HHS Public Access

Author manuscript

Curr Osteoporos Rep. Author manuscript; available in PMC 2022 August 01.

Published in final edited form as:

Curr Osteoporos Rep. 2021 August ; 19(4): 403–416. doi:10.1007/s11914-021-00690-y.

Finite Element Analysis of Fracture Fixation

Gregory S. Lewis, PhD[1,*], **Dominic Mischler, MSc**[2], **Hwabok Wee, PhD**[1], **J. Spence Reid, MD**[1], **Peter Varga, PhD**[2]

[1]Department of Orthopaedics and Rehabilitation, Pennsylvania State University, Hershey PA, USA

[2]AO Research Institute Davos, Davos, Switzerland

Abstract

Purpose of review: Fracture fixation aims to provide stability and promote healing, but remains challenging in unstable and osteoporotic fractures with increased risk of construct failure and nonunion. The first part of this article reviews the clinical motivation behind finite element analysis of fracture fixation, its strengths and weaknesses, how models are developed and validated, and how outputs are typically interpreted. The second part reviews recent modeling studies of the femur and proximal humerus, areas with particular relevance to fragility fractures.

Recent findings: There is some consensus in the literature around how certain modeling aspects are pragmatically formulated, including bone and implant geometries, meshing, material properties, interactions, and loads and boundary conditions. Studies most often focus on predicted implant stress, bone strain surrounding screws, or interfragmentary displacements. However most models are not rigorously validated.

Summary: With refined modeling methods, improved validation efforts, and large-scale systematic analyses, finite element analysis is poised to advance the understanding of fracture fixation failure, enable optimization of implant designs, and improve surgical guidance.

Keywords

finite element analysis; fracture fixation; biomechanics; plate; nail; screw

Clinical motivation

The management of bone fractures constitutes a significant societal burden.[1] The impact on an individual patient spans a broad spectrum including pain, loss of work, and temporary disability. In severe fractures, there can be permanent disability. This burden is worsened in situations in which bone union does not occur, or a fracture fixation construct mechanically fails prior to bone union (Fig. 1). These nonunion scenarios often require additional surgery

*Corresponding author: Gregory S. Lewis, greglewis@psu.edu.

in the form of new implants, with or without biologic augmentation. Nonunion also severely prolongs patient disability[2,3] and imparts an additional significant economic burden.[4,5]

As the population ages, the increased incidence of osteoporosis has resulted in a parallel rise in fragility fractures associated with compromised bone density and bone quality, such as in the proximal femur, proximal humerus, distal radius, and spine.[1,6] The increase in the incidence of total knee and total hip procedures[7] has also resulted in the rapid increase in fractures around these implants, i.e. periprosthetic fractures (Fig. 1C–E), as these elderly patients remain active.[8] An interprosthetic femur fracture in an elderly osteoporotic patient between a total hip and a total knee replacement constitutes a singular challenge in reconstructive orthopaedic surgery.[9]

In developed countries, the vast majority of displaced long bone fractures in adults are surgically stabilized with a metallic implant, such as plate and screws (Fig. 1H), or intramedullary nail (Fig. 1A). A fracture fixation implant is designed and applied to provide two benefits to the patient. The first is to create an appropriate mechanical/biologic condition at the fracture site for healing. The second is to provide enough stability to allow immediate functional use of the injured part and thus minimize the fracture-associated disability discussed above. If a fracture is simple, and the major fragments can be perfectly reduced surgically with compression by the implant, then a situation of “absolute stability” is created in which the bone will heal primarily without the formation of callus. Immediate load sharing by the bone ends will also shield the implant from stress. More commonly, a variable gap will exist at the fracture site following surgery. Fixation of such fractures via bridge plating, intramedullary nailing, or external fixation creates a situation of “relative stability” in the fracture gap which requires the synthesis of secondary healing tissues by the body.

With appropriate mechanical conditions, i.e. interfragmentary strain within the fracture gap on a spectrum initially described by Perren et al.[10,11], the healing progresses and the callus gradually stiffens (granulation tissue, cartilage, then bone) eventually resulting in restoration of load transmission through the bone and offloading the implant.[12,13] Moderate compressive axial strains (less than ~ 40% strain) promote healing, whereas low-to-high shear strains are believed to be inhibitory.[14–16] During the healing of a relative stability construct, especially in patients with impaired biology for endochondral and intramembranous bone formation, the implant undergoes a significant cyclic loading history and can suffer a fatigue fracture prior to bone union. Many human and animal studies have supported the importance of interfragmentary strains in fracture healing.[13–15,17] Hypertrophic nonunions show abundant callus volume without bridging bone, indicating a mechanically induced nonunion, e.g. due to a compliant fixation and overstimulated gap. Studies have also reported that atrophic nonunion sites are vascularized and contain viable stem cells[18], supporting the theory that mechanics (e.g. an overly rigid fixation) also can play a role in many of these nonunions.[10] Furthermore there is a lack of approved pharmacological agents for improving fracture healing.[19]

The fixation construct of an implant applied to a fractured bone has a complex mechanical behavior, both at the time of implantation (primary stability) and post-operatively during the healing phase (secondary stability). This complexity is a result of the bone geometry specific to the fracture location, the internal bone architecture and material properties, the specific implant configuration and characteristics, the implant/bone interaction, the post-operative loading profile, and finally the biologic response of the patient. It is precisely this complexity that makes the finite element analysis (FEA) approach so attractive when analyzing these phenomena. Once an FEA model is validated, the opportunities for investigation, design, and education are extraordinary as discussed below. When thoughtfully applied, FEA will provide an increasingly important computational framework for the development of improved implants, more personalized preoperative planning, and better surgeon education,[20–22] resulting in improved fracture care, fewer nonunions and fixation failures, and less fracture-related patient disability.

FEA overview

This paper provides a concise summary of FEA of fracture fixation biomechanics, intended for the general reader of this journal. We have attempted to use plain language and avoid overly technical aspects. Although the second part of the paper focuses on recent applications of FEA toward studying the fracture fixation mechanics of the femur and proximal humerus, it is beyond the scope of this paper to provide a systematic review of the entire research topic, including studies focused on other anatomic locations.

FEA, used widely in many fields, can be utilized for a variety of purposes in orthopaedics, which have been previously categorized as either: (1) fundamental understanding; (2) implant design; or (3) preoperative planning.[21] Additional purposes are emerging including detection of nonunion[23] and surgeon education. In FEA, displacements, strains, and stresses are computed throughout the entire bone and implant structure—a unique capability that is generally unavailable in other computational and experimental methods (Fig. 2).

At the core of FEA is spatial discretization: dividing a complex 3D geometry into a mesh of very small elements connected at nodes. The elements are deformable, unlike in rigid body musculoskeletal models, allowing for predictions of stresses and strains. The force-displacement equations modeling these simpler geometries can be readily computed, then assembled for the entire structure. Most simulations of fracture fixation assume elastic behavior, i.e. a proportional relationship between stress and strain; advanced material models allow damage and plasticity. Interfaces between sliding components can be modeled with frictional contact. FEA numerically solves for the displacements of all the nodes of the model simultaneously, which leads to computed stress and strain distributions. Most FEA studies solve for static equilibrium of the structure for prescribed boundary conditions (external forces and fixed points/surfaces), neglecting dynamic, inertial effects. However, an alternative (forward dynamic) solution process can be used for dynamic problems or ones with very complex contact.

Strengths and weaknesses of FEA

Biomechanical testing with cadavers remains the "gold standard" for providing the ground truth on ex vivo primary stability assessment of fracture fixation constructs. However, this testing is expensive, requires valuable human tissue, has low throughput and is therefore not well suited for optimization of complex problems that require a systematic and efficient evaluation strategy. In turn, FEA has three main advantages over experimental studies. The first advantage is inherent in computational models: they facilitate a complete inspection of the makeup of the model, as well as the predicted results throughout the entire structure. Understanding of cause-effect mechanical relationships is facilitated, and available data is more complete. In experimental models, certain aspects like material behavior are obfuscated, and measurements such as internal strains are difficult or impossible.

A second advantage of FEA is that it can be efficient and inexpensive relative to experiments. Once a valid modeling procedure is in place, changing numerical parameters including implant or bone material properties can be done with ease. New implant designs can be tested *in silico* without the need to manufacture them. Parametric studies with many input variables are possible with FEA,[24,25] unlike experiments that, in best case, still rely on paired comparisons, capable of investigating a single selected aspect and involving potential confounding factors related to within-pair symmetry. The possibility to investigate different implant configurations within the same bone is one of the key advantages of FEA simulations over biomechanical testing. It should be noted though that re-meshing models following an implant change can be time consuming, simulation times can range from hours to weeks, and simulation convergence is challenging for certain problems.

A third advantage of FEA is that it can hypothetically be used clinically for patient-specific predictions and planning, although this area is not well developed in fracture fixation analyses. With these advantages, finite element simulations may effectively complement, partially or fully replace biomechanical experiments for some investigations, providing further insights and accelerating research and development. However, validated models and outcome measures should be used to provide meaningful and clinically relevant results.

Limitations of FEA primarily arise from the deviation of models from clinical reality, as discussed further below. FEA is completely virtual and thus introduces simplification in all aspects. Conversely, cadaveric experimental models introduce simplifications in only certain aspects such as fracture geometry, healing status, loads and boundary conditions. The greater abstraction of FEA also makes it more susceptible to misunderstanding and errors in implementation and interpretation.

Aspects of a model

Geometry:

Bone and fracture geometries, like other model properties, can be either generic or subject-specific.[26] 3D bone geometries can be accurately derived from computed tomography (CT) scans using image segmentation software (Figs. 2A,B, 3). Cancellous bone is typically modeled as a continuum, although micro-FE models of cadavers with explicit representation of trabeculae have been derived from micro-CT scans.[27] FEA results are sensitive to some aspects of bone geometry, e.g. locations where loads and boundary conditions are applied, and canal geometry in the case of intramedullary nailing. Fracture geometries are almost always modeled by virtual osteotomies (Fig. 2C), although realistic patterns derived from CT are possible (Fig. 3). Comminuted (highly fragmented) fractures are typically modeled by removing the comminuted zone, with the rationale that the zone has negligible load transfer. FEA models of clinical fracture fixation, like their benchtop counterparts, usually consider only the initial phase following surgery without any primary or secondary bone healing present. Precise implant geometries enable more accurate determination of stresses for the particular implant (Figs. 2D,H); but generic implant geometries can be useful when the study seeks generalizable knowledge. Screw shafts are often modeled as simple cylinders,[28] fixed to bone (Figs. 2D, 3).

Mesh:

Investigators select among element types and sizes with consideration of implant and bone geometric complexity, and desired balance between solution time and accuracy (Fig. 2E). Sophisticated modern software is used to generate finite element meshes in a semi-automated manner, with consideration of element quality parameters (e.g. aspect ratio). Tetrahedral elements are often used because of geometric complexity. Because solution accuracy generally improves with a denser mesh and/or element complexity (e.g. quadratic vs. linear), especially at critical locations, mesh convergence studies should be performed when deciding an appropriate mesh density. With improvements in computational efficiency, the number of elements in typical orthopaedic FEA models has grown to hundreds of thousands, or up to several millions in microFE simulations.

Materials:

Implant materials are engineering materials and can be adequately modeled with homogeneous, isotropic, linear elastic properties. Bone material behavior, however, is much more complex. Although bone is viscoelastic, it is almost always considered elastic, which is probably adequate because of relatively low physiologic loading rates involved.[29] Most models assume linear elasticity and do not attempt to simulate post-failure behavior, with some notable exceptions.[30] Heterogeneity in material properties is sometimes considered; subject-specific models can map local material properties to elements based on quantitative CT scans according to relationships between Hounsfield units, density, and elastic modulus (Fig. 2F).[31–33] Inclusion of bone's heterogeneity is important for accurate simulations for some problems.[34] In generic homogeneous models, osteoporotic bone is simulated with a decreased elastic modulus. Cortical thinning and periosteal apposition has also been incorporated into geometry.[35] Bone's direction-dependency in properties is sometimes considered, but the assumption of isotropy is most common, with a Poisson's ratio of ~0.3.

Interactions:

The interactions between surfaces of plates or nails, screws, and bone can be complex and require some simplifying assumptions in FEA models. Connections between bone and simplified threadless screw shafts are most often modeled as fully bonded, with the rationale that there are negligible motions at these interfaces during sub-failure conditions.

However, this assumption does affect the local stress environment, and more accurate connections have been proposed.[36] Locking screw threaded connections with plates are also usually modeled as fully bonded, although more accurate compliant connections have been proposed.[37] Traditional (nonlocking) screws are more complex to model; their surgical insertion process develops tension within the screw, higher peri-screw bone strains, compression between the plate and bone, and (with dynamic compression plating) interfragmentary compression. Extramedullary plates and intramedullary nails can separate or slide with bone during mechanical loading, and these interactions can be modeled with Coulomb frictional contact.[38] The presence of frictional contact between bone fragments at the fracture site results in load transfer, which greatly offloads implants. This contact can be intermittent upon loading. There is uncertainty in the above frictional coefficients in physiologic situations, although this may not affect model accuracy unless sliding is significant. Modeling contact necessitates nonlinear, incremental finite element solution procedures which sometimes can encounter convergence challenges. (Geometric nonlinearity, associated with sizeable displacements and rotations, is also inherent in many of these problems.)

Loads and boundary conditions:

Loads applied to fracture fixation constructs *in vivo* are cyclic and variable in nature. FEA typically focuses on a quasi-static analysis of a peak loading condition during one cycle; the investigator considers the cyclic effects in subsequent analysis outside of FEA. External loads applied to bones are primarily due to joint and muscle forces (Fig. 2G). Fortunately, in vivo studies using instrumented joint replacements have provided reliable data on joint loads.[39] Greater uncertainty exists in muscle forces, which are themselves derived from modeling estimates.[40] Depending on postoperative rehabilitation plans, assist devices, and patient compliance, loads may be reduced in the immediate postoperative period. Boundary conditions entail constraining model degrees of freedom to prevent rigid body motions; a simple example is fixing surface nodes on the bone end that is opposite to where the external forces are applied. But *in vivo* physiological constraint conditions are not straightforward, and in some problems boundary conditions must be carefully considered as they can have a substantial effect on results.[26,37,41,42]

Basic outcome measures:

The typical FEA solution consists of displacements throughout the structure, and strains and stresses derived from these displacements (Fig. 2H). Interfragmentary displacements at the fracture site influence the course of healing;[14,43] relative displacements between fragment ends can be resolved into axial and shear components and normalized by the fracture gap size to estimate interfragmentary strains. Displacement at the point of load application can be used to determine an overall construct stiffness. Although stiffness does not have clear clinical relevance, it can be measured reliably in experiments for validation purposes. In implants and screws, peak stresses are examined (Fig. 3), as they relate to the potential for static yield or cyclic fatigue failure. Prediction of bone failure more often uses a strain criteria than a stress criteria.[26,44,45] Sub-failure bone stress and strain may also have relevance for potential stress shielding and bone resorption.[46,47]

Advanced predictions

Implant and screw fatigue:

Normal fracture healing with bone bridging results in substantial offloading of fracture fixation implants and screws over time. However, in cases of biologically impaired healing, especially comminuted fractures of the lower limb with minimal cortical contact at the fracture site, implants (including screws) bear substantial cyclic tensile stresses that do not decrease over time. These scenarios carry additional risk of fatigue failure, characterized by a sudden brittle-like fracture of the implant.[48–50] Fatigue failure initiates at stress concentrations such as screw holes.[51] Basic methods to assess fatigue life of engineering materials can use FEA-predicted peak stress, which is the most often used approach in FEA studies of fracture fixation. More accurate predictions involve consideration of the precise implant material properties and surface finish, intraoperative factors like plate prebending,[52] non-reversed and multiaxial nature of physiologic loading, and change in loading over time. In regulatory assessment of medical devices, because of uncertainty in FEA predictions of fatigue of implants, FEA is often used to determine worst case design configurations which are then tested with cyclic loading experiments. Other specific types of hardware failure under cyclic loading, such as failure of variable angle threaded connections between plates and screws,[53] would require alternative prediction approaches.

Screw-bone interface and its failure:

In many constructs prior to healing, forces are transmitted between bones and implants primarily through the bone-screw interface, stability of which is therefore of high importance. FEA is ideal for providing insights into these details that are not assessable experimentally. The mechanical environment in the cortical bone region around screws was investigated with FEA to understand the influence of modeling choices[54,55], quantify the induced strains[56], evaluate the effects of fixation concept[35] and pilot hole size[57], and to explain peri-screw bone resorption[46] and screw loosening.[58] Most FEA studies on screw fixation in trabecular bone focused on optimizing primary stability in the challenging osteoporotic condition.[59,60] Using continuum FEA models, initial stiffness[61], peri-screw bone strain[62] and ultimate force[63] were found to predict failure. MicroFE models, including the trabecular microarchitecture and screw threads, are generally better suited for such analyses,[64,65] although they are computationally expensive and thus challenging for whole bone-implant constructs. Most microFE studies focused on stress distributions[66] and fixation stiffness[67,68] that can be accurately predicted when considering the damage caused during insertion.[69] Pull-out was the most frequently investigated failure mode; nevertheless, the failure process was usually not simulated as surrogate measures from linear elastic analyses showed good predictions.[70,71] Simulating more complex failure processes such as perforation requires the inclusion of post-elastic material properties and contact, which can improve prediction accuracy over linear analyses.[30]

Fracture healing effects:

Despite the importance of fracture healing in mitigating risk of fatigue failure, few FEA models of clinical fixation constructs have included consideration of it, instead modeling a worst-case stress scenario prior to healing. Inclusion of a 3D fracture callus having finite elements of increasing stiffness was used recently to show the importance of healing in preventing fatigue failure of high tibial osteotomy plates.[72] Simpler spring elements at the fracture gap have also been used.[73] FEA has also been investigated as a potential tool to assess the quality of ongoing fracture healing.[23,74–76]

Verification & validation

Verification, validation, and other activities related to model credibility, as described in depth elsewhere,[77–80] have fundamental importance in orthopaedic computational models with potential to impact patient care and safety. These activities should be guided in part by the model's purpose, including context of use and associated risks.[80] Verification includes e.g. analysis of simplified benchmark problems of known solution, and the aforementioned mesh convergence testing. Sensitivity studies and uncertainty quantification are appropriate especially for model inputs with substantial uncertainty and large impact on the outcomes, such as bone modulus and load direction.

Validation requires a careful selection of a comparator. For FEA models of clinical fracture fixation, cadaver experiments are considered gold standard; although their loads/boundary conditions are a simplified abstraction of clinical reality and involve some undesirable mechanical compliance, and certain measurements cannot be made or are noisy. Outcome measurements that can be compared to FEA results include interfragmentary displacements, overall construct stiffness,[25] bone or implant[81] surface strains, and construct failure under cyclic loading.[62] Experiments with synthetic bones can be appropriate for investigations focused on implant mechanics and interfragmentary displacements, when screw-bone interface failure is not of primary consideration.[25,81,82] Scientific rigor and statistical approach (if any) vary substantially among studies that include a benchtop validation component.[83]

Comparison of FEA predictions to clinical data, which some consider the ultimate validation, is a developing area with few examples in the literature. Potential clinical data include presence of construct failure, healing status, and data from instrumented implants.[84] Construct and interfragmentary displacements have been recently measured using weightbearing CT[85] and radiostereometric analysis.[86,87] Models comparing treatment options can be compared to statistical differences observed clinically between study groups from a cohort study or from large-scale registry data. Or, patient-specific FEA models can be compared to clinical data at the individual subject level, such as callus formation viewed on radiographs.[14]

Applications in femur fracture fixation

Rates of nonunion/failure of femur fracture fixation have been reported as exceeding 10%.[88] Higher rates have been observed for complex femur fractures, including periprosthetic femur fractures (Fig. 3).[89,90] Nonunion and revision surgery for femur fractures imposes substantial burden on the patient (Fig. 1).[3] The femur is subject to loads of several times bodyweight during normal ambulation.[39] Due to the eccentricity of load application through the femoral head, load-induced stresses are further exacerbated through bending, especially for lateral extramedullary implants. Most FEA studies of femur fracture fixation focus on unstable extra-articular fractures.

Twenty-four recent, relevant publications that used FEA analyses to investigate the biomechanical competence of femur fracture fixations were identified in our non-systematic review (Supplementary Table 1). [14,38,47,73,81,82,91–108] In the following, the number of studies associated with each characteristic is indicated in parentheses. Studies mostly focused on fractures of the femoral neck (6), intertrochanteric region (7), and distal femur (8). Computer simulations were applied to analyze three main scenarios: I) comparison of different implants (8); II) the optimal use of existing plates, nails, and screws (11); and III) options to improve existing implants by optimizing their design (4). The most often examined implant type was intramedullary nail (13), followed by locking plate (7), cannulated screws (5), sliding hip screws (4), the combination of intramedullary nail and locking plate (1) and the combination of screws and medial buttress plate (2). Subject-specific bone geometry was used in 13 studies; however, nine of these used only a single patient. Continuum modelling of bone was used in all studies. Bone material properties in models were mostly separated homogeneous compartments for cortical and trabecular bone (14), or using CT-bone mineral density (BMD) based heterogeneous properties (8). The assumption of bone isotropy was used in all papers but one, which used a transverse isotropic model for cortical bone. Only a single study considered bone’s post-elastic material behavior to simulate failure.[98] The bone-screw interface was modelled as bonded in 12 studies and with contact in four studies, with five studies not describing this interaction and others not including screws. Loading and boundary conditions of the fixation constructs included hip joint force with additional muscle forces (6), or without muscles (16). Multiple loading cases were included in two studies. All models were solved with an implicit FEA approach. Systematic parametric analysis, with hundreds of models, was performed in two studies.[38,105] Main outcome measures in the above studies included fracture gap motion (10), implant stress (18), and overall construct displacement/stiffness (11).

Intertrochanteric femur fractures, a prevalent fracture in elderly patients, are typically fixed with intramedullary nailing. Eberle et al.[81] reported that for cephalomedullary nail fixation, subtrochanteric fractures resulted in the highest nail stresses, followed by pertrochanteric, then followed by lateral neck fractures. Sensitivity analyses showed dependence of stresses on angle of insertion of the nail in the frontal plane. The recent results of Tucker et al.[38] were in general agreement with the findings of Eberle et al. regarding effect of fracture locations. Tucker et al. reported that larger, closer fitting nail diameters reduced axial and shear interfragmentary motions. They also reported on reduced stability associated with unreduced/comminuted fractures. Ali et al.[92] reported that for nail fixation of more realistic (although simulation-derived) intertrochanteric fracture geometries, load transfer and nail stress were substantially influenced by inter-subject variability in fracture geometry. Goffin et al.[96,109] reported studies focused on risk of screw cut-out through the femoral head, as determined by local bone strains. In one subject-specific model fixed with a sliding hip screw, they reported lower strains with inferior positions of the lag screw.[109] They also reported reduced strains associated with bone compaction around a helical blade in simulated osteoporotic bone.[96] Recent studies also investigated alternative designs and materials for proximal femur nails. Wang et al.[106] simulated the effects of lower modulus nails. Although not specifically demonstrated in the study, reduced modulus implants may have some advantages with respect to cut-out in poor quality bone. Li et al. [100] examined the mechanics of a modified nail design with an additional feature intended to better stabilize the medial cortex in unstable fractures.

Femoral neck fractures have a variety of fixation options including cannulated screws, sliding/dynamic hip screw, and locking plates. Related FEA studies generally have more application to younger patients; in elderly patients, displaced femoral neck fractures are treated often by hemiarthroplasty. Most recent FEA studies of these constructs focused on implant stresses and fragment displacements under loading. A combination of sliding hip screw with additional cannulated screws was more effective than sliding hip screw alone to prevent shear rotation and separation of fragments and reduce the stress in the implants.[94,104] Li et al. reported that applying a medial buttress plate improved stability and reduced shear rotation of the proximal fragment.[99]

Distal femur fractures can be repaired with either plates or nails. For plate fixation, studies have demonstrated the importance of the plate material and working length (distance across the fracture between the inner-most screws) in controlling the axial and shear interfragmentary motions important for healing.[14,47,73] Recent studies have also investigated innovative design modifications of the plate and locking screws, intended to increase axial interfragmentary motions.[82,110]

Applications in proximal humerus fracture fixation

Another clinically challenging topic is the treatment of osteoporotic proximal humerus fractures. Implant fixations enable early functional recovery; however, their benefit versus conservative treatment has been debated.[111–113] Despite the development of the state-of-the-art locking plate technology, the rate of mechanical failures has remained high, up to 36%[114], with screw cut-out and perforation being the most frequent implant-related complications.[115] These outcomes may be improved by enhancing implant designs and clinical guidelines for applying these fixations. Implant fixation of proximal humerus fractures is a complex and multifactorial problem, with age, bone mineral density, fracture complexity and reduction quality being prominent risk factors.[116] A further challenge for fixation strategies is the highly heterogeneous bone stock distribution within the humeral head.[117–119] FEA may help to accelerate research and development towards improved implants and treatment strategies.[120,121]

Thirty relevant publications that used FEA to investigate the biomechanical competence of proximal humerus fracture fixations were identified in our non-systematic review (Supplementary Table 2).[24,27,30,36,62,65,67,68,122–143] In the following, the number of studies associated with each characteristic is indicated in parentheses. Computer simulations were applied to analyze three main scenarios: I) comparison of different implants (9); II) the optimal use of existing locking plates (13); and III) options to improve existing implants by optimizing their design (3). Others focused primarily on the effect of bone stock quality (2), modelling approaches (2), or experimental validation (1). The most often examined implant type was locking plate (25), followed by single screw (5), intramedullary nail (2) and K-wires (1). Subject-specific bone geometry was used in 24 studies; however, six of these used only a single patient. Continuum FE (cFE) modelling of bone was used in most studies (25); the microarchitecture of trabecular bone was considered in microFE simulations investigating screws (4) only and in a single study on construct stability. Bone material properties in cFE models were mostly simplified as being homogeneous (4), separated for cortical and trabecular bone (10), or CT BMD based heterogeneous (12). Considering heterogeneity was found to be influential at fracture fixation simulations of other anatomical locations.[34] All microFE models used homogeneous properties on the tissue level; inclusion of heterogeneity was shown not to be influential.[144] The assumption of isotropy was used in all papers; however, meso-scale anisotropy is inherently included in microFE models. Only a single study considered bone's post-elastic material behavior to simulate failure.[30] The bone-implant interface was modelled primarily as bonded in most cFE studies (26), contact or a pseudo-threaded approach was used only in three papers. MicroFE simulations used tied interfaces, except for one study applying a soft per-implant bone region simulating damage during screw insertion[69] and another non-linear approach utilizing contact conditions.[30] Loading and boundary conditions of the fixation constructs mimicked physiological activities (11) or simplified conditions from experimental setups (19). Multiple loading cases were included in 13 studies. All cFE models were solved with implicit approach. MicroFE simulations utilized special parallel solvers to efficiently handle large model sizes and one study used an explicit technique to solve the nonlinear problem.[30] Systematic parametric analysis and optimization, with up to thousands of models, was performed in nine studies, requiring fully automated simulation workflows.[24]

Most studies used construct stiffness and/or axial fracture gap motion as the main outcome measure (14), generally aiming to seek maximum rigidity. Less than half of those studies (6) validated stiffness experimentally or used a different measure for validation such as bone surface strain.[125] While the relevance of rigidity has been shown for single screws, the clinical relevance of stiffer constructs has not been clearly demonstrated, especially considering that overly stiff fixations can be inhibitory for secondary healing.[145] Some studies aimed to minimize shear-type gap motion (3), which is believed to be detrimental for healing.[14–17] Interfragmentary contact pressure in well-reduced fractures was used in a single paper as measure of stability.[132] Another frequently used metric was implant stress, being subject to minimization, aiming to avoid implant damage (12) but without validation. Nevertheless, failure of the metal components is not the most often occurring complication in the proximal humerus fixations.[115] Several studies based their conclusions on one of these metrics or their combinations. Stability of single screw fixations in pull-out and the effectiveness of cement augmentation were shown to be strongly determined by the volume fraction of the peri-implant bone region.[67,68] Construct stability was improved, and implant stress reduced by implant selection[124], combining lateral and medial plating[129,130], placing calcar screws[142], establishing medial cortical contact[136], fracture reduction with impaction[123], as well as via augmentation of locking plates with cement at the screw tips or with additional intramedullary strut increase stability.[122] Design features of plates were shown to be influential. Plate holes that allow either a locking or nonlocking screw placement (combi holes) were associated with higher stress concentration and higher shear motion in the gap compared to locking holes.[143] Construct stiffness was increased by more proximal orientation of the calcar screws[131] and longer threading of the screw.[134]

Another frequently used outcome measure was the stress or strain in the bone region in the direct or indirect vicinity of the screws. Stress of screw-bone interface was found to be better distributed in double plating versus a single lateral locking plate[133] and reduced by the addition of calcar screw, achieving medial cortical contact[142], augmenting the screw tips[132] or the humeral head with cement[125], changing the angles of medical screws[131], and selecting more elastic implant materials.[125] Stress within the bone cannot be measured directly and therefore none of these findings were validated. Several studies investigated bone strain. Deformations were shown to be highly affected by bone quality and loading mode.[135] Detailed analyses indicated that the accurate strain distribution within the peri-screw bone region cannot be reproduced when using homogeneous properties[65] or bonded bone-screw interfaces[36] in cFE models. Nevertheless, the assumption concerning the interface was shown not to affect the statistical findings between different implant configurations when the average compressive principal strain is evaluated in the bone regions around the locking screws within the humeral head.[36] Moreover, the latter measure was demonstrated to be an experimentally validated surrogate for cyclic screw cut-out failure[62] that is one of the most frequent failure modes of these fixations.[115] Using this strain measure, it was shown that the predicted cut-out risk could be reduced by using longer screws[126], appropriately selecting the screw number and configuration in comminuted and non-well reduced fractures,[36,139] especially by maximizing screw spread.[128] Furthermore, cement augmentation of the screw tips was demonstrated to be beneficial[24] especially when prioritizing the calcar screws.[141] Using locking plates that sit more proximally or even proximalizing the implant indicated lower cut-out failure risk.[127] Parametric optimization found improvements with more proximally oriented screw trajectories within the humeral head.[138] Novel plate designs including a medial strut decreased the predicted cut-out risk.[140] Only a single computational study investigated screw perforation failure, showing that non-linear microFE models provide accurate predictions.[30]

Conclusion and future directions

FEA is by far the most widely used computational tool for investigating internal mechanics associated with orthopaedic surgery, including fracture fixation. Sophisticated FEA software has been refined and verified over many years across a wide variety of industries and fields. With improved approaches for applying FEA to orthopaedics, and increased computational power, there is growing acceptance of the use of FEA for development and governmental regulation[146] of implants, scientific investigation, and surgical decision making. *In silico* trials hold potential for systematic, efficient evaluation of fracture fixation methods in a scientifically rigorous manner that considers ‘biologic’ variability.[79] However, FEA is particularly prone to nuanced method variations, and even errors, that can provide believable but misleading results. With model validation being absent in most studies, or performed only in ex vivo settings in others, the results must always be interpreted with care and require clinical corroboration. Moving forward, established best practices for biomechanical model verification, validation, and credibility can be adapted to the fracture fixation field. Validation efforts should be based on the clinical question and corresponding model outcome(s). Carefully designed benchtop experiments with reliable outcome measurements can be used to validate FEA-predicted mechanics, and innovative approaches will bring us closer to true clinical validation. FEA studies hold great potential to advance the understanding of fracture fixation failure, help to improve guidelines, contribute to surgical education, and support the development of new, optimized implant designs via systematic analyses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

GSL, HW, and JSR were supported by the National Institute of Biomedical Imaging and Bioengineering (1R01EB029207-01). DM and PV were supported by the AO Foundation via the AOTRAUMA Network (Grant No.: AR 2018/01).

Conflicts of interest/Competing interests:

GSL receives research support for an unrelated project from Arthrex Inc. JSR and GSL have received materials for a biomechanical research project from Depuy Synthes (Johnson and Johnson). GSL and JSR are co-inventors on the patent: "Individualized preoperative planning system and method." JSR is consultant for Depuy Synthes (Johnson and Johnson) and Osteocentric, and stockholder for ROMtech. None of the above indirectly related interests has influenced the present paper. No other competing interests are present.

References

1. Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. J Bone Miner Res. 2007;22:465–75. [PubMed: 17144789]
2. Brinker MR, Hanus BD, Sen M, O'Connor DP. The devastating effects of tibial nonunion on health-related quality of life. J Bone Joint Surg Am. 2013;95:2170–6. [PubMed: 24352770]
3. Brinker MR, Trivedi A, O'Connor DP. Debilitating Effects of Femoral Nonunion on Health-Related Quality of Life. J Orthop Trauma. 2017;31:e37–42. [PubMed: 27755332]
4. Hak DJ, Fitzpatrick D, Bishop JA, Marsh JL, Tilp S, Schnettler R, et al.Delayed union and nonunions: epidemiology, clinical issues, and financial aspects. Injury. 2014;45 Suppl 2:S3–7.
5. Rupp M, Biehl C, Budak M, Thormann U, Heiss C, Alt V. Diaphyseal long bone nonunions - types, aetiology, economics, and treatment recommendations. Int Orthop. 2018;42:247–58. [PubMed: 29273837]
6. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006;17:1726–33. [PubMed: 16983459]
7. Maradit Kremers H, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, et al.Prevalence of Total Hip and Knee Replacement in the United States. J Bone Joint Surg Am. 2015;97:1386–97. [PubMed: 26333733]
8. Abdel MP, Watts CD, Houdek MT, Lewallen DG, Berry DJ. Epidemiology of periprosthetic fracture of the femur in 32 644 primary total hip arthroplasties: a 40-year experience. Bone Joint J. 2016;98-B:461–7. [PubMed: 27037427]
9. Scolaro JA, Schwarzkopf R. Management of Interprosthetic Femur Fractures. J Am Acad Orthop Surg. 2017;25:e63–9. [PubMed: 28252475]
10. Elliott DS, Newman KJH, Forward DP, Hahn DM, Ollivere B, Kojima K, et al.A unified theory of bone healing and nonunion: BHN theory. Bone Joint J. 2016;98-B:884–91. [PubMed: 27365465]
11. Perren SM. Physical and biological aspects of fracture healing with special reference to internal fixation. Clin Orthop Relat Res. 1979;175–96.

12. Cheng C, Shoback D. Mechanisms Underlying Normal Fracture Healing and Risk Factors for Delayed Healing. Curr Osteoporos Rep. 2019;17:36–47. [PubMed: 30671884]

13. Einhorn TA, Gerstenfeld LC. Fracture healing: mechanisms and interventions. Nat Rev Rheumatol. 2015;11:45–54. [PubMed: 25266456]

* 14. Elkins J, Marsh JL, Lujan T, Peindl R, Kellam J, Anderson DD, et al.Motion Predicts Clinical Callus Formation. J Bone Joint Surg Am. 2016;98:276–84. [PubMed: 26888675] This study developed semi-patient specific models of a series of patients. Correlations between predicted interfragmentary motions (axial and shear) and clinical callus formation were examined.

15. Augat P, Burger J, Schorlemmer S, Henke T, Peraus M, Claes L. Shear movement at the fracture site delays healing in a diaphyseal fracture model. J Orthop Res. 2003;21:1011–7. [PubMed: 14554213]

16. Claes LE, Meyers N. The direction of tissue strain affects the neovascularization in the fracture-healing zone. Medical Hypotheses. 2020;137:109537. [PubMed: 31901879]

17. Epari DR, Kassi J-P, Schell H, Duda GN. Timely fracture-healing requires optimization of axial fixation stability. J Bone Joint Surg Am. 2007;89:1575–85. [PubMed: 17606797]

18. Panteli M, Pountos I, Jones E, Giannoudis PV. Biological and molecular profile of fracture non-union tissue: current insights. J Cell Mol Med. 2015;19:685–713. [PubMed: 25726940]

19. Kostenuik P, Mirza FM. Fracture healing physiology and the quest for therapies for delayed healing and nonunion. J Orthop Res. 2017;35:213–23. [PubMed: 27743449]

20. Lewis GS, Wee H, Vicory J, Armstrong AD, Reid JS. Virtual Simulation for Interactive Visualization of 3D Fracture Fixation Biomechanics. J Am Acad Orthop Surg. 202184. doi: 10.5435/JAAOS-D-20-01322. Epub ahead of print..

21. Taylor M, Prendergast PJ. Four decades of finite element analysis of orthopaedic devices: Where are we now and what are the opportunities?Journal of Biomechanics. 2015;48:767–78. [PubMed: 25560273]

22. Lambert S, Mischler D, Windolf M, Regazzoni P, Dell'Oca AF, Gueorguiev B, et al.From creative thinking to scientific principles in clinical practice. Injury. 2021;52:32–6. [PubMed: 33004202]

23. Dailey HL, Schwarzenberg P, Daly CJ, Boran SAM, Maher MM, Harty JA. Virtual Mechanical Testing Based on Low-Dose Computed Tomography Scans for Tibial Fracture: A Pilot Study of Prediction of Time to Union and Comparison with Subjective Outcomes Scoring. J Bone Joint Surg Am. 2019;101:1193–202. [PubMed: 31274721]

24. Varga P, Inzana JA, Gueorguiev B, Südkamp NP, Windolf M. Validated computational framework for efficient systematic evaluation of osteoporotic fracture fixation in the proximal humerus. Med Eng Phys. 2018;57:29–39. [PubMed: 29728330]

25. Wee H, Reid JS, Chinchilli VM, Lewis GS. Finite Element-Derived Surrogate Models of Locked Plate Fracture Fixation Biomechanics. Ann Biomed Eng. 2017;45:668–80. [PubMed: 27554672]

26. Pankaj PPatient-specific modelling of bone and bone-implant systems: the challenges. Int J Numer Method Biomed Eng. 2013;29:233–49. [PubMed: 23281281]

27. Steiner JA, Hofmann UAT, Christen P, Favre JM, Ferguson SJ, van Lenthe GH. Patient-specific in silico models can quantify primary implant stability in elderly human bone. Journal of Orthopaedic Research. 2018;36:954–62. [PubMed: 28876466]

28. Wieding J, Souffrant R, Fritsche A, Mittelmeier W, Bader R. Finite element analysis of osteosynthesis screw fixation in the bone stock: an appropriate method for automatic screw modelling. PLoS One. 2012;7:e33776. [PubMed: 22470474]

29. Morgan EF, Unnikrisnan GU, Hussein AI. Bone Mechanical Properties in Healthy and Diseased States. Annu Rev Biomed Eng. 2018;20:119–43. [PubMed: 29865872]

30. Panagiotopoulou VC, Ovesy M, Gueorguiev B, Richards RG, Zysset P, Varga P. Experimental and numerical investigation of secondary screw perforation in the human proximal humerus. Journal of the Mechanical Behavior of Biomedical Materials. 2021;116:104344. [PubMed: 33524891]

31. Fleps I, Bahaloo H, Zysset PK, Ferguson SJ, Pálsson H, Helgason B. Empirical relationships between bone density and ultimate strength: A literature review. J Mech Behav Biomed Mater. 2020;110:103866. [PubMed: 32957183]

32. Helgason B, Perilli E, Schileo E, Taddei F, Brynjólfsson S, Viceconti M. Mathematical relationships between bone density and mechanical properties: a literature review. Clin Biomech (Bristol, Avon). 2008;23:135–46.

33. Nobakhti S, Shefelbine SJ. On the Relation of Bone Mineral Density and the Elastic Modulus in Healthy and Pathologic Bone. Curr Osteoporos Rep. 2018;16:404–10. [PubMed: 29869752]

34. Synek A, Chevalier Y, Baumbach SF, Pahr DH. The influence of bone density and anisotropy in finite element models of distal radius fracture osteosynthesis: Evaluations and comparison to experiments. J Biomech. 2015;48:4116–23. [PubMed: 26542787]

* 35. MacLeod AR, Simpson AHRW, Pankaj P. Reasons why dynamic compression plates are inferior to locking plates in osteoporotic bone: a finite element explanation. Computer Methods in Biomechanics and Biomedical Engineering. Taylor & Francis; 2015;18:1818–25.This study modeled the two fundamentally different types of plate-screw connection mechanisms, applied to either healthy or simulated osteoporotic bone.

36. Inzana JA, Varga P, Windolf M. Implicit modeling of screw threads for efficient finite element analysis of complex bone-implant systems. Journal of Biomechanics. 2016;49:1836–44. [PubMed: 27157243]

37. MacLeod A, Simpson AHRW, Pankaj P. Experimental and numerical investigation into the influence of loading conditions in biomechanical testing of locking plate fracture fixation devices. Bone Joint Res. 2018;7:111–20. [PubMed: 29363522]

* 38. Tucker SM, Wee H, Fox E, Reid JS, Lewis GS. Parametric Finite Element Analysis of Intramedullary Nail Fixation of Proximal Femur Fractures. J Orthop Res. 2019;37:2358–66. [PubMed: 31254411] This study investigated combined effects of nail diameter, nail length, nail material, and presence of distal fixation screws for nine clinically important fracture patterns.

39. Bergmann G, Graichen F, Rohlmann A, Bender A, Heinlein B, Duda GN, et al.Realistic loads for testing hip implants. Bio-Medical Materials & Engineering. 2010;20:65–75. [PubMed: 20592444]

40. Heller MO, Bergmann G, Kassi J-P, Claes L, Haas NP, Duda GN. Determination of muscle loading at the hip joint for use in pre-clinical testing. J Biomech. 2005;38:1155–63. [PubMed: 15797596]

41. Heyland M, Trepczynski A, Duda GN, Zehn M, Schaser K-D, Märdian S. Selecting boundary conditions in physiological strain analysis of the femur: Balanced loads, inertia relief method and follower load. Med Eng Phys. 2015;37:1180–5. [PubMed: 26521092]

42. Speirs AD, Heller MO, Duda GN, Taylor WR. Physiologically based boundary conditions in finite element modelling. J Biomech. 2007;40:2318–23. [PubMed: 17166504]

43. Klein P, Schell H, Streitparth F, Heller M, Kassi J-P, Kandziora F, et al.The initial phase of fracture healing is specifically sensitive to mechanical conditions. Journal of Orthopaedic Research. 2003;21:662–9. [PubMed: 12798066]

44. Bayraktar HH, Morgan EF, Niebur GL, Morris GE, Wong EK, Keaveny TM. Comparison of the elastic and yield properties of human femoral trabecular and cortical bone tissue. J Biomech. 2004;37:27–35. [PubMed: 14672565]

45. Schileo E, Taddei F, Cristofolini L, Viceconti M. Subject-specific finite element models implementing a maximum principal strain criterion are able to estimate failure risk and fracture location on human femurs tested in vitro. Journal of Biomechanics. 2008;41:356–67. [PubMed: 18022179]

46. Feng X, Lin G, Fang CX, Lu WW, Chen B, Leung FKL. Bone resorption triggered by high radial stress: The mechanism of screw loosening in plate fixation of long bone fractures. Journal of Orthopaedic Research. 2019;37:1498–507. [PubMed: 30908687]

47. Gee A, Bougherara H, Schemitsch EH, Zdero R. Biomechanical design using in-vitro finite element modeling of distal femur fracture plates made from semi-rigid materials versus traditional metals for post-operative toe-touch weight-bearing. Med Eng Phys. 2021;87:95–103. [PubMed: 33461680]

48. Kandemir U, Augat P, Konowalczyk S, Wipf F, von Oldenburg G, Schmidt U. Implant Material, Type of Fixation at the Shaft, and Position of Plate Modify Biomechanics of Distal Femur Plate Osteosynthesis. J Orthop Trauma. 2017;31:e241–6. [PubMed: 28394844]

49. Klima ML. Comparison of Early Fatigue Failure of the TFNa and Gamma 3 Cephalomedullary Nails in the United States From 2015 to 2019. Journal of Orthopaedic Trauma. 2021;35:e39. [PubMed: 32569070]

50. McDonald TC, Lambert JJ, Hulick RM, Graves ML, Russell GV, Spitler CA, et al.Treatment of Distal Femur Fractures With the DePuy-Synthes Variable Angle Locking Compression Plate. J Orthop Trauma. 2019;33:432–7. [PubMed: 31259799]

51. Zhang JY, Tornetta P, Jones B, Zheng Y, Whitten A, Cartner J, et al.Locking Hole Inserts: Effect of Insertion Torque on Fatigue Performance and Insert Loosening in Locking Plates. J Orthop Trauma. 2019;33:120–4. [PubMed: 30768531]

52. Parr WCH, Wang T, Tan C, Dan MJ, Walsh WR, Morberg P. Fatigue implications for bending orthopaedic plates. Injury. 2021;

53. Tidwell JE, Roush EP, Ondeck CL, Kunselman AR, Reid JS, Lewis GS. The biomechanical cost of variable angle locking screws. Injury. 2016;47:1624–30. [PubMed: 27324325]

54. MacLeod AR, Pankaj P, Simpson AHRW. Does screw–bone interface modelling matter in finite element analyses?Journal of Biomechanics. 2012;45:1712–6. [PubMed: 22537570]

55. Moazen M, Mak JH, Jones AC, Jin Z, Wilcox RK, Tsiridis E. Evaluation of a new approach for modelling the screw-bone interface in a locking plate fixation: a corroboration study. Proc Inst Mech Eng H. 2013;227:746–56. [PubMed: 23636756]

56. Torcasio A, Zhang X, Van Oosterwyck H, Duyck J, van Lenthe GH. Use of micro-CT-based finite element analysis to accurately quantify peri-implant bone strains: a validation in rat tibiae. Biomech Model Mechanobiol. 2012;11:743–50. [PubMed: 21898099]

57. Affes F, Ketata H, Kharrat M, Dammak M. How a pilot hole size affects osteosynthesis at the screw–bone interface under immediate loading. Medical Engineering & Physics. 2018;60:14–22. [PubMed: 30061066]

58. Pankaj P, Xie S. The risk of loosening of extramedullary fracture fixation devices. Injury. 2019;50:S66–72. [PubMed: 30955874]

59. Steiner JA, Ferguson SJ, van Lenthe GH. Computational analysis of primary implant stability in trabecular bone. J Biomech. 2015;48:807–15. [PubMed: 25579993]

60. Wirth AJ, Müller R, van Lenthe GH. Computational analyses of small endosseous implants in osteoporotic bone. Eur Cell Mater. 2010;20:58–71. [PubMed: 20665437]

61. Van den Abbeele M, Valiadis J-M, Lima LVPC, Khalifé P, Rouch P, Skalli W. Contribution to FE modeling for intraoperative pedicle screw strength prediction. Comput Methods Biomech Biomed Engin. 2018;21:13–21. [PubMed: 29226718]

* 62. Varga P, Grünwald L, Inzana JA, Windolf M. Fatigue failure of plated osteoporotic proximal humerus fractures is predicted by the strain around the proximal screws. J Mech Behav Biomed Mater. 2017;75:68–74. [PubMed: 28697401] This validation study included 19 specimen-specific finite element models and corresponding cadaveric cyclic loading experiments. Average strain computed around the screws was found to correlate strongly with number of cycles to failure, forming the basis for follow-up investigations of surgical variations.

63. Widmer J, Fasser M-R, Croci E, Spirig J, Snedeker JG, Farshad M. Individualized prediction of pedicle screw fixation strength with a finite element model. Comput Methods Biomech Biomed Engin. 2020;23:155–67. [PubMed: 31910656]

64. Marcián P, Borák L, Zikmund T, Horáčková L, Kaiser J, Joukal M, et al.On the limits of finite element models created from (micro)CT datasets and used in studies of bone-implant-related biomechanical problems. J Mech Behav Biomed Mater. 2021;117:104393. [PubMed: 33647729]

65. Wirth AJ, Müller R, Harry van Lenthe G. The discrete nature of trabecular bone microarchitecture affects implant stability. Journal of Biomechanics. 2012;45:1060–7. [PubMed: 22284426]

66. Ruffoni D, Wirth AJ, Steiner JA, Parkinson IH, Müller R, van Lenthe GH. The different contributions of cortical and trabecular bone to implant anchorage in a human vertebra. Bone. 2012;50:733–8. [PubMed: 22178777]

67. Wirth AJ, Goldhahn J, Flaig C, Arbenz P, Müller R, van Lenthe GH. Implant stability is affected by local bone microstructural quality. Bone. 2011;49:473–8. [PubMed: 21609793]

68. Wirth AJ, Müller R, van Lenthe GH. Augmentation of peri-implant bone improves implant stability: quantification using simulated bone loss. J Orthop Res. 2012;30:178–84. [PubMed: 21853456]
69. Steiner JA, Christen P, Affentranger R, Ferguson SJ, van Lenthe GH. A novel in silico method to quantify primary stability of screws in trabecular bone. Journal of Orthopaedic Research. 2017;35:2415–24. [PubMed: 28240380]
70. Chevalier Y, Matsuura M, Krüger S, Fleege C, Rickert M, Rauschmann M, et al.Micro-CT and micro-FE analysis of pedicle screw fixation under different loading conditions. Journal of Biomechanics. 2018;70:204–11. [PubMed: 29336820]
71. Wirth AJ, Mueller TL, Vereecken W, Flaig C, Arbenz P, Müller R, et al.Mechanical competence of bone-implant systems can accurately be determined by image-based micro-finite element analyses. Arch Appl Mech. 2010;80:513–25.
72. MacLeod AR, Serrancoli G, Fregly BJ, Toms AD, Gill HS. The effect of plate design, bridging span, and fracture healing on the performance of high tibial osteotomy plates. Bone Joint Res. 2019;7:639–49. [PubMed: 30662711]
73. Märdian S, Schaser K-D, Duda GN, Heyland M. Working length of locking plates determines interfragmentary movement in distal femur fractures under physiological loading. Clinical Biomechanics. 2015;30:391–6. [PubMed: 25716162]
74. Matsuura Y, Rokkaku T, Suzuki T, Thoreson AR, An K-N, Kuniyoshi K. Evaluation of Bone Atrophy After Treatment of Forearm Fracture Using Nonlinear Finite Element Analysis: A Comparative Study of Locking Plates and Conventional Plates. The Journal of Hand Surgery. 2017;42:659.e1–659.e9. [PubMed: 28552442]
75. Schwarzenberg P, Klein K, Ferguson SJ, von Rechenberg B, Darwiche S, Dailey HL. Virtual mechanical tests out-perform morphometric measures for assessment of mechanical stability of fracture healing in vivo. Journal of Orthopaedic Research. 2021;39:727–38. [PubMed: 32970350]
76. Shefelbine SJ, Simon U, Claes L, Gold A, Gabet Y, Bab I, et al.Prediction of fracture callus mechanical properties using micro-CT images and voxel-based finite element analysis. Bone. 2005;36:480–8. [PubMed: 15777656]
77. Erdemir A, Mulugeta L, Ku JP, Drach A, Horner M, Morrison TM, et al.Credible practice of modeling and simulation in healthcare: ten rules from a multidisciplinary perspective. J Transl Med. 2020;18:369. [PubMed: 32993675]
78. Henninger HB, Reese SP, Anderson AE, Weiss JA. Validation of computational models in biomechanics. Proc Inst Mech Eng H. 2010;224:801–12. [PubMed: 20839648]
79. Viceconti M, Pappalardo F, Rodriguez B, Horner M, Bischoff J, Musuamba Tshinanu F. In silico trials: Verification, validation and uncertainty quantification of predictive models used in the regulatory evaluation of biomedical products. Methods. 2021;185:120–7. [PubMed: 31991193]
80. Assessing Credibility of Computational Modeling Through Verification and Validation: Application to Medical Devices. American Society of Mechanical Engineers; 2018.
81. Eberle S, Gerber C, von Oldenburg G, Hungerer S, Augat P. Type of hip fracture determines load share in intramedullary osteosynthesis. Clin Orthop Relat Res. 2009;467:1972–80. [PubMed: 19333673]
82. Epari DR, Gurung R, Hofmann-Fliri L, Schwyn R, Schuetz M, Windolf M. Biphasic plating improves the mechanical performance of locked plating for distal femur fractures. Journal of Biomechanics. 2021;115:110192. [PubMed: 33385868]
83. Burkhart TA, Andrews DM, Dunning CE. Finite element modeling mesh quality, energy balance and validation methods: a review with recommendations associated with the modeling of bone tissue. J Biomech. 2013;46:1477–88. [PubMed: 23623312]
84. Ernst M, Richards RG, Windolf M. Smart implants in fracture care - only buzzword or real opportunity?Injury. 2020;9021.
85. Liu SZ, Cao Q, Osgood GM, Siewerdsen JH, Stayman JW, Zbijewski W. Quantitative Assessment of Weight-Bearing Fracture Biomechanics Using Extremity Cone-Beam CT. Proc SPIE Int Soc Opt Eng. 2020;11317.

86. Finnilä S, Moritz N, Strandberg N, Alm JJ, Aro HT. Radiostereometric analysis of the initial stability of internally fixed femoral neck fractures under differential loading. J Orthop Res. 2019;37:239–47. [PubMed: 30273993]

87. Galea VP, Botros MA, McTague MF, Weaver MJ, Vrahas MS, Malchau H, et al.Radiostereometric Analysis of Stability and Inducible Micromotion After Locked Lateral Plating of Distal Femur Fractures. J Orthop Trauma. 2020;34:e60–6. [PubMed: 31794438]

88. Zura R, Xiong Z, Einhorn T, Watson JT, Ostrum RF, Prayson MJ, et al.Epidemiology of Fracture Nonunion in 18 Human Bones. JAMA Surg. 2016;151:e162775. [PubMed: 27603155]

89. Campbell ST, Lim PK, Kantor AH, Gausden EB, Goodnough LH, Park AY, et al.Complication Rates after Lateral Plate Fixation of Periprosthetic Distal Femur Fractures: A Multicenter Study. Injury. 2020;51:1858–62. [PubMed: 32482424]

90. Giaretta S, Momoli A, Porcelli G, Micheloni GM. Diagnosis and management of periprosthetic femoral fractures after hip arthroplasty. Injury. 2019;50 Suppl 2:S29–33.

91. Albareda-Albareda J, Gabarre-Raso S, Rosell-Pradas J, Puértolas-Broto S, Ibarz-Montaner E, Redondo-Trasobares B, et al.Biomechanical behavior of retrograde intramedullary nails in distal femoral fractures. Injury. 2021;

92. Ali AA, Cristofolini L, Schileo E, Hu H, Taddei F, Kim RH, et al.Specimen-specific modeling of hip fracture pattern and repair. J Biomech. 2014;47:536–43. [PubMed: 24275435]

93. Arnone JC, Crist BD, Ward CV, El-Gizawy AS, Pashuck T, Rocca GJD. Variability of human femoral geometry and its implications on nail design. Injury. Elsevier; 2021;52:109–16.

94. Cordeiro M, Caskey S, Frank C, Martin S, Srivastava A, Atkinson T. Hybrid triad provides fracture plane stability in a computational model of a Pauwels Type III hip fracture. Comput Methods Biomech Biomed Engin. 2020;23:476–83. [PubMed: 32160804]

95. Gabarre S, Albareda J, Gracia L, Puértolas S, Ibarz E, Herrera A. Influence of gap size, screw configuration, and nail materials in the stability of anterograde reamed intramedullary nail in femoral transverse fractures. Injury. 2017;48 Suppl 6:S40–6. [PubMed: 29162240]

96. Goffin JM, Pankaj P, Simpson AHRW, Seil R, Gerich TG. Does bone compaction around the helical blade of a proximal femoral nail anti-rotation (PFNA) decrease the risk of cut-out?: A subject-specific computational study. Bone Joint Res. 2013;2:79–83. [PubMed: 23673407]

97. Herrera A, Albareda J, Gabarre S, Ibarz E, Puértolas S, Mateo J, et al.Comparative analysis of the biomechanical behavior of anterograde/retrograde nailing in supracondylar femoral fractures. Injury. 2020;51 Suppl 1:S80–8.

98. Lee WC, Chou SM, Tan CW, Chng LS, Yam GJM, Chua THI. Intertrochanteric fracture with distal extension: When is the short proximal femoral nail antirotation too short?Injury. 2020;

99. Li J, Yin P, Zhang L, Chen H, Tang P. Medial anatomical buttress plate in treating displaced femoral neck fracture a finite element analysis. Injury. 2019;50:1895–900. [PubMed: 31455504]

100. Li J, Han L, Zhang H, Zhao Z, Su X, Zhou J, et al.Medial sustainable nail versus proximal femoral nail antirotation in treating AO/OTA 31-A2.3 fractures: Finite element analysis and biomechanical evaluation. Injury. 2019;50:648–56. [PubMed: 30827705]

101. Li J, Wang M, Zhou J, Zhang H, Li L. Finite element analysis of different screw constructs in the treatment of unstable femoral neck fractures. Injury. 2020;51:995–1003. [PubMed: 32151421]

102. Mortazavi J, Farahmand F, Behzadipour S, Yeganeh A, Aghighi M. A patient specific finite element simulation of intramedullary nailing to predict the displacement of the distal locking hole. Med Eng Phys. 2018;55:34–42. [PubMed: 29576461]

103. Peng MJ-Q, Xu H, Chen H-Y, Lin Z, Li X, Shen C, et al.Biomechanical analysis for five fixation techniques of Pauwels-III fracture by finite element modeling. Computer Methods and Programs in Biomedicine. 2020;193:105491. [PubMed: 32388067]

104. Samsami S, Augat P, Rouhi G. Stability of femoral neck fracture fixation: A finite element analysis. Proc Inst Mech Eng H. 2019;233:892–900. [PubMed: 31203740]

105. Sarwar A, Gee A, Bougherara H, Kuzyk PRT, Schemitsch EH, Zdero R. Biomechanical optimization of the far cortical locking technique for early healing of distal femur fractures. Med Eng Phys. 2021;89:63–72. [PubMed: 33608126]

106. Wang C, Li X, Chen W, Wang C, Guo Y, Guo H. Three-dimensional finite element analysis of intramedullary nail with different materials in the treatment of intertrochanteric fractures. Injury. 2020;

107. Zeng W, Liu Y, Hou X. Biomechanical evaluation of internal fixation implants for femoral neck fractures: A comparative finite element analysis. Comput Methods Programs Biomed. 2020;196:105714. [PubMed: 32858283]

108. Zhang W, Hao M, Chang Z, Wu Y, Tang P, Chen H. Comparison of a multidimensional cross locking plate versus a locking compression plate for the treatment of femoral shaft nonunion: Finite element analysis. Med Eng Phys. 2020;83:106–11. [PubMed: 32507679]

109. Goffin JM, Pankaj P, Simpson AH. The importance of lag screw position for the stabilization of trochanteric fractures with a sliding hip screw: a subject-specific finite element study. J Orthop Res. 2013;31:596–600. [PubMed: 23138576]

110. Sarwar A, Gee A, Bougherara H, Kuzyk PRT, Schemitsch EH, Zdero R. Biomechanical optimization of the far cortical locking technique for early healing of distal femur fractures. Med Eng Phys. 2021;89:63–72. [PubMed: 33608126]

111. Fjalestad T, Hole MØ, Hovden IAH, Blücher J, Strømsøe K. Surgical treatment with an angular stable plate for complex displaced proximal humeral fractures in elderly patients: a randomized controlled trial. J Orthop Trauma. 2012;26:98–106. [PubMed: 21804410]

112. Handoll HH, Keding A, Corbacho B, Brealey SD, Hewitt C, Rangan A. Five-year follow-up results of the PROFHER trial comparing operative and non-operative treatment of adults with a displaced fracture of the proximal humerus. Bone Joint J. 2017;99-B:383–92. [PubMed: 28249980]

113. Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J. Internal fixation versus nonoperative treatment of displaced 3-part proximal humeral fractures in elderly patients: a randomized controlled trial. J Shoulder Elbow Surg. 2011;20:747–55. [PubMed: 21435907]

114. Kralinger F, Blauth M, Goldhahn J, Käch K, Voigt C, Platz A, et al.The Influence of Local Bone Density on the Outcome of One Hundred and Fifty Proximal Humeral Fractures Treated with a Locking Plate. J Bone Joint Surg Am. 2014;96:1026–32. [PubMed: 24951739]

115. Panagiotopoulou VC, Varga P, Richards RG, Gueorguiev B, Giannoudis PV. Late screw-related complications in locking plating of proximal humerus fractures: A systematic review. Injury. 2019;50:2176–95. [PubMed: 31727401]

116. Krappinger D, Bizzotto N, Riedmann S, Kammerlander C, Hengg C, Kralinger FS. Predicting failure after surgical fixation of proximal humerus fractures. Injury. 2011;42:1283–8. [PubMed: 21310406]

117. Hepp P, Lill H, Bail H, Korner J, Niederhagen M, Haas NP, et al.Where should implants be anchored in the humeral head?Clin Orthop Relat Res. 2003;139–47.

118. Kamer L, Noser H, Popp AW, Lenz M, Blauth M. Computational anatomy of the proximal humerus: An ex vivo high-resolution peripheral quantitative computed tomography study. Journal of Orthopaedic Translation. 2016;4:46–56. [PubMed: 30035065]

119. Schiuma D, Brianza S, Tami AE. Development of a novel method for surgical implant design optimization through noninvasive assessment of local bone properties. Medical Engineering & Physics. 2011;33:256–62. [PubMed: 20980189]

120. Castro-Franco AD, Mendoza-Muñoz I, González-Ángeles Á, Cruz-Sotelo SE, Castañeda AM, Siqueiros-Hernández M. Trends in the Characterization of the Proximal Humerus in Biomechanical Studies: A Review. Applied Sciences. Multidisciplinary Digital Publishing Institute; 2020;10:6514.

121. Ye Y, You W, Zhu W, Cui J, Chen K, Wang D. The Applications of Finite Element Analysis in Proximal Humeral Fractures. Comput Math Methods Med [Internet]. 2017 [cited 2021 Mar 25];2017. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5610852/

122. Chen H, Zhu Z, Li J, Chang Z, Tang P. Finite element analysis of an intramedulary anatomical strut for proximal humeral fractures with disrupted medial column instability: A cohort study. International Journal of Surgery. 2020;73:50–6. [PubMed: 31783165]

123. Chen Y-N, Chang C-W, Lin C-W, Wang C-W, Peng Y-T, Chang C-H, et al.Numerical investigation of fracture impaction in proximal humeral fracture fixation with locking plate and intramedullary nail. Int Orthop. 2017;41:1471–80. [PubMed: 28120001]

124. Čukelj F, Knezević J, Kodvanj J, Bandalović A, Ostojić M, Bilan K, et al.Computer representation of osteosynthesis stability in locking plates used for the treatment of osteoporotic proximal humerus fractures. Psychiatria Danubina. Medicinska Naklada Zagreb; 2014;26:14–9.

125. Feerick EM, Kennedy J, Mullett H, FitzPatrick D, McGarry P. Investigation of metallic and carbon fibre PEEK fracture fixation devices for three-part proximal humeral fractures. Medical Engineering & Physics. 2013;35:712–22. [PubMed: 22989528]

126. Fletcher JWA, Windolf M, Grünwald L, Richards RG, Gueorguiev B, Varga P. The influence of screw length on predicted cut-out failures for proximal humeral fracture fixations predicted by finite element simulations. Arch Orthop Trauma Surg. 2019;139:1069–74. [PubMed: 30895465]

127. Fletcher JWA, Windolf M, Richards RG, Gueorguiev B, Buschbaum J, Varga P. Importance of locking plate positioning in proximal humeral fractures as predicted by computer simulations. J Orthop Res. 2019;37:957–64. [PubMed: 30690786]

128. Fletcher JWA, Windolf M, Richards RG, Gueorguiev B, Varga P. Screw configuration in proximal humerus plating has a significant impact on fixation failure risk predicted by finite element models. Journal of Shoulder and Elbow Surgery. 2019;28:1816–23. [PubMed: 31036421]

129. He Y, He J, Wang F, Zhou D, Wang Y, Wang B, et al.Application of Additional Medial Plate in Treatment of Proximal Humeral Fractures With Unstable Medial Column. Medicine (Baltimore) [Internet]. 2015 [cited 2021 Mar 25];94. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4616805/

130. He Y, Zhang Y, Wang Y, Zhou D, Wang F. Biomechanical evaluation of a novel dualplate fixation method for proximal humeral fractures without medial support. Journal of Orthopaedic Surgery and Research. 2017;12:72. [PubMed: 28499398]

131. Jabran A, Peach C, Ren L. Biomechanical analysis of plate systems for proximal humerus fractures: a systematic literature review. BioMedical Engineering OnLine. 2018;17:47. [PubMed: 29703261]

132. Kennedy J, Feerick E, McGarry P, FitzPatrick D, Mullett H. Effect of calcium triphosphate cement on proximal humeral fracture osteosynthesis: a finite element analysis. J Orthop Surg (Hong Kong). 2013;21:167–72. [PubMed: 24014777]

133. Kim H, Lee W, Choi S, Kholinne E, Lee E, Alzahrani WM, et al.Role of Additional Inferomedial Supporting Screws in Osteoporotic 3-Part Proximal Humerus Fracture: Finite Element Analysis. Geriatr Orthop Surg Rehabil. SAGE Publications Inc; 2020;11:2151459320956958.

134. Le L, Jabran A, Peach C, Ren L. Effect of screw thread length on stiffness of proximal humerus locking plate constructs: A finite element study. Medical Engineering & Physics. 2019;63:79–87. [PubMed: 30554981]

135. Maldonado ZM, Seebeck J, Heller MOW, Brandt D, Hepp P, Lill H, et al.Straining of the intact and fractured proximal humerus under physiological-like loading. J Biomech. 2003;36:1865–73. [PubMed: 14614940]

136. Mendoza-Munoz I, Gonzalez-Angeles A, Gil-Samaniego-Ramos M, L-Avitia R, Gonzalez-Toxqui C. Evaluation of significant effects on locking plates design for a 2-part fracture of the surgical neck of the humerus using finite element and statistical analysis. Biomedical Research; 2018 [cited 2021 Mar 25]; Available from: https://www.biomedres.info/abstract/evaluation-of-significant-effects-on-locking-plates-design-for-a-2part-fracture-of-the-surgical-neck-of-the-humerus-using-finite-e-10296.html

137. Mischler D, Babu S, Osterhoff G, Pari C, Fletcher J, Windolf M, et al.Comparison of optimal screw configurations in two locking plate systems for proximal humerus fixation - a finite element analysis study. Clin Biomech (Bristol, Avon). 2020;78:105097.

138. Mischler D, Windolf M, Gueorguiev B, Nijs S, Varga P. Computational optimisation of screw orientations for improved locking plate fixation of proximal humerus fractures. Journal of Orthopaedic Translation. 2020;25:96–104.

139. Tilton M, Armstrong AD, Wee H, Hast MW, Manogharan G, Lewis GS. Finite Element-Predicted Effects of Screw Configuration in Proximal Humerus Fracture Fixation. Journal

of Biomechanical Engineering [Internet]. 2020 [cited 2021 Mar 25];142. Available from: 10.1115/1.4045907

140. Tilton M, Lewis GS, Bok Wee H, Armstrong A, Hast MW, Manogharan G. Additive manufacturing of fracture fixation implants: Design, material characterization, biomechanical modeling and experimentation. Additive Manufacturing. 2020;33:101137.
141. Varga P, Inzana JA, Fletcher JWA, Hofmann-Fliri L, Runer A, Südkamp NP, et al.Cement augmentation of calcar screws may provide the greatest reduction in predicted screw cut-out risk for proximal humerus plating based on validated parametric computational modelling: Augmenting proximal humerus fracture plating. Bone Joint Res. 2020;9:534–42. [PubMed: 32922762]
142. Yang P, Zhang Y, Liu J, Xiao J, Ma LM, Zhu CR. Biomechanical effect of medial cortical support and medial screw support on locking plate fixation in proximal humeral fractures with a medial gap: a finite element analysis. Acta Orthop Traumatol Turc. 2015;49:203–9. [PubMed: 26012943]
143. Zhang Y-K, Wei H-W, Lin K-P, Chen W-C, Tsai C-L, Lin K-J. Biomechanical effect of the configuration of screw hole style on locking plate fixation in proximal humerus fracture with a simulated gap: A finite element analysis. Injury. 2016;47:1191–5. [PubMed: 26975793]
144. Gross T, Pahr DH, Peyrin F, Zysset PK. Mineral heterogeneity has a minor influence on the apparent elastic properties of human cancellous bone: a SRμCT-based finite element study. Comput Methods Biomech Biomed Engin. 2012;15:1137–44. [PubMed: 22263706]
145. Perren SM. Evolution of the internal fixation of long bone fractures. The scientific basis of biological internal fixation: choosing a new balance between stability and biology. J Bone Joint Surg Br. 2002;84:1093–110. [PubMed: 12463652]
146. Baumann AP, Graf T, Peck JH, Dmitriev AE, Coughlan D, Lotz JC. Assessing the use of finite element analysis for mechanical performance evaluation of intervertebral body fusion devices. JOR Spine. 2021;4:e1137. [PubMed: 33778409]

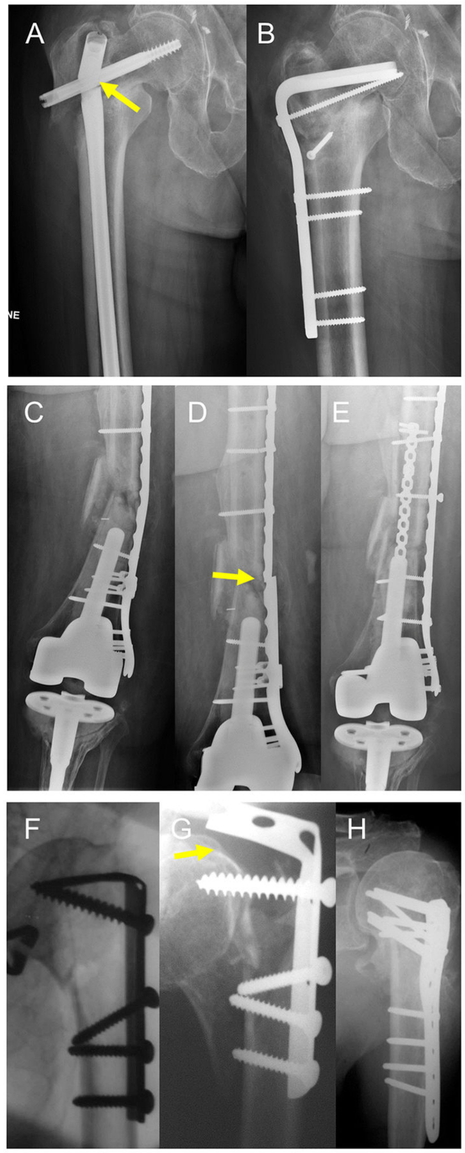
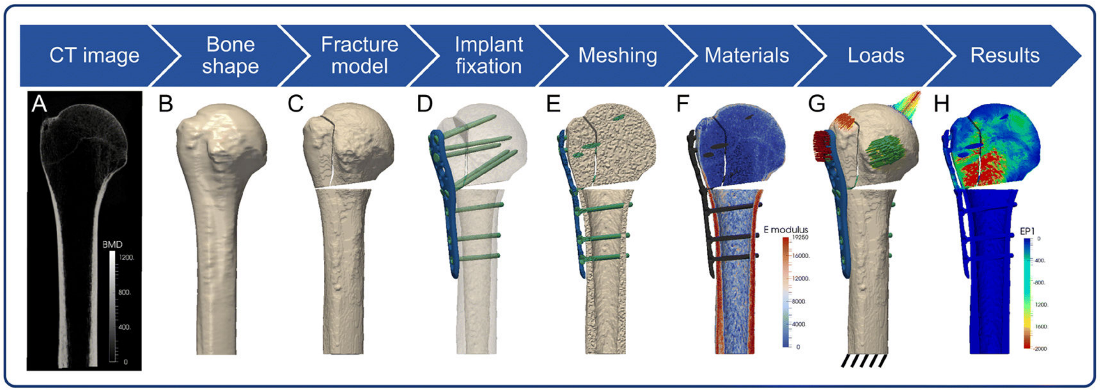


Figure 1.

Radiographs from three patient cases (three rows of images). (*A*) A 72 y/o man sustained an intertrochanteric hip fracture that was stabilized with an intramedullary nail. After six months, the fracture did not heal and the nail sustained a fatigue fracture where the lag screw enters the neck of the femur (arrow). The patient was unable to walk without a walker. (*B*) He underwent revision surgery with placement of a different implant in compression (laterally based plate) which resulted in eventual healing of the fracture. (*C*) A 69 y/o man suffered a fracture above his revision knee replacement following a motorcycle accident. He was initially stabilized with a lateral plate. He was unable to restrict his weight bearing and sustained bending of his plate over three months. (*D*) Eventually, this plate fractured (arrow), requiring (*E*) complex reconstructive surgery with two plates and bone shortening, which eventually resulted in union. (*F*) 78 y/o woman sustained an osteoporotic proximal humerus fracture, initially stabilized with a blade plate and non-locking screws. (*G*) Early failure of the construct resulted, with pullout of the blade (arrow) and screws. (*H*) Revision surgery using an anatomic specific plate with locking screws resulted in successful union.



Pasted Layer

Figure 2.
Overview of finite element analysis workflow (adapted from [24], with permission from Elsevier).

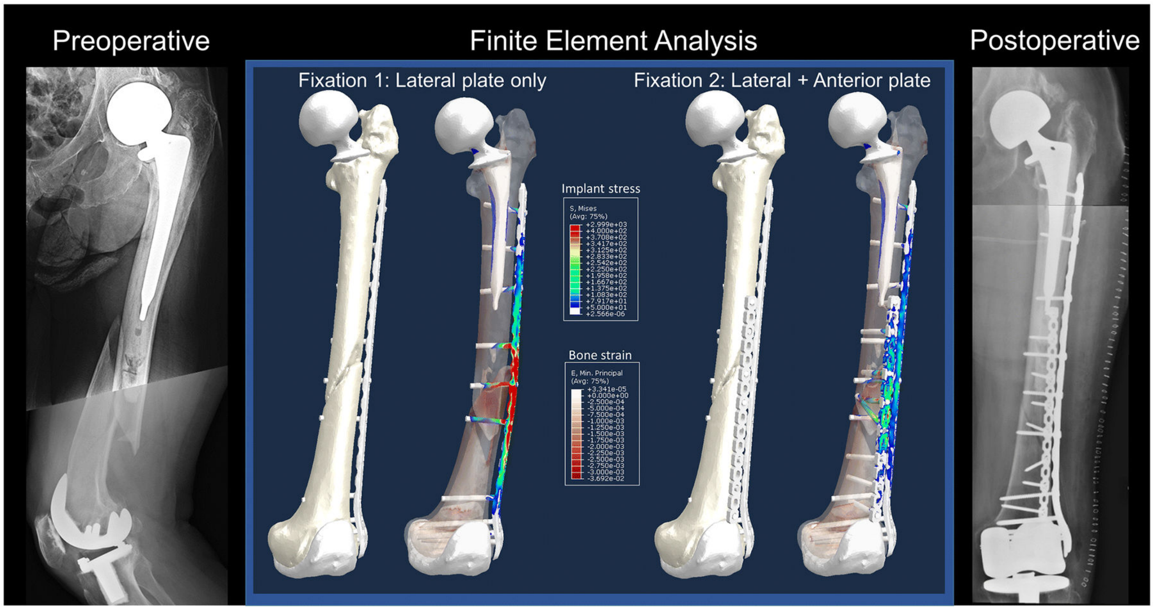


Figure 3.
Example of finite element analysis comparing two fixation options for a challenging periprosthetic femur fracture.