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Mapping anisotropy improves QCT-based finite element estimation of hip strength in pooled stance and side-fall load configurations

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ABSTRACT

Hip fractures are one of the most severe consequences of osteoporosis. Compared to the clinical standard of DXA-based aBMD at the femoral neck, QCT-based FEA delivers a better surrogate of femoral strength and gains acceptance for the calculation of hip fracture risk when a CT reconstruction is available. Isotropic, homogenised voxel-based, finite element (hvFE) models are widely used to estimate femoral strength in cross-sectional and longitudinal clinical studies. However, fabric anisotropy is a classical feature of the architecture of the proximal femur and the second determinant of the homogenised mechanical properties of trabecular bone. Due to the limited resolution, fabric anisotropy cannot be derived from clinical CT reconstructions. Alternatively, fabric anisotropy can be extracted from HR-pQCT images of cadaveric femora. In this study, fabric anisotropy from HR-pQCT images was mapped onto QCT-based hvFE models of 71 human proximal femora for which both HR-pQCT and QCT images were available. Stiffness and ultimate load computed from anisotropic hvFE models were compared with previous biomechanical tests in both stance and side-fall configurations. The influence of using the femur-specific versus a mean fabric distribution on the hvFE predictions was assessed. Femur-specific and mean fabric enhance the prediction of experimental ultimate force for the pooled, i.e. stance and side-fall, (isotropic: $r^2 = 0.81$, femur-specific fabric: $r^2 = 0.88$, mean fabric: $r^2 = 0.86$, $p < 0.001$) but not for the individual configurations. Fabric anisotropy significantly improves bone strength prediction for the pooled configurations, and mapped fabric provides a comparable prediction to true fabric. The mapping of fabric anisotropy is therefore expected to help generate more accurate QCT-based hvFE models of the proximal femur for personalised or multiple load configurations.

1. Introduction

Hip fractures lead to mortality, morbidity and high health care costs. The effective prevention of hip fractures requires an accurate diagnosis of osteoporosis, which is currently based on measurement of areal bone mineral density (aBMD) measured by dual energy x-ray absorptiometry (DXA). However, the majority of fractures occur in patients with aBMD above the diagnostic threshold [1–3]. This reflects the fact that aBMD alone has high specificity but low sensitivity. Alternatively, Kopperdahl et al. [4] defined femoral strength thresholds, which were based on finite element (FE) analysis, equivalent to aBMD diagnostic criterion. Based on clinical data, a combination of FE-based femoral strength and aBMD identified more individuals at high fracture risk than aBMD alone [4]. FE analysis was also shown to estimate the failure load more accurately than radiography, DXA or quantitative computed tomography (QCT) [5]. FE approaches based on computer tomography (CT) have been applied extensively throughout the past decades to simulate the mechanical behaviour of the proximal femur [6–17]. With availability of quantitative CT (QCT) in hospitals, QCT-based FE analyses have been increasingly included in hip studies and clinical evaluation of drug treatments against osteoporosis [18,19]. To evaluate the ability in predicting bone strength, QCT-based FE models of the proximal femur were validated based on mechanical tests in which proximal femora were tested in the one-legged stance [20–24] or unprotected side-fall configuration [10,14,17,25–27]. To a lesser extent, QCT-based FE models of the proximal femur were validated in both configurations [5,12,28,29].

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Homogenised, voxel-based FE (hvFE) models can be generated by converting re-coarsened QCT image voxels to hexahedral cubic elements. A homogenised material property is assigned to each element that is based on a statistically representative volume element (RVE) of the material [30]. Homogenised elastic and yield properties are best predicted by bone volume fraction (BV/TV) and fabric anisotropy of trabecular bone [31,32], but QCT images are lacking information on trabecular microstructure due to the limited resolution. Therefore, bone is usually assumed to behave isotropically in QCT-based FE models of the proximal femur [33]. Several approaches were proposed to extract fabric tensors from QCT images, but fabric anisotropy cannot be derived accurately [34–36]. On the other hand, anisotropic homogenised FE models based on high resolution peripheral QCT (HR-pQCT) improved the prediction of stiffness [11] and experimental bone strength [13,37]. Enns-Bray et al. [14,15] proposed a method to map femoral anisotropy from HR-pQCT into QCT-based FE models by using the direct mechanics [38] and then the mean intercept length (MIL) method [39,40]. However, both studies involved only linear FE analyses of the proximal femur in a single load configuration. Little is known about the effect of including HR-pQCT derived fabric anisotropy into QCT-based, geometrically and materially non-linear hvFE of the human proximal femur in different loading configurations.

Alternatively, trabecular fabric anisotropy can be estimated from the HR-pQCT image of a dissected femur with multiple approaches [41–45]. Taghizadeh et al. [45] showed that averaged fabric anisotropy is a close approximation of patient-specific anisotropy and can be used in FE models. Chandran et al. [46] used a more systematic approach by selecting a mean femur with the closest shape and intensity to the femurs of a database ($n = 71$). To our best knowledge, none of aforementioned approaches were tested for QCT-based hvFE models. We employed the latter single-template approach to obtain the natural fabric distribution of a mean human proximal femur and to build anisotropic hvFE models using CT scans of clinical quality. In this study, fabric anisotropy from the HR-pQCT images of the femur-specific and the mean femur were mapped to QCT-based hvFE models and non-linear FE analyses were performed to compute stiffness and strength.

The goal of this study was to assess the effect of including femur-specific or mean fabric anisotropy on the predictive ability of non-linear QCT-based hvFE models of the human proximal femur, as compared with experimentally measured stiffness and strength in two loading configurations.

2. Materials and methods

Seventy-two human proximal femora (35 males, 37 females, age 77 ± 11 years, range 46–96 years) were obtained from body donors prepared by the Division of Anatomy of the Medical University of Vienna. Collection and preparation procedures were approved by the ethics commission of the Medical University of Vienna. Informed consent was obtained from all donors. Sample preparation, imaging and mechanical testing of femora were explained in detail elsewhere [12,13]. According to the calculated T-score from DXA, 29 of the femora were osteoporotic, 22 were osteopenic and 21 were normal. The procedures are explained here briefly.

2.1. Imaging and testing

QCT scanning

Each femur was scanned with a clinical QCT (Brilliance 64, Philips, Germany; intensity: 100 mA; voltage: 120 kV; voxelsize: $0.33 \times 0.33 \times 1.0\,\mathrm{mm}^3$) with a calibration phantom (BDC phantom, QMR GmbH, Germany) for converting the Hounsfield unit (HU) scale to equivalent BMD scale in mgHA/cc. The BMD range was restricted to −100 and 1400 mgHA/cc to decrease the effect of residual air bubbles and other artefacts [12].

HR-pQCT scanning

Each femur was also scanned with an HR-pQCT (Xtreme CT, Scanco, Switzerland; intensity: 900 µA, voltage: 60 kVp, voxel size: $0.082 \times 0.082 \times 0.082\,\mathrm{mm}^3$). The scanned images were converted from HU to BMD scale following the manufacturer's calibration procedure. Similarly to QCT, the BMD range was restricted to −100 and 1400 mgHA/cc [13].

Mechanical tests

A femur of each pair was randomly selected to be tested in a one-legged stance and side-fall configuration. In stance configuration, the cranial portion of the femoral head was embedded in polyurethane (PU). In side-fall configuration, the medial portion of the femoral head and the lateral portion of the greater trochanter were embedded in PU. The shaft was fixed in both configurations. A custom-made bearing was used to reduce transverse forces/moments by allowing rotation and 2 translations perpendicular to the loading axis. Each femur was compressed to failure by a servo-hydraulic testing machine (Mini-Bionix, MTS systems, USA) at a rate of 5 mm/min. Femoral ultimate force was defined as the maximum compressive load. The stiffness was the maximum slope of the linear part of the load-displacement curve [12].

2.2. QCT-based hvFE model generation

The QCT images of the femora were cropped proximally, upsampled along the scanning axis to isotropic voxel size of 0.33 mm, rotated to an experimental position (stance or side-fall configuration), masked and coarsened to a resolution of 3 mm. A filling out algorithm was used to find the outer contour of each image. Image processing was done with the software MEDTOOL (www.dr-pahr.at). Due to the equivalent performance of voxel and smooth mesh FE models in a recent QCT-based clinical study [47], it was decided to use the simpler voxel mesh in this study. An hvFE model of each femur was therefore generated by converting image voxels to linear hexahedron elements. Each voxel was assigned its local voxel BMD values. The calibration relationship between BMD and BV/TV is provided in Dall'Ara et al. [12].

Image registration

Grayscale HR-pQCT images were segmented in the original coordinate system with the manufacturer's software (Scanco Medical, Switzerland). Both grayscale and segmented HR-pQCT images were pre-oriented (left/right and top/bottom) along the experimental position by using the flipping function in MIPAV software (http://mipav.cit.nih.gov). Rotated QCT images were upsampled to 82 µm isotropic voxels. In the following description of the image registration methodology, HR-pQCT and QCT images refer to pre-oriented HR-pQCT and upsampled rotated QCT images, respectively.

A mean femur closest to all the femurs of the available collection was selected. To do so, each donor femur image was registered to all the femora to quantify the distance metric based on the logarithm of the left stretch tensor of the gradient of the non-rigid transformation [46]. Based on this calculation, the femur with the minimal cumulated distance metric to all other femora was chosen to be the mean femur, which was then excluded from the analysis. Therefore, the femur dataset included the remaining 71 femora. Subsequently, image registrations were performed by using the software ELASTIX [48] to calculate two types of transformations.

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