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REVIEW

Computed tomography-based finite element analysis to assess fracture risk and osteoporosis treatment

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Abstract

Finite element analysis (FEA) is a computer technique of structural stress analysis and developed in engineering mechanics. FEA has developed to investigate structural behavior of human bones over the past 40 years. When the faster computers have acquired, better FEA, using 3-dimensional computed tomography (CT) has been developed. This CT-based finite element analysis (CT/FEA) has provided clinicians with useful data. In this review, the mechanism of CT/FEA, validation studies of CT/FEA to evaluate accuracy and reliability in human bones, and clinical application studies to assess fracture risk and effects of osteoporosis medication are overviewed.

Key words: Finite element analysis; Bone mechanics; Hip fracture; Osteoporosis; Vertebral fracture; Fracture risk

Core tip: Finite element analysis (FEA) is a computer technique of structural stress analysis developed in engineering mechanics. With the faster computers, better FEA, using computed tomography (CT) has been developed. This CT-based finite element analysis (CT/FEA) has provided clinicians with useful data. In this review, the mechanism of CT/FEA, validation studies of CT/FEA to evaluate accuracy and reliability in human bones, and clinical application studies to assess fracture risk and osteoporosis treatment are overviewed.

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INTRODUCTION

Finite element (FE) method is a calculation technique

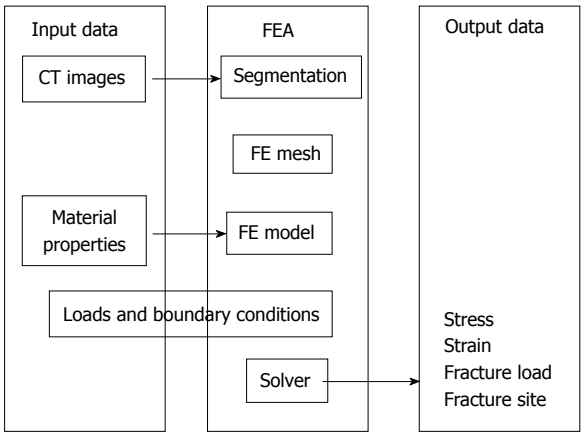

Figure 1 Steps involved in construction, analysis, and output data of computed tomography-based finite element analysis for human bones. FEA: Finite element analysis; CT: Computed tomography.

using computers to solve structural mechanics problems. With FE, approximate solutions of boundary value problems are solved. The concept of the FE is the subdivision of the mathematical complex structure into independent components of simple geometry. The number of components is finite, therefore the components are called "finite elements". The response of the mathematical model is considered to be discrete model obtained by connecting or assembling the collection of all elements. When examining artificial and natural systems such as bridge, building, airplane, and skeleton, the disconnection-assembly concept occurs. Calculation of structural mechanics problems using FE consists of dividing the structure into finite elements, and then each element is assigned by the element equations to the problem, followed by recombining all sets of element equations into the whole structure for the final calculation.

Finite element analysis (FEA) is a practical application of FE for performing structural analysis. FEA consists of using mesh generation techniques for dividing a complex structure into small simple elements and using software program with FE algorithm. FEA has been improved over the past 40 years and become an indispensable tool to assess structural mechanics of human tissues such as bones. In 1972, FEA was first applied in orthopedic biomechanics to calculate stress of human bones[1]. Since then, FEA has been widely applied to assess the human bone mechanics[2]. When the faster computers have been available, improved FEA and more advanced imaging modalities have been developed. The FEA using 3-dimensional (3D) computed tomography (CT) data was applied and was used to assess vertebral bone strength clinically in the early 1990s[3]. This so-called "computed tomography-based finite element analysis (CT/FEA)" has provided clinicians with useful data. Clinical applicability of CT/FEA of human bones might depend on accuracy, reliability, the ease of use, and usefulness. The purpose of this review article is to overview the mechanism of CT/FEA, validation studies of CT/FEA to evaluate accuracy and reliability in human bones, and clinical application studies to assess fracture risk and osteoporosis treatment.

MECHANISM OF CT/FEA FOR HUMAN BONES

There are three major stages, *i.e.*, pre-process, solution, and post-process, in CT/FEA for human bones[4]. The stages are summarized in Figure 1. The FE model is generated in the first pre-process stage and the problem of the model is solved by FE solver in the second solution stage. The solved results are analyzed in the post-process stage. The first step of CT/FEA is to acquire CT images of human bones, and then transfer the data to FE modeling system. After CT data are acquired, the region of interest (ROI) is segmented and mesh generation is proceeded. The quality and accuracy of the FE model is highly dependent on the ROI segmentation and mesh generation. A 3D image constructed with CT scanning is called voxel. In order to create FE model accurately and good quality, it is essential to define the anatomical bone shapes and segment the ROI accurately. After the ROI is segmented and the 3D bone geometry is obtained, mesh generation procedure can be done. There are several mesh generation techniques. In voxel based mesh generation technique, a pre-defined voxels from the CT scanning constitutes elements. In voxel based mesh, there is no surface or solid bodies. On the other hand, geometrical model with surface points is generated in structure based mesh procedure. Structure based mesh can generate more complex mesh and shell-solid mesh. In shell-solid mesh, component is modeled with two types of elements. Trabecular bone is modeled using solid elements. Outer surface of the trabecular bone, cortical bone or cortical shell is modeled using thin plate shell elements.

After FE model is generated, material properties of the each element in the model is assigned. The density of the each element is defined using the correlations between the Hounsfield unit (HU) value of the CT and the apparent density. The Young's modulus of the element is defined using the equations between the density and the mechanical properties of the bone. Regarding FE modeling of the human bone, there are two problems: (1) material properties of the cortical bone and the trabecular bone are very different; and (2) the material properties distribution within the cortical bone and the trabecular bone is not homogeneous. One of the methods to deal with the first problem is to use shell-solid mesh and model the cortical bone and trabecular bone using two types of elements. Cortical bone is constructed with "shell" elements. Trabecular bone is modeled using "solid" elements. It is essential to assure that assigned bone stiffness is connected to the assigned bone mineral density (BMD). The HU value of a voxel is connected to the bone stiffness. The HU values of a CT image are applied to define the

appropriate bone stiffness in the FE model.

An essential procedure to define material properties in FE model consists of calibrating the CT density, relating the voxel value to BMD, and accurately defining Young's modulus of the bone. For this purpose, a calibration phantom, which consists of known concentration of calcium hydroxyapatite, is used in CT image acquisition. By normalizing the HU values with the known concentration of the calibration phantom, an equation between CT density and BMD of the bone is established. It is shown that the apparent density and the mechanical properties of the bones are related with equations using power laws[5].

It is preferable that trabecular bone shows anisotropic mechanical behavior. Therefore, CT/FEA with anisotropic properties of the bones is assumed to be more accurate. In some studies, no significant difference was shown between the results by isotropic CT/FEA models and by CT/FEA orthotropic models[6]. But another study indicated a significant difference between the isotropic CT/FEA models and orthotropic CT/FEA models[7].

The final step is to apply the loads and boundary conditions in FE model. Boundary conditions defines that assigned nodes of the elements are limited in their degrees of freedom and are constrained. The constrained nodes are fixed or prescribed to move in a fixed amount. The applied loads work for deforming the element and producing internal stress. The solver works to solve the equilibrium between applied loads and internal material stress under the loads and boundary conditions. The location of the fixed element is defined by constraining the assigned nodes of the element completely. It is essential to apply the accurate loads and boundary conditions to fairly assess the mechanical behaviors in bone in daily activities.

CT/FEA SOLUTION AND CLINICAL APPLICATION

In order to apply CT/FEA in human bones, two important characteristics of bone have to be considered. First, bone is failed because of overstress or insufficient bone strength. Second, bone is adapting and remodeling by the applied loads and stresses, known as Wolff's law. Because of this bone tissue adaptation process, the mechanical properties of bone are changed.

In our increasingly aging societies, there are more patients with osteoporosis. Osteoporotic patients have much higher bone fracture risk due to insufficient bone strength. Fracture often occurs at hip, spine, humerus, and forearm. To determine whether pharmacological intervention for osteoporosis is needed, accurate fracture risk assessment is helpful. Traditionally, measurement of BMD by dual energy X-ray absorptiometry (DXA) has been the standard method for diagnosing osteoporosis. However, BMD itself is not able to predict the actual fracture in a reliable way. It has been reported that many patients which have normal BMD developed fractures due to osteoporosis[8]. The correlation between BMD and experimental fracture load was reported 45%-57%[9,10]. Recently, fracture risk assessment tool (FRAX) was developed to assist with clinical treatment decisions. FRAX was developed by the World Health Organization Collaborating Center for Metabolic Bone Diseases and calculates the 10-year probability of major osteoporosis related fractures (hip, spine, humerus, and forearm)[11-13]. FRAX can only be used in untreated patients. FRAX is useful for primary screening for osteoporosis and related fractures, but not useful for assessing therapeutic effects.

In CT/FEA, the stress and strain distributions are able to be assessed. Stress, strain, fracture load, and fracture site are assessed as a post-processing stage. Fracture is defined, and fracture load and fracture site are predicted with fracture criterion. For assessing the failure of engineering and biological materials, stress-based criteria or strain-based criteria have been used. Fracture criteria of bone include von Mises stress[14-16], Drucker-Prager stress[16-18], maximum principal strain[19], maximum principal stress[19], and minimum principal strain[17]. Some studies reported that bone fracture is regulated by strain and stress[20,21].

VALIDATION OF CT/FEA

After FE model with material properties is constructed, loads and boundary conditions are assigned, and CT/FEA solver solved the model simulation, the results are transformed into a useful output data, *i.e.*, stress, strain, fracture load, fracture site, to meet the investigation purpose. In addition, accuracy and validity of the CT/FEA should be shown through validation of the model. By comparing CT/FEA output data with the measured values in mechanical testing, CT/FEA can be validated and verified. It has been impossible to measure strains or stresses inside the trabecular bone structure with conventional methods. Therefore, strains at the bone surface are experimentally assessed, and it is considered that a validation of the surface strains substitutes for validation of the strains and stresses inside the bone. Strain gauges can measure strains at the site it attached. With strain gauges, strains at the some parts of specimen surface can be measured through mechanical testing. Recently, full-field strain measurement techniques that can measure surface strains throughout the specimen have been improved. Digital image correlation technique has been used for the measurement of surface strains during mechanical testing[22-24]. Digital image correlation has been successfully used for validation of the CT/FEA of the proximal femur[25].

For clinicians, fracture load, fracture pattern, and fracture site are the most useful data. There are some *ex-vivo* validation studies of CT/FEA analyzing the fracture load and then evaluate the accuracy by performing mechanical testing with human cadaveric

Table 1 Validation studies of the proximal femur

Ref.	Software	Variable	R^2	Slope
Cody *et al*[9]	EBE-PCG	One-legged stance fracture load	0.84	0.85
Keyak *et al*[14]	ABAQUS	Stance configuration fracture load	0.75	0.99
Keyak *et al*[14]	ABAQUS	Fall configuration fracture load	0.90	1.24
Keyak[27]	ABAQUS	Stance configuration fracture load	0.93	1.15
Bessho *et al*[18]	Mechanical Finder	Stance configuration fracture load	0.96	0.94
Bessho *et al*[18]	Mechanical Finder	Principal strain	0.93	0.91
Tanck *et al*[15]	MARC	Stance configuration fracture load	0.92	1.07
Derikx *et al*[16]	MSC (von-Mises criterion)	Stance configuration failure force	0.91	0.92
Derikx *et al*[16]	MSC (Drucker-Prager criterion)	Stance configuration failure force	0.91-0.94	0.93-1.01
Dragomir-Daescu *et al*[28]	ANSYS Mechanical APDL	Sideways fall fracture load	0.86	1.36

Used software of finite element analysis, validation variables, cross-validation R^2 values, and slope of the regression line are summarized.

Table 2 Validation studies of the spine

Ref.	Software	Variable	R^2	Slope
Silva *et al*[29]	ABAQUS	10 mm thick vertebral section yield load	0.91	0.86
Martin *et al*[30]	ADINA	Failure load	0.79	0.57
Crawford *et al*[31]	ABAQUS	Compressive strength	0.86	0.72
Imai *et al*[17]	Mechanical Finder	Failure load	0.96	0.88
Imai *et al*[17]	Mechanical Finder	Minimum principal strain	0.70	0.93
Kinzl *et al*[33]	ABAQUS	Apparent strength	0.92	1.02

specimens. For hip, validation studies indicated that CT/FEA might be able to predict femoral strength more than quantitative CT (QCT) or DXA[9] and was able to assess fracture site of the proximal femur[26]. Nonlinear CT/FEA showed more accurate predictions of fracture load at proximal femur[27]. Using shell-solid meshing, nonlinear CT/FEA analyzed fracture loads of the proximal femurs as well as principal strains of the surface of the femoral bones accurately[18]. Using Drucker-Prager yield criterion, CT/FEA could predict femoral bone strength and fracture site better than using von Mises yield criterion[16]. Validation studies of simulating a sideways fall on the hip revealed that CT/FEA predicted fracture loads and fracture patterns with a high degree of accuracy[28]. The validation studies of the proximal femur are summarized in Table 1.

Regarding spine, the cadaver studies have validated and verified that CT/FEA predicts failure loads and fracture patterns for vertebral sections with 10 mm thickness[29]. *Ex-vivo* validation studies of CT/FEA analyzing vertebral bones demonstrated that CT/FEA could predict vertebral compressive strength more accurate than BMD[30] and QCT[31]. Nonlinear CT/FEA using shell-solid meshing and Drucker-Prager yield criterion was able to predict distribution of minimum principal strains of the vertebra, vertebral strength, fracture pattern, and fracture site accurately[17,32]. Nonlinear FEA using high-resolution peripheral quantitative CT could predict vertebral strength well and the analyzed pressure distributions were qualitative agreement with the experiments measured by pressure sensitive films[33]. The validation studies of the spine are summarized in Table 2.

ASSESSMENT OF FRACTURE RISK AND OSTEOPOROSIS TREATMENT USING CT/FEA

Based on validation and verification with the cadaver studies, CT/FEA has been applied clinically in the assessment of fracture risk and osteoporosis treatment. In clinical data, the hip fracture risk index in discriminating hip fracture derived from CT/FEA was significantly better than total hip BMD and DXA-based structural engineering models[34]. The strength of the proximal femur varies depending on the specific force configuration.

In fall configuration, the force magnitudes and directions can be influenced by many biomechanical factors such as body weight, height, and position. The study to assess the relationship between femoral bone strength by nonlinear CT/FEA and incident hip fracture in multiple loading conditions, posterolateral loading in men and posterior loading in women were most strongly associated with incident hip fracture[35].

As for vertebral fracture, nonlinear CT/FEA had higher discriminatory power for vertebral fracture than lumbar spine BMD by DXA and volumetric BMD by QCT[36,37]. Consequently, CT/FEA has the potential to replace DXA and QCT in discriminating osteoporosis related fractures.

Regarding osteoporosis treatment, CT/FEA was useful for assessing teriparatide and alendronate medication effects at the lumbar spine[38]. In addition, a study using nonlinear CT/FEA clinically showed that vertebral compressive strength by CT/FEA was a significantly

better predictor for vertebral fracture than BMD, and was able to assess medication effects significantly earlier than BMD[36,37].

CONCLUSION

Osteoporosis related hip fractures and vertebral fractures have become a major social problem because the elderly population continues to increase. It is essential to assess fracture risk, start medication, and prevent fractures in the management and treatment of osteoporosis. In this article, the mechanism of CT/FEA, validation studies of CT/FEA for human bones, and clinical application studies to assess fracture risk and osteoporosis treatment are reviewed. CT/FEA accurately assesses bone strength and fracture site and is useful for assessing fracture risk and medication effects on osteoporosis. CT/FEA also assesses bone strength under various loading configurations normally seen in daily living activities[39]. With CT/FEA in the diagnosis and management of osteoporosis, patients and their clinicians are able to tailor a treatment plan according to a patient's specific clinical scenario.

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