SIMULATION–BASED DESIGN OF PATIENT–SPECIFIC
FEMORAL LOCKING PLATE USING TOPOLOGY
OPTIMIZATION

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SIMULATION-BASED DESIGN OF PATIENT-SPECIFIC FEMORAL
LOCKING PLATE USING TOPOLOGY OPTIMIZATION

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and hereby certify in their opinion it is worthy of acceptance.

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To

My Parents, Vimal and Atmaram Gholawade,

*For making me your whole world and giving me the best childhood. All
that I am or hope to be, I owe it you.*

My Grandparents, Tarabai and Rajaram Gholawade,

For your constant unconditional love and care.

My Friends and Siblings, for keeping me sane and grounded.

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ABSTRACT

Femoral locking plates are orthopedic implants used in closed reduction of the fractured femur. These orthopedic implants designed using conventional methods apply finite element analysis to evaluate their performance. The main drawbacks of such methods are isotropic assignment of bone material, lack of consideration to patient data and not accounting the influence of muscle forces. The effect of muscular forces in reducing femoral strain distributions and the impact of anisotropic assignment of bone material can make a substantial difference to the expected performance response. Giving due consideration to the key factors like femoral muscle forces, biological variability, and patient's bone geometry and its microstructure is essential for effective design of internal fixation devices. Therefore, a simulation-based design approach is employed which encompasses medical imaging segmentation, finite element analysis, Taguchi design methodology and topology optimization. A finite element model of a locking plate system with a diaphyseal femoral fracture is generated to investigate the device performance. The model includes all physiological loading conditions – hip contact, knee contact, and muscle forces - associated with a normal walking gait cycle. In conjunction with Taguchi design method, topology optimization is used to make the implant lighter without affecting its structural integrity

Keywords: Locking compression plates, orthopedics biomechanics, internal fixation

Chapter 1. Introduction

1.1 Femoral fractures and Locking Compression Plate

A femoral fracture is the bone fracture that involves the femur. Since the femur is the longest and strongest bone in the human body, femoral fractures are generally the result of a high-energy trauma. The long straight part of the femur is called the femoral shaft and a fracture anywhere along this length of the bone is called a femoral shaft fracture. In United States alone, the incidence of femoral shaft fractures ranges from 9.5 to 18.5 per 100,000 annually[1]. Thirty-seven percent of runners suffer from various stress fractures. The femur accounts for 11% of stress fractures and roughly 53% of these fractures are femoral shaft fractures[1]. Femoral shaft fractures are further classified according to the pattern and location of the fracture and the condition of the skin and muscle above the fractured bone. This classification will be covered in depth in later sections.

It is unusual for femoral shaft fractures to be treated without surgery. It is estimated that every year in the United States, 3.6 million orthopedic operations are performed and of the 10 most frequented operations, four necessitate metallic implants (e.g., plate, external fixator)[2]. The most commonly used methods for treatment of femur fractures are external fixation, intramedullary nailing and femur plates[3]. Femur plates can be further categorized as conventional plates and locking plates. When using a conventional plate, fixation is achieved through the friction between the bone and plate, which in many cases has caused disturbance in the blood supply to the bone[2]. To

overcome this drawback, one of the successful alteration employed was to reduce the contact between the plate and bone which led to development of limited-contact dynamic compression plate (LC-DCP)[4]. Design improvements in conventional and compression plates led to the development of locking plates. The main advantage of locking plate is that they are not pressed to the bone and therefore do not need to be contoured exactly to fit the bone. Locked plates are used in conjunction with a technique known as minimally invasive plate osteosynthesis or more commonly known as MIPO. Treating fractures with locked plates along with MIPO techniques improves callus formation with an increased chance of accelerated recovery[5]. However, one of the disadvantages of using locked plates over conventional plate is that screws can only be placed perpendicular to the plate whereas conventional plate offers placement of screws at varying angles. Thus, Locking Compression Plate (LCP) was a result of combining the conventional hole with the threaded hole to accommodate both type of screws. Since the LCPs can be used as a compression plate as well as locking plate, it is currently the preferred method for most femur fractures by orthopedicians around the world.

Femoral fracture treatment has undergone a paradigm shift over the last fifteen years. Designing a *patient-specific* implant is now possible due to advancement in modeling and simulation packages. Furthermore, increased reliability and biocompatibility of metal additive manufactured parts has made it possible to have anatomically conforming implants which has advantages of both compression and locking plates.

1.2 Current trends in development of orthopedic devices

The design, development and pre-clinical testing of orthopedic implants is reaching its peak with the increased understanding of fundamentals of biomechanical processes in human body. It is further accelerated with the advancement in the methods of extracting patient data using computerized tomography (CT) scans and magnetic resonance (MR) imaging of the musculoskeletal system[6]. In addition, stringent laws by administrative bodies like Medical Device Directive (Europe) and Food and Drug Administration (USA) to regulate the design process of medical devices has made computer-aided design as a fundamental part of the design process. This ensures that the whole design process is managed and planned in a systematic and repeatable manner [7].

Finite Element (FE) analysis has been an integral part of orthopedic biomechanics for four decades now[8]. The finite element modelling in orthopedic biomechanics can be divided into a basic five-step procedure which includes (i) development of the basic model, the application of appropriate material properties, loading and boundary conditions, (ii) describing the preliminary mechanical environment of the bone–implant system, (iii) capturing the time dependent behaviour in adaptive simulations, (iv) the design and application of computer based experiments and (v) determining suitable performance metrics [8]. Following the above mentioned approach, multidisciplinary teams of scientists and engineers are able to get closer in simulating the *in vivo* conditions using a FE model on a computer, which generally are harder to replicate in biomechanical

testing. As a result, CAD modeling combined with FE analysis has enabled engineers to verify the design before clinical testing. This is vital in product development phase as initial flaws in design can be ratified without spending much resources on prototype testing.

The design of orthopedic implants has come a long way from traditional prototyping and experimental methods based on trial and error to a more standardized engineering design approach. Even with the current advancements in manufacturing technologies, the implants are still manufactured using conventional methods such as CNC [9]. The flexibility that additive manufacturing provides during the design phase is yet to be fully acknowledged. Presently, the implants are designed around a 'standardized femur model' in order to accommodate the wide geometric variation among bone anatomy of patients [10]. This also facilitates manufacturing and helps in comparability and reproducibility of the research findings [11]. While adoption of this method has been quite successful, the failure rate of implants is on the rise too. Revision surgery is performed to replace or compensate for a failed implant and it is estimated that if the current trend continues, then the number of revision surgeries may increase to 66% by 2030 [12]. Failure of implant has adverse physiological as well psychological effects on the patient. The recovery process is hampered and there is a substantial increase in total expenditure.

Although, there are wide range of factors that cause an implant failure, most of them can be attributed to the design of the implant. Thus, a more comprehensive approach in the design process is necessary to reduce these failures.

1.3 Additive Manufacturing and Topology Optimization

The evolution of additive manufacturing (AM) from a non-commercialized technology to a mainstream manufacturing process is quite phenomenal. Shorter product development cycle, higher demand for customized product, lower manufacturing lead time, and new business models were the key growth drivers for innovations in AM materials and technologies. The AM industry is anticipated to grow to more than \$22 billion dollars by 2020 [13]. The positive impact of additive manufacturing has been witnessed in following areas: (1) personalized healthcare products to improve quality of life, (2) higher manufacturing sustainability, and (3) simple supply chain to increase efficiency and responsiveness to demand fulfillment [14].

Traditional design approaches don't make the most of new manufacturing methods, like additive manufacturing, which are removing design constraints and opening up new possibilities. The capabilities of AM to produce topology optimized macro-structure parts as well as complex porous parts are of particular interest to orthopedic industry. Unlike shape or parametric optimization, topology optimization is a method to determine whether a certain point in the structure should be void or solid. The optimal shape of a part is often organic and counterintuitive, so designing it requires a different approach. The simulation packages make it easy to perform the lightweighting of parts, extracting the CAD shape and quickly verifying the optimized designs. The innovation in AM has changed the design landscape by making it possible to build virtually any shape, without regard for the design for manufacturability rules.

However, the AM-related standards are still under development. The International Organization for Standardization (ISO/TC 261) and American Society for Testing and Materials (ASTM F42) are working towards producing a set of global standards that are applicable to most AM processes, applications and materials [13]. The development of AM standards is one of the principal challenges of AM growth. Furthermore, lack of understanding of design for additive manufacturing is restricting the overall penetration of AM in manufacturing industry. As a result, the design engineers cannot entirely benefit from AM and realize its true potential.

Chapter 2. Literature Review

2.1 Biomechanics of Locked Plate Technology

The necessity to improve the treatment of femur fractures has enabled interesting innovations in fixation techniques and devices. Conventional plating procedures focused on the main goal of anatomical reduction of the fracture. The dynamic compression plate used in the process relies on the frictional force created between bone and the plate by the bone screws, for a stable fixation [15]. With the increase in axial loading, screw toggle increases and leads to plate loosening due to reduced friction. The major drawback of compression plating is that it severely affects the periosteal blood supply due to plate-bone frictional interface and compromises the vascularity of the fracture [16]. Also, the screw purchase is a huge problem in osteoporotic bone cases.

Many of these problems are solved by the locking plates. The frictional interface between bone and plate is not required in locking plate as they follow the biomechanical principle of external fixators [16]. A single beam is created when no movement occurs between the construct and its parts (no toggle). Locking plates are designed to be single beam fixators. This fixed-angle device converts axial loads into compressive loads, rather than shear force as in conventional plating. Locking plates work well with the minimally invasive insertion techniques and maintain the soft-tissue attachments to the bone-preserving blood supply. The union occurs by secondary bone healing through callus formation [17]. However, locking plate has its own disadvantages. After placement of

screws through plate into the bone, the particular bone segment cannot be manipulated by insertion of additional screws or by compression devices. Surgeons have to be extra careful when using a locking plate and need a variety of techniques such as 'no-hands' traction, femoral distractors, and percutaneous clamps [16]. A poorly reduced fracture using a locked plate usually results in a nonunion.

2.2 Design of Locking Compression Plate (LCP)

Robert Frigg developed the locking compression plate (LCP) in 2001 [18]. This plate is an ideal combination of the two concepts (compression plate & locking plate) mentioned earlier. LCP allows placement of locking head screws as well as compression screws which gives it more stability and better fracture reduction. The LCP system converts the shear forces into compressive forces at the screw bone interface, which is beneficial in fracture fixation as compact or cortical bone has higher compressive strength than shear strength [19]. Additionally, there is little to no stress concentration as load is evenly distributed amongst the component screws due to higher angular stability of locked screws. For successful healing of a fracture- the surgical approach used, sequence of screw placement, and the length and position of the plate are one of the many critical factors.

The research findings on engineering factors and their effect on the plate design by the researchers worldwide, has helped orthopedicians to gain better understanding into the failure of implants. Lee et al., [20] attempted to identify the best number and positions of LCP screws to achieve fixation stability using a simulation based particle swarm

optimization algorithm. LCP with six locking screws was selected, with three screws on each side of the fracture segment. They concluded that increasing number of screws greater than six had no significant effect on performance and found a strong correlation between length of plate and fixation stability. A finite element model of locked plating in femoral shaft fractures was developed by Schwartz et al [21]. They found out that minimizing the interface gap leads to lower peak stress values. This study reaffirmed that more number of screws does not necessarily lead to reduced stress. In 2007, Smith et al conducted an in-depth study to provide practical information and tips for the practising orthopedic surgeons [16]. They concluded that at least three or four plate holes should be left empty at the level of the fracture, in order to achieve a larger area for stress distribution on the plate. Furthermore, the length of the plate should be twice the length of fracture zone. This study gave a good insight on how a custom plate can be more advantageous for the patient as well as the surgeon. Brinkman et al conducted a biomechanical testing to study the effect of different factors on the plate performance [22]. They came to the conclusion that increased working length, a greater distance of the plate to the bone, an increased gap size and a shorter plate all negatively influenced the stability of the construct. The stability of plate-bone construct usually decides the outcome of the recovery process. To study how stability can be controlled in the locked internal fixators, Stoffel et al performed a biomechanical testing of a LCP [23]. The study concluded that having more than three screws per bone fragment did not have significant effect on the stability and increasing distance of the plate to the bone resulted in decreased construct stability.

Majority of the studies simulating the femur and the locking plate, approximate the physiological loading by considering only the abductor muscles and the ilio-tibial band [11]. Using a finite element model, Pauwels et al attempted to investigate the influence proximal femoral muscles on femur [24]. He came to the conclusion that the bending moments in the bone shaft were substantially low due to the tension from the iliotibial band. Duda et al., demonstrated the importance of including muscles forces to reproduce the physiological loading in the femur [11]. They found that a simplified loading condition, produced strain difference as high as 26% in comparison to loading condition where all muscles forces are included. Thus, using simplified loading for a bone plate construct, leads to overdesigning of the plate, which can further lead to the failure of the fracture treatment. The biomechanics community has made great advances due to the newer technologies for modeling musculoskeletal systems. There are open source softwares that allow users to develop, analyze and visualize models of the human musculoskeletal system. Wagner et al., carried out a whole-body musculoskeletal inverse dynamics analysis to achieve realistic loading and boundary conditions for finite element analysis of femur [25]. They observed 8% reduction in stress values, reiterating the importance of including muscle forces in finite element models.

2.3 Clinical Significance

The successful treatment of fractures using Locking Compression Plate (LCP) requires meticulous preoperative planning and highest consideration to biomechanical principles integrated in its design. The LCP system has many benefits when it comes to

internal fixation of femoral shaft fractures, however, the number of implant breakage cases due to intraoperative technical errors, screw pull-out, improper placement of plate and screws are escalating [26]. Hence, a careful investigation of these parameters and their effect on performance of the plate is essential. For instance, the working length of the plate has shown to play a vital role in stress distribution in LCP as well as its fixation stability [20]. Similarly, number of screws and screw configuration are critical factors in reducing the fracture and maintaining the required stiffness of the implant.

Usually, the surgeons follow the same procedure which 'worked well' in the past and don't use an engineering approach in their techniques. As intraoperative errors are one of the main causes of failure of implants, designing a plate which is easier to work on can help counter this problem to some extent. Additionally, designing a patient-specific LCP after careful investigation of the factors affecting the performance of implant can reduce the failure rate of the implant as well as make it less tedious for the surgeons to perform the surgery.

The objective of this study is to provide a simulation-based approach to design a patient-specific locking compression plate with optimized parameters for a femoral shaft fracture. There are four important aspects of this objective: (1) using real patient data, (2) determining the effect of muscle forces on stress and strain distribution in the designed plate and bone construct using realistic loading/boundary conditions as well as material properties, (3) performing Taguchi design optimization, (4) topological optimization of the final design. The four core techniques used in the proposed approach are Medical Imaging, FEM and parametric & topology optimization. The intent is to

provide a methodology that will aid in selection of the plate length, screw density, screw configuration, plate type (material & thickness), thereby helping surgeons to make informed decisions backed by engineering analysis.

Details of the each step of the methodology are outlined in Chapter 4, and the results obtained using this approach are discussed in Chapter 5. The fundamentals of Orthopedics Biomechanics, Finite Element Analysis and Optimization are reviewed in Chapter 3.

Chapter 3. Background

3.1 Anatomical Overview

3.1.1 Medical Terminology

This study will mainly focus on the femur bone and its associated muscle groups. Further understanding of content within this field of work requires knowledge of anatomical terminology that is not primarily germane to engineering practice. As a result, the following section defines key anatomical terms that assist in describing and defining biological structures as well as relationships

Fig. 1 Body planes

Planes of the body:

1. Frontal Plane (Coronal Plane) - A vertical plane running from side to side;
divides the body or any of its parts into anterior and posterior portions
2. Sagittal Plane (Lateral Plane) - A vertical plane running from front to back;
divides the body or any of its parts into right and left sides
3. Transverse Plane (Axial Plane) - A horizontal plane; divides the body or any of
its parts into upper and lower parts.

Table 1. Basic Terms

Sr. No.	Term	Definition
1.	Proximal	nearest to the top of the body
2.	Distal	nearest to the bottom of the body
3.	Inferior	beneath or lower
4.	Superior	above or higher
5.	Lateral	part closest to the outside of the body
6.	Medial	part closest to the inside or midline of the body
7.	Anterior	before or in front
8.	Posterior	behind or in back

Fig. 2 Left femur

3.1.2 Tissue Mechanics: Bone

In order to withstand the incredible amounts of forces during daily activities, the femur contains an osseous architecture that gives rise to incredible strength and rigidity. This specific material configuration consists of a composite arrangement of cortical and cancellous tissues. The highly dense outer layer of the femur that contributes to its overall strength is primarily composed of cortical bone. In addition to its incredible weight bearing properties, cortical tissue operates as a system of passageways that allow nerves

and blood vessels to supply oxygen and nutrients to the rest of the body. In contrast, cancellous tissue is known for its high porosity, large surface area, and vascularity around areas with minimal mechanical stress. Cancellous bone's low density produces a softer and weaker material; however, it allows for increased flexibility. This composite structure is one of the many naturally created biological materials that combine incredible structural properties with efficient function.

In terms of chemical composition, osseous femoral tissue contains bone cells that have organic and inorganic phases. The organic composition of bone minerals consists of a triple helix structure of multiple proteins in the form of type I collagen. In contrast, the inorganic phase of bone contains calcium phosphates and calcium carbonates minerals known as hydroxyapatite. The precise configuration of both organic and inorganic components allows bones to maximize durability and strength while minimizing brittleness.

The various regions of the femur can be categorized into the diaphysis, epiphysis, and metaphysis (Figure 3). The diaphysis pertains to the shaft of the femoral bone that houses the medullary cavity that stores bone marrows. During maturity, the diaphysis region grows from its ends until the growth plates close once an individual reaches adulthood. The epiphyses are the large ends of the bone that grow from separate ossification centers, while the metaphysis is the region that lies between the diaphysis and epiphysis. At the proximal end of the femur, the epiphysis and metaphysis are comprised of: (1) a head that allows for articulation with the pelvis' acetabulum, (2) a neck to permit wide range articulation, and (3) trochanters that give leverage for muscle

to rotate the thigh around its axis. The culmination of each component gives rise to the incredible ability that the femur has to grow and support the human body.

Fig. 3 General form of a long bone [27]

3.1.3 Tissue Mechanics: Skeletal Muscle

Dynamic movement of the human body is controlled by the somatic nervous system through voluntary contractions of activated skeletal muscle cells, known as myocytes. The contraction of muscles can be described via the sliding filament theory in which myofilaments, actin and myosin, slide past one another to cause the sarcomere to shorten. This process occurs when calcium is released from the sarcoplasmic reticulum to initiate bonding of actin and myosin filaments to create a cross bridge. Chemical energy stored from the breakdown of adenotriphosphate (ATP) is attached to myosin and is stored as mechanical potential energy. This potential energy is the result of a change in the shape of the myosin molecule in which the myosin head is “cocked; resulting in a high-energy and extended position. The high energy is then released when adenodiphosphate (ADP) is expended to produce a power stroke, which moves the myosin heads and pull the actin filaments closer together. Once the ADP is fully expended, ATP molecules reattach to the myosin head to allow the myosin filament to revert back to its original shape. This process continues to occur when the presence of calcium is maintained.

With over twenty different muscle groups that are either attached or wrapped around the femoral bone, various combinations of muscle activations are stimulated to produce precise movements of the lower extremity. The figure below depicts an anterior view of the femoral muscle groups that are of interest within the present work. The main muscle group covering the anterior side of the femur are the quadriceps muscles, which include the rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius. On

the posterior portion, the muscles of the hamstring include the semitendinosus, semimembranosus, and biceps femoris. The sartorius is a femoral muscle is not attached to the femur, but does transverse and wraps around the other muscles group. The specific muscle groups of the femur pertaining to the current work will be discussed further in the methodology section.

Fig. 4 Muscles of the femur [28]

3.2 Finite Element Method

3.2.1 Introduction

The Finite Element Method (FEM) is a numerical approach that is utilized to describe and analyze physical systems that involve complicated physics, geometry, and boundary conditions. This particular method is performed by dividing a domain into a collection of smaller subdomains. In doing so, each subdomain can be described by various governing equations and approximated via variational methods. By approximating such solutions, representation of complicated functions can be transformed into simplified polynomials. FEM's ability to represent various complicated functions gives rise to its wide utilization in many engineering applications, such as structural, thermal, seismic, crash, fluid flow, and electromagnetics. It has become accepted as the standard analysis software technique due to its generality and suitability for computer implementation.

3.2.2 Methods to solve engineering problems

Engineering problems can be categorized into three distinct classifications: analytical, numerical, and experimental. The analytical method is a classical approach that yields accurate results and a closed form solution. However, its application can only be applied to simple problems and structures, such as cantilever beams or support beams. Secondly, numerical methods generate mathematical representations that produce approximate solutions based upon specified assumptions. It is a cost-effective method that saves time and material resources through computational analysis. Lastly,

experimentation provides actual and realistic measurements of the system. This method may prove to be considerably time consuming and expensive to set up and perform; however, these methods yield results that derive from real life physical phenomena. This study will make use of the numerical method approach via finite element analysis by simulating realistic loading conditions and “virtual surgeries” that would not be ideal to reproduce due to the numerous iterations that are necessary for the study.

3.2.3 General principles of Continuum Mechanics

The field of continuum mechanics seeks to analyze the kinematics and mechanical behavior of materials when modeled as a continuous mass. Its principles are essential in the formulation of FEM elemental equations that derive from governing equations. The assembling of such continuum mechanics equations allow for the response of materials and systems - subject to various loading conditions - to be interpreted. In order for the reader to effectively understand the mechanics behind the finite element method, it is imperative to understand the constitutive equations and behavior of material responses described below.

Consider a straight bar that has a constant cross-sectional area, A , and is subjected to external tensile forces, F .

Fig. 5. Straight bar with cross sectional area, A , and external tensile forces, F

$$\sigma = \frac{F}{A} \quad (2.1)$$

In addition to the stresses that are generated, deformation of the material in the form of strain, ε , is also created. In doing so, a material's original length, l_o , is transformed to a deformed length. This physical characteristic can be expressed as a ratio between the change in deformation, Δl , and its original length:

$$\varepsilon = \frac{\Delta l}{l_o} \quad (2.2)$$

When materials are introduced to the stresses and strains mentioned prior, a physical phenomenon known as the Poissons effect occurs. This effect describes how the compression of a material in one direction can yield an expansion in the other two directions that are perpendicular to the applied load. By comparing the transverse contraction strain, $\varepsilon_{transverse}$, to longitudinal extension strain $\varepsilon_{longitudinal}$, the Poisson's ratio is obtained as:

$$\nu = -\frac{\varepsilon_{transverse}}{\varepsilon_{longitudinal}} \quad (2.3)$$

A typical stress-strain curve, shown in Figure 5, illustrates an essential relationship that describes the behavior of material when pulled in tension. This graph is employed as a tool by many engineers and scientists to archive known material response in order to predict how a material may behave.

Fig. 6 A typical stress-strain curve

In the linear region of the curve, the stress-strain relationship follows Hooke's Law in which:

$$\sigma = \varepsilon E \quad (2.4)$$

where σ is stress, ε is strain, E is the modulus of elasticity and is the tendency of a material to deform when it is exposed to forces.

As the stress-strain curve transitions to nonlinearity – no longer obey Hooke's law - it reaches a point in which the material begins to yield. This specific location is known as the yield strength and signifies the introduction of dislocations within the crystal structures of the material. The curve will then reach a maximum stress level where the material can no longer endure further stresses without failure, the ultimate strength. The region between the yield strength and ultimate strength is referred to as strain hardening, a region where strengthening of material occurs through plastic deformation. Material necking decreases the cross-sectional area as a result of localized strain; this occurs

between the ultimate strength and fracture point. Lastly, if the material is loaded beyond its load carrying capacity, fracture of the material will ensue.

Linear analyses require deformations to be small, material behavior to be linear, dynamic effects to be neglected, and that no gaps or overlaps occur during the deformation of the solid. In the case that these requirements are not met, a nonlinear analysis may be more suitable.

In order to define material stresses in three-dimensional space, the Cauchy stress tensor is utilized following a right-handed Cartesian coordinate system seen below:

$$[\sigma] = \begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} = \begin{bmatrix} \sigma_{xx} & \tau_{xy} & \tau_{xz} \\ \tau_{yx} & \sigma_{yy} & \tau_{yz} \\ \tau_{zx} & \tau_{zy} & \sigma_{zz} \end{bmatrix} \quad (2.5)$$

The stress tensor contains three normal forces; σ_{xx} , σ_{yy} , *and* σ_{zz} , as well as six shear forces; σ_{xy} , σ_{xz} , σ_{yz} , σ_{yx} , σ_{zx} , and σ_{zy} . A relationship among the six shear forces that yields equilibrium of forces is given by:

$$\sigma_{xy} = \sigma_{yx}, \quad \sigma_{xz} = \sigma_{zx}, \quad \text{and} \quad \sigma_{yz} = \sigma_{zy} \quad (2.6)$$

As a result of the equilibrium forces generated, the stress tensor can be consolidated into six independent stress components in the following stress vector:

$$\{\sigma\} = \begin{Bmatrix} \sigma_{xx} \\ \sigma_{yy} \\ \sigma_{zz} \\ \tau_{xy} \\ \tau_{xz} \\ \tau_{yz} \end{Bmatrix} \quad (2.7)$$

In addition, six independent strain components can also be represented as a single strain vector:

$$\{\varepsilon\} = \begin{Bmatrix} \varepsilon_{xx} \\ \varepsilon_{yy} \\ \varepsilon_{zz} \\ \varepsilon_{xy} \\ \varepsilon_{xz} \\ \varepsilon_{yz} \end{Bmatrix} \quad (2.8)$$

Furthermore, the relationship between stress and strain, which obeys Hooke's Law, can also be described in terms of the material stiffness matrix:

$$\{\sigma\} = [C]\{\varepsilon\} \quad (2.9)$$

The material stiffness matrix, C , consists of a system of material constants, modulus of elasticity, and Poisson ratio; which are required to define material behavior. The manipulation of such variables allows material property definitions for many material models such as isotropic, anisotropic, and orthotropic. Assembling of such equations is pivotal in generating elemental equations that are used to solve for approximate solutions in the finite element method.

3.2.4 Variation Principles and Methods

The application of variational methods plays a prominent role in FEM for its ability to approximate solutions of differential equations. Natural phenomena cannot simply be represented with one dynamic variable. Hence, the utilization of differential equations is ideal to describe the many laws governing natural phenomena. By utilizing variational methods to approximate such dynamic equations, it allows for proper methods of finding approximate solutions to these problems.

The principle behind variational methods works by finding the extremum, such as the maximum or minimum, or specific values of a function with respect to its problem variables. This system includes all intrinsic features of the problem, which may be governing equations, boundary conditions, initial conditions, or constraint conditions. Configuration of elemental integral formulations through variational methods in the finite element method makes use of two main types; weak and weighted-residuals. The formulation of weak forms of governing equations involves the Ritz method while development of weighted-residuals includes the Petrov-Galerkin, Galerkin, least squares, and collocation methods.

Traditionally, the application of variational formulations is performed by constructing a functional that is equivalent to the governing equations of the problem. The sections below will outline the procedures that are done for the formulation of a weak form integral through the Ritz method. In the Ritz method, the weak form contains both the governing differential equations and the natural boundary conditions of the

problem. As a result, it requires weaker continuity on the approximate solution than the original differential equation.

3.2.5 Theory of Finite Element Analysis

The finite element method is a numerical method that utilizes mathematical models to computationally obtain approximate solutions for the mathematical models. More general, Finite Element Analysis (FEA) is an application of the finite element method that can be utilized to perform analyses on structural systems and other applications. The process of FEA can be defined through six basic steps [29]. The initial phase divides the geometrically complex domain, Ω , into a collection of simple subdomains known as finite elements that vary from triangular to quadrilateral shapes. These elements are then connected at their vertices, known as nodes, and have important interpolation properties. Each finite element, Ω_e , is then viewed as an independent domain by itself. When all finite elements are assembled, the collection of elements is called the finite element mesh. Secondly, the algebraic equations using principle governing equations are developed over each finite element at the nodes of each element. At this step of the analysis, the physical process is approximated by functions of polynomials via interpolation functions. The third phase involves the assembling of element equations utilizing continuity and balance of physical quantities to interpret the entire problem. The next steps involves the imposition of boundary conditions, solution of assembled equations, and post processing of the results to yield values such as stress, strain, etc.

In order to formulate the finite element models of three-dimensional elasticity problems, governing equations must first be established. The governing strain-displacement relations are seen below:

$$\varepsilon_{xx} = \frac{\partial u_x}{\partial x}, \varepsilon_{yy} = \frac{\partial u_y}{\partial y}, \varepsilon_{zz} = \frac{\partial u_z}{\partial z} \quad (2.10)$$

$$2\varepsilon_{xy} = \frac{\partial u_x}{\partial y} + \frac{\partial u_y}{\partial x}, 2\varepsilon_{xz} = \frac{\partial u_x}{\partial z} + \frac{\partial u_z}{\partial x}, 2\varepsilon_{yz} = \frac{\partial u_y}{\partial z} + \frac{\partial u_z}{\partial y} \quad (2.11)$$

where ε is the strain and u is the deformation along the x , y , and z directions.

Additionally, this strain-displacement relation can also be represented in matrix form:

$$\varepsilon = \mathbf{D}\mathbf{u}, \varepsilon = \begin{Bmatrix} \varepsilon_{xx} \\ \varepsilon_{yy} \\ \varepsilon_{zz} \\ 2\varepsilon_{xz} \\ 2\varepsilon_{xy} \\ 2\varepsilon_{yz} \end{Bmatrix}, \mathbf{D}^T = \begin{bmatrix} \partial/\partial x & 0 & 0 & \partial/\partial z & 0 & \partial/\partial y \\ 0 & \partial/\partial y & 0 & 0 & \partial/\partial z & \partial/\partial x \\ 0 & 0 & \partial/\partial z & \partial/\partial x & \partial/\partial y & 0 \end{bmatrix} \quad (2.12)$$

where ε is strain along the x , y , and z directions, $\mathbf{D}$ is the conductivity matrix, and $\mathbf{u}$ is displacement.

The equations of motion that describes the system in terms of stress, displacement, and a body vector forces can then be described as:

$$\frac{\partial \sigma_{xx}}{\partial x} + \frac{\partial \sigma_{xy}}{\partial y} + \frac{\partial \sigma_{xz}}{\partial z} + f_x = \rho \frac{\partial u_x}{\partial t^2} \quad (2.13)$$

$$\frac{\partial \sigma_{xy}}{\partial x} + \frac{\partial \sigma_{yy}}{\partial y} + \frac{\partial \sigma_{yz}}{\partial z} + f_y = \rho \frac{\partial u_y}{\partial t^2} \quad (2.14)$$

$$\frac{\partial \sigma_{xz}}{\partial x} + \frac{\partial \sigma_{yz}}{\partial y} + \frac{\partial \sigma_{zz}}{\partial z} + f_z = \rho \frac{\partial u_z}{\partial t^2} \quad (2.15)$$

or

$$\mathbf{D}^T \boldsymbol{\sigma} + \mathbf{f} = \rho \ddot{\mathbf{u}} \quad (2.16)$$

where f_x , f_y , and f_z denote the components of body force vector along the x, y, and z directions, respectively, σ is stress, and ρ is the density of the material.

The constitutive equations that relate the stress and strain is seen in the following equation:

$$\begin{Bmatrix} \sigma_{xx} \\ \sigma_{yy} \\ \sigma_{zz} \\ \sigma_{xy} \\ \sigma_{xz} \\ \sigma_{yz} \end{Bmatrix} = \begin{bmatrix} c_{11} & c_{12} & c_{13} & 0 & 0 & 0 \\ c_{21} & c_{22} & c_{23} & 0 & 0 & 0 \\ c_{31} & c_{32} & c_{33} & 0 & 0 & 0 \\ 0 & 0 & 0 & c_{44} & 0 & 0 \\ 0 & 0 & 0 & 0 & c_{55} & 0 \\ 0 & 0 & 0 & 0 & 0 & c_{66} \end{bmatrix} \quad (2.17)$$

or

$$\boldsymbol{\sigma} = \mathbf{C} \boldsymbol{\varepsilon} \quad (2.18)$$

where c_{ij} ($c_{ji}=c_{ij}$) are the elasticity constants for an orthotropic medium with the material principal directions, x_1, x_2 , and x_3 , coinciding along the x, y, and z directions. The c_{ij} variable can be expressed in terms of the engineering constants - E_1 , E_2 , E_3 , ν_{12} , ν_{13} , ν_{23} , G_{12} , G_{13} , and G_{23} - for an orthotropic material.

This problem requires two types of boundary conditions; natural and essential boundary conditions. The natural and essential boundary conditions are as follows:

$$\left. \begin{aligned} t_x &\equiv \sigma_{xx}n_x + \sigma_{xy}n_y + \sigma_{xz}n_z \equiv \hat{t}_x \\ t_y &\equiv \sigma_{xy}n_x + \sigma_{yy}n_y + \sigma_{yz}n_z \equiv \hat{t}_y \\ t_z &\equiv \sigma_{xy}n_x + \sigma_{yz}n_y + \sigma_{zz}n_z \equiv \hat{t}_z \end{aligned} \right\} \text{ on } \Gamma_\sigma \quad (2.19)$$

and

$$\mathbf{u} = \hat{\mathbf{u}} \text{ on } \Gamma_u \quad (2.20)$$

where t is traction, σ is stress, Γ_σ is the natural boundary condition, and Γ_u is the essential boundary condition.

The principle of virtual displacements for the given three-dimensional elasticity problem is then expressed in vector form as:

$$0 = \int_{\Omega_e} [(\mathbf{D}\delta\mathbf{u})^T \mathbf{C}(\mathbf{D}\mathbf{u}) + \rho \mathbf{u}^T \ddot{\mathbf{u}}] d\mathbf{x} - \int_{\Omega_e} (\delta\mathbf{u})^T \mathbf{f} d\mathbf{x} - \oint_{\Gamma_e} (\delta\mathbf{u})^T \mathbf{t} ds \quad (2.21)$$

where $\mathbf{D}$ is the conductivity matrix, $\mathbf{u}$ is displacement, t is traction, and f is the body force vector.

The finite element approximation is assumed to be in the form:

$$\mathbf{u} = \begin{Bmatrix} u_x \\ u_y \\ u_z \end{Bmatrix} = \psi \Delta, \quad \mathbf{w} = \delta \mathbf{u} = \begin{Bmatrix} w_1 = \delta u_x \\ w_2 = \delta u_y \\ w_3 = \delta u_z \end{Bmatrix} = \psi \delta \Delta \quad (2.22)$$

where $\mathbf{u}$ is displacement along the x, y, and z directions, ψ is the interpolation function, Δ is the gradient vector, $\mathbf{w}$ is the weight function, δ is the Kronecker delta, and

$$\psi = \begin{bmatrix} \psi_1 & 0 & 0 & \psi_2 & 0 & 0 & \dots & \psi_n & 0 & 0 \\ 0 & \psi_1 & 0 & 0 & \psi_2 & 0 & 0 & \dots & \psi_n & 0 \\ 0 & 0 & \psi_1 & 0 & 0 & \psi_2 & 0 & \dots & 0 & \psi_n \end{bmatrix} \quad (2.23)$$

and

$$\Delta = \{u_x^1 \quad u_y^1 \quad u_z^1 \quad u_x^2 \quad u_y^2 \quad u_z^2 \quad \dots \quad u_x^n \quad u_y^n \quad u_z^n\} \quad (2.24)$$

By substituting equations (2.23) and (2.24) into the statement of the principle of virtual body, the finite element model of a three-dimensional elastic body yields the following equation:

$$\mathbf{M}^e \ddot{\Delta}^e + \mathbf{K}^T \Delta^e = \mathbf{F}^e + \mathbf{Q}^e \quad (2.25)$$

$$\mathbf{K}^e = \int_{\Omega_e} \mathbf{B}^T \mathbf{C} \mathbf{B} dx, \quad \mathbf{M}^e = \int_{\Omega_e} \rho \psi^T \psi^e dx \quad (2.26)$$

$$\mathbf{F}^e = \int_{\Omega_e} \psi^T \mathbf{f} dx, \quad \mathbf{Q}^e = \oint_{\Gamma_e} \psi^T \mathbf{t} ds \quad (2.27)$$

It should be noted that the element mass matrix $\mathbf{M}^e$ and stiffness matrix $\mathbf{K}^e$ are of order $3n \times 3n$ and the element load vector $\mathbf{F}^e$ and the vector of internal forces $\mathbf{Q}^e$ is of order $3n \times 1$, where n is the number of nodes in a finite element.

After a domain is divided into specific subdomains of a particular shape function, an approximating function, known as an interpolation function, is assigned to interpret deformation of shapes. Interpolation functions are then defined by its field variables and nodes. Integration at these particular nodes yields the necessary values of desired field variables for that particular elemental domain. Interpolation functions of three-dimensional space have the following form:

$$\sum_{i=1}^n \psi_i^e(x, y, z) = 1, \quad \psi_i^e(x_j, y_j, z_j) = \delta_{ij} \quad (2.28)$$

Specifically, for a four-node tetrahedral element, the interpolation function is:

$$u(x, y, z) = a_0 + a_1x + a_2y + a_3z \quad (2.29)$$

In evaluating the element matrices numerically, the geometry of the elements can be described by the transformation equations:

$$x = \sum_{i=1}^m x_i \phi_i(\xi, \eta, \zeta), \quad y = \sum_{i=1}^m y_i \phi_i(\xi, \eta, \zeta), \quad z = \sum_{i=1}^m z_i \phi_i(\xi, \eta, \zeta) \quad (2.30)$$

where ξ, η, ζ are element coordinates.

Under these transformations, the master tetrahedral elements transform to the arbitrary tetrahedral elements shown below:

$$[J] = \begin{bmatrix} \frac{\partial x}{\partial \xi} & \frac{\partial y}{\partial \xi} & \frac{\partial z}{\partial \xi} \\ \frac{\partial x}{\partial \eta} & \frac{\partial y}{\partial \eta} & \frac{\partial z}{\partial \eta} \\ \frac{\partial x}{\partial \zeta} & \frac{\partial y}{\partial \zeta} & \frac{\partial z}{\partial \zeta} \end{bmatrix} = \begin{bmatrix} \frac{\partial \hat{\psi}_1}{\partial \xi} & \frac{\partial \hat{\psi}_2}{\partial \xi} & \cdots & \frac{\partial \hat{\psi}_m}{\partial \xi} \\ \frac{\partial \hat{\psi}_1}{\partial \eta} & \frac{\partial \hat{\psi}_2}{\partial \eta} & \cdots & \frac{\partial \hat{\psi}_m}{\partial \eta} \\ \frac{\partial \hat{\psi}_1}{\partial \zeta} & \frac{\partial \hat{\psi}_2}{\partial \zeta} & \cdots & \frac{\partial \hat{\psi}_m}{\partial \zeta} \end{bmatrix} \begin{bmatrix} x_1 & y_1 & z_1 \\ x_2 & y_2 & z_2 \\ \vdots & \vdots & \vdots \\ x_m & y_m & z_m \end{bmatrix} \quad (2.31)$$

$$\begin{Bmatrix} \frac{\partial \psi_i^e}{\partial x} \\ \frac{\partial \psi_i^e}{\partial y} \\ \frac{\partial \psi_i^e}{\partial z} \end{Bmatrix} = [J]^{-1} \begin{Bmatrix} \frac{\partial \psi_i^e}{\partial \xi} \\ \frac{\partial \psi_i^e}{\partial \eta} \\ \frac{\partial \psi_i^e}{\partial \zeta} \end{Bmatrix} \quad (2.32)$$

where J is the Jacobian matrix.

3.3 Structural Optimization

3.3.1 Introduction

The field of structural optimization attempts to maximize structural systems in order to best sustain intended loads. In doing so, structural optimization seeks to find optimal configurations without having to explicitly enumerate and evaluate all possible alternatives. More recently, structural optimization has become an area of particular interest in orthopedics and medical devices. Various studies on optimization and parametric analysis on the geometry of intramedullary rods and femoral fixation plates have been performed [30]. In addition, the utilization of probabilistic risk analysis in conjunction with optimization techniques with hip prosthesis are also prevalent [31]. The evolution of high-speed computation has led a wave of structural optimization methods that can evaluate complicated structural systems numerically with reduced time and increased accuracy.

3.3.2 Setting up the Optimization Problem

The application of structural optimization to generate a system that yields an optimal configuration requires clear identification and definitions of design variables, objective function, and state variables [32]. In order for a structure to be improved or optimized, allowance of structural changes of various parameters must be permissible. The selection of such parametric changes, or design variables, allows possible alternate design configurations to be generated and analyzed. In addition, the establishment of objective

functions gives a basis in which performance of the structural system can be measured. This basis of performance is a scalar function that must depend explicitly or implicitly on the design variables. Lastly, identification and defining of constraints are imperative in creating limitations in the working system. The imposition of boundaries provides limits to the system in order for it to properly operate and delineate the system from areas that are not of interest. In the general case, these structural optimization requirements can be represented in the following equation:

$$\begin{aligned}
 &\textbf{minimize } f(x) \\
 &\textbf{such that } g_j(x) \geq 0 \quad j = 1, \dots, n_g \\
 &\quad h_k(x) = 0 \quad k = 1, \dots, n_e
 \end{aligned} \tag{2.33}$$

where, x denotes a vector of design variables with components x_i , $i=1,\dots,n$, $h_j(x)$ is the equality constraints, and $g_j(x)$ is the inequality constraints $g_j(x)$.

The optimization problems that are prevalent in this work pertain to the linear optimization technique. This type of optimization is deemed linear when both the objective function and constraints are considered linear functions of the design variables, also known as a linear combination. If this statement is true, the expression can take the following form:

$$f(x) = c_1x_1 + c_2x_2 + \dots + c_nx_n = \mathbf{c}^T \mathbf{x} \tag{2.34}$$

where, $f(x)$ is the objective function, x_i are the design variables, and c_i are the constraints. In the case where the objective function and constraints are described as nonlinear

functions of the design variables, utilizing of nonlinear programming would be more suitable for the analysis.

3.3.3 Optimization Types

Conventionally, structural optimization is categorized into three distinct groups: size, shape, and topology optimization[33, 34]. Sizing optimization pertains to optimizing a structure based on a typical sizing, such as determining the optimal thickness distribution of a linearly elastic plate or beam. In this type of optimization, the main feature of the sizing problem is that the structural domain of the design model and state variables is known and fixed throughout the entire optimization process. Shape optimization refers to determining the optimal form or contour that is associated with the boundary of the structural domain. A shape is defined by the oriented boundary curves or boundary surfaces of the body. The shape problem is defined on a domain which is now the design variable. Lastly, topology optimization is concerned with finding the optimal layout or distribution of features in a structure within a specified domain. This field involves determining features such as the number and location of holes, and the connectivity of the domain.

3.3.4 Parametric Analysis using Taguchi Design of Experiments

The Taguchi method of parametric design is a robust experiment process that seeks to obtain an optimal combination of design parameters in order to achieve the lowest cost solution. The method is a prime candidate for evaluation of orthopedic

implant devices due to its ability to quantify how design parameters can affect mechanical performance. The Taguchi method utilizes orthogonal arrays, signal-to-noise ratios, and analysis of variance (ANOVA). In order to accommodate many design factors simultaneously and assure a balanced comparison of factor levels that result in meaningful and verifiable conclusions, the Taguchi method makes use of orthogonal arrays. In particular, this study will make use of an L18 orthogonal array which assesses seven different factors at three various levels and one factor at two levels, as shown below:

Table 2. L18 Orthogonal Array

Experiment No.	Factor A	Factor B	Factor C	Factor D	Factor E	Factor F	Factor G	Factor H
1	1	1	1	1	1	1	1	1
2	1	1	2	2	2	2	2	2
3	1	1	3	3	3	3	3	3
4	1	2	1	1	2	2	3	3
5	1	2	2	2	3	3	1	1
6	1	2	3	3	1	1	2	2
7	1	3	1	2	1	3	2	3
8	1	3	2	3	2	1	3	1
9	1	3	3	1	3	2	1	2
10	2	1	1	3	3	2	2	1
11	2	1	2	1	1	3	3	2
12	2	1	3	2	2	1	1	3
13	2	2	1	2	3	1	3	2
14	2	2	2	3	1	2	1	3
15	2	2	3	1	2	3	2	1
16	2	3	1	3	2	3	1	2
17	2	3	2	1	3	1	2	3
18	2	3	3	2	1	2	3	1

The Taguchi method employs signal-to-noise ratios, which are logarithmic functions that transform a measured response into a signal-to-noise ratio and serve as the objective function of optimization. In the application of optimizing an orthopedic fixation implant that reduces overall stresses, the “smaller is better” signal-to-noise ratio would be utilized and can be described as:

$$S/N = -10 \log\left(\sum \frac{y_i^2}{n}\right) \quad (2.35)$$

where, y_i is measured response and n is the number of experiments.

When utilizing this particular S/N ratio, larger values of the ratio correspond to a better performance response.

Furthermore, the main effects analysis determines the optimal combination of design parameters and specified levels while the ANOVA determines the error variance and quantifies the relative importance of each investigated factor. In order to test the significance of main effects and interactions, ANOVA compares the mean square against an estimate of the experimental errors at specified confidence levels. This can be performed by first calculating the total sum of square deviations, in which:

$$SS_T = \sum_{i=1}^n (n_i - n_m)^2 \quad (2.36)$$

where, n is the number of experiments in the orthogonal array, n_i is the mean S/N ratio for the i th experiment, and n_m is the total mean of the S/N ratio.

As a result, the percent contribution can be calculated by:

$$\rho = \frac{SS_d}{SS_T} \quad (2.37)$$

where, SS_d is the sum of the squared deviations.

The Taguchi method of optimization allows for the study of various internal fixation plate design parameters in such a manner that experimental and simulation time is minimized. As a result, the techniques of the Taguchi method allow for simplification of experimental design, data analysis, and prediction of optimal configurations

Chapter 4. Methodology

The flowchart shown in fig. 6 illustrates the simulation-based methodology proposed for the design and optimization of patient-specific implant. Although the comprehensive process is systematic in nature, there exists a significant degree of freedom in exactly how the steps are carried out for a specific application and what software packages are used. The methodology is open-ended and allows for the adaptation to various design scenarios. The ultimate goal is to obtain a design that is as close to the optimal as possible prior to prototyping.

Fig. 7 Design Methodology flowchart

4.1 Medical Imaging Analysis

The first step of this process is to obtain the patient data. The patient data is usually obtained in the form of computer tomography (CT) scans or as magnetic resonance imaging (MRI) scans. In this study, CT scans were utilized. The scans are characterized as a 3-D array of voxel intensity data, where each voxel intensity value represents the tissue density at a finite location. The more voxels in each CT slice (or 2-D layer, usually orientated in the axial direction), the higher the image's resolution will be. Additionally, the smaller the slice thickness, the higher the resolution will be in the sagittal and coronal planes. The image data is typically saved as a series of DICOM (digital imaging and communications in medicine) files, with each file representing a 2-D slice of the 3-D array.

Fig. 8 Using gray scale to map the bone (Mimics)

Commercial software packages such as Amira (Thermo Scientific, 2017) and Mimics (Materialize, 2017) can be utilized to segment the voxel data into regions of cortical bone, cancellous bone, and other various tissue types. Once the series of DICOM files are loaded into the program, built-in automated tools can be used to make the initial selection of the type of tissue(s) desired to be modeled. This is accomplished by defining a voxel intensity range that represents the tissue, and then selecting which continuous region(s) of tissue it applies to as represented in figure 8. Alternatively, the voxel intensity range can be applied to the entire image.

Fig. 9 Clockwise from top left: front view, top view, sagittal view and rendered 3D model

With either of these automated techniques, it is highly probable that numerous unwanted small holes will be present within the segmented voxel region. Additionally, unwanted islands may be selected outside of the desired bone tissue region. This is shown in figure 10. These undesirable artifacts require a second segmentation phase involving manual selection/removal techniques. This is accomplished by viewing each slice layer-by-layer – in all three Cartesian orientations – and performing the necessary “touch-ups”. For bone tissue modeling, manual segmentation is especially crucial for cancellous bone and thin cortical bone regions.

Fig. 10 CAD Rendering: before post-processing

Fig. 11 CAD Rendering: after post-processing

4.1.1 Specimen Sample

A 32 year-old male presenting with a non-comminuted diaphyseal fracture (left thighbone) who underwent CT for pre-surgical evaluation.

Fig 12 X-ray scan of the patient

4.2 CAD Modeling

4.2.1 Femur Model

It is well-known fact that each bone anatomy is unique. Fundamental biological and environment processes have given rise to a myriad of skeletal size and shape variations across the human population. Many orthopedic implant designs may utilize the same size and shape configuration for its implant to treat various types of injuries and patients. However, contrasting device performances may occur due to differing human skeletal structures.

Majority of studies in the past have focused on creating an “average femur model” to accommodate the entire femoral population to produce optimal implant shapes and sizes [30]. Despite minimizing the variability in femur models and many improvements in the existing plate designs, failure rate of implants has seen a steady rise. These studies failed to acknowledge the potential of additive manufacturing. Due to rapid advancements in the field of additive manufacturing, it is now possible to 3D print biocompatible parts with complex geometry. The product cycle time of additive manufacturing is same that of as conventional manufacturing [35]. Thus, the advantage of using additive manufacturing gives designers the flexibility to have plate design which precisely matches the bone anatomy of the patient. Prior studies have already shown the advantages of using such a plate for fracture recovery as well as ease of handling for orthopedicians during surgery [19, 36-38].

One of the ‘patient-specific design’ aspect of this study is designing a plate which matches the unique size and shape of the bone. After recreating a 3D model from CT scans using Mimics, another module (3-Matic) of the same software is utilized to create a CAD model of the plate. The recreated femur model is then imported into 3-Matic. The model was assigned a right-handed Cartesian coordinate system with the origin located at the centroid of the femoral posterior cruciate insertion site. The xyz-coordinate system is as follows: 1.) the x-axis is pointing ventrally, 2.) the y-axis is pointing laterally, and 3.) the z-axis is pointing proximally. Femoral muscle group attachment data and orientations were acquired from Julius Wolff Institute for Biomechanics and Musculoskeletal Regeneration, Berlin, Germany and scaled to the patient femur [11, 39, 40]. This is performed by creating datum points for femoral muscle groups in accordance to average anthropometric measurements of femoral muscle origins and insertion sites, as seen in figure 13 and table three.

Table 3. Corresponding femoral muscle group names to location on Average Femur

No.	Muscle	No.	Muscle
1	Gastrocnemius lateralis	13	Gluteus maximus 1
2	Gastrocnemius medialis	14	Quadratus femoris
3	Adductor magnus caudal	15	Gluteus medius
4	Adductor magnus cranial	16	Gluteus minimus
5	Biceps femoris	17	Piriformis
6	Adductor longus	18	Obturator internus, gemellus
7	Vastus lateralis	19	Obturator externus
8	Vastus medialis	20	Psoas major, iliacus
9	Vastus intermedius	21	Adductor brevis
10	Gluteus maximus 3		
11	Adductor minimus	Note:	●= front face
12	Pectineus		○= back face

Fig.13 Spatial location of femoral muscle groups

4.2.2 Patient-specific plate

Section 4.2.1 discussed the shortcomings in the current plate design and how it affects the patient and to some extent the surgeon handling it. Figure 14 shows one of the plate designs obtained from Taguchi design of experiments. As seen from the figure, the interface gap is minimum and the plate follows the bone anatomy accurately. This feature cannot be incorporated into plate design derived from ‘average femur’ model which often results in wrong placement of the plate by surgeon and eventually plate failure. There are many such factors which are discussed at length in section 4.5.

The CAD modeling was done in 3-Matic according to design obtained from Taguchi DOE. The finished models of femur and plate were meshed in 3-Matic and exported back to Mimics for material assignement which is discussed in next section.

Fig 14. Left to Right: Front view, Side view

4.3 Finite Element Model

4.3.1 Material Properties

The behaviors of materials are influenced by many structural properties such as the modulus of elasticity, Poisson's ratio, shear strength, and yield strength. In order to correctly predict the response of complex systems, finite element models must assign realistic material properties to its elements. In doing so, calculations of nodal displacement can be generated with increased accuracy and precision. In previous studies, to save computational time due to increased complexity, the material assignment for femur was done as linear elastic and isotropic. The femur was composed of solid cancellous structure with outer cortical shell. Figure 15 shows femur bone with such geometry and material assignment.

Fig 15. Fracture model in a past study [30]

Although past research had deemed modeling of cortical and cancellous bones of the femur as isotropic materials as acceptable, recent studies have shown the inaccuracy of the results due to this assumption [41]. The study further shows the accurate results obtained with assigning anisotropic properties to trabecular bone structure using micro-CT images. Voxel-based studies have shown to predict the anisotropic mechanical properties of bone accurately [42]. The current study has adopted the same of approach for anisotropic assignment of material.

Mimics uses following material expressions for gray-value based assignment of material:

1. Density expression: The density expression can be used for translating the gray value of an element to a density. To do this, an empirical expression of the form $\rho = \alpha + \beta * GV$ can be entered to convert the gray value into a density value. This method can also be used to export gray values: if $\rho = 0 + 1 * GV$ is used as a density expression, the representatives of each interval are written out as densities.
2. Elastic Modulus expression: Based on the density value, following expression was used to define the Modulus of Elasticity

Table 4. E-Modulus expression

Apparent density r (Kg/m³)	R²	Axis	Young's modulus E (MPa)	R²
$r = 1.067 * HU + 131$	0,84	A-P	$E = 0.004 * r ^ 2.01$	0,91

- Poisson expression: Similarly, based on the density value, an expression can be entered to define the Poisson coefficient for each material.

Fig. 16 Expressions for material assignment

Fig. 17 Sectional view of femur after material assignment

4.3.2 Loading Conditions

Applications of loading conditions in biomechanical finite element models are essential in representing realistic physiological loading conditions. The proper selection of orientation, direction, and magnitude of joint reaction and muscle forces allow for appropriate elemental and nodal deformations. These definitions are especially critical in modeling the impact of muscle on the behavior of the femoral bone. Current preclinical assessments of the femoral locking plate systems are based upon the assumption that the hip joint reaction force is the primary load in the system. However, literature has shown the appropriateness of including femoral muscle groups in modeling the biomechanics of the lower extremity. The implementation of muscular forces not only allows for improved model representation, but it also yields insight on stress shielding that occurs within the osseous specimen.

The present study will incorporate femoral muscle force outputs that are associated with a normal walking gait cycle. Muscle force magnitude data (Table 5) will be assigned to their corresponding node coordinates created in Section 4.1 [11]. The direction of the force will originate from the muscular origin and is directed towards its insertion site.

In addition, the joint patella contact force – obtained from vasti, rectus femoris, and patellar ligament – is located at the ventral groove between the medial and lateral condyles.

Table 5. Loading conditions at 10, 30, 45 and 70% gait cycle

Name of force	Attachment (mm)			Force at 10% gait cycle (N)			Force at 30% gait cycle (N)			Force at 45% gait cycle (N)			Force at 70% gait cycle (N)		
	x	y	z	x	y	z	x	y	z	x	y	z	x	y	z
Joint contact hip	-7.93	-56.6	433.42	-510.63	665.76	-1131.89	-399.59	812.5	-1435.34	-466.34	962.62	-1911.22	-68.12	4.94	-47.79
Joint contact patella	27.71	-10.7	13.4	123.18	65.61	-27.03	14.32	2.73	5.42	342.94	34.41	164.95	15.95	8.09	30.49
Joint contact knee :															
posterioro-lateral1	-5.12	20.99	0.03	0	0	718.3	0	0	807	0	0	1287.38	0	0	-22.08
anterio-medial1	2.85	-20.04	-0.14	0	0	239.43	0	0	269	0	0	429.13	0	0	7.36
central	0	0	0	-99.66	60.75	-0.01	-98.36	108.58	-0.01	-134.61	113.43	-0.02	-14.49	34.95	0.01
posterioro-lateral2	2.67	24.96	-0.53	-339.36	0	0	-280.31	0	0	-137.02	0	0	-22.84	0	0
anterio-medial2	2.89	-29.98	-0.29	476.24	0	0	475.18	0	0	797.97	0	0	56	0	0
posterioro-medial	-13.16	-16.08	-0.97	0	-339.36	0	0	-280.31	0	0	-137.02	0	0	25.71	0
anterio-lateral	24.92	12.84	1.58	0	110.34	0	0	-19.9	0	0	-119.14	0	0	22.84	0
Gluteus maximus 1	-5.72	10.25	407.51	71.13	-71.72	75.19	50.18	-87.92	90.85	35.1	-87.87	90.95	0	0	0
Gluteus maximus 2	-13.13	2.57	349.89	27.33	-58.78	75.97	10.05	-69.16	85.76	0.08	-57.73	70.32	0.2	-0.45	0.55
Gluteus maximus 3	-11.63	10.88	392.17	36.06	-12.13	-27.76	0	0	0	0	0	0	0	0	0
Gluteus medius 1, 2, 3	-4.53	8.61	410.56	161.1	-118.59	149.1	128.07	-164.71	201.36	111.23	-179.68	221.4	3.57	-4.89	5.53
Gluteus minimus 1, 2, 3	0	0	413.68	136.5	-92.37	36.25	152.51	-177.49	78.5	186.22	-193.69	92.98	22.29	28.45	7.97
Tensor fasciae latae	6.34	15.38	393.23	3.23	51.09	-18.95	35.26	-20.26	-26.34	51.42	-40.7	-40.04	6.43	-3	5.58
Piriformis	1.7	-7.48	413.66	22.71	-47.98	42.95	15.17	-77.9	68.03	5.35	-77.9	67.03	2.89	-6.42	5.44
Obturator externus	-5.7	-11.09	407.19	0	0	0	0	0	0	0	0	0	0.55	-0.41	0.07
Quadratus femoris	-17.75	-29.26	367.18	20.34	-22.79	32.46	0	0	0	0	0	0	0	0	0
Obturator internus,															
Gemellus superior & inferior	0.86	-10.42	410.57	11.96	-18.98	20.66	12.43	-36.77	39.19	7.07	-35.18	37.2	2.15	-3.92	4.14

Pectineus	-16.52	-11.14	339.48	0	0	0	0	0	0	1.3	-1.01	1.12	2.38	-1.06	1.32
Vastus medialis	15.54	-21.93	180.83	82.9	-6.1	-259.22	0	0	0	2.93	0.18	-8.09	0	0	0
Vastus intermedius	21.31	-16.8	199.26	0	0	0	0	0	0	9.13	5.01	-62.06	0	0	0
Vastus lateralis	16.7	1.23	217.3	0	0	0	0	0	0	69.58	-25.73	-215.72	0	0	0
Gastrocnemius lateralis	-17.85	26.8	11.43	-22.75	5.96	-52.93	-126.98	21.72	-159.16	-292.75	37.74	247.83	-19.04	-3.33	-4.72
Gastrocnemius medialis	-24.7	-24.5	10.28	0	0	0	-6.77	2.3	-8.42	-5.71	0.04	-4.77	0	0	0
Biceps femoris, caput breve	-0.91	-1.59	204.26	-0.1	9.17	-48.81	-4	10.97	-60.16	-15.09	11.31	-90.02	-0.64	0.17	-2.21
Adductor magnus caudal	3.59	-27.65	41.85	6.44	-7.45	61.2	0	0	0	0	0	0	0	0	0
Adductor magnus cranial	1.42	-23.97	276.17	30.22	-49.77	63.83	0	0	0	0	0	0	0	0	0
Adductor minimus	7.39	-21.54	174.37	9.53	-20.47	51.26	0	0	0	0	0	0	0	0	0
Adductor longus	-3.18	-5.67	216.09	0	0	0	0	0	0	1.86	-1.9	2.81	11.45	-7.62	13.25
Adductor brevis 1	-15.62	-6.94	339.59	0	0	0	0	0	0	0	0	0	0.4	-0.29	0.26
Adductor brevis 2	-11.37	-11.32	311.71	0	0	0	0	0	0	0	0	0	0.37	-0.28	0.31
Psoas major, iliacus	-12.22	-33.5	370.43	0	0	0	51.47	-24.37	44.32	115.24	-62.89	114.51	32.41	-7.41	20.43

4.3.3 Boundary Conditions

The region of interest in this particular study is the femoral model and components of the locking plate system. By limiting the finite element system to these constituents, modeling of the upper body extremity and constituents below the femoral condyle can be omitted. By constraining the model to these parameters, it allows for increase computational efficiency without compromising model accuracy and validity. Since the model is balanced with the joint contact forces of the hip and knee – in conjunction to the all femoral muscle groups – only rigid body motions at the distal end

of the model were constrained. The fixed constraint at both distal condyles creates zero degrees of freedom at the knee joint.

4.3.4 Mesh Quality

The quality of mesh plays a significant role in the accuracy and stability of numerical computations. In order to assess the mesh quality of a model, quality metrics such as mesh orthogonally, expansion, aspect ratio, and Jacobian ratio are utilized. When dealing with tetrahedral meshes, these quality standards are more stringent than their hexahedral counterparts. This is due to the fact that tetrahedral elements are more prone numerical errors, inaccurate results, and high computational times.

Fig. 18 Mesh Element quality

Although hexahedral elements may alleviate these nuisances, the versatility of tetrahedral elements to represent complex shapes such as the bone deems it more suitable. By abiding the strict mesh quality standards when utilizing a tetrahedral mesh to model the femoral bone, it can be utilized as a representative model that can yield accurate results. For meshing of all the parts, SOLID185 tetrahedral elements were used.

4.3.5 Convergence

Convergence studies are analytical methods to determine optimum mesh configurations and quality of calculated solutions. Solutions that converge provide mesh sizes that are ideal and results that are acceptable; however, solutions that do not converge may yield inaccurate conclusions and require additional mesh configurations. Reconfiguration of meshes to finer detail may result in improved model representation; however, may not be necessary if the solution converges at coarser mesh sizes. The mesh analysis method is performed by refining a mesh and observing whether multiple outputted results can converge to a single correct solution. There are two techniques to perform such convergence analyses, the h-method and the p-method. The h-method is executed by increasing the number of elements within the model, while the p-method increases the complexity of shape function by increasing polynomial order. The tetrahedral elements that were utilized in this study were analyzed via the h-method analysis. Mesh refinement was increased over an interval and von Mises stresses were observed to converge at a common solution. In addition to the mesh's ability to converge solutions, it was also able to yield an optimum mesh size of 1,124,538 tetrahedral

elements with an optimal global size of three mm. Figure 17 shows force convergence from one of the simulations.

Fig. 19 Force convergence

4.4 Topology Optimization

Topology optimization, a variant of shape optimization, takes a slightly different approach to optimize structures. This method is concerned with “laying out material in an optimal manner”, whereas the previously described approach is more dependent on the initial design variables (i.e. number/orientation of sides, holes, and other features are not permanent [43]). Techniques for solving FEM-integrated topology optimization include the solid isotropic material with penalization (SIMP) method, topology optimization by penalty (TOP) method [44], and dynamic implicit boundary-based moving superimposed finite element method (s-FEM) [45]. Several popular commercial CAD/FEA software packages, such as SolidWorks and ANSYS Workbench, have adopted a similar design of experiments (DoE) approach for structural optimization [46, 47].

The present study uses topology optimization module in ANSYS. After the non-linear structural analysis of the femur-implant assembly, topology optimization is linked to the structural analysis project. The objective of the optimization problem was set for minimizing the compliance or maximizing the stiffness. In the optimization region, only implant body was selected as a design region and the rest of the assembly was in exclusion region, as shown in figure 19. The design constraints were mass and stress values. This values depend on the number of different factors like type of fracture (comminuted, non-comminuted), minimum factor of safety required from the implant, required stiffness of the plate, and bone condition [45]. For the patient under consideration, after accounting all the mentioned factors, the limit on mass reduction was set to not more than 30%.

Fig. 20 Optimization region selection

The optimization process is iterative one, where the convergence to optimum solution can be obtained by adjusting the values of response constraints as required by the application. The output of the optimization is often an organic shape which is further processed can be further process in software package which accepts STL file, usually ANSYS Spaceclaim or 3-Matic. This study used 3-Matic. The design validation of the post-processed part is carried out to check the stress levels and factor of safety.

4.5 Taguchi Design of Experiments

The performance of femoral locking plates is highly dependent of various factors such as material selection, device dimensions, device placement, screw configuration, and overall bone health. In order to understand the effects of such parameters, a large number of experiments are required to adequately assess the interactions and main effects of the system. In addition to the impractical number of iterative experiments to be performed, the challenging and expensive tasks of implementing time-dependent static and dynamic loads make traditional biomechanical testing methods inefficient. Therefore, a deterministic Taguchi design optimization technique will be employed to yield an optimal implant design configuration with maximal structural integrity and reliability.

A three-dimensional finite element femoral fracture model utilizing the plating system and Femur model is created using Mimics and 3-Matic and imported into ANSYS. Femoral bone material properties, loading conditions, boundary conditions, mesh quality, and mesh convergence established in section 4.3. The interlocking screws were then inserted at appropriate locations following the recommendations and techniques used in literature [20].

4.5.1 Screw Type: Biocortical and Unicortical

Bicortical and unicortical interlocking screws were both utilized to fix the plate to the diaphysis of the femur. The functionality behind usage of either screw result in reduced stresses along the plate and reduce stress shielding along the femoral shaft.

Bicortical screws are characterized by a screw that enters through the lateral portion of the diaphysis and a screw tip that is anchored on the medial side. In contrast, a unicortical screw is distinguished by insertion into the lateral side of the diaphysis and anchored by a single cortical wall; does not enter medial cortical wall. The metaphysis and epiphysis will always be secured with bicortical screws for proper fixation.

Fig. 21 Plate with unicortical screws (left) and plate with bicortical screws (right)

4.5.1 Screw Density

Screw density may also contribute to varying degrees of stress distribution on the plate and femoral shaft. Higher screw density ratios may result in stress shielding of the bone; in contrast, lower screw densities may not allow for proper implant to bone fixation; resulting in failure. The screw density is calculated by dividing the number of screws utilized for the fixation by the available screw slots. In particular to the locking plate, three screw densities will be assessed during this investigation, 0.30, 0.50 and 0.60.

4.5.2 Fracture zone

For every femoral shaft fracture, a fracture zone can be defined as an area below and above the fracture line, which is structurally the weakest. Orthopedicians while performing surgery define a fracture zone based on their best judgement and experience. While attaching the plate to the bone, they avoid using screws in the fracture zone. The usage of screws in fracture zone can result into further comminution of fracture, lower screw purchase as well less stability of the entire plate-bone construct. A 'standard plate' has holes throughout the entire length of the plate and the surgeon chooses to leave the holes adjacent to fracture zone empty. Prior studies have shown that the screw holes are the areas where the stress concentration is maximum [5, 7, 15, 17, 20, 22]. The plate should have maximum strength adjacent to the fracture zone and thus this feature is incorporated in this study by defining a fracture zone, where holes are eliminated. The fracture gap is 5 mm, hence the fracture zone of 15 mm on each side of the fracture line is defined for the distal and proximal fracture segment. Along with fracture zone, different

distances between the screw holes on the plate on each side of the fracture segment are tested. This is done to determine if the distances between screw holes has any effect on the performance of the plate. Screw hole distances of 20 mm, 25 mm and 30 mm are checked.

4.5.3 Plate Thickness and Length

Three different plate thicknesses and plate lengths are considered. The thickness of the plate directly correlates to the stress-shielding phenomena. Using a thicker plate can result in stress shielding, whereas a thinner plate can result in implant failure [16]. Plate thickness of 3.5 mm, 4.5 mm and 6.5 mm were considered.

The plate length affects the plate stability [16, 20, 21]. A shorter plate can negatively affect the stability of plate, whereas a longer plate can result into higher stiffness which could either lead to stress-shielding or implant breakage [16]. Longer plates can also be really hard to work with and may also lead to implant failure due to misplacement of plate due to intraoperative error [26]. Ideally, depending on the fracture condition, the length of the plate should be determined. But, for the ease of manufacturability

4.5.4 Implant Material Properties

Due to their biologically inert properties and high anti-corrosive properties, surgical grade medical alloys such as Ti6Al4V titanium alloy and 316L stainless steel are commonly used for orthopedic implants. In addition, low modulus titanium alloys, such as Ti Grade II have become of greater interest in the orthopedic world due to its similarity

in mechanical properties of cortical bone. As a result, these three materials have been selected in the current parametric study. The modulus of elasticity, Poisson's ratio, and yield strength of Ti Grade II, Ti6Al4V, and 316L stainless steel is obtained from literature and shown below.

Table 6. Material properties of orthopedic implants [48]

Material	Modulus of Elasticity (MPa)	Poisson's Ratio	Yield Strength (MPa)
Ti Grade II	103,000	0.30	329
Ti6Al4V	112,700	0.28	905
316L Stainless Steel	186,400	0.29	690

4.5.5 Orthogonal Array

The current study will evaluate how different design parameters mentioned in the sections earlier will affect the overall implant performance. These factors were selected prior based upon their potential influence to implant performance. The investigated design factors and their alternate levels are presented in Table 7 and are assembled in an L18 Taguchi orthogonal array in Table 8.

The array defines eighteen simulation conditions that guarantee proper testing of each pairwise combination; in doing so, this reduces the number of required simulations needed from 2189 configurations to 18. The objective of this optimization problem will be to minimize peak stress concentrations within the plate.

Table 7. Parametric Design Factors and their Levels

FACTORS	LEVELS		
	1	2	3
A. Screw Type	Unicortical	Bicortical	
B. Number of Screw Holes	6	8	10
C. Screw density	0.3	0.5	0.6
D. Distance of screw holes from the fracture zone	3 mm	5 mm	10 mm
E. Material of plate	Ti Grade II	316L SS	Ti6Al4V
F. Thickness of plate	3.5 mm	4.5 mm	6.5 mm
G. Distance between the screw holes on each side of the fracture fragment	20 mm	25 mm	30 mm
H. Plate type	Short (140 mm)	Medium (200 mm)	Long (280 mm)

Table 8. Taguchi orthogonal array for simulations

Sr. No.	Screw Type	Number of Holes	Screw density	Distance of holes from the fracture zone	Material	Thickness	Distance on each side	Length
1	1	1	1	1	1	1	1	1
2	1	1	2	2	2	2	2	2
3	1	1	3	3	3	3	3	3
4	1	2	1	1	2	2	3	3
5	1	2	2	2	3	3	1	1
6	1	2	3	3	1	1	2	2
7	1	3	1	2	1	3	2	3
8	1	3	2	3	2	1	3	1
9	1	3	3	1	3	2	1	2
10	2	1	1	3	3	2	2	1
11	2	1	2	1	1	3	3	2
12	2	1	3	2	2	1	1	3
13	2	2	1	2	3	1	3	2
14	2	2	2	3	1	2	1	3
15	2	2	3	1	2	3	2	1
16	2	3	1	3	2	3	1	2
17	2	3	2	1	3	1	2	3
18	2	3	3	2	1	2	3	1

In present design and engineering practice, it is customary to implement a factor of safety when dealing with structural stability. The factor of safety is a performance measure of a structure that can be calculated by dividing the material strength by the maximum load of the structure. In the case of medical devices, a factor of safety must be selected that is sufficiently high that device failure can be prevented under extreme physiological conditions. Therefore, the current study will assess the femoral fracture model with the locking system during peak joint hip reaction forces - 30 percent gait - during a normal walking gait cycle and utilize the factor of safety as the performance response. In doing so, the investigation will utilize the greater-the-better SNR metric to obtain the optimal configuration.

A linear elastic and static structural analysis is performed for each simulation of the bone-implant construct.

Chapter 5. Results

5.1 Influence of Anisotropic Material Properties

5.1.1 Strain distribution on intact femur

In addition to observing simulation results and effect of all factors at different levels, the intact femur model will be assessed for strain distribution levels at four cross section levels- the intertrochanteric, subtrochanteric, proximal diaphyseal, and distal diaphyseal, as shown in figure 21. Each cross section will give insight on various strain distributions that may arise across the femoral shaft.

Fig. 22 Four level cross reference plans of Average femur for calculation of strain distributions

In addition, analysis at each level will serve as a means for FE model validation against similar performed investigations. Figure 22 compares the simulation strain results from the intact femoral model with simplified loading conditions [49], with the inclusion of all the muscle forces [49] and anisotropic material properties at 30% gait cycle with the simplified loading configuration with isotropic material properties. Unlike the simplified loading configuration, there was less variation in strain values when moving from the proximal portion of the femur to the distal aspect.

Fig. 23 Maximum Principal Strain at 30% gait cycle

5.2 Parametric Design Optimization

The simulation results from the deterministic parametric design optimization are illustrated in table 9. For all nine simulations, the computed maximum von Mises stress is substantially lower than the yield strengths of Ti Grade II, Ti6Al4V, and 316L stainless steel, as indicated by the factor of safety.

Table 9. Taguchi simulation results

Simulation No.	Material	Maximum von Mises stress (MPa)	Factor of Safety
1	Ti Grade II	248.81	3.7379
2	Ti6Al4V	26.762	9.3415
3	316L SS	67.199	3.7203
4	Ti6Al4V	314.06	1.256
5	316L SS	32.616	7.6649
6	Ti Grade II	18.423	13.57
7	Ti Grade II	45.172	5.345
8	Ti6Al4V	66.157	3.7789
9	316L SS	47.974	5.2112
10	316L SS	45.77	5.4621
11	Ti Grade II	291.66	2.2005
12	Ti6Al4V	107.47	2.32623
13	316L SS	194.24	1.2871
14	Ti Grade II	184.86	1.3524
15	Ti6Al4V	43.396	5.7609
16	Ti6Al4V	38.932	6.4215
17	316L SS	44.363	5.634
18	Ti Grade II	5924.6	0.04

Simulation 6 resulted in smallest local maximum stress of 18.423 MPa while simulation 18 generated the largest peak stress of 5924.6 MPa. Hence, simulation 6 design has the highest factor of safety, whereas simulation 18 has the lowest. This wide difference in values can be attributed to the combination of all the eight factors with their respective levels for a particular design.

Simulation 1

Simulation 2

Simulation 3

Simulation 4

Simulation 5

Simulation 6

Simulation 7

Simulation 8

Simulation 9

Simulation 10

Simulation 11

Simulation 12

Simulation 13

Simulation 14

Simulation 15

Simulation 16

Simulation 17

Simulation 18

Fig. 24 Stress distribution in plate: Loading at 30% gait cycle

5.2.1 Taguchi Analysis

For each response parameter, the level with the greatest signal-to-noise ratio corresponds to the optimal design parameter, highlighted in green. The optimum predicted design configuration was not one of the original eighteen simulations performed.

Table 10. Response Table for Means (von mises stress)

FACTORS	LEVELS		
	1	2	3
A. Screw Type	96.35	763.92	
B. Number of Holes	131.28	131.27	1027.87
C. Screw Density	147.83	107.74	1034.84
D. Distance from fracture zones	165.04	1055.14	70.22
E. Material of Plate	1118.92	99.46	72.03
F. Thickness of Plate	113.24	1090.67	86.5
G. Distance between holes	37.31	110.11	1142.99
H. Plate type	1060.22	103	127.19

Fig. 25 Mean Effects Plot

Table 11. Response Table for Signal to Noise Ratios: Smaller the better

FACTORS	LEVELS		
	1	2	3
A. Screw Type	-35.74	-40.29	
B. Number of Holes	-39.36	-38.23	-40.55
C. Screw Density	-40.29	-37.13	-40.72
D. Distance from fracture zones	-41.08	-42.29	-34.77
E. Material of Plate	-46.07	-36.68	-35.39
F. Thickness of Plate	-38.16	-44.35	-35.63
G. Distance between holes	-38.26	-90.98	-48.9
H. Plate type	-42.67	-35.72	-39.75

Fig. 26 S/N ratio

Table 12. Main effects response parameters

FACTORS	LEVELS		
	1	2	3
A. Screw Type	<u>Unicortical</u>	Bicortical	
B. Number of Screw Holes	6	<u>8</u>	10
C. Screw density	0.3	<u>0.5</u>	0.6
D. Distance of screw holes from the fracture zone	3 mm	5 mm	<u>10 mm</u>
E. Material of plate	Ti Grade II	316L SS	<u>Ti6Al4V</u>
F. Thickness of plate	3.5 mm	4.5 mm	<u>6.5 mm</u>
G. Distance between the screw holes on each side of the fracture fragment	<u>20 mm</u>	25 mm	30 mm
H. Plate type	Short (140 mm)	<u>Medium (200 mm)</u>	Long (280 mm)

Table 13. ANOVA results of Taguchi design analysis

Source	DOF	SUM OF SQUARES	MEAN OF SQUARES	F-Value	P-Value
Screw Type	1	2005416	2005416	1.08	0.062430378
Number of Holes	2	3215524	16077662	0.87	0.100102112
Screw Density	2	3295855	1647928	0.89	0.102602888
Distance from fracture zones	2	3542670	1771335	0.96	0.111288343
Material of Plate	2	4272068	2136034	1.16	0.142868417
Thickness of Plate	2	3928894	1964447	1.06	0.122309953
Distance between holes	2	4589282	2294641	1.24	0.110286457
Plate type	2	3574853	1787426	0.97	0.132993264
Error	2	3697877	1848938		0.115118189
Total	17	32122439			1

An analysis of variance (ANOVA) was performed on the eight parametric factors, as shown in Table 13. The performance of plate was significantly affected by material selection in which it yielded the greatest percent contribution of 14.28%. Plate length was found to have the second highest percent contribution and followed by plate thickness. The screw type resulted in the least contribution to the performance of the designed LCP. The results obtained from ANOVA comply with the result obtained in a past study [49].

The plate designed with optimum parameters is analyzed in ANSYS following the same procedures as described in the Methodology section. Table 15 shows the result from FE simulation for the plate design with optimum parameters. The maximum stress induced is lower than that obtained from all the simulation designs, indicating a good design with a high factor of safety.

Fig. 27 Stress distribution in plate: Loading at 30% gait cycle

Table 14. Optimum Design Parameters Configuration

Parameters	Value
A. Screw Type	Unicortical
B. Number of Screw Holes	8
C. Screw density	0.5
D. Distance of screw holes from the fracture zone	10 mm
E. Material of plate	316L SS
F. Thickness of plate	6.5 mm
G. Distance between the screw holes on each side of the fracture fragment	20 mm
H. Plate type	Medium (200 mm)

Table 15. FEA results for plate with optimum parameters

Maximum von Mises Stress (MPa)	Factor of Safety (FOS)
24.74	10.104

5.3 Topology Optimization

As discussed in previous section, the plate design with optimal parameters is analyzed to check stress levels and factor of safety. The analyzed plate design is linked to topology optimization module in ANSYS for further reduction in mass without losing the structural integrity. The results obtained from topology optimization are shown in figure 26.

Fig. 28 Result from topology optimization

The iteration process is initiated with retaining 95% of mass retention and stopped at 70% mass retention. The step size chosen was 2.5% and after each optimization, design validation was carried out to check the stress values. Hence, one topology optimization cycle consisted of optimization, design modification and design validation. The details of the result are shown in table 16. The final reduction in mass and volume is 30%.

Table 16. Topology Optimization Result

Parameter	Initial	Final
Mass (kg)	0.13007	9.1309e-002
Volume (mm ³)	16570	11632

After considering the inputs from topology optimization, final plate design with optimum design parameters was designed and analyzed for stress values.

Fig. 29. Final plate design

The maximum stress induced is 45.55 MPa with a Factor of Safety 5.48, which is appropriate for biomechanical testing [50]

Table 17. Result for modified Plate after topology optimization

Maximum von Mises Stress (MPa)	Factor of Safety (FOS)
45.55	5.48

Chapter 6. Conclusion and Future Work

6.1 Conclusion

Modern numerical computational methods allow for increased accuracy and realistic modeling of biomechanical systems. However, the degree of accuracy and validity of the overall model is limited by the information provided in regards to various loading conditions and assignment of material properties. In particular, modeling of the femoral fracture, due consideration should be given to influence of muscle forces as well as material properties of bone. When appropriate muscle groups are considered and included along with realistic material properties, strain magnitudes showed similar values to those reported from in vivo measurements in humans. If femoral muscle groups are neglected, this presents overestimation of tensile and compressive strains. Thus, generating unrealistic displacements and strain magnitudes that exceed normal physiological range. The results from this study indicate the need to consider anisotropic bone properties as well as muscle force loads to realistically model bone-plate construct.

The study-design of this research is comparative as well parametric in nature to maximize the potential of finite element simulations. Improper material assignment, lack of fundamental understanding of the behavior of the system (e.g. muscle force loads) and choosing either parametric or comparative design-study are few of the major shortcomings of the finite element studies of orthopedic devices [51]. This study attempts to overcome these shortcomings with a more realistic and accurate modeling. It will

provide a good insight to surgeons in having a streamlined process for internal fracture fixation.

6.2 Recommendations and Future Work

- Empirical data for finite element validation
- Dynamic Loading conditions
- Metal additive manufacturing of the plate
- Biomechanical Testing

References

1. Nikolaou, V.S.M., PhD, et al., *Use of Femoral Shaft Fracture Classification for Predicting the Risk of Associated Injuries*. Journal of Orthopaedic Trauma, 2011.
2. Danielle L.Miller, T.G., *A review of locking compression plate biomechanics and their advantages as internal fixators in fracture healing*. Clinical Biomechanics, 2007. **22**(10): p. 1049-1062.
3. M.Ehlinger, G.D., P.Adam, F.Bonnomet, *Distal femur fractures. Surgical techniques and a review of the literature*. Orthopaedics & Traumatology: Surgery & Research, May 2013. **99**(3): p. 353-360.
4. M.Perren, S., *Evolution and rationale of locked internal fixator technology: Introductory remarks*. Injury, September 2001. **32**(2): p. 3-9.
5. Bolhofner, B.R., B. Carmen, and P. Clifford, *The results of open reduction and Internal fixation of distal femur fractures using a biologic (indirect) reduction technique*. Journal of Orthopaedic Trauma, August 1996. **10**(6): p. 372-377.
6. Hatice Tuba Sanal, S.A., *Computerized Tomography in the Evaluation of Musculoskeletal System*, in *Musculoskeletal Research and Basic Science*. Springer, Cham. p. 165-182.
7. G.A Aitchison, D.W.L.H., J.J Parry, D.E.T Shepherd, and S.G Trotman, *A Review of the Design Process for Implantable Orthopedic Medical Devices*. The Open Biomedical Engineering Journal, 2009. **3**: p. 21-27.
8. Mark Taylor, P.J.P., *Four decades of finite element analysis of orthopaedic devices: Where are we now and what are the opportunities?* Journal of Biomechanics, March 2015. **48**(5): p. 767-778.
9. Katrana, N.J., N.A. Winslow, and J.M. McDaniel, *Patient-specific fracture fixation instrumentation and method*. 2017, Google Patents.
10. Arnone, J.C., et al., *An integrated computer-aided engineering approach for parametric investigation of locked plating systems design*. Journal of Medical Devices, 2010. **7**(2): p. 411-417.
11. Duda, G.N., et al., *Influence of muscle forces on femoral strain distribution*. Journal of Biomechanics, 1998. **31**(9): p. 841-846.
12. Bhandari, M., et al., *Clinical and Economic Burden of Revision Knee Arthroplasty*. Clinical Medicine Insights. Arthritis and Musculoskeletal Disorders, 2012. **5**: p. 89-94.
13. Thompson, M.K., et al., *Design for Additive Manufacturing: Trends, opportunities, considerations, and constraints*. CIRP Annals, 2016. **65**(2): p. 737-760.
14. Huang, S.H., et al., *Additive manufacturing and its societal impact: a literature review*. The International Journal of Advanced Manufacturing Technology, 2013. **67**(5): p. 1191-1203.
15. Frigg, R., *Locking Compression Plate (LCP). An osteosynthesis plate based on the Dynamic Compression Plate and the Point Contact Fixator (PC-Fix)*. Injury, 2001. **32**(Supplement 2): p. 63-66.
16. Smith, W.R., et al., *Locking plates: tips and tricks*. JBJS, 2007. **89**(10): p. 2297-2307.
17. Henderson, C.E., et al., *Locking plates for distal femur fractures: is there a problem with fracture healing?* Journal of orthopaedic trauma, 2011. **25**: p. S8-S14.
18. Frigg, R., *Development of the locking compression plate*. Injury, 2003. **34**: p. 6-10.
19. Egol, K.A., et al., *Biomechanics of locked plates and screws*. Journal of orthopaedic trauma, 2004. **18**(8): p. 488-493.

20. Lee, C.-H., et al., *Simulation-based particle swarm optimization and mechanical validation of screw position and number for the fixation stability of a femoral locking compression plate*. Medical Engineering & Physics, 2014. **36**(1): p. 57-64.
21. Schwartz, B.E., et al., *A Finite Element Model of Locked Plating in Femoral Shaft Fractures*. Open Journal of Orthopedics, 2014. **4**(04): p. 104.
22. Brinkman, J.-M., et al., *Biomechanical testing of distal femur osteotomy plate fixation techniques: the role of simulated physiological loading*. Journal of experimental orthopaedics, 2014. **1**(1): p. 1.
23. Stoffel, K., et al., *Biomechanical testing of the LCP—how can stability in locked internal fixators be controlled?* Injury, 2003. **34**: p. 11-19.
24. Pauwels, F., *Über die mechanische Bedeutung der größeren Kortikalisstruktur beim normalen und pathologisch verbogenen Röhrenknochen*, in *Gesammelte Abhandlungen zur funktionellen Anatomie des Bewegungsapparates*. 1965, Springer. p. 236-249.
25. Wagner, D.W., et al., *Combined musculoskeletal dynamics/structural finite element analysis of femur physiological loads during walking*. Multidiscipline Modeling in Materials and Structures, 2010. **6**(4): p. 417-437.
26. Strauss, E.J., et al., *The current status of locked plating: the good, the bad, and the ugly*. Journal of orthopaedic trauma, 2008. **22**(7): p. 479-486.
27. Bartel, D.L., D.T. Davy, and T.M. Keaveny, *Orthopaedic Biomechanics: Mechanics and Design in Musculoskeletal Systems*. 2006: Pearson/Prentice Hall.
28. Netter, F.H., *Atlas of Human Anatomy, Professional Edition E-Book: including NetterReference.com Access with Full Downloadable Image Bank*. 2014: Elsevier Health Sciences.
29. Reddy, J.N., *Introduction to Finite Element Method*. 2005, Naperville, Illinois: McGraw-Hill Science/Engineering/Math.
30. Arnone, J.C., *A comprehensive simulation-based methodology for the design and optimization of orthopaedic internal fixation implants*, in *Mechanical & Aerospace Engineering*. 2011, University of Missouri. p. 220.
31. Nicolella, D.P., et al., *The effect of three-dimensional shape optimization on the probabilistic response of a cemented femoral hip prosthesis*. Journal of Biomechanics, 2006. **39**(7): p. 1265-1278.
32. Haftka, R.T., Z. Gurdal, and M.P. Kamat, *Elements of Structural Optimization*. 1990, Dordrecht, Netherlands: Kluwer Academic Publishers.
33. Spillers, R.W. and K.M. MacBain, *Structural Optimization*. 2009, New York: Springer.
34. Arora, J.S., *Guide to Structural Optimization*. 1997, New York, NY: American Society of Civil Engineers.
35. Kafara, M., et al., *Comparative Life Cycle Assessment of Conventional and Additive Manufacturing in Mold Core Making for CFRP Production*. Procedia Manufacturing, 2017. **8**(Supplement C): p. 223-230.
36. Mehin, R., et al., *A biomechanical study of conventional acetabular internal fracture fixation versus locking plate fixation*. Canadian Journal of Surgery, 2009. **52**(3): p. 221.
37. Perren, S.M., *Evolution of the internal fixation of long bone fractures: the scientific basis of biological internal fixation: choosing a new balance between stability and biology*. Bone & Joint Journal, 2002. **84**(8): p. 1093-1110.
38. Fulkerson, E., et al., *Fixation of diaphyseal fractures with a segmental defect: a biomechanical comparison of locked and conventional plating techniques*. Journal of Trauma and Acute Care Surgery, 2006. **60**(4): p. 830-835.

39. Brand, R.A., et al., *A model of lower extremity muscular anatomy*. Biomechanical Engineering, 1982. **104**(304-310).
40. Brand, R.A., D.R. Pedersen, and F. J.A., *The sensitivity of muscle force predictions to changes in physiological cross-sectional area*. . Journal of Biomechanics, 1986. **19**(9): p. 589-596.
41. Nazemi, S.M., D.M. Cooper, and J.D. Johnston, *Quantifying trabecular bone material anisotropy and orientation using low resolution clinical CT images: a feasibility study*. Medical engineering & physics, 2016. **38**(9): p. 978-987.
42. Wang, J., et al., *Trabecular plates and rods determine elastic modulus and yield strength of human trabecular bone*. Bone, 2015. **72**: p. 71-80.
43. Calvel, S. and M. Mongeau, *Black-box structural optimization of a mechanical component*. Computers & Industrial Engineering, 2007. **53**(3): p. 514-530.
44. Bruns, T., *Topology optimization by penalty (TOP) method*. Computer Methods in Applied Mechanics and Engineering, 2007. **196**(45): p. 4430-4443.
45. Fraldi, M., et al., *Topological optimization in hip prosthesis design*. Biomechanics and Modeling in Mechanobiology, 2010. **9**(4): p. 389-402.
46. Kurowski, P., *Engineering Analysis with SolidWorks Simulation 2013*. 2013: SDC publications.
47. Lee, H.-H., *Finite Element Simulations with ANSYS Workbench 17*. 2017: SDC publications.
48. Gonzalez, M., et al., *Low modulus Ti-Nb-Hf alloy for biomedical applications*. Journal of Materials Science and Engineering, 2014. **42**: p. 691-695.
49. El-Gizawy, A.S., L. Eap, and X. Ma. *Reliability Based Design of Femoral Locking Plate Systems*. in *ASME 2016 International Mechanical Engineering Congress and Exposition*. 2016. American Society of Mechanical Engineers.
50. Okazaki, Y., *Development trends of custom-made orthopedic implants*. Journal of Artificial Organs, 2012. **15**(1): p. 20-25.
51. Taylor, M. and P.J. Prendergast, *Four decades of finite element analysis of orthopaedic devices: where are we now and what are the opportunities?* Journal of biomechanics, 2015. **48**(5): p. 767-778.