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Estimation of mechanical stiffness by finite element analysis of ultrasound computed tomography (UCT-FEA); a comparison with X-ray μCT based FEA in cancellous bone replica models

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ABSTRACT

The mechanical integrity of a bone is determined by its quantity and quality. Conventional mechanical testing is the 'gold standard' for assessing bone strength, although not applicable *in vivo* since it is inherently invasive and destructive. A mechanical test measurement of stiffness ($N\,mm^{-1}$) provides an accurate estimate of strength, although again inappropriate *in vivo*. Several non-destructive, non-invasive, *in vivo* techniques have been developed and clinically implemented to serve as surrogates for bone strength assessment including dual-energy X-ray absorptiometry along with axial and peripheral quantitative computed tomography, and quantitative ultrasound. Finite element analysis (FEA) is a computer simulation method that predicts the behaviour of a structure such as a bone under mechanical loading, being previously combined with *in vivo* bone imaging, reporting higher predictions of mechanical integrity than imaging alone.

We hypothesised that ultrasound computed tomography (UCT) may be combined with FEA, thereby predicting the stiffness of bone. The objective of this study was to apply finite element analysis to UCT derived attenuation images of trabecular bone replica samples, thereby providing an estimate of mechanical stiffness that could be compared with both a gold standard mechanical test and a surrogate X-ray μCT-FEA.

Replica bone samples were 3D-printed from four anatomical sites (femoral head, lumbar spine, calcaneus and iliac crest), with two cylindrical volumes of interest extracted from each sample. Each replica sample was scanned by X-ray μCT and a bespoke UCT system, from which finite element analysis was performed to estimate mechanical stiffness. The samples were then mechanically tested, yielding the gold standard stiffness value.

The coefficient of determination (R^2) to estimate mechanical test derived stiffness was 99% for μCT-FEA and 84% for UCT-FEA. In conclusion, UCT-FEA is a promising tool for estimating the mechanical integrity of a bone. This study demonstrated that UCT-FEA, based upon quantitative attenuation images, provided a comparable estimation of gold standard mechanical-test stiffness and therefore has significant potential clinical utility for osteoporotic fracture risk assessment and quantitative assessment of musculoskeletal tissues.

1. Introduction

The mechanical integrity of bone is determined by two factors; bone quantity and bone quality. Bone quantity is generally expressed as bone density ($g\,cm^{-3}$), and may be defined as tissue density (bone mass divided by tissue volume or apparent density (bone mass divided by sample volume). Bone quality reflects the properties such as bone shape, cortical thickness, trabecular architecture, mineralization, and presence of micro-fractures [1].

Conventional mechanical testing is the 'gold standard' for assessing bone strength, although not applicable *in vivo* since it is inherently invasive and destructive. A mechanical test measurement of stiffness ($N\,mm^{-1}$) provides an accurate estimate of strength, although again inappropriate *in vivo*. Several non-destructive, non-invasive, *in vivo* techniques have been developed and clinically implemented to serve as surrogates for bone strength assessment. Dual energy X-ray absorptiometry (DXA) provides a measure of areal bone mineral density (BMD, $g\,cm^{-2}$; bone mineral content divided by scan area), and is widely used to diagnose osteoporosis [2–4]. However, it is only a moderate predictor of fracture risk [5,6], being a non-volumetric measure of bone quantity but not bone quality [3]. X-ray quantitative computed tomography (QCT) allows volumetric bone density assessment, with the

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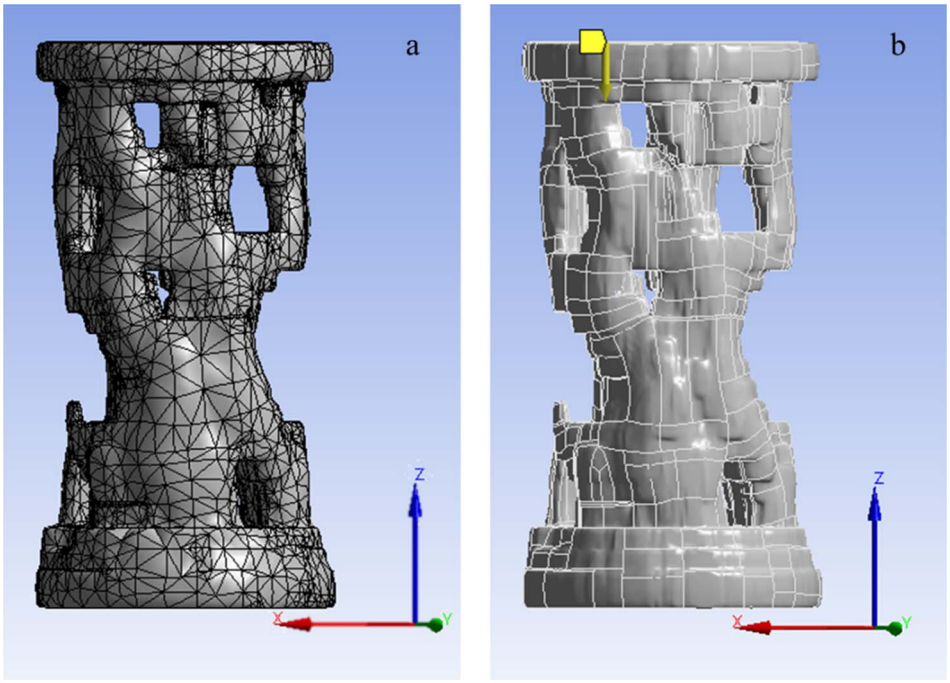

Fig. 1. The FEA simulation process consists of dividing the structure into regular-shaped finte-elements (a), onto which constraints and loads (indicated with the yellow arrow on the top) are applied (b). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

provision of separate analysis for cortical and trabecular components [7,8] with a voxel size typically of 500 μm. It is however relatively expensive, and delivers a significantly higher radiation dose to the subject that DXA [9]. For in vitro bone samples, micro-computed tomography (μCT) is considered the gold standard for bone microstructure imaging, with voxel sizes ranging from a few μm to 100 μm [10].

The clinical utility of Quantitative Ultrasound (QUS) to assess the mechanical of bone was first described by Langton et al. [11]. Being non-ionizing, it is ideal for triage assessment of the general population. QUS parameters of velocity and attenuation are dependent upon both bone quantity and bone quality, providing a prediction of fracture risk comparable to DXA [12–15].

Finite element analysis (FEA) is a computer simulation method that predicts the behaviour of a structure such as a bone under mechanical loading [16,17]. The structure is divided into a number of regular-shaped parts, termed finite elements that are interconnected at nodes, as shown in Fig. 1a. Density, Young's modulus and Poisson's ratio values are prescribed to each finite-element, with constraints and loads (compressive or tensile) applied to the structure at defined locations, as indicated in Fig. 1b. The displacement of each node is then determined by solving inter-connected simultaneous equations following Newton's First Law, that integrate the material properties, loads, constraints and geometry of the test sample. Finite element analysis is again sensitive to both bone quantity and bone quality, the output parameter generally being a prediction of mechanical stiffness ($N\,mm^{-1}$).

FEA has previously been combined with *in vivo* bone imaging, reporting higher predictions of mechanical integrity than imaging alone [18–21].

Ultrasound computed tomography (UCT) has the capability to create 3D quantitative analysis images, being operator independent and providing high resolution images with a voxel size down to 0.2 mm [22–25]. Clinical applications to date have predominantly considered breast tissues [26–28], although it has also been used to assess long bones [29]. Ultrasound attenuation computed tomography has previously been reported for bone imaging of human cadaver heads [30], legs of lambs [31], turkey and dog limbs [32].

We hypothesised that UCT may be combined with FEA, thereby predicting the stiffness of bone; to the authors' knowledge, this has not previously been reported. The objective of this study was to apply finite element analysis to UCT derived attenuation images of trabecular bone replica samples, thereby providing an estimate of mechanical stiffness that could be compared with both a gold standard mechanical test and X-ray CT-FEA.

2. Material and methods

2.1. Cancellous bone replica samples

The study utilised externally-sourced μCT-derived binary data sets (bone/void) of 4 mm cuboid human cancellous bone samples from four anatomical sites (femoral head, lumbar spine, calcaneus and iliac crest); the isotropic voxel dimension being 14 μm (28 μm for calcaneus). Two cylindrical volumes of interest were extracted from each sample, equivalent to a natural tissue diameter of 2.6 mm; the voxel dimensions were then uni-axially magnified by a factor of 11 to facilitate 3D printing, the resulting cylinders measuring 30 mm in diameter and 44 mm in length. To facilitate consistent mechanical test loading, a 2 mm thickness flat-parallel end-plate of 30 mm diameter was attached to the top of each sample design, and a second end-plate of 4 mm thickness attached to the bottom of each sample design, additionally serving as a sample holder for subsequent UCT imaging. The samples were 3D printed by a ProJet 3510 SD (3D Systems, Rock Hill, USA) using a plastic material (VisiJet M3 Crystal). Fig. 2 shows a photograph of the printed samples.

2.2. X-ray μCT scanning

The 3D-printed cancellous bone replica models were X-ray micro CT (μCT) scanned (μCT 40, Scanco Medical, Brütisellen, Switzerland) in air at 45 kVp and 177 μA, with an isotropic voxel size of $36 \times 36 \times 36\,\mu m^3$ and a sample time of 750 ms. Each scan contained 1400 slices which were exported to DICOM format for further processing. Each DICOM stack was imported using the image processing package Fiji [33], a distribution of ImageJ [34]. A region of interest (ROI) was manually selected, corresponding to the diameter of the sample. The outer region was removed and the ROI converted into a binary image stack which was downscaled by a factor of 0.25, thereby reducing the stack size