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What is the future of patient-specific vertebral fracture prediction?

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ABSTRACT

This paper aims to introduce a few alternative methodologies for prediction of vertebral fractures, the most common type being fragility fracture in the elderly. Current methods, such as DXA, for diagnosing osteoporosis and predicting the risk of vertebral failure, are often not accurate thereby preventing those patients at risk from receiving adequate treatment. Robust fracture prediction models for vertebral fracture risk should not only include BMD, as measured by DXA, but should incorporate a wide range of factors including bone geometry, bone mineral distribution within the vertebral body, daily living activities, and spine musculature. One promising technique is finite element modeling, which has been developed over the past several decades and implements clinical imaging, such as quantitative computed tomography (QCT), and engineering fundamentals to more accurately predict the risk of fracture. Other imaging tools that assess bone mineral distribution and structure at the microscopic level include micro-CT or high-resolution peripheral QCT (HR-pQCT). These newer techniques hold the promise of more accurate diagnosis of osteoporosis and those at risk for vertebral insufficiency fractures before they occur.

Osteoporosis, characterized by bone loss, bone micro-architectural deterioration, abnormal changes in bone matrix, and the presence of microcracks, leads to reduced skeletal strength and an increase in fracture risk.[1] With the rapid growth of the aging population in the United States, the incidence and prevalence of vertebral fractures due to this condition will reach epidemic proportions in the next decades. Despite fracture risk increasing with age, and affecting both men and women,[2] there is no clear prevention for vertebral fractures, with current diagnostic tools incompletely characterizing fracture prediction and risk. This article discusses current methodologies used for prediction of vertebral fractures with additional evidence associated with fractures and spine deformity, and future considerations to prevent bone failure.

1. QCT/FEA

While DXA is currently considered the goal standard for osteoporosis diagnosis and fracture risk prediction, it is important to note the shortcomings of using areal BMD (aBMD) as a single unit of merit and the sole predictor for vertebral fractures. The accuracy of DXA-measured aBMD is affected by osteophytes, vascular calcifications and the presence of scoliosis. Additionally, studies have shown DXA as an imperfect tool for predicting fracture risk, missing a significant number of the people who go on to have an osteoporotic bone failure, and reporting a high percentage of subjects with t-scores better than the osteoporotic threshold of −2.5 presenting with fractures.[3] For this reason, quantitative computed tomography-based finite element analysis (QCT/FEA)

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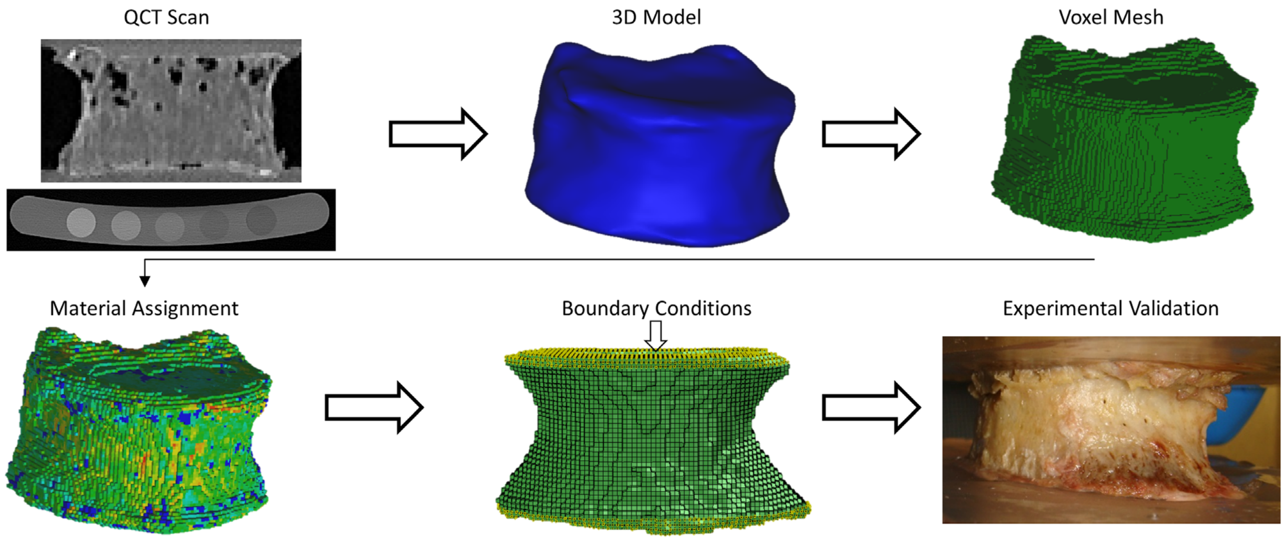

Fig 1 – Overview of QCT-based FEA modeling. CT scans with a calibration phantom (QCT) are used to get patient-specific properties. DICOM images from the scans are then segmented to obtain a 3D model, and after meshing the model with voxel elements, material properties are assigned to each element based on Hounsfield unit (HU) values from the images. Boundary conditions mimicking various loading conditions of daily living are then applied to the model to obtain fracture properties.

has been implemented to develop more robust tools that can account for the three-dimensional bone geometry as well as volumetric distribution of minerals, while providing information about the location of the fracture within the bone resulting from various normal and traumatic loading conditions.[4–6] This may allow for a more accurate future state of predicting the risk and location of vertebral fractures.

QCT-based FEA has been widely reviewed in the literature, however, a brief description of the process is provided here (Figure 1). A CT scan comprised of voxels ranging in gray scale values [Hounsfield units (HU)] is used as the template for creating a patient-specific finite element (FE) model. When developing voxel-based FE models, the CT voxels are converted to FE elements and material properties are assigned to each element depending on tissue type. These material properties are based on empirical equations from the literature relating BMD,[7] obtained using a calibration phantom and HU values within the element, to Young's modulus. Depending on the type of load to be modeled, boundary conditions are implemented to simulate physiological loading conditions. In order to simulate fracture of the bone, failure criteria equations are used which, when exceeding a user-defined set limit (strain, stress, pressure, etc.) in the element, will either reduce the elements' stiffness,[8] remove it from the model,[9] yielding the vertebral fracture load. A different approach used for modeling fracture in vertebra is QCT/X-FEM, which contrary to the above methods, is able to model the discontinuities associated with the propagating crack.[10]

When developing fracture predictive models it is important to consider the clinical translational aspects, and as such, parameters implemented in research need to represent those used in the clinical setting. A main input in model development is the CT scan acquired of the patient, which contains patient-specific bone geometry and bone mineral distribution. It is well established that CT acquisition settings (current (mA), voltage (kVp), and image reconstruction algorithms) can affect the HU value of the CT voxels. When developing fracture predictive tools using QCT-based FEA, imaging protocols that provide improved bone contrast and image quality are desired, so that bone geometry can be easily segmented and bone tissue local inhomogeneities can be certainly observed. However, previous studies have shown that protocols usually implemented in the research community, which differ from those used during routine clinical examinations, might lead to different bone fracture properties estimations.[11–13] It is important for researchers and the research community to account for these differences and implement methodologies that can be translated to the clinic, either by standardizing CT acquisition protocols or implementing additional techniques that consider these differences.

While validated QCT-based FEA modeling can already be implemented clinically, the time and computing power necessary to accurately create these models and obtain fracture properties is still costly and time prohibitive. As these techniques become more refined and imaging and computing processes improve, QCT-based FEA modeling may become a reality in the clinical setting for patient-specific fracture properties prediction.

2. Micro-CT and HR-pQCT-based FEA

Unlike QCT, micro-CT and high-resolution peripheral quantitative computed tomography (HR-pQCT) can assess the micro-architectural morphology of bones. Models developed using these imaging modalities can range in resolutions as high as 5 μm (micro-CT) and 80 μm (HR-pQCT). Additionally, cortical and trabecular bones can be analyzed independently to assess structural parameters such as cortical porosity (Ct. Po), cortical thickness (Ct.Th), number of trabeculae (Tb.N), trabecular thickness (Tb.Th), and trabecular separation (Tb.Sp). Several studies have implemented these imaging