for the model generation process is a CT data set of the fractured bone. In the first step (Fig 5 - M1), a triangular surface mesh is created for each bone fragment using semi-automatic threshold segmentation.

In step two (Fig 5 - M2), the fracture is virtually reduced by positioning the bone fragments together. Implants, e.g. standard plates and screws are selected from a known database for virtual fracture fixation. To obtain a model of the fixated bone, Boolean subtraction operations are performed between the meshes of the bone fragments and the fixation hardware.

In the third step (Fig 5 - M3), a volumetric mesh is created by constrained Delaunay tetrahedralization from Delaunay triangulated surfaces. All tetrahedral elements are quadratic 10 nodes, and a circumradius to shortest edge ratio below 2.

In step four (Fig 5 - M4), mechanical properties are assigned to all elements (bone elements and implants). Each bone element $e_i$ is assigned an elastic modulus $E_{e_i}$, using an elasticity-density relationship as described elsewhere (Zannoni et al, 1998)

$$E_{e_i} = a \rho_{e_i}^b$$  \hspace{1cm} \text{Equation (1)}

where $\rho_{e_i}$ is the apparent density of the bone element in g/cm³, the value being determined from the local corresponding radiographic density in Hounsfield units (HU). Correlation between apparent density and HU is obtained using a standard linear based calibration. The specific elasticity-density relationship used is determined by user preferences (Wirtz et al, 2000; Helgason et al, 2007; Keyak, et al., 1998) Poisson's ratio is 0.3 (Wirtz et al, 2000), properties of implants are assigned according to manufactures data.
Model generation is implemented using AmiraDev4 software. In-house developed code and open source libraries were embedded into AmiraDev. Specifically, boolean subtraction between the implants and the surface mesh of the bone fragments are carried out using an open source library. (Opencascade 5.2) Automated volumetric meshing is carried out using the TetGen V1.4 open source library [http://tetgen.berlios.de/].

2.3 Comparative biomechanical analysis

Once the model generation is accomplished in the preplanning environment, a text file containing all model information is created. This includes; grid topology for bone and implants, material properties of all elements and surface definitions. The text file is imported into a FEA software. Two separate FEA simulations are carried out; one for the fixated bone model and another for a virtually intact bone model. For both models, fixated and intact, the external load and boundary conditions are identical.

*Fixated model*—Contact conditions between surfaces are defined as follows; a soft contact condition (exponential relationship between gap distance and pressure) is used for metal to metal surfaces such as screw heads to plate and for bone to bone surfaces. The soft contact condition ensures relatively fast convergence. Surfaces representing contact between screw threads and bone are bonded. In cases where there is a multi fragment fracture, only the fragments which are fixated in the real surgical procedure are modeled. Material properties of implants are assigned according to data of supplied by manufacture.

*Intact model*—all the fragments are fused with a "tie" condition at fracture surfaces and metal implants are removed. Cavities created by the removal of the implants are filled with elements with material properties similar to neighboring elements.
The simplified boundary conditions included fixating the distal tip of the femur shaft and a hip contact load equal to 2.5 times the patient's body weight is applied to the femur head. (The magnitude of the load has no implications on the results, since it is reduced when the two models are divided).

For both models, the topology of the bone grid is identical. This fact enables computing the ratio of any field-output variable with a relatively simple algorithm embedded inside the FEA software environment. As described in the introduction, principle strain was chosen as the field-output variable of most interest. The relationship between the principle strain in the fixated model to that of the principle strain in the intact model provided the dimensionless indicator SR defined as:

\[
SR = \frac{(\varepsilon_{\text{principle}})_{\text{fixated}}}{(\varepsilon_{\text{principle}})_{\text{int actd}}}
\]

Equation (2)

Once the SR value was computed for each element, strain shielded and over strained patterns were graphically visualized (Fig 6) and quantified for different regions of interest in femur shaft and head.
Figure 6 – Three dimensional Strain Ratio (SR) patterns. The comparative biomechanical analysis generates patterns of SR for each type of fixation. (a) The colored regions designate over-strained regions (SR>1). Dark blue designates SR=1. (b) The colored regions designate strain-shielded regions (SR<1). Dark red designates low SR values.
2.4 Comparing different fracture fixation devices

The main achievement of implementing a patient-specific modeling methodology into the clinical environment would be its ability to demonstrate the discrepancy between different fracture fixation solutions. In this study we choose to compare the biomechanical difference between an inter-medullar proximal femur fixating device (PFNA synhes®) and a proximal femur extra-medullary fixating device (DHS Richards®). Comparing clinical outcome between these two fixation types has been of great interest to the orthopaedic community and was thoughtfully discussed in the literature (Adams et al, 2001; Baumgaertner et al, 1998; Harrington et al, 2002; Hardy et al, 1999; Saudan et al, 2002).

For each fracture fixation device the entire procedure described in sections 2.3 and 2.4 was carried out. For each option SR values in the shaft regions and femur head fragment were quantified and presented graphically. At first, one specific patient model was used while carrying out extensive sensitivity tests for different parameters which may affect the analysis results. The second stage included four patient models and one cadaver model.

For all the models the average element length was below 2mm ensuring good tradeoff between numerical accuracy and computational weight (Viceconti et al, 2004) and in the asymptotic region of convergence for the required SR parameter.

2.5 Sensitivity tests for a specific patient model

The model used to carry out the sensitivity tests was constructed from a fractured femur of a 81 year old male. The femur was fractured into four fragments intertrochanteric fracture; shaft, femur head, lesser trochanter and greater trochanter. The fracture was classified as a 31-A2 fracture according to AO/OTA classification.
The patient was CT scanned (GE Lightspeed16, KVP 120 slice thickness 1.25 mm pixel spacing 0.86X0.86 mm). The whole procedure described in paragraphs 2.2 and 2.3 was carried out for two implant types; intra-medullar and extra medullar. Sensitivity checks were performed for uncertainties of the following parameters: elasticity-density relationship, implant material and force configuration (Table 1). The average SR value was calculated for each of the following sections; proximal, medial and distal part of the femur shaft. The medial part started 1 cm above the first screw of the side plate and ended at the tip of the intra-medullar nail (figure 8).

Table 1 – The different model input variables used for the sensitivity tests.

<table>
<thead>
<tr>
<th>Elasticity-density relationship</th>
<th>Implant stiffness GPa</th>
<th>*simplified Load configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) $E = 3790\rho_{app}^3$</td>
<td>110</td>
<td>Hip contact</td>
</tr>
<tr>
<td>(2) $E = 10500\rho_{ash}^{2.29}$</td>
<td>110</td>
<td>Hip contact</td>
</tr>
<tr>
<td>(3) $E = 6950\rho_{app}^{1.49}$</td>
<td>110</td>
<td>Hip contact</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>Hip contact</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>Hip contact + proximal tensor fascia latae</td>
</tr>
</tbody>
</table>

Comparative biomechanical analysis was carried out for different model input variables. All Boundary conditions were fully identical in all models. The process was performed for an intra-medullar and extra-medullar fixation device.

(1) Carter and Hayes, 1977
(2) Keller, 1994
(3) Morgan et al., 2003

* only hip contact was modeled.
Figure 7– Image of a fractured femur created by the CT data set. The surface model is created in AmiraDev implementing a maximal intensity projection (MIP) technique. The surface model is used for first assessment of fractured femur.

Figure 8– One patient model fixated with two implant types. After virtually reducing the fracture, two models were generated: (a) intra-medullar and (b) extra-medullar. Both models were analyzed for average SR values in the head, proximal region of shaft, medial shaft and distal shaft for different model input variables as described in Table 1.
Sensitivity of implant positioning

Sensitivity of implant positioning (femoral neck/head sliding screw) and load location was examined separately for the femur head while keeping all other parameters constant.

The slide screw was positioned at 16 different locations. Seven locations were placed along the center line which is a line parallel to the femoral neck and intersects the apex. Nine additional locations were chosen at all the nine zones as described by Cleveland et al; superior, central, and inferior thirds and anterior, central, and posterior thirds (Cleveland, et al., 1959) For each of the nine zones three different load locations were applied; -30 anterior, central and +30 posterior (Fig 9). For each case the volume of elements exceeding a SR threshold value greater than 4 was calculated (to be referred as the threshold volume TH-V). The TH-V parameter was chosen for a few reasons; 1) the volume of elements inside the bone tissue exceeding a strain threshold affect the probability of failure (Taylor and Kuiper, 2001) 2) Finite element studies aiming at fracture prediction assume that a number of contiguous elements exceeding a certain failure criterion indicate fracture location (Keyak, et al., 1998; Keyak and Rossi., 2000; Keyak et al, 2001) 3) in general locations having a large percentage of elements exceeding a certain failure criterion indicate a higher probability for failure (Helgason et al, 2009; Schileo et al, 2008) The value of the threshold parameter SR can be chosen arbitrarily if its purpose is conducting pure sensitivity tests, yet the value SR=4 seemed to be appropriate based on fatigue failure theory. It is well established that the number of load cycles required for failure \( N_{\text{fail}} \) is inversely proportional to the applied strain range \( s \):

\[
N_{\text{fail}} = k s^{-q}
\]

Equation (3)
Where \( k \) and \( q \) are coefficients (Carter and Caler, 1985; Martin et al, 1995). Taking \( q=10 \), an increase of strain values by a factor of four (\( SR=4 \)) would decrease \( N_{\text{fail}} \) by a magnitude of \( 4^{10} \). This would mean that if a lifelong \( N_{\text{fail}} \) is approximately 40 million cycles (Scaffhler et al, 1990) that \( N_{\text{fail}} \) would be reduced to an estimated value less than 1000 cycles which is less than one month of normal activity (Taylor and Quiper, 2001).

True tip to apex distance (T-TAD) was measured for each case. The T-TAD measurement differs from the regular Tip to apex distance (TAD) which represents the summation of two orthogonal projections (Baumgaertner et al, 1995) It was not possible to retain the TAD from the T-TAD which was measured directly from the three dimensional model. The TAD has been found as a significant predictor for slide screw cut out of perto-trochanteric fractures fixat ions (Baumgaertner et al, 1995; Walton et al, 2007).

Results were presented numerically and graphically separately for locations along the center-line and for the peripheral zones. This was required due to the fact that relationship between the T-TAD and TAD can be assumed constant along the center line but not the case when the slide screw tip is positioned in the peripheral zones.

![Figure 9 - Positioning of the slide screw in the femur head.](image)

Comparative biomechanical analysis was performed while placing the slide-screw tip in all nine zones and for each zone three different loads were applied. All together 27 configurations were carried out for the same specific femur head.
2.6 Patient models

In addition to the cadaver model, the CT scans of four patients with a fractured proximal femur schedule for surgery were selected for this study. All patients had multi-fragmental fractures with varying instability and bone condition (Table 2). Bone condition was assessed as follows, a five bin histogram representing volume of bone (in percentage) as a function of Young-modulus was created. Bone quality was graded based on volume percentage of elements with a Young modulus greater than 12500 MPa.

Table 2 – The data of the fractured femurs.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>*Volume percentage</th>
<th>**Fracture classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadaver</td>
<td>F</td>
<td>---</td>
<td>70†</td>
<td>6%</td>
<td>31-A1.1</td>
</tr>
<tr>
<td>Patient #1</td>
<td>M</td>
<td>82</td>
<td>72</td>
<td>2.7%</td>
<td>31-A2.2</td>
</tr>
<tr>
<td>Patient #2</td>
<td>F</td>
<td>73</td>
<td>66</td>
<td>3.5%</td>
<td>31-A2.2</td>
</tr>
<tr>
<td>Patient #3</td>
<td>M</td>
<td>81</td>
<td>65</td>
<td>2.3%</td>
<td>31-A2.2</td>
</tr>
<tr>
<td>Patient #4</td>
<td>M</td>
<td>83</td>
<td>68</td>
<td>1.7%</td>
<td>31-A2.2</td>
</tr>
</tbody>
</table>

* volume percentage of elements having a Young-modulus greater than 12500 MPa.
**based on AO/OTA classification
† approximation

The following parameters were used for all the models:

(1) Elasticity-density relationship – \( E = 6950\rho_{app}^{1.49} \) (Morgan et al, 2003)

(2) Implant material – Titanium alloy 110 GPa

(3) Element type – a modified 10 node quadratic element

(4) Load configuration – Hip contact (Heller et al, 2005)

(5) Boundary condition – the distal end of the femur was fixated.
The methodology was examined separately for the femur shaft and for the femur head for each case and implant type.

**Shaft response**

In order to examine and compare differences in implant types a graph describing SR value as a function of location along the femur shaft was constructed for each case (four patients and one cadaver). This was achieved by dividing the femur shaft into segments of 2cm and computing the average SR value of all the elements for each segment.

A simplified load configuration, including a hip contact force, was applied. It is obvious that addition of all known muscle insertions (Heller et al, 2001; Heller et al, 2005) would change the calculated SR values (Bistakos et al, 2005; Speirs et al, 2007). It was chosen to apply a simple load configuration which can be repeated consistently thus creating a standardized biomechanical test which enables comparison between two fixative solutions for different patient-specific models.

**Head fragment**

For each case (cadaver and patients) the slide screw tip was positioned in all nine zones and in additional two locations along the center-line. Comparative biomechanical analysis was carried out for each specific implant location. The TH-V was calculated for each case. Correlation between T-TAD and TH-V was examined. The effect of slide screw positioning on the shaft response was not examined.
Results

3.1 Preliminary mechanical tests with cadavers

The force-displacement plot produced from the axial loading test (Fig 10a) indicates that, the relationship between force and displacement could be approximated as a linear until sudden failure occurs. This was observed at a force of 2 [kN] and 1.3 [kN] for cadaver1 and cadaver2-R (right) respectively. Pearson's correlation coefficient was 0.9989 and 0.999 for cadaver1 and cadaver2-R respectively. This sudden failure mode is associated with thread release in the femur head as a result of eccentric force causing rotation of the femur head around the DHS screw (Fig 10b). Cadaver2-L (left) experienced thread release at a force of 1.6 [kN] and in general responded in a less linear mode (Pearson's correlation coefficient was 0.9864). A more non-linear response was observed after thread release. This is most likely related to crushing of some bone tissue in contact with the threads and shaft of the DHS screw (Fig 10c), and continuing of the screw loosening.
Figure 10 – Mechanical testing of the cadavers. (a) A force vs deflection plot created by an Instron 5544 uniaxial testing machine. The kinks in the plots are related to mechanical failure associated to sudden thread release. (b) An example of a mechanical failure. The femur head is rotated as a result of eccentric force. (c) The gap between the metal implant and bone tissue are a result of crushing of trabecular bone. Bone crushing creates non-linear effects.
3.2 Preliminary grid quality convergence tests

The range of the average element size was 2.135mm to 4.17mm across the different meshes. In the distal region, the average SR value was almost constant (Figure 11), the percentage difference between the highest and lowest values was 0.3%. In the proximal region, which included the implant interface mesh refinement average SR value seemed to become asymptotic for a grid with an average element length of 2.2 mm. The percentage difference between the highest and lowest values was 5.3%. Maximum displacement changed by 3.95%. Computation time for the finest mesh increased by 555% with respect to that of the coarsest mesh.

Fig 11 – Sensitivity of SR values to changes in grid quality. Average SR values for the proximal and distal regions. Results seem to become asymptotic for average element length of 2.2 mm.
3.3 Sensitivity tests for a specific patient model

The values in Table 3 present the percentage difference in average SR value for each section and implant type. Figures 12a, 12b present the average SR values for each section and implant type.

Table 3 – The sensitivity tests results

<table>
<thead>
<tr>
<th>Region</th>
<th>Elasticity relationship</th>
<th>Implant material</th>
<th>Force configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PFNA</td>
<td>DHS</td>
<td>PFNA</td>
</tr>
<tr>
<td>Head</td>
<td>1%</td>
<td>1.8%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Proximal</td>
<td>3.4%</td>
<td>20%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Medial</td>
<td>4.5%</td>
<td>8.4%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Distal</td>
<td>3.2%</td>
<td>15%</td>
<td>0.15%</td>
</tr>
</tbody>
</table>

The results show the largest percentage difference in average SR values for each section; head, proximal, medial and distal regions for each implant type.

Elasticity relationship – The intra-medullar fixation is not sensitive to changes in elasticity-density relationship. The extra-medullar fixation device exhibited higher sensitivity to changes in elasticity relationship. The major contribution for high sensitivity values in the femur shaft comes from the large difference between the Morgan relationship to the other two relationships.

Implant material - Sensitivity to change of implant material was also limited for the intra-medullar implant (Figure 12a). A 36% increase in material elasticity (110GPa to 150GPa) created a maximum difference of 11.6% in the medial region but was very limited in the other regions (Figure 12b). The extra-medullar device again was more sensitive.
Load configuration - Both fixation types were sensitive to change in load configuration. High sensitivity to change load configuration were expected (Bistakos et al, 2005; Speirs et al, 2007).

In general, changes in average SR values in the femur head were totally insensitive to changes in model parameters. The extra-medullar device exhibits higher sensitivity to model input variables.

Figure 12– Average SR values for the distal, medial, proximal and head of fixated femur. SR values are calculated for the proximal, medial and distal regions for different parametric configurations. (a) for the intra-medullar fixation device (b) for the extra-medullar fixation device

Fig 12a – The sensitivity test results for intra-medullar implant

Fig-12b – The sensitivity test results for extra-medullar implant

M_T – Morgan elasticity-density and Titanium implant
C_T – Carter and Hayes elasticity-density and Titanium implant
K_T – Keller elasticity-density and Titanium implant
M_T2- Morgan elasticity-density and increased material type
M_T_A - Morgan elasticity-density, Titanium implant and additional abductor.
Sensitivity to implant positioning in femur head fragment

Placement of slide screw along center line - When placed along the center line at true TAD values greater than 10mm, TH-V increased monotonously as a function of true TAD (Fig 13). When regressing for an exponential function correlation value was \( R^2 = 0.9996 \) for the data created by the SR>4 threshold. For values of true TAD lower than 10mm TH-V values increased. This is more noticeable for data created by lower thresholds (SR<3 and SR<2).

Figure 13 – The threshold volume values along the femur head center line. Threshold volume (TH-V) values as a function of true tip to apex distance (TAD) along the center-line. A deflection point was detected at a true TAD of approximately 10 mm.

Placement of slide screw in peripheral zones

Figure-14 presents the TH-V for each of the nine zones for three different load locations.

The center superior region exhibited the least TH-V, but this was the only region where a substantial number of elements on the proximal surface of the femur head exceeded this value (Fig 14b, 14c). Proximity of the slide screw tip to the surface of
the femoral head, and the fact that low torque of the femur head around the simulated screw thread creates a relatively low volume of elements which exceed the threshold value.

The center-center region exhibited the lowest values. The average value for all load locations was 2.36 cm$^3$ and variability between the three loads was 0.14 cm$^3$. The highest values and range between different load locations were measured in the inferior zones (anterior and posterior). The values for the inferior-posterior zone was 6±4.7cm$^3$ and for the inferior-anterior 11.3±4.75cm$^3$. The range of TH-V values between the different load locations implies that during a gait cycle the range of strains will also be high implying on high alternation and risk of fatigue failure. (Carter and Caler, 1985; Taylor and Kuiper, 2001)
Figure 14 – The threshold volume values in the peripheral zones of the femur head for different load configurations.

The slide-screw was positioned in all nine zones. Three different load locations were applied (a) central (b) -30° posterior and (c) +30° anterior. The results present TH-V values in cm³ (d) the range of TH-V values between the different load locations.
Correlation between TH-V and the true TAD for all zones (except the superior-center) was also examined (Fig 3.6a). Correlation between TH-V and T-TAD was poor; $R^2 = 0.3266$ against an exponential function. The range of TH-V (Fig 14d) for the three load locations ($\max\text{(TH-V)} - \min\text{(TH-V)}$ for a specific zone) correlated better against an exponential function; $R^2 = 0.6647$ (Fig 15b).

![Figure 15 – Correlation of threshold volume values with true tip to apex distance](image)

(a) The red markers present TH-V values as a function of true TAD. The blue markers present the range of TH-V ($\max\text{-}\min$) as a result of load positioning change. (b) A color gradient for the case where the slide screw was positioned in the center-superior zone. (c) An isolated display-group of elements having a SR value greater than 4 (TH-V). Most of the elements are located on the surface of the proximal femur head.
3.4 Patient models

Femur shaft – SR distribution

The following graphs (Fig 16 and 17) show the average SR value along the shaft.

One evident result is that stable fractures (cadaver, patient #1) respond in a similar way to the different fixation methods. However when the fracture is unstable the load bearing of the femur shaft is much more significant. The peak results with the intra-medullar device (PFNA) were; SR=305% for patient #2, SR=263% for patient #3 and SR=930% for patient #4.

While the peak results with the extra-medullar device (DHS) were; SR=148% for patient #2, SR=194% for patient #3 and SR=210% for patient #4. The peak values (for the intra-medullar device) occurred at the proximal region where the plate barrel pierces the femur. In this region bone matter is crushed by the plate barrel insertion. SR values further down the shaft are reduced; In case of patients #2 and #3, the mean SR values for the segments below the plate barrel were 95% and 83% respectively.

The high SR values, especially in case of patient #4, would probably be reduced if more muscle insertions were simulated, especially the adductors and hip flexors, but in general the results coincide with the assumption that the an intra-medullar fixation device is designed to be a load sharing device (Browner et al, 2003). For the given fracture types, which are classified as proximal per-trochanteric simple (only 2 fragments AO/OTA 31-A1) for the cadaver and pertrochanteric multifragmentary (AO/OTA 31-A2.2) for all other cases, the extra-medullar fixation device created a more similar SR profile for all cases (Fig 17).
Figure 16– Individual graphs of SR values along the shaft of all the fixated femurs. The graphs show average SR values as a function of location along the femur shaft for segments 2 cm thick. Simulations were performed for a simplified loading condition (hip contact). Other boundary conditions were consistent for all cases.
Figure 17– Biomechanical response along the shaft for the intra-medullar and extra-medullar fixation devices.
(a) Grouped graphs representing response to intra-medullary fixation for all cases and (b) Grouped graphs representing intra-medullary fixation for all cases.
The intra-medullary fixation, in general creates higher SR values in variability between cases is higher.
Femur head – slide screw positioning

The true TAD values, for all the models, ranged between 11.8mm to 17.8mm for all nine zones. The slide screw was positioned in two more locations along the center-line with true TAD values ranging from 14.79mm to 36.2mm.

Along the center line for the presented range of true TAD, the TH-V increases as true TAD increases (Figure 18). This was the case for all models. Although not presented, values of TH-V increased for true TAD values below 10 mm.

Figure 18- Positioning of the slide screws along the center line for all cases. For each case the slide-screw tip was positioned in two locations along the center-line. TH-V rises as true TAD is increased.

However, when placing the slide-screw tip in one of the nine zones, no correlation exists between the true TAD values and TH-V values.

Table 3.1 and figure 3.9 summerize the results of the following section.

The center-center zone creates the lowest TH-V value for all five cases, 0.0548±0.022 cm$^3$. The center-superior zone exhibited low TH-V values, 0.14±0.13 cm$^3$ but created
high SR values on the proximal surface of the femur head in proximity to the slide-screw tip (Figure 3.6A, 3.6B).

When examining the horizontal planes (AP projections), the inferior zones always exhibit larger TH-V values, variability and range than the center and superior (Table 4). This is probably associated with the relatively large torque applied to the femur head when the screw is positioned in the inferior regions.

<table>
<thead>
<tr>
<th>Zone</th>
<th>TH-V [cm$^3$]</th>
<th>STDEV [cm$^3$]</th>
<th>Max-Min (TH-V) [cm$^3$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center-Inferior (CI)</td>
<td>3.33</td>
<td>2.59</td>
<td>6.62</td>
</tr>
<tr>
<td>Center-Center (CC)</td>
<td>0.055</td>
<td>0.022</td>
<td>0.06</td>
</tr>
<tr>
<td>Center-Snterior (CS)</td>
<td>0.14</td>
<td>0.13</td>
<td>0.297</td>
</tr>
<tr>
<td>Anterior-Inferior (AI)</td>
<td>5.25</td>
<td>5.33</td>
<td>13.12</td>
</tr>
<tr>
<td>Anterior-Center (AC)</td>
<td>3.2</td>
<td>3.9</td>
<td>9.18</td>
</tr>
<tr>
<td>Anterior-Superior (AS)</td>
<td>2.49</td>
<td>2.67</td>
<td>5.99</td>
</tr>
<tr>
<td>Posterior-Inferior (PI)</td>
<td>6.34</td>
<td>7</td>
<td>18.23</td>
</tr>
<tr>
<td>Posterior-Center (PC)</td>
<td>4.25</td>
<td>3.62</td>
<td>9.5</td>
</tr>
<tr>
<td>Posterior-Superior (PS)</td>
<td>3.03</td>
<td>2.34</td>
<td>5.05</td>
</tr>
</tbody>
</table>

The anterior and posterior zones resemble in response and profile. This implies that from the morphological aspect the anterior zones resemble the anterior zones, but if the true thread design is taken into account (direction, pitch, friction etc) one zone may have an advantage against the other regarding probability of failure.

When examining differences between patients, the cadaver case exhibited the lowest values for all zones with an exception in the center-center zone. This is probably associated with the fact the cadavers bone condition was good opposed to all the other patients which suffered from different degrees of osteo-perosis.
A comparative analysis was performed for all nine zones in each case. The bars represent the average value for all cases. The inferior zones exhibit the largest threshold volume values in all AP planes. The CC location exhibits the smallest TH-V values. The results of the cadaver were substantially lower than all other cases.


**Discussion**

**4.1 Summery of current research**

In this study, a new patient-specific finite element based workflow, employing maximal principal strain ratio (SR) as a primary field-output variable was presented. At first, preliminary tests were carried out. These tests included experimental axial loading tests of three cadaveric fixated femoral neck osteotomies and grid quality convergence tests. Afterwards, sensitivity to change in model input variables was carried out applied with a CT data set of one patient specific model. In the last phase a retrospective study with five different patient data sets was performed.

*Preliminary tests*

The axial loading tests approved that the fixated femoral neck osteotomy that simulate proximal femur fracture construct, has a linear force-strain response until a failure load is reached. Failure occurred mostly because of torque applied to femur head around the slide screw axis. This type of failure mode is expected when the slide screw is not located along the center line. Failure due to fatigue, which is the major cause of failure, was not examined.

The grid quality convergence tests showed that SR values are relatively insensitive to mesh refinement, less than a 3.5% change for the proximal region and less than 1% for the distal region. The proximal section which includes the penetration of the implant was more sensitive than the distal section that is comprised of pure bone material. For the proximal section the average SR value seems to become asymptotic for a grid with an average element length of 2.1 mm. Our findings agree with those presented in other studies which showed that an average element size of 2 mm provides the optimum regarding accuracy and computation time (Viceconti et al, 2004).
Phase I – one patient model

One CT data set of a patient with fracture of the femoral neck was used. The whole workflow was performed for two common fixation devices that are routinely use; intra-medullar and extra-medullar and for different locations of the slide screw tip in the femur head. Average SR values in the femur head and proximal, medial and distal shaft regions were calculated for both fixation solutions. Changes in average SR values in the femur head are not discussed in this section since changes were minor.

Sensitivity to density-based elasticity relationship

When examining the sensitivity of the intra-medullar fixation device by itself, it was found to be totally insensitive to elasticity relationship changes. This result is in agreement with other results published (Weinans et al, 2000) which checked sensitivity to a stem implant. On the other hand, the extra-medullar fixation device was found to be much more sensitive to elasticity relationship change especially when comparing the Morgan relationship to the other relationships in the shaft regions. The difference in sensitivity profiles can be related to two factors; the extra-medullar device (plate and screws) bares a higher percentage of the load compared to the intra-medullar device which is a load sharing device (Browner et al, 2003). This results in higher sensitivity of SR values which are in essence an expression of stress shielding. Another factor is the penetration of implants through cortical and trabecular bone tissue in the proximal region (plate barrel) and the compression screws in the medial region. When comparing the two fixation types, the proximal region exhibited the largest sensitivity, 20.4% difference. As explained previously, the proximal region was pierced by the plate barrel.

The models created with the Morgan (Morgan et al, 2003) elasticity relationship contributed mostly to divergence. Models created with the Carter (Carter and Hayes,
1977) and the Keller (Keller, 1994) elasticity relationships resembled. The maximum difference when using these relationships was 4.1% in the proximal region for the extra-medullar device.

*Change in load configuration*

The addition of a load insertion generated relatively large changes in average SR values. This was true when examining each implant type separately and for values representing the difference between the two implants. These results are in agreement with other studies that examined the affect of load configuration changes on strain values and bone loss. Bitsakos et al simulated bone loss after a total hip procedure using adaptive remodeling theory. Changing load configuration from simplified to realistic caused a change of up to 40% in some regions (Bistakos et al, 2005). Another study showed that the choice of boundary conditions influenced both the strain magnitudes and the mode of deflection of the intact femur (Speirs et al, 2007). In vivo tibial strain measurements showed that tension strains changed by 29% as a result of muscle fatigue (Milgrom et al, 2007).

High sensitivity to load configuration raises a dilemma between obtaining realistic SR values opposed to performing a non-realistic simplified but consistent and standardized loading scenario. If real SR values are of importance then realistic load configurations are to be used. Simulating realistic load configurations imposes a number of challenges for a clinical workflow; 1) it will be difficult to be consistent for different patients CT data sets and 2) it will be time consuming. A simplified and repetitive loading configuration would provide a consistent standard that would enable comparison between different patients and reduce the time required for model preparation.
Sensitivity to implant material

Change if implant material was also found to substantially affect average SR values in extra-medullar device. The intra-medullar device was less sensitive to implant material. Other studies that assessed sensitivity of stress shielding to implant material examined a cemented stem implant (Bistakos et al, 2005; Weinans et al, 2000) which was bonded at its interface with the bone. These studies showed relatively high sensitivity to implant material. In our models the intra-medullar device was not bonded, this probably lowered the sensitivity. Uncertainty of implant material elasticity can be expected to be low since it is manufactured in a standardized process. For these reason it is not a major cause for concern regarding uncertainties in model output.

Slide screw positioning

Our main goal in this section was to check if TH-V values, which represent probability for failure for screw migration and cut out, are with agreement with clinical experience and if relevant clinical data can be extracted. This failure mode was chosen for a few reasons; 1) it is of great clinical importance and 2) probability of failure has been correlated to several variables in clinical studies. Baumgaertner et al showed high significance between cut out failure and TAD. Walton et al also found correlation between TAD and cut out failure for unstable A3 type fractures. Davis et al found that cut out rate was much more frequent when the slide screw tip was positioned in zones other than the center zone. Higher rate of cutting-out was also found when the perceived distance between the implant tip and the femoral articular surface was less than 10mm.

Along the center line, correlation between TH-V and true TAD was strong when regressed against an exponential function ($R^2=0.9996$). It was also shown that when
the screw tip was placed along the center line near the articular surface at distances below 10mm, TH-V values increased. This is in agreement with Davis et al.

In peripheral zones correlation between true TAD and TH-V was weak. This was the case for all load configurations when inspected separately. When examining the range of results for each zone, correlation with true TAD was much stronger when regressed against an exponential function ($R^2 = 0.6647$). TH-V ranges were smallest in the center plane with the center-center zone exhibiting the smallest ranges of TH-V values. In the center-superior zone where the slide screw tip is in proximity to femur head proximal surface (region where force is applied) TH-V values and ranges of values were also relatively small. These results are in agreement with Davis et al and Baumgartner et al. To summarize, when increasing the true TAD along the center line, a deflection point was identified indicating the existence of an optimal location for slide screw positioning. The TH-V values increased when true TAD was less than or greater than this optimal location. The overall result is in agreement with reported data. When increasing true TAD at peripheral zones it was the range of TH-V values that better agreed with reported results. We therefore may conclude, that when assessing probability for failure, it is of great importance to simulate different loading configurations which may be related to alterations during a gait cycle.

Clinical studies have demonstrated asymmetry regarding rate of screw cut out. The anterior-center and anterior-inferior had lower cut out rates than the counter posterior zones. This can be a result of a few reasons; 1) asymmetry in load during a gait cycle, 2) proximity of superior-anterior zone to femur head surface in the region of applied load, 3) large torque (inferior zone) and 4) counter clock wise torque tends to release screw lock. In our study, the above mentioned asymmetry was not demonstrated due
to simplification of simulation constraints and boundary conditions (screw thread was simplified to a bonding condition and symmetric force locations).

**General remarks**

These findings show that uncertainties are different for different types of fixation devices. A load sharing device will exhibit different sensitivity than a load bearing device. Regions with an implant piercing through cortical and trabecular bone tissue are expected to create larger uncertainties. Regions with an implant piercing mostly one bone tissue type (femur head) create small uncertainties especially when expected strains are small. Although the intra-medullar fixation device usually exhibited lower sensitivity, we should bear in mind that all sensitivity tests were performed with identical boundary conditions regarding implant to bone interface.

**Phase II – retrospective study**

The workflow was carried out with five CT data sets of fractured femurs. Shaft response was investigated for two fixation devices and sensitivity to slide screw positioning in all zones of femur head was also examined. Patients were randomly selected based on availability.

**Shaft response**

The shaft response for the cadaver and patient #1 was quite similar. Patients #2 and #3 exhibited a more substantial difference in shaft response between the two fixation devices. The average SR values along the medial and distal regions were less than 100% for the extra-medullar device as opposed to average SR values exceeding 250% for the intra-medullar device. Patient #4 exhibited the most substantial difference between the two devices, up to average SR values of 900% for the intra-medullar
opposed to SR values between 100% and 200% for the extra-medullar device. In general, it seems that shaft response is quite similar for stable fractures and the difference is more extreme as fracture becomes less stable. The intra-medullar device transfers more load to the bone shaft and has a more unique response for each case, the extra-medullar device response was more constant across all cases. We note that the values of SR would differ substantially if realistic load configuration would be simulated. Sensitivity to load configuration has been shown in the previous phase and in other studies (Bistakos et al, 2005).

The fact that one device creates substantially larger SR values does not imply that it is less preferable clinically. What has been demonstrated is that for a given consistent simplified loading configuration results are indeed patient specific and clear biomechanical differences can be identified for different fixation devices.

*Slide screw positioning*

Along the center line, TH-V values increase as a function of true TAD. Although not presented, when the screw tip is located very close to the apex (less than 10mm) TH-V values tend to increase.

The center-center zone generates the smallest TH-V values. These results agree with all clinical studies. The center-superior zone also generates small TH-V values but again most of the elements exceeding the SR threshold value are located on the proximal surface of femur head in proximity to the area where the load is applied. Another pattern identified is that for the anterior and posterior planes, the inferior region exhibits the largest TH-V values whereas the superior region generates the smallest values.

The cadaver exhibited substantially lower TH-V values for all zones. This is probably related to the fact that bone quality of the cadaver was much better than the patients. It
is not possible to determine, based on the small population in this study, that results will be patient specific concerning slide screw positioning in zones. It seems more reasonable that low TH-V values in the center-center zone would prevail for all cases.

4.2 Limitations of study

The most obvious limitation in this study is a small population. It is not possible to draw statistical conclusions from such a small population. Another limitation is the fact that we tested similar fracture types (AO/OTA 31-A2) while other fractures types, with different configuration such as a AO/OTA 31-A3 fracture were not examined.

Another aspect which is need to be proved and was not examined in this study is intra-observer repeatability of results. Identification of bone fragment surfaces requires expertise. This fact may result in geometry errors during the segmentation process. The influence of these potential errors on the final results of the work flow has not been investigated.

4.3 Further research

- A larger scale clinical study is requested. Such a study should be designed to enable intra-operative data (real implant location and implant used) to be used as model input. Post operative follow-up is essential if failure criterions are to be concluded.

- A cadaveric validation study for SR values should be carried out for two fixation devices.

- There is a need to establish a more coherent failure prediction criterion.
• Improving segmentation algorithms is required in order to enable full atomization of model construction. Specifically there is a need to enable automatic identification of articular surfaces and fracture surfaces.

4.4 Conclusions
A new patient specific workflow employing principal strain ratio (SR) as a field-output variable has been presented. Different fixation devices types and regions of interest, exhibit different sensitivity to uncertainty in model input variables. Sensitivity to controlled model input variables agree with known clinical experience and important clinical data may be extracted.

The ability to provide a failure prediction criterion is of clinical importance. This may be performed by combining a numerical indicator and visualization of results.

Simplification of the workflow can be achieved for clinical practice. Specifically the following issues should be addressed:

• Sub-modeling - if for example, the main concern in pertochanteric fixation failures is head screw cut out, than it is reasonable to ignore the shaft region. This would reduce the workflow time by approximately 80%.

• Simplified load configuration - implementing a simplified load configuration enables consistency which can be used to create standards. The same applies for boundary conditions such as contact at interfaces.

• Automatic segmentation – the segmentation process of articular surfaces and bone fragments is a "bottle neck". Improving automatic segmentation algorithms will eventually enable implementing the workflow within the required time limit of the clinical environment.
The workflow presented in this study, enables comparison between different fixation solutions and may be implemented for other anatomical regions. With further simplification and atomization, the workflow may be used as a preplanning tool which will assist the surgeons’ decisions regarding type of implant and positioning and it will help in post-operative patient treatment for example in weight barring and different loads recommendations.

To conclude, the workflow holds the potential to become part of the computerized tools and improve patient treatment and outcome.
Bibliography

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