Clinical Biomechanics 30 (2015) 703–712

Contents lists available at ScienceDirect

Clinical Biomechanics

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

Prediction of local proximal tibial subchondral bone structural stiffness using subject-specific finite element modeling: Effect of selected density–modulus relationship☆

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ARTICLE INFO

Article history:
Received 13 August 2014
Accepted 7 May 2015

Keywords:
Finite element modeling
Elastic modulus of bone
Density–modulus relationships for bone
Proximal tibia
Model validation

ABSTRACT

Background: Quantitative computed tomography based subject-specific finite element modeling has potential to clarify the role of subchondral bone alterations in knee osteoarthritis initiation, progression, and pain initiation. Calculation of bone elastic moduli from image data is a basic step when constructing finite element models. However, different relationships between elastic moduli and imaged density (known as density–modulus relationships) have been reported in the literature. The objective of this study was to apply seven different trabecular-specific and two cortical-specific density–modulus relationships from the literature to finite element models of proximal tibia subchondral bone, and identify the relationship(s) that best predicted experimentally measured local subchondral structural stiffness with highest explained variance and least error.

Methods: Thirteen proximal tibial compartments were imaged via quantitative computed tomography. Imaged bone mineral density was converted to elastic moduli using published density–modulus relationships and mapped to corresponding finite element models. Proximal tibial structural stiffness values were compared to experimentally measured stiffness values from in-situ macro-indentation testing directly on the subchondral bone surface (47 indentation points).

Findings: Regression lines between experimentally measured and finite element calculated stiffness had R^2 values ranging from 0.56 to 0.77. Normalized root mean squared error varied from 16.6% to 337.6%.

Interpretation: Of the 21 evaluated density–modulus relationships in this study, Goulet combined with Snyder and Schneider or Rho appeared most appropriate for finite element modeling of local subchondral bone structural stiffness. Though, further studies are needed to optimize density–modulus relationships and improve finite element estimates of local subchondral bone structural stiffness.

1. Introduction

Various research have suggested that subchondral bone is involved in the initiation and progression of cartilage degeneration and eventual osteoarthritis (OA). OA-related subchondral bone alterations are believed to increase local structural stiffness of subchondral bone (i.e., stiffness directly at the subchondral bone surface), thereby reducing subchondral bone's ability to transfer strain energy, leading to more energy being transferred through overlying cartilage (Radin et al., 1972). Stiffness gradients arising from variations in local subchondral bone structural stiffness are also thought to increase cartilage shear stresses (Radin and Rose, 1986). As well, local subchondral bone cyst presence is thought to increase intra-osseous stress distributions, leading to pain and disability (McErlain et al., 2011). Current theories regarding the role of subchondral bone in OA, though, are largely based upon animal or ex vivo cadaveric studies. Animal studies of OA initiation and progression, however, may not be applicable to the human OA process. There is also uncertainty regarding the validity of ex vivo cadaveric studies given that clinical OA status or pain symptoms are generally unknown. In order to better understand the role of subchondral bone in OA, in vivo methods are needed to monitor subchondral bone mechanical property variations in people living with OA.

☆ Funding sources: National Science and Engineering Research Council of Canada (NSERC).

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http://dx.doi.org/10.1016/j.clinbiomech.2015.05.002
0268-0033/

Subject-specific finite element (FE) modeling has potential to clarify the role of subchondral bone alterations in knee osteoarthritis (OA) initiation, progression, and pain initiation. These models can be evaluated computationally (and noninvasively) to assess local structural stiffness, stress and strain distributions, and various other mechanical parameters in vivo which cannot currently be measured experimentally. Quantitative Computed Tomography (QCT) has been widely used to provide both bone geometry and varying material properties for subject-specific FE models (referred to as QCT-FE). QCT images can be obtained rapidly (thereby minimizing noise due to patient movement) with relatively small isotropic voxel sizes (~0.5 mm). At the knee joint, ionizing radiation is also low due to the low presence of radiosensitive tissues (Johnston et al., 2009). Material properties (elastic modulus, E) are generally defined using imaged bone mineral density (BMD) and density–modulus (E-BMD) equations, which are typically derived from isolated compression testing of excised bone samples (Helgason et al., 2008a). The selected E-BMD equation is a key factor controlling FE model accuracy, as illustrated in a study by Austman et al. (2008). In this study, six different E-BMD equations reported in the literature were used to predict ulnar surface strain. Errors in surface strain prediction ranged widely from −15.3% to +92.4%. As such, appropriately selected E-BMD equations are critical to ensure accurate estimates of E and accurate QCT-FE models.

To our knowledge, only three subject-specific QCT-FE models have been used at the proximal tibia (Edwards et al., 2013; Gray et al., 2008; McErlain et al., 2011). One model was used to evaluate the possible role of subchondral cysts in OA-related pain (McErlain et al., 2011), but mechanical behavior was not validated. The other two models were developed and validated (via strain gauging Gray et al., 2008 and stiffness and strength testing Edwards et al., 2013) to simulate mechanical behavior under axial compression, bending and/or torsional loading. Though, in both studies, FE model validation was limited to strain and/or stiffness measures of bone located distal to the subchondral surface (~20 mm distal), not directly at the subchondral bone surface, which is most relevant for studies of OA initiation and progression as this region has the greatest potential to negatively affect overlying cartilage (Brown et al., 1984). As well, all three studies used E-BMD equations specific to bone from diaphyseal and/or proximal tibial epiphyseal and metaphyseal sites (Morgan et al., 2003; Rho et al., 1995), which may not be applicable for subchondral cortical and highly heterogeneous trabecular bone in the subchondral region. It is currently unknown which E-BMD relationship is most appropriate for characterizing the local structural stiffness of proximal tibial subchondral bone.

In situ macro-indentation testing—the preferred method for determining subchondral bone mechanical properties from various articulating bones, including the proximal tibia (Finlay et al., 1989; Harada et al., 1988; Johnston et al., 2011; Little et al., 1986; Yang et al., 1997) — may provide relevant assessments of the required E-BMD equations for input into proximal tibial FE models. In situ macro-indentation testing involves mechanical testing directly at the subchondral surface, typically with a flat cylindrical indentor (generally 3 to 4 mm in diameter), and is essentially a test of local structural stiffness. This test differs from micro-indentation which typically uses non-flat pyramidal diamond shaped indentors penetrated into the material. The penetration and yielding associated with micro-indentation testing makes measurement of stiffness challenging. Conversely, usage of a larger flat indentor ensures a sizable linear response for measuring stiffness. In comparison with isolated compression testing of excised bone samples, macro-indentation based measures of local structural stiffness are thought to be most representative of the in vivo condition (McKoy et al., 2000). This is important because, as the immediate support for overlying cartilage, representative characterizations of subchondral bone mechanical properties are essential for future FE studies investigating links between subchondral bone mechanics and cartilage integrity.

The objective of this study was to apply various E-BMD equations from the literature (seven trabecular-specific and two cortical-specific E-BMD equations) to QCT-FE models of the proximal tibia to identify which equation(s) best predicted (with largest explained variance and least amount of error) local subchondral bone structural stiffness derived using experimental in situ macro-indentation testing.

2. Methods

2.1. Tissue harvesting and classification

Eleven fresh frozen cadaveric proximal tibial samples from 8 donors (7 males and 1 female, ages ranging from 51 to 88 years (mean 76.2, standard deviation (SD) 9.2) were used in this study. Each sample was cut sagittally to obtain separate medial and lateral compartments. The participating surgeon (BAM) reviewed and excluded specimens with obvious structural pathology (e.g., late-stage OA), leaving 9 lateral and 4 medial compartments. The thirteen compartments were then wrapped in saline soaked towels and kept at a temperature of −20 °C prior to testing. Study approval was provided by the University of British Columbia Clinical Research Ethics Board (CREB #: H03-70308).

2.2. Sample preparation

Each medial/lateral compartment was thawed for 12 h at 20 °C then fixed in a potting system composed of a PVC outer shell and a support base made of gypsum potting material (Denstone, Modern Materials Inc., South Bend, IN, USA) and a Poly(methyl methacrylate) (PMMA) layer. The proximal 25 mm portion of each compartment was left exposed. To mimic the structural support of the excised contralateral compartment, a custom 'phantom' compartment was created out of PMMA and rigidly fixed to the PMMA potting layer and sealed surfaces of the tibial compartment. For registration purposes, four stainless steel fiducial markers of 1 mm diameter were inserted in the outer PVC shell.

2.3. CT imaging

Each potted compartment, including fiducials, was imaged using a clinical CT scanner (64-slice helical Aquilion 64, Toshiba Medical Systems, Tokyo, Japan) according to a previously validated QCT method (Johnston et al., 2009, 2011). Imaging parameters include: tube voltage: 120 kVp, tube current-time product: 150 mAs, bone standard reconstruction algorithm, 0.5 mm slice thickness and 0.5 mm × 0.5 mm in-plane pixel size. A QCT phantom (Model 3 T; Mindways Software Inc., Austin, TX, USA) was used to convert CT grayscale intensity values (Hounsfield units, HU) to equivalent volumetric bone mineral density BMD (g/cm^3 K_2HPO_4). With regard to BMD values below the indentation locations, average BMD of a 3.5 mm diameter region of interest (matching the indentor size) ranged from 0.19 to 0.64 g/cm^3 (mean 0.43, SD 0.11 g/cm^3) across a depth of 0–2.5 mm from the subchondral surface and 0.08–0.42 g/cm^3 (mean 0.26, SD 0.09 g/cm^3) across a depth of 2.5–5 mm from the subchondral surface (Johnston et al., 2011).

2.4. Mechanical indentation testing

Macro-indentation tests were performed by a single researcher (JDJ) using a novel mechanical indentation test setup which combined compressive indentation with iterative milling, as previously described in detail (Johnston et al., 2011). In brief, the testing apparatus was comprised of a right angle drill and a load-cell (250 N, accuracy: 0.1 N, LC101-50, Omega Engineering, Stamford, CT, USA) mounted to a material testing machine (Instron 8874, Instron Corp., Canton, MA, USA), combined with a 5 degree-of-freedom positioning stage to control specimen rotation and translation (Fig. 1). Test sites on each compartment were defined according to anterior–posterior and central-peripheral dimensions (Fig. 2). A total of 47 test sites from 13 specimens were included in this study. The location of the subchondral cortical bone surface was first identified using a compression needle test (Herzog