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Comparison of 3D finite element analysis derived stiffness and BMD to determine the failure load of the excised proximal femur

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Abstract

Introduction: Bone mineral density (BMD) is currently the preferred surrogate for bone strength in clinical practice. Finite element analysis (FEA) is a computer simulation technique that can predict the deformation of a structure when a load is applied, providing a measure of stiffness (N mm^{-1}). Finite element analysis of X-ray images (3D-FEXI) is a FEA technique whose analysis is derived from a single 2D radiographic image.

Methods: 18 excised human femora had previously been Quantitative Computed Tomography scanned, from which 2D BMD-equivalent radiographic images were derived, and mechanically tested to failure in a stance loading configuration. A 3D proximal femur shape was generated from each 2D radiographic image and used to construct 3D-FEA models.

Results: The coefficient of determination (R^2%) to predict failure load was 54.5% for BMD and 80.4% for 3D-FEXI.

Conclusions: This ex-vivo study demonstrates that 3D-FEXI derived from a conventional 2D radiographic image has the potential to significantly increase the accuracy of failure load assessment of the proximal femur compared with that currently achieved with BMD. This approach may be readily extended to routine clinical BMD images derived by dual energy X-ray absorptiometry.

Keywords: BMD, bone strength, failure load, finite element analysis, proximal femur

Introduction

Currently, there is no accurate non-invasive measure of overall bone strength. However, the most commonly used measurement to diagnose osteoporosis is based on assessment of bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA), performed on the assumption that it is a reliable surrogate for the mechanical failure load of the bone being measured. Several experimental validation studies have reported on this, with various R^2 values reported including 79% for femoral neck BMC, n=61 [**1**], 42% for femoral neck BMD, n=58 [**2**], 89% for total hip BMD against pelvic fracture load, n= 9 [**3**], 76% and 72% for total femoral BMC and BMD respectively, n = 54 [**4**]. An enhancement of DXA-derived BMD is Hip Strength Analysis (HSA) based upon a combination of cross-sectional area and cross-sectional moment of inertia, yielding an improvement in prediction of proximal femur strength from 62% for femoral neck BMD to 79% for HSA in an experimental study of 20 femora. [**5**]. The ability of a stereo-radiographic technique based upon biplanar acquisitions for reconstruction of the proximal femur to predict stance failure load of the human proximal femurs was assessed by Le Bras et al [**6**]. In a study of 12 excised femurs that were experimentally tested in a stance loading configuration, failure load was predicted by total hip BMD with R^2 = 41%, which increased significantly to 84% when a multiple linear regression model was considered, additionally incorporating femoral head diameter and mid-femoral neck cross-sectional area.

Finite Element Analysis

Finite element analysis (FEA) is a computer simulation technique that can predict the deformation of a structure such as a bone when a load is applied, providing a measure of stiffness (N mm^{-1}). In this technique, the structure is divided into a number of discrete, finite elements whose geometry is defined by points on the elements called nodes. Each element is prescribed material properties, namely Young's modulus and Poisson's ratio in the case of a static, elastic analysis of a structure composed of isotropic materials. Complex models of structures having irregular geometries and heterogeneous material properties can be created by an assembly of elements, to which constraints (fixed displacements) and loads may be applied. The displacements of the nodes are calculated by solving inter-related simultaneous equations that incorporate the material properties, geometry, loads and constraints, and that prescribe Newton's first law.

Finite element analysis of a bone such as the proximal femur is dependent on the overall size and shape of the bone (hip axis length, neck-shaft angle, anteversion of femoral head, etc.) which is described by the geometry of the elements, and on the material properties of each element, most importantly Young's modulus, which in turn is related to the density of the bone represented by each element **[7]**. A number of studies, over a significant number of years, have reported the utility of 3D FEA based upon CT image data to predict the mechanical integrity of the proximal femur [**8-15**]. With reference to this current paper, it has been demonstrated that in a stance loading configuration, a 3D finite element method derived from CT scan data explained at least 20% more of the variance in strength of the proximal femur than areal density, with R^2 values of 83.7% and 57.4%, respectively [**13**]. However, because of the high costs and high radiation dose, CT scans are not routinely used in clinical assessment of osteoporosis. DXA, on the other hand, is relatively easier and less expensive to obtain and hence an FEA technique based upon the derived 2D radiographic images of DXA might provide a readily available improved prediction of bone strength compared with conventional areal BMD.

The aim of this paper is to apply a 3D proximal femur shape derived from a single 2D radiographic image of the subject's femur to create a subject-specific and versatile 3D finite element model (3D-FEXI). It is hypothesised that 3D-FEXI would serve as a more accurate surrogate of bone strength than BMD.

Methods

The approach in this paper has two parts: a) creation of versatile 3D finite element models (3D-FEXI) from a combination of an average 3D shape template of the proximal femur that is warped to the size and shape of individual 2D BMD radiographic images of subjects' femurs, and b) correlation of measured failure load of excised proximal femurs with 3D-FEXI derived stiffness and areal Total Hip BMD, and comparison thereof.

Generation of BMD radiographic image from CT scan data

18 femora from 8 males and 10 females; age 52–92 years had previously been scanned by computed tomography (CT) at University of California. Each femur was immersed in water and placed atop a calibration phantom for CT scanning on a GE 9800 Research Scanner (GE Healthcare Technologies, Waukesha, WI) with a K_2HPO_4 (KHP) calibration phantom 320 × 320 matrix, and 1.08 mm pixels [**9**]. CT numbers were therefore expressed as concentration of K_2HPO_4, [KHP] (mg cm^{-3}), Scans were obtained using 80 kVp, 280 mAs, with a 3 mm slice thickness and the standard reconstruction technique adopted.

A ray casting technique was applied to the historical CT scan data for each proximal femur to create a 2D mapping of BMD, expressed as a 256 level grey-scale bitmap. Initially, each voxel of the 3D CT scan was converted into volumetric mineral density (mg cm^{-3}) using a two-stage regression manipulation.

i) conversion of [KHP] (g cm^{-3}), into ash density, ρ_{ash} (g cm^{-3}) = 0.0526 + 1.22*[KHP]; [**17**], and
ii) conversion of ash density (ρ_{ash}) into volumetric mineral density (mg cm^{-3} calcium hydroxyapatite equivalent from quantitative CT) = 1.192* (1000ρ_{ash}) – 83.19 using an equation from reference [**18**] that has been rearranged, where a factor of 1000 has been included to convert ρ_{ash} to mg cm^{-3};

The bone mineral mass for each 3D voxel is the product of its volumetric mineral density and volume. By dividing the sum of bone mineral masses along a line of voxels normal to each 2D pixel coordinate by the pixel cross-sectional area yields the simulated areal BMD for that pixel. Averaging the individual pixel BMD values over the corresponding region of interest yields the areal BMD for a proximal femur, equivalent to 'Total Hip' BMD derived from a DXA scan.

Creation of 3D Shaped Proximal Femur from a single 2D Radiographic Projection

A 3D shape corresponding to the resulting BMD image was generated by warping an average 3D shape template of the proximal femur to the size and shape of the BMD image **[19]**. For each proximal femur, the landmark configuration of the 3D template grid was first aligned to the landmark configuration of the BMD image using Generalised Procrustes Analysis. The 3D template grid was then warped using Thin Plate Splines, resulting in the creation of a 3D shape approximating that of the proximal femur in the 2D BMD image. This process is illustrated in Figure 1.

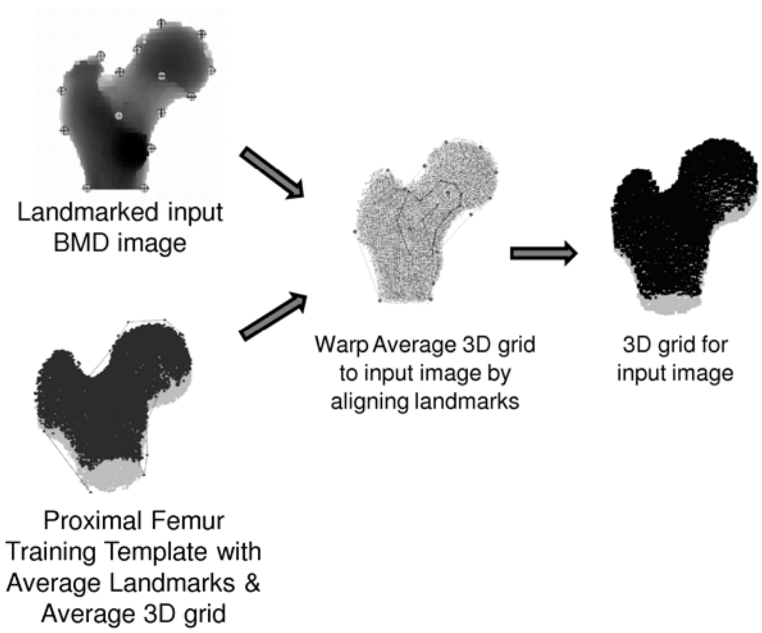


Figure 1: Transformation of the 3D Shape Template to an individual 2D radiographic projection to create an Individual 3D model.

Finite Element Analysis of X-ray Images (3D-FEXI)

Finite element analysis of X-ray images (3D-FEXI) is a FEA technique developed to analyse a conventional 2D radiographic image of a bone such as the proximal femur, providing a measure of bone stiffness (N mm^{-1}). This generically involves a number of steps, namely:

1. A 3D volumetric density voxel mapping is derived by assigning a constant volumetric density (CVD, mg cm^{-3}), equal to the 2D pixel BMD divided by the bone depth from the warped 3D template, to each voxel along the line normal to each 2D pixel.

2. A 3D Young's modulus (E) volumetric voxel mapping is derived via a two-part regression manipulation:
    a. conversion of volumetric density into ash density (g cm^{-3}) = (69.8 + 0.839*CVD)/1000; [**18**], and
    b. conversion of ash density (ρ_{ash}) into Young's modulus (MPa) = 14900* $\rho_{ash}^{1.86}$; [**20**] noting that this equation applies to samples of both trabecular and cortical bone.
3. A constant Poisson's ratio (v) of 0.4 [**21**] is assumed for all voxels.
4. The 3D bone model is orientated as appropriate for the desired loading configuration, for example, inclination and anteversion of the femoral shaft and neck respectively to the loading force.
5. Simulated support and loading platens, to facilitate uniform loading across the bone surfaces are added, as appropriate for the desired loading configuration.
6. The bone model is meshed prior to finite element analysis utilising unit meshing for each voxel.
7. The support and loading platens are restrained as appropriate for the desired loading configuration.
8. A defined load is applied evenly over the loading platen.
9. The finite element analysis is solved, from which stiffness (N mm^{-1}) is derived by dividing the applied load by the displacement of the upper loading platen.

For this particular study, the created 3D proximal femur finite element model was stored as a discrete regular 3D voxel map. Each finite element consisted of an 8-node solid rectangular prism corresponding to the constantly sized voxel. The finite element analysis was performed using ANSYS (ANSYS Inc., PA) which had a finite element node limit of 127000 nodes for an academic licence. Hence, the voxel maps describing the bone were trimmed and re-sampled at 80% of the original resolution, the resultant voxels being 1.35 mm x 1.35 mm x 3.75 mm. A bespoke computer program was written in Matlab (Mathworks Inc., MA) to convert the 3D voxel map into a finite element model with the orientation, restraint and loading simulating a stance configuration mechanical loading test, as shown in Figure 2. This involved aligning the shaft of the proximal femur to an angle of 70^{o} to the ground without anteversion. The femoral head was loaded with the distal end of the shaft restrained in all directions. A simulated steel support platen (E = 200 x 10^3 MPa, v = 0.3; [**22**]) 37.5 mm thick was incorporated at the bottom of the femoral shaft and restrained in all three orthogonal directions. A horizontal simulated steel loading platen 37.5 mm thick was incorporated above the top of the femoral head. A simulated resin support platen ([ITW Devcon, Danvers, MA, USA]; E = 7.163 x 10^3 MPa, assumed v = 0.3) was positioned between the loading platen and the top of the femoral head, being moulded to match the shape of the femoral head and used to provide uniformly distributed loading at the femoral head. A vertical load of 1 kN was uniformly applied over the top of the horizontal loading platen which was restrained to only allow vertical displacement. Dividing the applied load by the resultant platen displacement yielded the stiffness of the bone (N mm^{-1}). The 3D-FEXI model is shown in Figure 3, illustrating a) a cut-away view demonstrating the internal femoral structure and distribution of Young's modulus values, and b) a stance orientated and platened proximal femur.

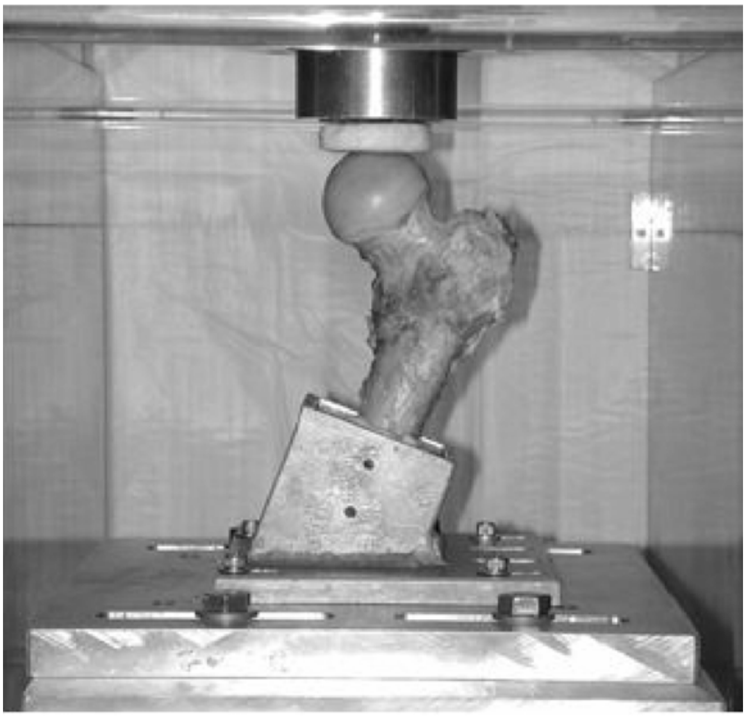
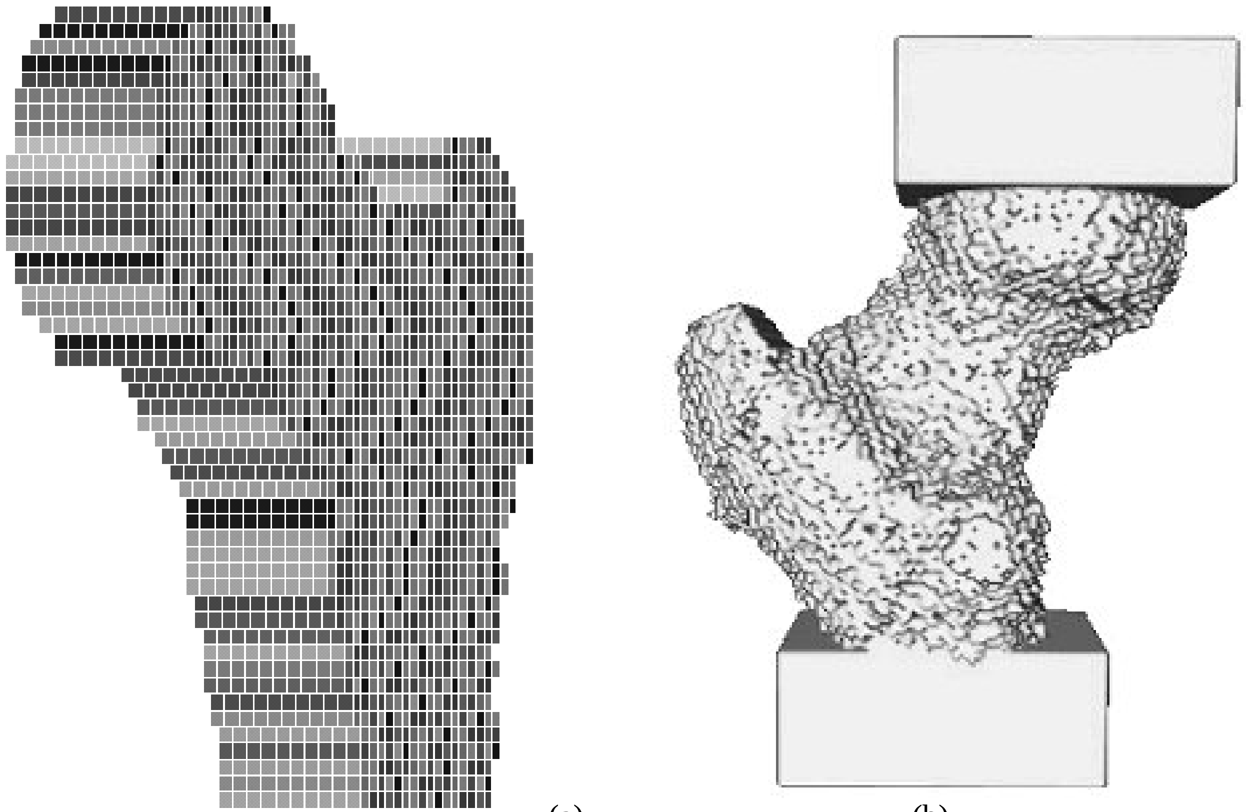


Figure 2: Mechanical test that is replicated by FEXI. In this scenario, the load is applied to the femoral head at 20° to the shaft in the coronal plane.



(a) (b)

Figure 3: The 3D-FEXI model, illustrating a) a cut-away view demonstrating the internal femoral structure and distribution of Young’s modulus values, and b) the created proximal femur and incorporated platens implementing a ‘stance’ loading condition, c.f. photograph of experimental test shown in Figure 2.

Experimental Mechanical Test

The 18 excised femora have previously been studied in terms of experimental failure load in a stance loading configuration **[9]**. All specimens were thawed and mechanically tested using loading conditions analogous to those that were modelled by finite element analysis (Figure 2). The distal end of each proximal femur was held in place by embedding it in a polymethylmethacrylate (PMMA) block. Displacement was applied to the femoral head at 0.5 mm s^{-1} (MTS 858 Test System; MTS, Eden Prairie, MN). A custom PMMA cup moulded, but not bonded, to the top of each femoral head distributed the applied load. The maximum load achieved during mechanical testing was defined as F_{Meas}.

Results

Plots for the prediction by a) areal BMD and b) 3D-FEXI of the experimental mechanical failure load of the proximal femur are shown in Figure 4. The coefficient of determination (R^2%) to predict failure load was 54.5% for BMD and 80.4% for 3D-FEXI.

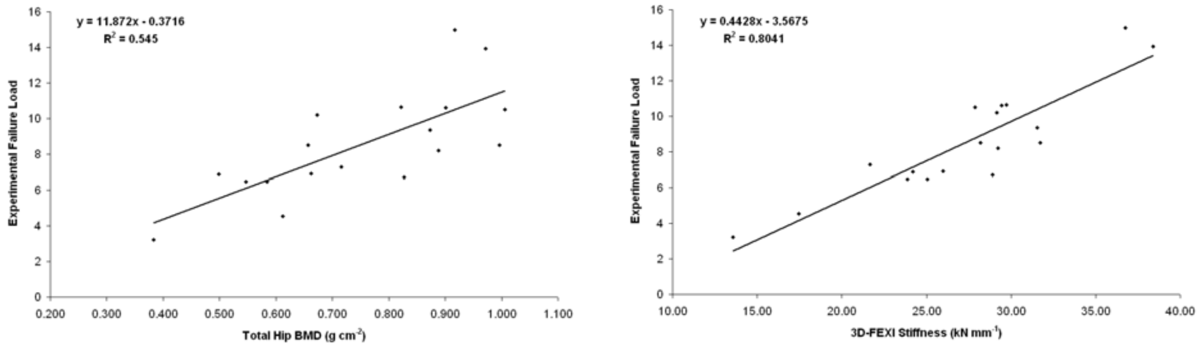


Figure 4: Prediction of experimentally derived failure load stiffness by a) areal BMD and b) 3D-FEXI.

Discussion

This ex-vivo study demonstrates that 3D-FEXI derived from conventional 2D BMD images has the potential to significantly increase the accuracy of failure load assessment of the proximal femur compared with that currently achieved by areal BMD alone. The correlation (R^2%) of 80.4% for 3D-FEXI with failure load is statistically comparable to the previously reported values of 79% and 83.7% for hip strength analysis **[5]** and conventional 3D FEA derived stiffness from CT scan data **[13]**, respectively.

It should be noted that the 2D BMD images were derived from the original CT scan data and not from DXA. Future scientific and clinical validation studies should consider implementation of DXA-derived BMD images to evaluate the true clinical performance of 3D-FEXI. For implementation of a conventional DXA hip scan, the proximal femur image would first be exported as an 8-bit greyscale bitmap. The grey level of each pixel would then be converted into BMD by creating a subject-specific regression between average grey level with BMD, reported from the subject's DXA report, for the proximal femur sub-regions of Trochanter, Neck, Shaft and Total (defined as (ΣBMC / Σarea of the other three sub-regions). Segmentation of the proximal femur is achieved using a semi-automatic contour detection program thereby deleting adjacent surrounding tissues and other bones. It should be noted however that the acetabulum will still be present overlying the femoral head. The 2D BMD mapping would then be converted into a 3D FEA model as described within this paper.

This paper describes the simulation of the proximal femur loaded in a stance configuration, a decision governed by the availability of corresponding mechanical test data. It is accepted however that it is highly unlikely that femurs fail in this loading configuration. The flexibility of the 3D-FEXI technique however readily offers the opportunity to incorporate alternative loading configurations, for example, a fall loading configuration could be implemented whereby the femoral shaft would be inclined at an angle of 30 degrees along with 20 degree anteversion of the femoral neck.

It is recognised that there is a potential technical concern related to assessment of excised bones at room temperature where fatty marrow may leak out of the marrow cavity leaving air spaces behind. The occurrence of this would be difficult to confirm, but would result in reduced tissue densities in affected regions of the specimens, as measured within this study by QCT. However, if this was a significant problem, the previous study of these femurs [**10**], in which CT-based FEA was used to predict fracture load, could not have produced such a strong correlation (R^2 = 92.5%).

It should be stressed that this paper describes initial scientific validation of the 3D-FEXI technique using a relatively small sample size, which will inherently limit the generalisation of the conclusions. In addition to fundamental assumptions related to prediction of strength from stiffness and derivation of volumetric bone density derived from integrated bone mineral content and bone depth, there are a number of issues that warrant further investigation. As previously stated, scientific and clinical evidence based upon DXA-derived images is required. Further, precision and reproducibility should be investigated.

The strong prediction of failure load by 3D-FEXI stiffness compared to conventional areal BMD suggests that a combination of routine DXA scans along with the implementation of a shape model and application of finite element analysis may offer the opportunity to significantly improve prediction of osteoporotic hip fracture risk within the routine clinical environment. One option would be to replace BMD within a fracture risk prediction model based on risk factors, since 3D-FEXI derived stiffness is an alternative (but potentially improved) surrogate for mechanical integrity.

In conclusion, this ex-vivo study demonstrates that 3D-FEXI derived from a conventional 2D radiographic image has the potential to significantly increase the accuracy of failure load assessment of the proximal femur compared with that currently achieved with areal BMD. This technique could be readily incorporated into routine DXA assessment.

Conflict of Interest

Associate Professor Keyak and Dr Pisharody declare that they have no conflict of interest or disclosures. Professor Langton declares that he is the named inventor of a filed patent that incorporates the concept of the 3D shape derived from a single projection 2D radiographic image and subsequent derivation of a finite element model.

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