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9 FINITE ELEMENT MODELING AND ANALYSIS APPLICATIONS IN OSTEOGENESIS IMPERFECTA

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INTRODUCTION

Understanding the biomechanics of bones in persons with osteogenesis imperfecta (OI) is a key component to further understanding the disease, optimizing treatment and quality of life, as well as injury prevention. However, it is not feasible to study bone biomechanics in vivo. Thus, modeling may play a key role in understanding how OI bones respond to the loading experienced during various activities, especially ambulation. Biomechanical modeling can provide insight into bone fracture risks, such as type and location, from single applied loads or repetitive loading. One method for obtaining this information is via a finite element analysis (FEA). FEA is a general technique for mathematically approximating solutions to boundary-value problems.[1] It is a powerful computational tool with numerous applications. These numerical methods are used to obtain an output from a system of differential equations in response to boundary condition inputs in many scenarios. FEA allows for the discretization of a structure into numerous subparts (elements) for analysis. Elements represent regular straight-side geometric 2-D or 3-D shapes that enclose a finite area or volume.[2] Field output variables (stress, strain, etc.) are explicitly calculated at each vertex (node) of every element.[3] These outputs provide information that corresponds to bone strength and, therefore, location and risk for potential fractures.

General FEA Applications

Overall, FEA can also be used to model thermal and dynamic fatigue responses. Several software packages exist to perform FEA. These allow the user to either create or import a model, choose the shape and size of the elements that make up the structure, designate material properties and apply boundary and initial conditions. FEA is becoming a reliable method for mechanical analysis of materials, especially in fatigue testing, as it reduces the testing time. Benefits of FEA include: increased accuracy, enhanced design and better insight into critical design parameters, virtual prototyping, fewer hardware prototypes, a faster and less expensive design cycle and increased productivity.[4] It is also useful in flow dynamics analysis, thermal effects, molecular level analysis and crack propagation.[5, 6] A valid model can considerably shorten the development of a new product or process and allow for testing that could not otherwise be completed.

FEA Applications in Biomechanics

Since its introduction into biomechanics in 1972, FEA has been widely used in orthopaedic biomechanics and the assessment of bone mechanical properties.[7,8] A major benefit of FEA is the ability to perform non-invasive evaluations of biological structures. Finite element (FE) models also demonstrated beneficial clinical applications. Mechanical stresses in bones cannot be measured in living subjects without the use of an invasive surgical procedure.[9] Patient-specific FE models allow estimations of in vivo response of bone to various loading conditions. FE models have been developed for long bones as well as the skull, vertebrae, pelvis, metacarpals and scapula.[10,11] FEA was used as early as 1972 by Brekelmans and colleagues to investigate the stresses acting in human bone under physiologic loading conditions.[10] Gupta and colleagues developed and validated a 3-D FE model of the human scapula.[11] The model was based on geometry and material properties, such as density, which were taken from computed tomography (CT) data. Unlike previous solid models, the model created by Gupta et al used a combination of shell (2-D) and solid (3-D) elements. The researchers used fresh cadaver bones with mounted strain gages as a reference to assess the accuracy of the model's stress and strain analysis of the scapular surface.[11]

While several studies have been completed using FEA, there is no standard analysis criterion for fracture prediction in long bones. Bosisio et al looked

at combining inverse FEA with quantitative ultrasound and peripheral quantitative CT to assess the mechanical properties of the distal radius and fracture risk in osteoporosis patients.[16] Taddei and colleagues used FEA to study the mechanical strength of a femoral reconstruction in pediatric oncology.[17] Their study examined the proximal femur reconstruction of a child afflicted with Ewing sarcoma in an effort to evaluate the risk of fracture. The loading conditions in the FE model were comprised of the hip joint reaction force and abductor muscle force. Taddei et al based risk of fracture upon the ratio between the bone tissue strength and the predicted von Mises equivalent stress.[17] Other criteria for fracture that have been used by various research groups include: distortion energy, Hoffman and a strain-based Hoffman analogue (used for anisotropy), maximum normal stress, maximum normal strain, maximum shear strain, maximum shear stress, Coulomb-Mohr, and modified Mohr failure theories (used for anisotropic, elastoplastic materials). Gómez-Benito, García-Aznar and Doblaré argue that these criteria are not sufficient for the anisotropic behavior of bone. Therefore, they implemented the Cowin fracture criterion based on the Tsai-Wu model which takes into account the anisotropy and porosity of bone.[18] Both of these studies, and others, focused on the proximal femur rather than the entire femur and neither accounted for the full muscle contributions to the intrinsic forces of the bone.

The proximal femur is most commonly studied as most fractures occur at this site and are frequently seen in elderly and obese patients as well as those with osteoarthritis and hip implants. Trauma research has recently led to the development and validation of a lower-limb, non-linear, 3-D FEA model to study the effects of car-pedestrian impact on the thigh.[19,20] More sophisticated models account for the individual muscle forces. These forces can significantly alter the loading distribution on the femur.[19,21-25] This knowledge led to the development of a muscle standardized femur (MSF) model.[24,25] Most proximal femur fracture prediction studies model a static quasi-axial loading scenario, which closely replicates single limb stance during the gait cycle. However, these studies do not take loading from other directions into account. Grassi et al recently completed a study validating a model to replicate forces on the adult human proximal femur during a fall scenario.[26]

FEA Applications in OI

Patient-specific FE models have been an effective tool for both bone strain and fracture strength assessment.[12,13] They are used alongside motion

analysis for gait pathologies, rehabilitation, and sports training. One important developing application is the use of FEA to predict fractures in OI.[14,15] Fracture prediction in OI patients may lead to altered prescription of activities and improved physical therapy.

While several groups are examining adult femoral fracture risk and bone strength using FE models, studies on pediatric bone are scarce. Even rarer is the availability of information on fracture risk and strength of pediatric bones in OI. Across all types of OI, poor bone quality poses major orthopaedic and rehabilitation challenges. All treatments are performed with the goal of maximizing function, minimizing deformity, maintaining patient comfort and allowing for independent living. Treatment strategies are generally personalized based on motor function, functional needs and fracture risk. However, fracture risk is difficult to evaluate and is not quantitatively assessed in the clinical environment. Numerous factors contribute to fractures in OI patients including, but not limited to: altered bone material properties, geometry and loading. Therefore, these are three key components for a predictive model of OI long bone fracture. Models are currently being developed to examine the fracture risk assessment and validity of FEA applied to the whole OI femur.[14, 15] Ideally, these analyses will allow the implementation of better patient-specific models for persons with OI which will provide quantitative guidelines for activity limitations to increase function and reduce fracture risk.[27]

METHODS

FE Parameters for Patient-Specific Models

Key contributions to any FE model, including that of a long bone, include: the geometry of model, boundary and loading conditions and material properties. Changes in any of these parameters can affect the output of the model. All of these factors can be dependent on the patient whose bone is being modeled.

Long Bone Geometry

Current methods employ a digital image to determine the size and amount of femoral bowing by matching the size (length and width) and level of bowing from planar x-rays. Ideally, model geometry would be directly obtained from individual CT scans. Several groups have worked on creating automated FE models from 3-D images. Most of the methods use reconstruction of CT

images to obtain patient-specific geometry and material properties. Converting a CT scan into a 3-D image file for modeling is more computationally intensive than using a "standard" geometry, but it provides a better option for a patient-specific match of geometry.[7] However, this is not feasible for children, especially those with OI, due to the high levels of radiation involved in CT scans and the high number of x-rays already acquired clinically. As CT radiation is reduced through technical advances, individual scans may become feasible. Reduced radiation exposure to obtain more accurate geometry increases the validity of the resulting models. Appropriate model geometry is essential in determining the locations of the femur that are at risk for fracture as well as the level of the risk across the entire femur (stress, strain, etc.). The effects of altering the geometry were examined to emphasize the importance of patient-specific geometry.

Boundary and Loading Conditions

Boundary and loading conditions are fundamental to an accurate FE model. They describe the allowed motion of the structure being modeled as well as the external loads. For the current patient-specific model of the femur, the modeled load scenario replicates normal ambulation. Thus, the boundary and loading conditions are obtained from gait kinematics and kinetics as well as internal muscle loading. Accurate boundary and loading conditions help replicate physiologic mechanical conditions of the femur during walking. The forces from muscle contractions during gait are estimated based on EMG activation patterns and literature.[28] The muscles are modeled as a force equal to a prescribed percentage of body weight during the various gait cycle phases. The lines of action are determined from gait kinematics and muscle origin and insertion locations on the femur. The effects of altering the loads from muscle forces were assessed to determine contributions to fracture risk in the OI femur.[14]

Material Properties

Material properties are a major determinant as to how a structure responds to loading. Structures can be defined as having the same response to mechanical loading regardless of loading direction (isotropic). Alternatively, their mechanical response may be dependent on loading direction (anisotropic). Another possibility is that the response of the material is the same in the transverse directions, but varies between the transverse and longitudinal directions (transverse isotropy). These distinctions are important when assigning material properties to an FE model. The OI femur

is currently modeled by our group as a linear elastic material, thus, Young's modulus (E) and Poisson's ratio (ν) are required inputs. We have modeled this femur as both isotropic and transversely isotropic based on literature and recent studies of OI bone specimens.[29] The isotropic model required E and ν, whereas the transversely isotropic model also required shear modulus (G) values.

Model Development

Our FE model of the OI femur was originally developed and analyzed in Abaqus CAE (Dassault Systèmes Simulia Corp.; Providence, RI) with geometry and gait dynamics derived from studies of a 12-year-old female with OI type I. This model was then used to examine parameter alteration effects on the fracture risk in the femur. Over the past few years, our FE models for fracture risk assessment of the OI femur have evolved to include isotropic tetrahedral elements as well as transversely isotropic hexahedral elements.[15, 29] The various versions follow developments to enhance model parameter with improved meshing techniques. The current model was meshed in IA-FEMesh to allow for hexahedral elements.[30] The model was altered and analyzed with Abaqus CAE. Figure 1 illustrates the improved mesh quality of the complex femoral geometry with the implementation of hexahedral meshes. Comparative analysis of the FE OI femur has been used to illustrate the importance of patient-specific parameters.[29]

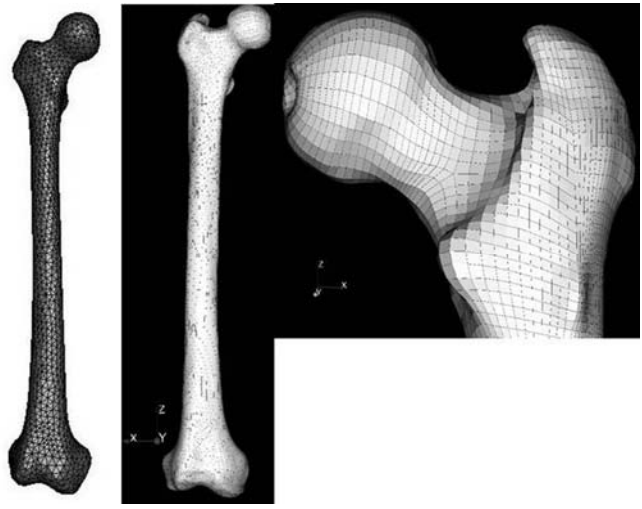

Figure 1. OI femur model with tetrahedral mesh (left) and improved hexahedral mesh (middle). A zoomed image shows the ability of the hexahedral mesh to follow the complex, curved geometry of the femoral head (right).

RESULTS

Each of the patient-specific parameters impacts the FEA results in the femoral OI model. Altering the force contributions from the femoral muscle attachments showed that stress sensitivity was greatest for loads from the gluteus medius and maximus muscles.[14] These stresses are direct contributing factors to femoral fracture risk. As stress increases, fracture risk also increases. Geometric alterations also affect the stress levels and fracture risk. A parametric study examining the effects of lateral bowing showed a positive linear increase in fracture risk with increased lateral bowing (Figure 2).[27] Other model alterations examine OI bone mechanical properties. Modeling the OI femur as a transversely isotropic material rather than an isotropic material not only affects the levels of stress, but also the stress distribution (Figure 3). The percent difference in maximum and minimum principal stresses along the longitudinal direction of a 15 mm laterally bowed OI femur showed a 5% and 7% increase, respectively, between the isotropic and transversely isotropic models.[29] The process of examining model parameter effects has continued with development of the FEA approach.

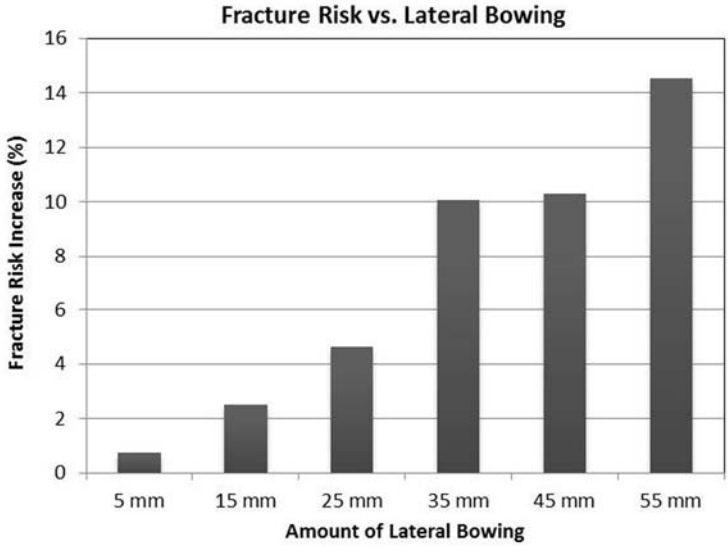

Figure 2. Fracture risk with increased lateral bowing of the OI femur.

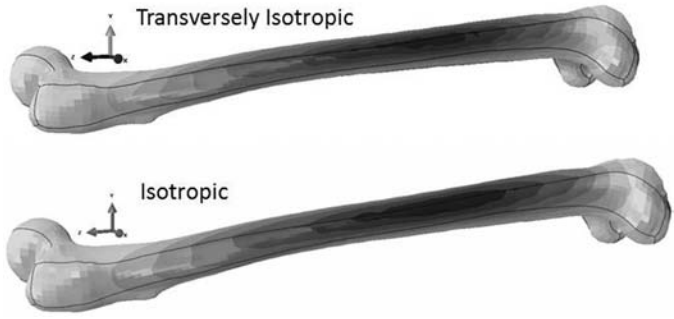

Figure 3. Contour plots of maximum principal stress on a 15 mm bowed femur for previous (top) and current (bottom) FE models. In the femoral diaphysis, stress levels increase from light to dark shading.

DISCUSSION AND CONCLUSIONS

Patient-specific parameters are essential to accurately employ FEA as a means to assess fracture risk in long bones of persons with OI. These include bone geometry, loading, and mechanical properties of OI bones. Ideally, bone geometry would be obtained from CT scans to reproduce exact 3-D geometries. However, this is often not feasible in OI patients due to high

levels of radiation exposure. In lieu of CT reconstruction, a 3-D model of long bone can be altered to match geometries measured through standard planar x-rays obtained clinically. This allows a 3-D model to be created without additional radiation exposure. A MATLAB (MathWorks; Natick, MA) program can be used to obtain various measurements from digital images of these x-rays. Our 3-D model can be modified in Abaqus CAE by altering the positions of the nodes (element vertices) of the appropriate area of the femoral diaphysis. Model loading includes both internal and external forces. Internal forces derive from contraction of muscles with origins/insertions on the modeled bone. External forces result from activities, such as gait. The parameter of greatest current interest is the mechanical properties of OI bone.

Our FE model for fracture risk assessment of the OI femur has been presented here with techniques suitable for application to any long bone. Orwoll et al. recently employed FE models to estimate vertebral bone strength in adults with OI.[31] Caouette et al. also recently published work on FE models for fracture risk assessment of the tibia in children with OI.[32] These are both discussed in more detail earlier in this text. Work has also been completed towards development of an FE model of the OI humerus.[33,34] In OI patients who use assistive devices for ambulation, humeral injuries become a greater concern than in those without assistive devices. Current study indicates that crutch walking results in high humeral loading.[35]

Accurate patient-specific FE models to assess fracture risk in long bones can help direct treatment and activity prescriptions in children with OI. Knowledge about the likelihood and location of bone fracture may also allow advances that improve the safety of various recreational and rehabilitative activities. Improved bone geometry, loading and material characterization parameters will allow continued advancement of FE models applied to quantitatively assess fracture risk in children with OI.

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ABBREVIATIONS

OI	Osteogenesis imperfecta
FEA	Finite element analysis
FE	Finite element
CT	Computed tomography
MSF	Muscle standardized femur
E	Young's modulus
ν	Poisson's ratio
G	Shear modulus

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