Medical Engineering and Physics 000 (2017) 1–9

Contents lists available at ScienceDirect

Medical Engineering and Physics

journal homepage: www.elsevier.com/locate/medengphy

MicroCT-based finite element models as a tool for virtual testing of cortical bone

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ARTICLE INFO

Article history:
Received 30 June 2016
Revised 27 March 2017
Accepted 26 April 2017
Available online xxx

Keywords:
Biomechanical testing
MicroCT-based FEM
Femur
Virtual testing

ABSTRACT

The aim of this study was to assess a virtual biomechanics testing approach purely based on microcomputed tomography (microCT or μCT) data, providing non-invasive methods for determining the stiffness and strength of cortical bone. Mouse femurs were μCT scanned prior to three-point-bend tests. Then microCT-based finite element models were generated with spatial variation in bone elastoplastic properties and subject-specific femur geometries. Empirical relationships of density versus Young's moduli and yield stress were used in assigning elastoplastic properties to each voxel. The microCT-based finite element modeling (μFEM) results were employed to investigate the model's accuracy through comparison with experimental tests. The correspondence of elastic stiffness and strength from the μFE analyses and tests was good. The interpretation of the derived data showed a 6.1%, 1.4%, 1.5%, and 1.6% difference between the experimental test result and μFEM output on global stiffness, nominal Young's modulus, nominal yield stress, and yield force, respectively. We conclude that virtual testing outputs could be used to predict global elastic-plastic properties and may reduce the cost, time, and number of test specimens in performing physical experiments.

1. Introduction

Knowledge of the elastic, yield, and failure properties of trabecular and cortical bone tissue is very useful in investigating the skeletal effects of drug treatments, aging, and disease. Mechanical testing has been considered as a standard tool for investigating various effects on the extrinsic (stiffness, yield force etc.) and intrinsic (Young's modulus, yield stress etc.) properties of bone for decades [1]. However, recent advances in medical image resolution and computer processor speed provide alternatives, reducing the need for invasive mechanical testing and replacing it with computational biomechanics to simulate in-vivo bone-loading conditions. This advancement provides the opportunity to assess bone strength through non-invasive methods, thus reducing the cost, time, and number of experiments [2].

The greatest challenge in the μFE modeling of bone is assigning the tissue-level material properties. There are a number of approaches in computational biomechanics for inputting the microscale bone material properties. One is using nanoindentation to measure bone material properties, such as stiffness and Young's modulus, for further μFE simulation [8,9]. In this method, the elastic properties of each element are assigned using the nanoindentation result as an input in the μFE model. Plasticity models must be included when the strains are larger than approximately 0.7%. The Pistoia criterion has been used to calculate postelastic parameters, such as whole bone failure [10,11]. In this method, empirical relationships have been developed to determine the failure load from linear elastic analysis. According to this criterion, failure occurs when more than 2% of tissue has been strained beyond 0.7% [11]. It should be noted that the elastoplastic models of bone at the microscopic level are distinct from those at the macroscopic level. Schwiedrzik et al. [12] carried out micropillar compression tests and reported that the plastic deformation of bone on a lamellar level was initiated at strains of magnitude 10–20%. Another alternative in assigning material properties to the model is considering μCT gray value distribution. As medical imaging improves, local material property assignment is achieved by converting grayscale value information into the material properties of the bone. The result is a heterogeneous specimen-specific FE model with non-uniform material property distribution that improves the accuracy of the μFE bone model. Bourne and Van Der Meulen [13] found, using a non-uniform μFE model for trabecular bone, improved predictions from the simulations.

Within the past 25 years, scientists have investigated the trabecular bone morphology followed by developing new three-dimensional finite element modeling (FEM) technologies based on microcomputed tomography (μCT) [3,4]. MicroCT-based FEM

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http://dx.doi.org/10.1016/j.medengphy.2017.04.011
1350-4533/

(μFEM) is widely used in medical research to analyze the trabecular bone structure at microscale, simulating microstructure stiffness and strength, and obtaining stress and strain distributions [5]. When the model is properly calibrated and validated, μFEM can be employed to reduce the amount of experimental testing required. Furthermore, μFEM offers benefits that are difficult to obtain from conventional mechanical testing, such as finding the behavior of bone under different multidirectional loading, and can be used in many configurations [6,7].

Cortical bone has often been considered homogeneous and simpler to describe than cancellous bone. Still, the large spread in resulting from mechanical tests for cortical bone is challenging [14]. Even with the development of advanced test techniques, it is still of interest to carry out the simple mechanical testing of cortical bone to get quick access to global performance. Typical examples are compression, tension, torsion, and bending tests. Of these, the three point bend test is easiest to use for long bones from rodents such as mice, requiring little manufacturing before the specimen is placed in the test machine [15]. Nominal Young's modulus can be obtained from such tests, using beam theory [16].

Validated specimen-specific cortical bone μFE models with non-uniform structures and materials are scarce in the literature [17]. In the current study, three-point-bend tests of mouse femur are carried out to find material properties of bone. All bones are μCT scanned prior to testing. Using the scan data for FE model generation, we can investigate the accuracy of global stiffness and strength predictions. The FE models account for spatial variation in bone elastoplastic properties and subject-specific femur geometries. We used empirical relationships of apparent density versus Young's moduli and yield stress to assign the material properties of each voxel [18–20]. As first pointed out by Schriefer et al. [21] and investigated by Kourtis et al. [22] with finite element analysis (FEA) of homogenous and perfectly cylindrical beams, three-point-bend tests consist of deformations in addition to beam bending and shear: the ovalization of the cortical shaft and local indentation at the load ram and supports. This is accounted for herein.

The aim of this study was to assess a virtual biomechanics testing approach where all input were obtained from detailed CT scans, i.e. predicting stiffness and strength only using numerical methods. The nonlinearity of both geometry and material properties was considered. Voxel-specific material properties were used instead of considering the average material properties for all elements and anatomic geometries instead of a simplified cylindrical geometry [23].

2. Materials and methods

2.1. Experimental animals

Twelve wild-type (WT) and 12 knockout (KO, lacking the gastric proton pump) female mice aged approximately 1 year and weighing approximately 29.7 and 27.4 g, respectively, were used in the current study. Note that these specimens are a part of a larger study addressing the possible link between extensive use of anti-acid stomach medication (proton pump inhibitors) and increased bone fracture risk. The KO mice mimic the gastric effect of the drug. See Aasarød et al. [24] for further details on medical aspects. The scope of the current study does not focus on comparison between the WT and KO groups, but includes some observations related to differences in global stiffness and strength. The reason for including both groups was to have a wider range of femur geometries and bone densities (e.g., the WT femur cross-sections were significantly larger than those for the KO). With this, we get a broader basis for assessing μFEM predictability. The Norwegian National Animal Research Authority approved the study. The mice were given standard diets for 12 months. After the mice were sacrificed, femurs were dissected from the body, cleaned of soft tissue, and μCT scanned. The right femurs were wrapped in bands saturated in 4% phosphate buffered saline (PBS) solution and stored at −80 °C until test day.

2.2. MicroCT recording, elasticity-density, and yield stress–density relationships

The femurs were scanned at 5 μm isotropic resolutions with SkyScan1172 (Skyscan, Kontich, Belgium), with a 0.5 mm aluminum filter, a current of 163 mA, and a voltage of 61 kV. The datasets were reconstructed using NRecon software (Skyscan). Image processing and finite element meshing were performed using commercial software (Mimics 16.0, Materialise, Leuven, Belgium). The bone properties were assigned based on μCT grayscale values converted to Hounsfield units using a calibration phantom. A linear relationship was assumed for Hounsfield units and bone apparent density [25]. Fig. 1a shows an example of the apparent density distribution of the cortical shaft (excluding metaphysis and epiphysis) for one specimen. The peak is slightly below the typical apparent density of 1.8 g/cm^3 employed for cortical bone [19]. It is noted that there is a significant scatter in the values and the hypothesis of a constant (or a narrow band) density for cortical bone can be questioned. For all of our FE analyses, a nonlinear relationship proposed by Wirtz et al. was considered to evaluate cortical bone Young's modulus in longitudinal direction from apparent density: $E = 2.065\rho^{3.09}$ ((GPa), density in g/cm^3) [18]. This relationship is obtained by combining the relationships presented by Lotz et al. [19] and Abendschein and Hyatt [26] to provide an improved equation linking cortical bone apparent density and Young's modulus. Poisson's ratio was set to 0.3. To check the influence of alternative relationships, the following were employed for some specimens: $E = -13.43 + 14.261\rho$ (GPa) [19] and $E = 2.79\rho^{2.58}$ (GPa) [27]. In addition, employing a relationship derived for cancellous bone [34], extrapolating to our cortical bone density regime, was investigated for a few specimens. The finite element yield stress assignment was based on Cory et al., which provided the following relationship for the compression yield stress of cortical bone: $\sigma_y = 53.4\rho^{1.64}$ (MPa) [20]. Using the nonlinear relationship from Wirtz et al. [18], the distribution of Young's modulus in the mid-span cross-section for one specimen is shown in Fig. 1b. All cross-sections have an elliptic shape at mid-length with a relatively constant thickness. The cross-section slenderness d/t is approximately 5, i.e., the femoral shaft cross-section is quite compact as opposed to a thin-walled cross-section.

2.3. Mechanical testing

Prior to testing, all samples were thawed and rehydrated in PBS solution for 24 h at room temperature. Three-point-bending tests were conducted with a material-testing machine (Model 5944, 2 kN single column machine, Instron Corp., Illinois, USA). The posterior surfaces of the femurs were facing downward on supports 8 mm apart. A triangular plunger provided the load application at the mid-span of the specimens (Fig. 2). To establish the contact between the plunger and the sample and to prevent sample rotation before testing, the plunger was moved downward slowly until the preloading force reached 0.7 N. Subsequently, the load was applied on the anterior surface of the femurs at a speed of 0.5 mm/min until fracture [28].

2.4. Data acquisition and statistical analysis

Force–displacement data were recorded at 10 Hz, providing force–displacement graphs. The yield force (F_y; N) and stiffness (S; N/mm) were calculated using these graphs. Two examples are

Please cite this article as: M. Ramezanzadehkoldeh, B.H. Skallerud, MicroCT-based finite element models as a tool for virtual testing of cortical bone, Medical Engineering and Physics (2017), http://dx.doi.org/10.1016/j.medengphy.2017.04.011