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Morphology based anisotropic finite element models of the proximal femur validated with experimental data

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ABSTRACT

Finite element analysis (FEA) of bones scanned with Quantitative Computed Tomography (QCT) can improve early detection of osteoporosis. The accuracy of these models partially depends on the assigned material properties, but anisotropy of the trabecular bone cannot be fully captured due to insufficient resolution of QCT. The inclusion of anisotropy measured from high resolution peripheral QCT (HR-pQCT) could potentially improve QCT-based FEA of the femur, although no improvements have yet been demonstrated in previous experimental studies.

This study analyzed the effects of adding anisotropy to clinical resolution femur models by constructing six sets of FE models (two isotropic and four anisotropic) for each specimen from a set of sixteen femurs that were experimentally tested in sideways fall loading with a strain gauge on the superior femoral neck. Two different modulus–density relationships were tested, both with and without anisotropy derived from mean intercept length analysis of HR-pQCT scans.

Comparing iso- and anisotropic models to the experimental data resulted in nearly identical correlation and highly similar linear regressions for both whole bone stiffness and strain gauge measurements. Anisotropic models contained consistently greater principal compressive strains, approximately 14% in magnitude, in certain internal elements located in the femoral neck, greater trochanter, and femoral head.

In summary, anisotropy had minimal impact on macroscopic measurements, but did alter internal strain behavior. This suggests that organ level QCT-based FE models measuring femoral stiffness have little to gain from the addition of anisotropy, but studies considering failure of internal structures should consider including anisotropy to their models.

1. Introduction

Finite element (FE) models of the proximal femur derived from clinical Quantitative Computed Tomography (QCT) rely on realistic material properties to accurately predict patient-specific bone strength *in vivo* [1]. The trabecular bone within the proximal femur exhibits anisotropic mechanical behavior due to its complex microarchitecture, which is difficult to resolve at clinical resolutions and therefore unavailable *in vivo*. Several studies have attempted to construct anisotropic FE models of the proximal femur with widely varied methods [2–9], however there is little agreement in the resulting outcome or the optimal approach, which can be partly attributed to a shortage of experimental validation studies focusing on anisotropy. Hence, the question remains whether anisotropic material properties improve QCT-based FE models of the proximal femur, which is highly relevant to the overall goal of translating this modeling technique into clinical practice.

The anisotropy of large anatomical regions can be measured incrementally from subsections taken from high-resolution peripheral QCT (HR-pQCT) scans with voxel sizes below 100 µm. The morphological anisotropy can be described using a fabric tensor [10], which can be measured using surface analysis tools such as the mean intercept length (MIL) method [11]. When implemented

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in organ-level FE models, elements representing trabecular bone are typically assigned orthotropic material properties. This requires a realistic degree of anisotropy (DA) and directionality that accurately reflects the mechanics of the underlying microarchitecture. The DA represents the ratio of material stiffness between orthogonal planes, while the directionality represents the three-dimensional orientation of those planes, also referred to as the material's principal directions. The anisotropy of an orthotropic stiffness tensor can be described using its eigenvalues and eigenvectors. The ratios between the first and second, and first and third eigenvalues together describe the DA of the tensor, while the eigenvectors describe its directionality.

While a variety of modulus–density relationships exist in the literature [12] no consistent model has been used in studies developing anisotropic organ-level models of the femur. A study by San Antonio et al. [5] constructed anisotropic femur models from QCT scans by combining the modulus–density relationship proposed by Keller [13] with the FE-based, density-DA relationships proposed by Yang et al. [14] and found differences in strain up to 14% between isotropic and anisotropic models. Another study, using directionality determined using simulated mechanical loading of micro-FE models of small bone volumes within the femur [15], found an average 26% decrease in whole bone stiffness ($n = 7$) between model types when loaded in a sideways fall, but no improvement in correlation between experimental and FE predicted whole bone stiffness [2]. An alternative approach combines fabric tensors with CT density to calculate the element compliance tensor [16]. This has improved proximal femur stiffness prediction by 4% and 42% for a single healthy and osteoporotic specimen, respectively, when compared to a micro-FE model gold standard [4]. Another study, using similar fabric anisotropy, found an improvement in ultimate strength prediction over isotropic models for stance but not sideways fall loading for 36 experimentally tested femur specimens [3], suggesting, conversely, that anisotropy does not improve these organ-level FE models in sideways fall configuration. Thus it remains unclear which anisotropic model is optimal for the proximal femur, and more specifically, which strategy results in the best prediction of whole bone stiffness. Furthermore, it is also unclear which modulus–density relationship and material mapping strategy provides an optimal combination with anisotropic properties, with a variety of previously published combinations available [3,5,6].

The purpose of this study was to investigate two important knowledge gaps surrounding anisotropic organ-level FE modeling of the femur. The first was to determine whether anisotropy improves whole bone stiffness prediction, instead of just ultimate strength, since stiffness is a closer indicator of whether the energy absorption properties are being modeled correctly, which is particularly important in an impact loading event such as a sideways fall [17]. The second was to determine the effect of combining morphometric anisotropy with different modulus–density relationships and material mapping strategies that have yielded good whole bone and local validation outcomes. This was done by testing two material mapping strategies that represent extremes of possible modulus–density relationships and partial volume artifact correction, instead of arbitrarily selecting from one of the numerous available methods. We hypothesized that anisotropic material properties will result in different local stress and strain behavior and improve the correlation between the FE models and experimental results.

2. Materials and methods

2.1. Specimens and experimental testing

A detailed description about the experiment has been published elsewhere [18]. Briefly, sixteen fresh frozen human femurs (15 women, 1 man, average age: 76 +/− 10 years) were acquired from a commercial tissue donation bank (National Disease Research Interchange, Philadelphia, PA) with no reported history of musculoskeletal or metabolic disease. Specimens were thawed at room temperature wrapped in saline-soaked gauze and scanned in HR-pQCT (XtremeCT, Scanco Medical, Switzerland) at 41 µm voxel size calibrated with a standardized hydroxyapatite phantom (0, 100, 200, 400 and 800 mg HA/cm^3). Specimens were potted in polymethylmethacrylate (PMMA), with a hinge at the distal ends that allowed free rotation in the anatomical frontal plane. The specimens were also imaged using dual-energy X-ray absorptiometry (DXA) as described by Gilchrist et al. [19]. PMMA pads, approximately 4 cm in diameter and 1.5 cm in height, were molded to the greater trochanter and femoral head for each specimen and acted as loading surface for the material testing system (8874, Instron Inc., Norwood, MA). Specimens were tested in a fall configuration [20] (Fig. 1), and were preloaded to 100 N over 5 repetitions then compressed at 0.5 mm/s up to half of the failure load predicted using areal bone mineral density (aBMD) [21]. Whole bone stiffness was calculated from load–displacement data adjusted for estimated cartilage deformation at the femoral head and machine compliance, which was measured directly by applying known loads to the frames and fixators [22]. A separate FE model was used to estimate cartilage compliance as described by Helgason et al. [18], assuming the femoral head was a spherical shape with a cartilage layer 1.47 mm thickness, based on average thickness of harvested specimens in a previous study [23]. Average cartilage deformation was between 0.11 mm and 0.20 mm at max experimental load [18]. Local changes in surface strain were measured with a rosette strain gauge (FRA-2-11-3LT Tokyo Sokki Kenkyujo Co., Tokyo, Japan) mounted on the anterior–superior surface of the femoral neck using cyanoacrylate and a standard mounting protocol [24]. This experimentally validated method has been effective for measuring external strains at this critical location known for fracture initiation [25], and was therefore useful for comparing the local mechanical behavior predicted by models with different material properties.

2.2. Continuum finite element models

The base FE models used in the present study are the same as the ones used in Helgason et al. [18]. The description of the FE mesh generation is only briefly described here for clarity. Reconstructed HR-pQCT scans were resampled to clinical CT resolution (0.615 mm) and segmented semi-automatically by identifying the periosteal surface (ITK SNAP, v2.2.0). Resampled HR-pQCT gray levels were converted to ash density based on hydroxyapatite (HA) content according to $\rho_{ash} = (\text{mgHA}/1000 + 0.09)/1.14$ [25]. Segmented images were meshed into 10-node tetrahedral elements (Ansys Workbench, v14.0, Altair Engineering Inc., USA). A mesh convergence analysis determined that 2.0 mm was the best compromise between computation cost and relative accuracy, as smaller elements were found to increase whole bone stiffness by approximately 4% at the cost of nearly eight times the computational time. Element modulus of elasticity was assigned using nodal interpolation of ash density values [26] and then averaging the nodal modulus into a single value per element which corresponds to material mapping method A according to the study of Helgason et al.. When selecting candidates for modulus–density-relationships, only studies that effectively captured both local deformation and whole bone properties from *in vitro* validation experiments were considered [25–29]. Two previously validated relationships were selected from studies that represent the softest [29] and stiffest [28] extremes. In the first, the ash density of each element was adjusted to apparent density according to $\rho_{ash} = 0.6\ \rho_{app}$ [25] then converted to a Young's modulus using the relatively