A CT-based high-order finite element analysis of the human proximal femur compared to in-vitro experiments

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Abstract

The prediction of patient-specific proximal femur mechanical response to various load conditions is of major clinical importance in orthopaedics. This paper presents a novel, empirically validated high-order finite element method (FEM) for simulating the bone response to loads. An accurate model of the bone geometry is constructed from a quantitative computerized tomography (QCT) scan using smooth surfaces for both the cortical and trabecular regions. Inhomogeneous isotropic elastic properties are assigned to the finite element model using distinct continuous spatial fields for each region. The Young modulus is represented as a continuous density function computed by a least mean squares method. p-FEMs are used to bound the simulation numerical error and to quantify the modeling assumptions. We validate the FE results with in-vitro experiments on a fresh-frozen femur loaded by a quasi-static force of up to 150 kgf at four different angles. We measure the vertical displacement and strains at various locations and investigate the sensitivity of the simulation. Good agreement was found for the displacements, and a fair agreement found in the measured strain in some of the locations. The presented study is a first step towards a reliable p-FEM simulation of human femurs based on QCT data for clinical computer aided decision making and optimization of cervical fracture surgery fixation.

Key words: Finite Element Analysis, p-FEM, Computed Tomography, Bone Biomechanics

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1 Introduction

Predicting the mechanical response of the proximal femur for individuals is of major clinical importance as a planning and analysis tool to assist orthopaedists in fracture treatment planning. The prediction can help surgeons determine whether a surgical or non-surgical treatment is preferable, and, when the treatment is surgical, to choose the optimal implant type, size, implant, and/or screw position. Predicting the mechanical response is nowadays very limited, as it depends on the geometrical complexity of the bone, its distinct cortical and trabecular internal regions, the anisotropic and inhomogeneous material properties which vary among individuals, and the inaccessibility to the living bone for validation.

Recent advances of quantitative computerized tomography (QCT) and high-order finite element (FE) methods open the possibility of performing reliable patient-specific mechanical simulations of loading conditions on the proximal femur. For example, QCT scan data has been used for the creation of accurate FE models of the femur in [1–6]. The accurate bone geometry can be obtained from the voxel coordinates. Herein we utilize the QCT data to generate an accurate geometrical representation of an individual bone, including a model of the internal surfaces that separate distinct trabecular and cortical regions in it. Thereafter, a p-finite element mesh can be semi-automatically constructed based on a geometrically accurate representation with smooth boundaries. A sequence of FE analyses with progressively higher accuracy and tight control of the numerical error may be performed by increasing the polynomial degree on same geometrical mesh. QCT information can also be correlated to the local density so as to provide inhomogeneous, region-specific distributions of the density within the bone used to determine a functional distribution of Young’s modulus.

Three dimensional (3D) finite element analysis (FEA) for orthopaedic application has been in use for over three decades ([7,8] and the references therein). Most of these FEAs provide an estimation on the risk of fracture, both for bones in general and for the femur in particular.

Although the bone is a complex biological tissue, the use of FEA is attractive because at the macro level it exhibits elastic linear behavior for loads in the normal range of regular daily activities [9]. The proximal femur consists of cortical (compact dense and hard tissue) and trabecular (cellular spongy tissue) regions [10]. The literature reports experimentally derived homogenized mechanical properties of both regions as well as isotropic Young’s modulus and other elastic constants (under the transversely isotropic/orthotropic assumption) of both regions as a function of the bone apparent density [9,11–16].

The bone density at every location may be estimated as Hounsfield units (HU) according to the voxels gray level intensity and may be thereafter correlated to the Young modulus.

The two most common methods currently in use for geometry construction and mesh generation are the voxel-based and the structure-based methods. The voxel-based method generates a FE mesh directly from the QCT data without any use of surfaces or solid bodies [17–19]. The mesh usually consists of 8-noded hexahedral elements, each enclosing a predefined cubic
volume containing a fixed number of QCT voxels [7]. The structure-based method generates first a geometrical model of the bone from the surface points determined from the QCT and then automatically generates a mesh from it [3–6,20,21]. In general, voxel-based models are easier to automatically generate and are sufficiently accurate to estimate deflections or interior material stresses. Structure-based models, on the other hand, are more accurate when surface strains and stresses are of interest [6–8].

Both methods require assigning inhomogeneous mechanical properties to the elements. The assessment and assignment to each element is usually performed according to an averaged value, based on the QCT HU values of the voxels inside the finite element volume [22]. In one approach, the element’s mechanical properties are derived from an averaged HU [17]. This may result in underestimated mechanical properties because the relationship between HU and Young’s modulus is known to be non-linear [17]. In another approach, the mechanical properties are first computed for each voxel and only then an averaged value is calculated [23].

Two additional factors greatly influence the results of an FEA analysis: the assignment of mechanical properties to a finite element, and the finite element size. Typically, mechanical properties are assigned based on averaged CT values and correlated to the bone density using linear relations [9,12,24,25]. This value is then used for Young modulus estimation, usually with power-law relations [3,11–13,15,16,26]. Regarding finite element size, there is usually a discrepancy between the CT pixel size (about 1 mm) and element sizes (5÷9 mm) used for density calculation and for mechanical properties evaluation tests. Although the influence of the finite elements size on the results has been reported [7,22], these studies usually focus on the computational accuracy versus meshing difficulties and computational times, with no mechanical or biological justifications for the characteristic size of elements in use. Keyak et al. reports that hexahedral 3 mm cubic elements are a good choice for a voxel based mesh [17,27]. However, Viceconti et al. show that further refinement can result in an increased error in FEA results [7]. Decreasing elements size does not lead necessary to convergence since both geometry and material assignment change from one model to the other. Furthermore, although some studies show good experimental correlation between FE model results and fracture load, to the best of our knowledge, only two studies investigate quantitatively the differences between strains computed by FEA and those measured experimentally on a femur bone [3,28]. In both, only partial agreement is found, suggesting the need for better simulations. In a recent FE study [8], the stresses in a femur are computed and shown to be in good correlation with the experimental observation. However neither displacements nor strains are reported although these are the measured quantities in in-vitro experiments.

Herein a new structure-based modeling method is presented. The method calls for using smooth surfaces for geometry representation and a continuous spatial field, independent of the mesh, for mechanical properties assignment. The accurate smooth representation of the bone geometry is extracted from the CT data. It includes an internal smooth surface that separates the cortical and trabecular regions. A FE mesh is automatically constructed based on large p-elements [29] using blending function methods for the element mapping, thus resulting in an accurate and smooth representation of the bone surface. p-FEMs allow the use of elements with large aspect ratios, enabling a tight control on the numerical errors.
over a fixed mesh, and provide very high convergence rates, yielding results superior to those obtained with conventional h-FEMs. The mechanical properties are determined from CT data and require several steps. First, for each region (cortical or trabecular) the HU-values are re-calculated at each voxel using moving average [30]. Next, the apparent density ($\rho_{\text{app}}$) is evaluated and a continuous spatial field, describing the density of the bone at each point according to its coordinates is approximated by least mean square methods (LMS). Finally the mechanical properties are evaluated within the FE analysis, according to the density at each integration point of the finite element without having to assign a discrete value for an entire element.

The thrust behind the suggested method is that the geometry should be represented as accurately as possible, and the Young modulus relation to the density be evaluated in a similar volume as the test specimens used for its estimation. Thus, the moving average is used so that at each point, the HU-values are averaged with an adequate surrounding volume (see a simplified concept in [22]). Another point of interest is that mechanical properties should be independent of the FE mesh and should be suitable for structure based mesh generation and for validation against in-vitro experiments in which strains are measured on the bone surface by strain-gages. Although the bone is known to be anisotropic and inhomogeneous, most studies assume an isotropic inhomogeneous material. We follow the same assumption and concentrate our attention on the geometry, mesh representation, and mechanical properties assignment for bones.

This paper is organized as follows. Section 2 describes in detail the p-finite element mesh generation and the inhomogeneous Young modulus determination from CT scans. An in-vitro experiment on a fresh frozen bone is also detailed. Section 3 summarizes the experiment observations, the FE results, and the various sensitivity tests performed on the model. A comparison between the FE results and experimental observations is provided. Section 4 provides an analysis of the results.

2 Methods and Materials

Herein we describe the proposed method for generating a p-FE model of the proximal femur and the procedure for identifying material parameters based on CT scans. Thereafter, the in-vitro experiments performed on human femurs to validate the FE results are described.

2.1 Finite element model and material parameter assignment

2.1.1 Geometric representation

A solid model is generated based on the CT data. First, two contours defining the inner and outer bone borders at each CT slice are determined with a semi-automated procedure.
The inner contour represents the internal border of the cortical bone and is determined only for slices where a cortical shell can be clearly visible (usually it cannot be obtained above the lesser trochanter). For the distal slices, the inner contour represents the medullar cavity surface, whereas for the more proximal slices, above the lesser trochanter, it represents the separating surface between cortical and trabecular regions. A minimum thickness of two pixels is required for the cortical layer so as to allow meshing with tetrahedral elements. When necessary, the cortical shell is thickened but assigned with low density properties to balance it and avoid overestimating the bone stiffness.

Thereafter the external and internal smooth surfaces are approximated and a solid body is generated using the CAD package SolidWorks-2004 (SolidWorks Corporation, MA, USA). The resulting 3D solid is then imported by the p-FE solver StressCheck (Engineering Software Research and Development Inc. St. Louis, MO, USA). The mesh is then generated by an auto-mesher using tetrahedral elements. The auto-mesher can generate elements with either exact geometrical (blending) mapping of the physical element onto the standard element, or with a simpler, second-order polynomial mapping. Both options are being used to investigate the sensitivity of the results to the mapping used in the FE analyses.

![Fig. 1. The steps for generating the p-FE model. a. Outer surface border points; b. Approximated smooth surface; c. Solid body having a cortical/trabecular separating surface; d. Meshed model with two different mesh regions.](image)

2.1.2 Material properties assignment

Bone mechanical properties are assumed to be isotropic linear elastic, with an inhomogeneous Young modulus and a constant Poisson ratio. This approach has been widely used in past FE studies on the proximal femur [2-4, 8, 17, 31]. The isotropicity assumption is widely accepted, especially in the trabecular bone where material principal directions are difficult to
predict using clinical QCT protocols. To describe the bone Young modulus, we propose to use a continuous spatial function independent of the mesh. This is in contrast with other reported FE studies, in which the bone Young modulus is a constant value within each element determined according to the averaged data within the element. We compute the Young modulus function by applying a moving average algorithm to average the HU data in each voxel based on a predetermined cubic volume surrounding it. Then a Least Mean Square (LMS) procedure to provide a polynomial approximation. This procedure is described in detail herein.

First, the HU values are recalculated using a moving average to handle noisy discrete data. The values are calculated in a pre-defined volume having a physical and mechanical interpretation similar to the specimen size used for the \( E(\rho_{\text{app}}) \) relation used in sequel. Then, the HU averaged data is converted to apparent density \( \rho_{\text{app}} \) using linear relations from the literature or from a phantom calibration. Next, a spatial polynomial is computed by LMS such that the apparent density is described by a continuous function for each bone region.

The moving average algorithm sums the HU values within a cube surrounding each voxel \( (S) \) and divides it by the number of non-empty cells within it \( (\tilde{N}) \), so it does not affect nearby surface values:

\[
S = \sum_{i=1}^{m_1} \sum_{j=1}^{m_2} \sum_{k=1}^{m_3} HU_{ijk}, \quad \tilde{N} = \sum_{i=1}^{m_1} \sum_{j=1}^{m_2} \sum_{k=1}^{m_3} \begin{cases} 1 & HU_{ijk} > 0 \\ 0 & HU_{ijk} = 0 \end{cases} \Rightarrow \overline{HU}_{IJK} = \frac{S}{\tilde{N}} (1)
\]

where \( i, j, k \) are the indices of voxel’s position within the averaged value cube and \( I, J, K \) are indices of voxel’s position within the entire CT scan data.

Subsequently, the apparent density values are evaluated based on the \( \overline{HU} \) data using a linear relationship. The spatial field is approximated using LMS, finding the best-fitting function(s) closest to a given set of \( N \) points by minimizing the sum of the residuals, i.e., the sum of the squares of the distances between the points and the function [32]:

\[
\rho_{\text{LMS}}(x, y, z) = \min \sum_{i=1}^{N} [\rho(x_i, y_i, z_i) - \rho_i]^2
\]

Both Cartesian and spherical coordinate systems are considered for the spatial representation. The Cartesian system is placed at the center of the distal face of the model, and a series of polynomial functions of up to fourth degree are used to approximate the field:

\[
\rho_{\text{app}}^{LMS} [g/cm^3] = \sum_{i=0}^{4} \sum_{j=0}^{4} \sum_{k=0}^{4} a_{ijk} x^i y^j z^k (3)
\]

Additional function series are used to represent the density within the femur head, related to a spherical system where the origin is situated in the head’s center:
\[
\rho_{\text{app}}^{LMS} [g/cm^3] = \sum_{i=0}^{3} \sum_{j=0}^{4} \sum_{k=0}^{4} a_{ijk} r^i f(j \theta) f(k \phi), \quad f(j \theta) = \begin{cases} 
\cos\left(\frac{j}{2} \theta\right) & \text{for } j \text{ even} \\
\sin\left(\frac{j+1}{2} \theta\right) & \text{for } j \text{ odd}
\end{cases}
\]  

Finally, the computed relationships \(E(\rho_{\text{app}})\) are used to obtain the continuous material properties representation (Table 1). Different relationships can be used for the cortical and trabecular regions based on the separation in the FE model. A constant Poisson ratio of 0.3 or 0.4 is chosen (the sensitivity to this value is minimal, as will be shown in the sequel).

Table 1
Summary of trabecular bone \(E(\rho_{\text{app}}) [MPa]\) relationship (\(\rho\) stands for \(\rho_{\text{app}} [g/cm^3]\))

<table>
<thead>
<tr>
<th>Bone region</th>
<th>No.</th>
<th>(E(\rho_{\text{app}})) Relationship</th>
<th>(n^#)</th>
<th>(R^2)</th>
<th>Testing method‡</th>
<th>Specimen size</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trabecular</td>
<td>(t.1)</td>
<td>(1310(\rho)^{1.40})</td>
<td>49</td>
<td>0.91</td>
<td>c</td>
<td>(\phi9) mm cylinder</td>
<td>[12]</td>
</tr>
<tr>
<td></td>
<td>(t.2)</td>
<td>(1.99 \times 10^3 \rho^{3.46})</td>
<td>297</td>
<td>0.75</td>
<td>c</td>
<td>(8) mm cube</td>
<td>[15]</td>
</tr>
<tr>
<td></td>
<td>(t.3)</td>
<td>(60 + 900\rho^2)</td>
<td></td>
<td></td>
<td>r</td>
<td>-</td>
<td>[33]</td>
</tr>
<tr>
<td></td>
<td>(t.4)</td>
<td>(1904\rho^{1.64})</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>[13]</td>
</tr>
<tr>
<td></td>
<td>(t.5)</td>
<td>(4607\rho^{1.30})</td>
<td>128</td>
<td>0.94</td>
<td>s</td>
<td>(10) mm cube</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td>(t.6)</td>
<td>(3790\rho^3\left(\frac{d \varepsilon}{d t}\right)^{0.06})</td>
<td>124</td>
<td></td>
<td>c</td>
<td>(\phi20.6) mm (\times) (5) mm cyl.</td>
<td>[34]</td>
</tr>
<tr>
<td></td>
<td>(t.7)</td>
<td>(2875\rho^3)</td>
<td></td>
<td></td>
<td>r</td>
<td>-</td>
<td>[4]</td>
</tr>
<tr>
<td></td>
<td>(t.8)</td>
<td>(1949\rho^{2.5})</td>
<td></td>
<td></td>
<td>o</td>
<td>-</td>
<td>[25]</td>
</tr>
</tbody>
</table>

| Cortical    | (c.1) | \(-13430 + 14261\rho\)          | 123     | 0.62   | b               | \(7 \times 5 \times 0.18 \div 0.4\) mm\(^3\) | [11] |
|             | (c.2) | \(2065\rho^{3.09}\)            |         |        | r               | -            | [13] |
|             | (c.3) | \(14 \times 10^3\rho - 6142\)  | 96      | 0.77   | s               | \(\approx\) 5 mm cube | [16] |
|             | (c.4) | \(1684\rho^{3.3}\)             |         |        | o               | -            | [25] |

# Number of specimens.
‡- c - compression, b - bending, s - ultrasonic, o - quoting other source
r - recalculated based on published data

Figure 2 presents the different relations for the cortical and trabecular bone. Note the large spread, especially for the trabecular bone. Although the linear elastic response of the bone is a widely accepted assumption, supported by many in-vitro experiments with a second-order visco-elastic response, the bone is definitely not an isotropic material but rather transversely isotropic. The difficulty in determining the inhomogeneous principle directions and the five required material parameters that determine Hooke’s law preclude at this time a more accurate FE analysis. Nevertheless, in the authors’ opinion, anisotropic material identification
is one of the most prominent contribution towards a reliable FE analysis, and will be investigated in the future.

Fig. 2. Relations between Young modulus and apparent density as reported in past publications for the trabecular (left) and cortical (right) bone.

2.1.3 FE solver

The resulting model is solved by the p-FE commercial package StressCheck. The advantages of p-FEMs over traditional h-FEMs ([29]) are: 1) the ability to describe the bone’s boundary accurately as p-FEMs apply the blending function mapping method; 2) the possibility of using elements with very large aspect ratios – this is required in the cortical region, where elements are thin and long; 3) the possibility of monitoring the numerical error by inspecting the convergence of the results as the polynomial degree is increased over a constant mesh; 4) the possibility of providing spatial functions to describe the inhomogeneous material properties within any element, and; 5) a considerably higher convergence rate compared to h-FEMs. In our studies, the degree of the polynomial of the shape functions (p-level) is increased from 1 to 5. Different loads and boundary constrains can be defined which will be described in the sequel for each model separately.

2.2 A FE comparison between voxel based analyses and the suggested method

Appendix A contains the numerical study that compares the results of the FE analysis resulting from existing voxel-based methods with the method presented herein. Several domains with increased complexity were considered to investigate the influence of three factors: 1) accurate surface representation; 2) continuous material representation, and; (3) element size.

The results show that both methods are in qualitative agreement. Nevertheless, our method shows a more realistic strain field and almost constantly lower displacements and strains.
compared to the voxel-based models. These results are consistent with [7], in which all structure-based models investigated show 15% stiffer response compared to the voxel-based model.

2.3 Fresh-frozen proximal femur FE model

A FE model of the fresh-frozen proximal femur was created from a CT scan acquired beforehand. The CT parameters were: 140 kVp, 250 mAs, 0.75 mm slice thickness, axial scan without overlap, with pixel size of 0.78 mm (512 pixels covering 400 mm field size). The CT data was segmented and a solid model was constructed according to the described method. A planar face was defined to determine the height of the applied force. The femur head was trimmed according to this plane prior to mesh construction using the auto-mesher. Four different regions were defined so in each one a different field is used for the density’s evaluation, one for the cortical region and three for the trabecular region (Figure 3).

![Figure 3](image)

Fig. 3. Four regions of the fresh-frozen bone model. The trabecular region was divided into three sub-regions, Low trabecular, Trochanter and Head, each with a different spatial field for the Young modulus.

A linear interpolation correlating the value for water ($HU \approx 0$) to $\rho_{app} = 0 \text{ g/cm}^3$ and the maximum bone HU value of 1700 (there were very few HU values above 1700) to maximum bone density $\rho_{app} = 1.9 \text{ g/cm}^3$ (as used by [22,26]):

$$\rho_{app}[\text{g/cm}^3] = 1.9 \frac{HU}{1700}$$  (5)

Density evaluation based on the $K_2HPO_4$ phantom present in the CT scan [35] resulted in very similar results.
A moving average was then computed using a cube containing $7 \times 7 \times 7$ voxels (edge size $\approx 5.4$ mm) for the trabecular region and a cube containing $3 \times 3 \times 7$ voxels for the cortical region. The cube sizes represent a similar volume to the smallest specimens considered in the studies on $E(\rho_{\text{app}})$. To appropriately approximate the apparent density in the trabecular region with a polynomial function, it was first divided into three parts: head, greater trochanter and low trabecular regions (Figure 3), each of them having a different function for Young modulus evaluation ($R^2 = 0.977 \div 0.982$). One cortical and two trabecular regions, are described in Cartesian coordinates whereas femur head spatial field is described in a spherical coordinate system situated in head’s center.

To investigate the sensitivity of the FE analysis, several $E(\rho_{\text{app}})$ relationships were considered (Table 1). As in [25], a constant Poisson ratio of 0.3 was used for the entire bone model, and the sensitivity of the results to this particular value was also checked.

To reproduce the loading experiment, we clamped the distal face of the bone at the location where it resides in the PMMA, and applied a pressure load with a resultant of 150 kgf enforcing zero displacement in transverse directions of the load. These boundary conditions best describe the effect of the pressing configuration assembled from a ball and a socket joint.

2.4 In-vitro experiments

To assess the reliability of the proposed FE model, we conducted two experiments on proximal femur specimens. The first was on an embalmed bone to validate the experimental procedure. The second was on a fresh-frozen femur within a period of 36 hours after defreezing. In both, we measured the displacements and strains under various loading configurations.

The experiments simulate a simple stance position configuration in which the femur is loaded through its head. In this loading condition, the force is applied in an inclination of $\approx 7^\circ$ to the shaft axis, along a virtual line that connects the femur head to the middle cavity in the
femur diaphysis (intercondylar fossa). A total of four inclination angles were considered: 0° for maximal sensitivity, 7° as in the natural stance posture, and 15° and 20° as in Keyak et al. [28]). Forces of up to 150 kgf were applied, corresponding to more than half an average body weight but smaller compared to bone’s linear response regime.

In the experiments, the load was increased monotonically at a slow displacement rate of 0.5 mm/min. Maximum loads were 50, 100, 150 kgf, applied to each of the four inclination angles. Each load case was repeated twice. A total of 24 experiments were performed for the 12 possible combinations (3 loads and 4 inclination angles). To explore the mechanical response sensitivity to the strain-rate, we applied 150 kfg load on the femur at 7° inclination at several displacement rates from 0.01 mm/min to 2 mm/min.

2.4.1 Experimental system

The experimental system includes a mounting jig, loading and measurement equipment, and data acquisition equipment. The experiment was performed using a displacement controlled machine (Instron 1115). The bone mounting jig was positioned on the Instron lower platform as shown in Figure 5. The jig was designed so as to allow bone clamping at several discrete inclination angles. The bone shaft was first positioned inside a steel cylinder (2) using six screws and fixed by embedding it into polymethyl-methacrylate (PMMA). The steel cylinder was welded to a flat plate positioned on a slider with its top face inclined to the required angle. Sliders with different slope angles position the bone in different inclination angles and allow femur head positioning directly below the load cell.

A Tedea-616 load cell with a load error ≤ 0.05% was used. A ball and socket joint with a steel ball between two brass cones was used to prevent moments acting on the load cell (Figure 5). A Solartron DFG5 Direct Current Linear Variable Displacement Transducer (DC-LVDT) measured the femur head vertical displacement. It was positioned on a stand arm.
with its core connected to the brass double-cone interface on femur’s head (Figure 5).

Strains were measured at four locations: two on the inferior and superior parts of the femur neck, and two on the medial and lateral femur shaft (Figure 6). A rosette (Vishay CEA-06-062UR-350), positioned on the lateral side of the shaft, and three uni-axial strain-gauges (Vishay CEA-06-062AQ-350) with 1.6 mm active length and 350Ω resistance were positioned at measurement locations. The strain gauges were connected to an eight-channel amplifier containing Vishay 2110B and four 2120B components. An eight-channel A/D converter (WaveBook/516 by IOTech) was used. Six channels were assigned for the strain gauges, one for the load-cell, and one for the LVDT readings. A sample rate of 10 Hz was used in all experiment to obtain measurement samples of less than 1µm displacement intervals for a testing machine velocity of 0.5mm/min. This high sample rate provides a good continuous signal with low noise. The A/D converter was connected to a laptop (Intel Pentium 4, 1.80GHz, 256MB) through LAN connection. IOTech’s WaveView software was used for data acquisition.

2.4.2 Preliminary embalmed bone experiment

An embalmed femur of a 56 years old female was used for in-vitro preliminary test to practice the test procedures to be subsequently used in the fresh-frozen bone experiment. The bone was aligned and mounted inside the cylindrical shaft and four relatively planar spots were defined on the bone surface for the three uni-axial strain gauges (neck superior, inferior and shaft medial) and for the rosette (shaft lateral). The stain-gauges were glued using a M-bond 200, as per Vishey-Micro-measurements specifications.

Five load steps were used for the test: $50 \div 250$ kgf at 50 kgf increments. The preliminary test was planned at an inclination angle of $20^\circ$, and was subjected to a higher load at the end of the experiment to determine the load at fracture. This test showed the elastic response -
all the strain gauges showed strain to load linear relation up to 120 kgf. Linear regression fit shows $R^2 > 0.99$ for all strain as a function of load. Bone mechanical response had very good repeatability on both days (with the exception of one loading "E" in the graphs). The difference between the results of each day was most likely due to the exact place where load was applied in each day (see discussion on the sensitivity to this position in the section on fresh-frozen experiment).

To investigate the inclination influence an additional experiment was performed at $0^\circ$ inclination angle. As expected, the bone inclined at $20^\circ$ is about 3.5 times stiffer than at the vertical posture (Figure 7). This ratio varies for the different measurement points due to the different mechanisms (compression and bending) that describe the strain field at those points.

![Fig. 7. Strain as a function of applied load (embalmed bone) at neck superior strain-gauge for two different inclination angles ($0^\circ$ and $20^\circ$)](image)

To ensure that the fresh-frozen bone will withstand the loading, the embalmed bone was subject to an increasing load until breakage at $\sim 400$ kgf. The first evidence of fracture occurred at 202 kgf. Consequently, a maximum load of 150 kgf was determined for the fresh-frozen femur experiment.

### 2.4.3 Fresh-frozen bone in-vitro experiments

A fresh-frozen femur of a 30 year-old male donor with no skeletal diseases was deep-freezed shortly after death. After de-freezing, the bone was affixed with six bolts to the cylindrical sleeve and fixed by PMMA after which strain gauges were attached after choosing areas with minimal curvature. Thereafter two CT scans were acquired. The mechanical experiments started six hours after bone mounting, long enough for the PMMA to cure.

The bone was repeatedly tested 39 times, with various maximum loads ($50 \div 150$ kgf) and inclination angles ($0^\circ$, $7^\circ$, $15^\circ$ and $20^\circ$).
The mechanical experiments lasted for two days. One procedure from the first day (150 kgf load at 7° inclination) was repeated at the start and at the end of the second day to verify that bone’s mechanical response (and therefore its mechanical properties) did not change. The bone was kept in refrigeration overnight and was deep-freezed again at the end of the experiments in case of further needs. The experiments during first day were for monotonic loadings at different inclination angles and maximal loading (Figure 8). On the second day, experiments to determine the sensitivity to loading rates were performed.

Fig. 8. Fresh-frozen experiments at different inclination angles (from left to right): 0°, 7°, 15°, 20°.

3 Results

3.1 In-vitro experimental results for the fresh-frozen bone

3.1.1 Linearity

A linear response was observed after 20 kgf preload (Figure 11) and can be noticed in all test results. All strain gauges show linear response to load ($R^2 > 0.998$) for the entire measurement range (see for example Figure 9).

3.1.2 Repeatability

Good repeatability was obtained, especially in adjacent tests (Figure 10). Two adjacent measurements show a difference of up to 5%. The maximum difference varies from of 3% to 19% for different measurements parameters. Two possible reasons for this difference are a change in the bone’s properties due to elapsed time or small changes in the precise location at which the load is applied to the bone.
3.1.3 Visco-elasticity

Two indications of visco-elastic behavior were noticed. One is the strain measure as a function of load magnitude during unloading: the unloading curve is not identical to the loading one. The other indication is the fact that load decreases as time passes after a given displacement is applied as shown in Figure 11. A similar behavior was also reported by Keyak et al. [28]. In few cases, an extra displacement of \( \approx 0.05 \) mm was applied to compensate for the decrease at load as seen at Figure 11 (5% during 40sec).

3.1.4 Load rate influence

To check the bone strain-rate sensitivity, we performed tests with various displacement rates in the range of \( 0.1 \div 2mm/min \). These displacement rates are equivalent to \( 2.3 \div 46 \) \( \mu strain/sec \) in the neck superior strain-gauge or \( 6.8 \div 130 \) \( \mu strain/sec \) in the shaft medial strain gauge. The strain rate differences were expected to introduce a 20% difference in bones stiffness according to (t.6). However, no such sensitivity was observed in the exper-
Fig. 11. Fresh-frozen load vis. time response for 150 kgf load at 15° inclination. Linear response is noticed after a 20 kgf preload.

iment. Displacement and strain response to monotonic loading was almost identical at all rates measured (Figure 12).

![Head's displacement vs. load and Strain (neck superior) vs. load](image)

**Fig. 12.** Fresh-frozen femur shows indifferent behavior to different strain rates (at 7° inclination): head’s displacement vis. load (left) and neck superior strain vis. load (right)

### 3.1.5 Inclination angle influence

Experiments with different inclination angles of the bone yielded unexpected results. At 7° inclination, the bone showed higher strain to load ratio than at the vertical posture (Figure 13). This is most likely caused by measurement error or by the bone’s shaft curvature that actually yields a different inclination angle. This behavior is also seen in displacements measured by the LVDT.
3.1.6 Displacements

Linear displacement/load ($\Delta z/\Delta F$) and strain/load ($\Delta \varepsilon/\Delta F$) ratios were computed for the experiment values and used in the sequel for comparison purposes with FE linear analysis results. The ratios are computed using linear regression based on the linear response range only (between 20 kgf to maximum load).

Table 2 summarizes bone displacement in the $z$ direction divided by the applied load ($\Delta z/\Delta F$) (mean values) as measured by the LVDT. In this and in subsequent Tables, $n$ is the number of experiments performed.

Table 2

<table>
<thead>
<tr>
<th>Inclination angle</th>
<th>n</th>
<th>mean</th>
<th>min</th>
<th>max</th>
<th>(max-min)/(2×mean) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$0^\circ$</td>
<td>5</td>
<td>3.01</td>
<td>2.53</td>
<td>3.54</td>
<td>16.8 %</td>
</tr>
<tr>
<td>$7^\circ$</td>
<td>13†</td>
<td>1.23</td>
<td>0.79</td>
<td>2.04</td>
<td>50.1 %</td>
</tr>
<tr>
<td>$15^\circ$</td>
<td>9</td>
<td>1.75</td>
<td>1.55</td>
<td>2.09</td>
<td>15.4 %</td>
</tr>
<tr>
<td>$20^\circ$</td>
<td>9</td>
<td>1.67</td>
<td>1.43</td>
<td>2.01</td>
<td>17.4 %</td>
</tr>
</tbody>
</table>

Note that the repeatability of the displacements/force measurements is within $\pm 17\%$ of the mean, except for the experiment at $7^\circ$ inclination. The experiment at $7^\circ$ inclination has a bad repeatability, thus will be ignored in the sequel.

3.1.7 Strains

Table 3 summarizes the mean values of strain/force response at the different locations. At the neck superior, neck inferior and shaft medial locations, the measured uniaxial strain is reported. At the shaft lateral location the principle strains computed from the rosette measurements are reported.
Table 3
Strain over load ratio [$\mu$ strain/kgf] as measured at four locations for different bone inclination angles.

<table>
<thead>
<tr>
<th>Location</th>
<th>Tilt angle</th>
<th>n</th>
<th>mean</th>
<th>min</th>
<th>max</th>
<th>(max-min)/(2\times mean) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0°</td>
<td>6</td>
<td>4.41</td>
<td>4.19</td>
<td>4.65</td>
<td>5.2 %</td>
</tr>
<tr>
<td>Neck</td>
<td>7°</td>
<td>13</td>
<td>4.85</td>
<td>4.49</td>
<td>5.21</td>
<td>7.5 %</td>
</tr>
<tr>
<td>Superior</td>
<td>15°</td>
<td>10</td>
<td>3.66</td>
<td>3.55</td>
<td>3.80</td>
<td>3.4 %</td>
</tr>
<tr>
<td></td>
<td>20°</td>
<td>10</td>
<td>3.02</td>
<td>2.90</td>
<td>3.28</td>
<td>6.3 %</td>
</tr>
<tr>
<td></td>
<td>0°</td>
<td>6</td>
<td>-12.7</td>
<td>-13.4</td>
<td>-11.3</td>
<td>8.3 %</td>
</tr>
<tr>
<td>Neck</td>
<td>7°</td>
<td>13</td>
<td>-13.4</td>
<td>-14.0</td>
<td>-11.3</td>
<td>10.1 %</td>
</tr>
<tr>
<td>Inferior</td>
<td>15°</td>
<td>10</td>
<td>-12.0</td>
<td>-12.3</td>
<td>-11.3</td>
<td>4.2 %</td>
</tr>
<tr>
<td></td>
<td>20°</td>
<td>10</td>
<td>-11.1</td>
<td>-11.3</td>
<td>-11.0</td>
<td>1.3 %</td>
</tr>
<tr>
<td></td>
<td>0°</td>
<td>6</td>
<td>-13.0</td>
<td>-13.7</td>
<td>-12.4</td>
<td>5.0 %</td>
</tr>
<tr>
<td>Shaft</td>
<td>7°</td>
<td>13</td>
<td>-12.6</td>
<td>-13.7</td>
<td>-11.4</td>
<td>9.1 %</td>
</tr>
<tr>
<td>Medial</td>
<td>15°</td>
<td>10</td>
<td>-7.42</td>
<td>-7.85</td>
<td>-7.24</td>
<td>4.1 %</td>
</tr>
<tr>
<td></td>
<td>20°</td>
<td>10</td>
<td>-4.53</td>
<td>-4.90</td>
<td>-4.32</td>
<td>6.4 %</td>
</tr>
<tr>
<td></td>
<td>0°</td>
<td>6</td>
<td>4.40</td>
<td>4.07</td>
<td>4.73</td>
<td>7.5 %</td>
</tr>
<tr>
<td>Shaft</td>
<td>7°</td>
<td>13</td>
<td>4.09</td>
<td>3.88</td>
<td>4.42</td>
<td>6.6 %</td>
</tr>
<tr>
<td>Lateral</td>
<td>15°</td>
<td>10</td>
<td>2.53</td>
<td>2.42</td>
<td>2.71</td>
<td>5.7 %</td>
</tr>
<tr>
<td>$\varepsilon_1$</td>
<td>20°</td>
<td>10</td>
<td>1.68</td>
<td>1.59</td>
<td>1.79</td>
<td>5.9 %</td>
</tr>
<tr>
<td></td>
<td>0°</td>
<td>6</td>
<td>-1.46</td>
<td>-1.53</td>
<td>-1.38</td>
<td>5.1 %</td>
</tr>
<tr>
<td>Shaft</td>
<td>7°</td>
<td>13</td>
<td>-1.44</td>
<td>-1.52</td>
<td>-0.05</td>
<td>54.5 %</td>
</tr>
<tr>
<td>Lateral</td>
<td>15°</td>
<td>10</td>
<td>-0.92</td>
<td>-0.98</td>
<td>-0.87</td>
<td>6.0 %</td>
</tr>
<tr>
<td>$\varepsilon_2$</td>
<td>20°</td>
<td>10</td>
<td>-0.63</td>
<td>-0.67</td>
<td>-0.58</td>
<td>8.7 %</td>
</tr>
</tbody>
</table>

3.1.8 Summary of the experimental results

The fresh-frozen femur response showed good linearity and repeatability. The visco-elastic behavior does not seem to have significant influence on the monotonic loading beyond the force of 20 kgf. Most of the collected data present an expected characteristic behavior. This indicates that the results may be used for comparison with the FEA.

An unclear response at 7° inclination relative to 0° inclination, and an uncertainty in the displacement measurements was observed. Therefore, the FEA comparison for the 7° inclination is questionable and should be probably discarded, but it is provided herein for completeness of presentation.
3.2 Fresh-frozen proximal femur FE model

3.2.1 FE model verification

The discretization error inherent in the FE model was investigated by increasing the polynomial degree of the shape functions from 1 to 5 over three different meshes with \( \approx 4200 \) to \( \approx 6000 \) elements. For verification purposes the boundary conditions on the femur’s head are 1 mm displacement in the direction of the inclination angle with zero displacements in perpendicular directions. The FE results show a small difference between the various FE models when the resultant force due to the 1 mm displacement is of interest (Figure 14), with about 3.2% difference between the finest and coarsest meshes. In all three models, the results for 3\(^{rd}\) polynomial with \( \approx 60,000 \) DOF is nearly converged numerically.

![Fig. 14. Resultant force (Fz) vs. DOF for different meshes under head displacement of 1mm (0° tilt).](image)

To the best of our knowledge, the determination of the Young modulus as a spatial field based on averaged data using moving average methods has not been investigated in the past. Therefore, it is important to investigate the results sensitivity to the volume of the box used for the averaging process. This investigation was performed separately for the trabecular and cortical regions. Three sets of spatial fields were determined according to three different volume sizes for moving average calculations on trabecular bone. The different volumes were \((3 \times 3 \times 3), (5 \times 5 \times 5)\) and \((7 \times 7 \times 7)\) voxels cubes. This corresponds to cube specimen with edge sizes of about 2.3\(mm\) to 5.5\(mm\). The smaller size is similar to typical elements size used in h-FE models [7, 31], while the bigger size is similar to reported test specimens (small) size. Material assignment used the (t.4) and (c.2) relationships, based on the different approximated spatial fields (one for each moving average cube size). This comparison is on the basis of bone’s model at 0° inclination, fully clamped in distal part, and head’s trimmed planar face is subjected to a 1 mm displacement.

Surprisingly, averaging trabecular bone data according to different moving average cube sizes does not show any significant effect on the analysis results (Figure 15). The resultant forces
are almost the same for all three cube sizes, with less than 1% difference (6662 N for 7 × 7 × 7 voxels cube vs. 6713 N for 3 × 3 × 3 voxels cube). Displacements and strains at several points agreed with less than 5% difference between models with different moving average box size.

The $E(\rho_{\text{app}})$ relationship used for the material assignment was found to have a significant influence on FE results. The following combinations of cortical and trabecular relations were investigated:

1. **Wirtz et al.**: Different relationships for cortical and trabecular regions according to (t.4) & (c.2).
2. **Lotz + Wirtz**: Cortical region properties are assigned according to (c.2). Trabecular properties are assigned according to (t.1).
3. **Carter and Hayes**: Same relationship is used both in cortical and trabecular regions. A strain rate of 0.01 sec$^{-1}$ is used in (t.6) resulting in (t.7).
4. **Cody et al.**: Different relations are assigned to trabecular and cortical regions according to (t.8) and (c.4).
5. **Keller**: Keller’s relation (t.2) is used in both regions of bone.

Lotz’s linear relation for cortical region (c.1) was not considered because it leads to negative Young’s modulus in some parts of the cortical spatial field where the density value is lower than 0.942 g/cm$^3$. Other relations used by Keyak et al. [1] and Martelli et al. [31] were not used herein because they are based on ash density and not on apparent density.

To investigate the sensitivity of the different relations were assigned to the FE model at 0° inclination under a 1 mm displacement constrain applied on the planar trimmed face (the density’s spatial field and all other model definitions remain unchanged). Different relationships yield significant differences in the FE results (Figure 16). The resultant force due to a 1 mm displacement using Wirtz’s relations is almost twice as compared to Keller’s relation (6662 N vis. 3381 N respectively). In these comparisons, the relations which best
predict the experimental displacement under a given load and distinguishing between cortical and trabecular bone is (t.8) and (c.4) denoted as Cody et al. [25].

To check the sensitivity of the Poisson ratio we examined values of 0.3, 0.35 and 0.4. We observed negligible influence when displacements or maximal principle strains are of interest. Only the transverse principle strains are slightly influenced.

We found that the height of the trimmed planar face on which the load is applied (see Figure 4) has a significant influence on the final result. This height may be estimated to an accuracy of ±1 mm, with a CAD software or from pictures taken during the experiment, due to the difficulty of exactly determining where the conic jig contacts the bone. To determine the sensitivity of the analysis to this height, we ran the analysis under a homogeneous material assumption ($E = 1000$ MPa, $\nu = 0.4$). Three different models with planar trimmed face at 3 mm intervals were considered. A 1 mm deflection was applied to the model on the trimmed surface with a constraint against transverse displacements. The computed resultant force shows large sensitivity to the trimmed surface height with $\approx 30\%$ difference between lowest and highest surface heights (the higher the planar trimmed face, the lower is the resultant force). The trimmed face height sensitivity increased by 33% (to 46%) after heterogeneous material properties were assigned. Examining a more complicated, yet more realistic cone shaped face for the contact surface shows only a small difference from the trimmed planar surface and therefore discarded.

Fig. 16. Resultant force [N] due to head displacement of 1 mm for 0° inclination angle: convergence of FEA resultant force according to several $E(\rho_{app})$ relations.

3.2.2 Model validation by experimental observations

To mimic the boundary conditions on femur’s head applied in the experiment we applied a uniform pressure over the entire trimmed planar surface in the axial direction while con-
straining the displacements perpendicular to the load direction. This pressure results in a non-uniform displacement field on that plane. Therefore, we averaged the displacement field extracted from the FE analysis (to be compared with the experimental measurements) over two lines passing through the center of area. From the different relationships $E(\rho_{app})$ considered in subsection 3.2, the one defined by Cody et al. provides the closest results compared to the experimental observations, and results reported in the sequel are obtained by using Cody et al. relationship.

A good prediction is achieved for two out of the four inclination angles, (Table 4 and Figure 17). An almost accurate prediction is obtained for load configuration of 15° and 20°, whereas for 0° and 7° a discrepancy exists. The experimental results for an inclination 7° are known to be questionable.

Fig. 17. FEA results using Cody et al. relations compared to experimental observations: Femur head displacement at 150 kgf compression at several inclination angles (error bars indicate min. and max. measured values).

Table 4
Displacement [mm] at 150 kgf load: FEA results using Cody et al. relations versus mean experimental measurements (%Δ refers to mean experimental measurement).

<table>
<thead>
<tr>
<th>Tilt angle</th>
<th>Experiment (mean value)</th>
<th>FEA</th>
<th>%Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>0°</td>
<td>0.45</td>
<td>0.35</td>
<td>-22%</td>
</tr>
<tr>
<td>7°</td>
<td>0.19</td>
<td>0.30</td>
<td>58%</td>
</tr>
<tr>
<td>15°</td>
<td>0.26</td>
<td>0.28</td>
<td>8%</td>
</tr>
<tr>
<td>20°</td>
<td>0.25</td>
<td>0.26</td>
<td>4%</td>
</tr>
</tbody>
</table>

We conclude that the predicted FE displacements are in very good agreement with the experimental observations, because the experimental error in the displacement is about 15% and for 7° it is about 50%.
In addition, we compared the FE strains and those measured in the experiment at the four different locations (Table 5). A closer correlation of the results is observed in the neck area than along the shaft. Even the relatively high difference of up to 66% at the neck superior location is considered to be in reasonable agreement compared to reported results by others [3, 28]. However, the FE strains along the shaft are not in good agreement with these measured in experiments.

An important observation in the FE model is the large strain gradients in the areas of interest. These large gradients in strain may be attributed to one of the following: 1) the geometrical irregularity of the surface; 2) the spatial field functional representation and several very distorted elements. For example, the FE principle strains at the location of the rosette show a difference of 78% between the upper and lower ends of the rosette.

<table>
<thead>
<tr>
<th></th>
<th>FE result</th>
<th>Experiment</th>
<th>%∆</th>
<th>FE result</th>
<th>Experiment</th>
<th>%∆</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neck Superior</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0°</td>
<td>1058</td>
<td>662</td>
<td>60%</td>
<td>-1874</td>
<td>-1954</td>
<td>-4%</td>
</tr>
<tr>
<td>7°</td>
<td>916</td>
<td>743</td>
<td>23%</td>
<td>-1813</td>
<td>-2029</td>
<td>-11%</td>
</tr>
<tr>
<td>15°</td>
<td>807</td>
<td>549</td>
<td>47%</td>
<td>-1766</td>
<td>-1806</td>
<td>-2%</td>
</tr>
<tr>
<td>20°</td>
<td>750</td>
<td>453</td>
<td>66%</td>
<td>-1744</td>
<td>-1662</td>
<td>5%</td>
</tr>
<tr>
<td><strong>Neck Inferior</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Shaft Medial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0°</td>
<td>-359</td>
<td>-1955</td>
<td>-82%</td>
<td>168</td>
<td>660</td>
<td>-75%</td>
</tr>
<tr>
<td>7°</td>
<td>-151</td>
<td>-1944</td>
<td>-92%</td>
<td>91</td>
<td>617</td>
<td>-85%</td>
</tr>
<tr>
<td>15°</td>
<td>68</td>
<td>-1112</td>
<td>-106%</td>
<td>57</td>
<td>380</td>
<td>-85%</td>
</tr>
<tr>
<td>20°</td>
<td>182</td>
<td>-679</td>
<td>-127%</td>
<td>55</td>
<td>252</td>
<td>-78%</td>
</tr>
</tbody>
</table>

|                  |           |            |    |           |            |    |
| **Shaft Lateral (ε1)** |           |            |    |           |            |    |
| 0°               |           |            |    |           |            |    |
| 7°               |           |            |    |           |            |    |
| 15°              |           |            |    |           |            |    |
| 20°              |           |            |    |           |            |    |

4 Discussion

Our FE analysis of the proximal femur is based on an accurate surface representation of the bone and the distinction between cortical and trabecular regions, generated from a CT scan, together with an inhomogeneous Young modulus represented by continuous spatial functions. Applying moving average to the CT data is also unique to the suggested method. Averaging the data for computational purposes is an accepted practice in all bone’s FE studies. This way, the Young modulus at each point in the mesh is independently determined by its close surrounding, rather than by voxels that are enclosed by the same element.
The moving average method is also necessary to compute the Young modulus based on data representing the same volume as specimens used for the $\rho(HU)$ relationship. Another numerical advantage of the moving average is the smoothing effect of the density, enabling the spatial field evaluation to be approximated by smooth polynomial functions.

The use of spatial field is well integrated in the p-FEM solver and can reduce numerical problems due to discrete jumps between adjacent elements. Possible disadvantages include large bone density gradients and the extra computational time needed for the field approximation. p-FEM reduces numerical errors due to singularities caused by an abrupt change in geometry or material properties. In addition, using high order p-element is advantageous because: 1) of the possibility to assess the numerical error without changing the mesh; 2) the use of elements with high aspect ratios in the cortical thin layer, and; 3) the high convergence rate resulting in converged strains on bone’s surface. These advantages, which keep the numerical errors under control, enable us to focus on the physical phenomena and allow direct solution verification and experimental validation using displacements and strains measurements.

The simplified models considered in the Appendix allow us to isolate the influence of the different material assignment methods. The maximum difference of 3% relative to the voxel based fine mesh is negligible compared to the modelling and experimental errors. For example, the correlation between QCT data and Young modulus is far less accurate (with $R^2 = 0.60 \div 0.92$) [9,11,12,15,24]. The advantage of using a structure-based model becomes evident when comparing the computed strains (and therefore stresses) in the cylindrical models. Voxel-based models show variations in the strain values close to the surface, while the structure-based p-FEM spatial field based models show a converged solution. The bone slice model exhibits the advantage of the new method thanks to the separation between the cortical and trabecular regions (up to the lesser trochanter). The stiffer behavior of p-FEM model is observed because of reducing the underestimated cortical shell stiffness due to average with trabecular density or air (near surface). Underestimation of bone Young’s modulus in voxel based methods was described by [23] and considered to be important.

Solving a physical problem using finite elements encompasses several error types. An idealization error is encountered when assumptions are made to describe the physical system by a mathematical model. A discretization error is introduced by solving the mathematical equations using numerical methods, i.e. FE methods. Measurement errors are of importance as well because the FEA should be validated against experimental measurements. Herein, we bring an error assessment and discussion following the differences found by comparing the FE results with in-vitro experimental observations.

Idealization errors associated with boundary conditions and material properties were among the most important errors considered in this research. The material properties are assumed to be linear elastic isotropic, with inhomogeneous Young modulus. An excellent elastic linear response was observed in the experiment, thus validating this assumption. The visco-elastic response, as measured during monotonic loading, is negligible. The bone response was indifferent to changes in strain-rates. However, we found that the isotropic assumption can indeed overestimate bone stiffness. The bone stiffness in the principal strain was reported
to be $1.7 \div 2.5$ times stiffer than in the transverse direction $[11,13,35]$. Although one may want to correlate the FE errors to that assumption alone, we must not forget that the bone is assumed to be remodelled such that for the experiment configuration (similar to stance posture) the material principle directions are oriented according to principal stresses, thus uniaxial properties might be satisfactory [36]. Nevertheless, the influence of transversely isotropic material properties on the results will be investigated in a future study.

The determination of the elastic parameters is of major importance in assessing idealization errors. We therefore numerically investigated it with various relations and values for $E$ and $\nu$. Young modulus determination based on the CT data includes two types of errors: one results from the computation of $\rho_{app}(HU)$ and the other from the relation $E(\rho_{app})$ (the error due $\rho_{LMS}(\rho_{app})$ is discussed in the sequel).

Even if one considers relations with $R^2 \geq 0.8$, by using two of those consequently, the final correlation quality can become quite low (yet both [35] and [11] report on good correlation of Young modulus directly from CT data). We found that using a specific relation for $E(\rho_{app})$ can cause a $100\%$ error in the displacement/force results alone. We thus conclude that a large experimental database of FEA studies is necessary to identify the best $E(\rho_{app})$ relationship. The relationship used by [25] is found to provide close results as measured in the experiment. Poisson ratio on the other hand, had almost no effect on the results. The strain measurements (a property found to be affected) were taken from nearly the principal direction and therefore should not be largely influenced by the arbitrary Poisson ratio used.

The separation of the bone into cortical and trabecular regions can be a source of error as well. Three errors should be considered: 1) neglecting the cortical shell above lesser trochanter; 2) position of separating border, and; 3) the thickening of the cortical shell near lesser trochanter. The influence of the three is difficult to assess. In our opinion, neglecting the thin cortical shell ($0.1 \div 0.4mm$) may affect the local strains, but not the global displacement. The inaccurate separation of the surface and cortical shell thickening may introduce errors. However, the use of the cortical relation (c.4) instead of the trabecular one (t.8) on a low density region having $\rho_{app} < 1.2g/cm^3$, leads to lower Young modulus evaluation and therefore cannot introduce the stiffer response showed by the model.

Three additional sources of error in the FEA are: 1) the geometric representation of the bone; 2) the density approximation by LMS, and; 3) the mesh itself. The geometric representation depends on the CT resolution, the smooth surface approximation, and the FE mapping. The first two errors have together an effect of less than $1mm$, taking into account a half pixel size plus the reported surface mean approximation error. This should not have a major affect on the model geometry and therefore on the displacement results. The mapping has no influence on the displacement results, and can slightly affect the strains. Note that abrupt density change – and therefore of the Young modulus – in the transition between regions can also lead to errors. This issue will be addressed in future work.

The LMS approximation of the density is a significant unknown. At first, it did not seem to have a real influence on the FE results – changing the volume used for averaging did
not result in large changes in the FE solution. However, additional numerical experiments are necessary to establish how averaging affects the results. The current study assumes that a moving average data should be a better source for material evaluation based on reported relations. Yet it cannot be proved or disproved based on the numerical comparison or mechanical test comparison.

Large variations of density along the entire trabecular bone necessitates the use of several functions to approximate it (see Figure 3 where we used 3 different functions in distinct regions). These functions introduce errors in strains along the regions borders, as discontinuity in the strain field was observed. Nevertheless, the strain-gauge location were at least two elements away from these borders and therefore this problem should not cause the large discrepancies in the strains.

The prediction of the mechanical response of the femur depends on the ability to approximate the density values using a continuous functions. The fields that were evaluated herein showed good approximation to the original values with \( R^2 > 0.97 \). Nevertheless, further investigation will be undertaken to examine if bases other than polynomials and trigonometric functions may provide a better approximation. In this research, higher polynomial degrees of the LMS approximation lead to ill-conditioned matrices. Therefore, the separation between cortical and trabecular regions is deemed to be essential due to different functional representation and to obtaining well-conditioned matrices, necessary to reliably evaluate the unknown coefficients representing the function. We conclude that the spatial field representation cannot be straightforwardly implemented in other structure based meshing methods such as [6,21]. Other complications could rise due to high density-gradients in osteoporotic region, but in this case several fields can be used, e.g. one for the healthy trabecular region and other for the osteoporotic one.

Finally, to evaluate experimental errors, it is important to consider the experimental data as a reference. The load and strains measurements are by far less significant than all other errors considered. However, the errors in the position and orientation of the strain gauges is about \( \pm 0.8 \) mm and about 16°. Such error may affect the result comparison. It is impossible to know which one is more reliable, so a definite model assessment cannot be done. An error in bone inclination angle measurement was addressed (although not described here) resulting in less than 2% difference in displacement due to a 1° inclination error.

To conclude, the model presented in this paper has been numerically verified and found to have good displacement prediction. Although it cannot be yet fully validated because of the strains prediction, the errors reported in this study are quite reasonable in view of past experiments of the proximal femur. We found that the two main factors that mostly influence the FEA reliability are the material properties assignment (both Young modulus evaluation and isotropic assumption) and the determination of the exact area subject to load. Both will be further investigated in the future to improve the analysis reliability. A larger experimental database to be generated (consisting of several bones) and further FE analyses incorporating anisotropic material properties are believed to have a prominent influence on the results.
5 Summary

A new method was described for a more reliable simulation of the mechanical response of bones based on an accurate representation of bone’s geometry, an accurate estimation of the trabecular-cortical interface, a spatial description of the inhomogeneous Young modulus, and a high order FE analysis. The thrust behind the new method stems from the desire to represent the bone geometry more accurately and from the desire to improve the evaluation of mechanical properties with experimental methods that were used to generate the correlations between QCT and mechanical properties. The resulting structured-based method showed superior performance compared to the common voxel-based method.

Model verification and validation against experimental results show an excellent prediction for the displacements due to load at three out of four inclination angles, and strains at two locations. Strain’s FE prediction at the other two locations were not in good correlation with the experimental observations. This model prediction will probably improve with the use of orthotropic material properties from QCT scans, to enable a more realistic simulation of the mechanical response of the femur.

Finally, as a service to the research community, we have made publicly available CT scans and FE mesh of the fresh-frozen bone as download at the URL address:
www.bgu.ac.il/~zohary/CT_FF.html

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A Appendix - Comparison study between voxel-based and structure-based models

In this Appendix, we compare the results of existing voxel-based methods to the proposed structure-based method with respect to three factors: 1) accurate surface representation; 2) continuous material representation, and; 3) element size. We do so in three domains of increasing complexity: a cube with straight faces, a quarter cylinder with a circular edge, and a portion of the proximal femur.

The domains are assumed to be isotropic inhomogeneous with a Young modulus defined according to the clinical CT scan of a 59 year old female femur (140 kVp, spiral scan, 2mm slice thickness with resolution of 0.863 mm pixel size). A linear interpolation is used for apparent density ($\rho_{app}$) evaluation as in (5). Distinct subregions for the trabecular and cortical parts are defined. Trabecular bone’s Young modulus is evaluated according to (t.4). For the cortical region a constant value of 16 GPa was used [3] herein, however any other spatial representation can be easily considered. A constant value of 0.4 for Poisson’s ratio was used for all elements, as in [28].
The voxel-based models were generated as follows:

1. **Data extraction:** A 3D array of voxel’s HU values was extracted from the CT scan.
2. **Mesh generation:** A voxel based mesh with hexahedral elements was generated using an automatic procedure which creates an element when the voxel’s HU value in its center is above a pre-defined threshold.
3. **Young modulus value:** First, \( \rho_{\text{app}} \) was estimated by linear interpolation of the HU value according to (5), followed by Young modulus evaluation according to (4).
4. **Young modulus assignment:** For each element, a constant Young modulus was assigned according to the averaged value of the enclosed voxels (rounded to 1 MPa).

**Cube dataset**

A 20 × 20.76 × 20.76 mm\(^3\) cube created from 10 CT slices × 24 pixels × 24 pixels was chosen in the femoral head. It was positioned so that its faces had a distance of at least 2 mm from the bone surface, to prevent partial volume voxel effects and prevent cortical bone influence. A series of six cubes were created with different mesh characteristics, with the material properties assignment method (Figure A.1). The first four models (numbered 1A-1D) are voxel-based models consisting of hexahedral elements with decreasing element size, containing 64 to 1440 elements. In each element the Young modulus is determined by averaging 240 CT-voxels for the 64 element mesh, to 8 CT-voxels for the 1440 element mesh. The other two models (1E-1F) are created by the suggested method: model 1E is meshed using 8 hexahedral p-elements; model 1F is auto-meshed by tetrahedral elements. The cubes are subject to a uniform pressure on one face, with symmetry constrains on three other faces. This comparison serves for evaluating the influence of Young modulus representation alone, because the geometry is well approximated.

![Model images](image-url)

Fig. A.1. Cubes comparison: Models A-D are voxel-based. Models E-F are p-meshed with a continuous function representing the Young modulus.

**Cylinder dataset**

A quarter cylinder, contained in the previous cube, with a radius of 20.7 mm and a height of 20 mm is considered herein. The first four voxel-based models (2A-2D) were meshed with hexahedral elements of decreasing size, representing progressively better the accuracy of the circular surface (Figure A.2). Models 2E-2F are p-FEM models, with material properties assigned using the suggested method. Model 2E has 24 p-elements with an exact surface...
representation achieved using blending functions mapping [29]. Model 2F is auto-meshed by tetrahedral p-elements with cylindrical edges described by second-order polynomials. Both axial pressure and an angular displacement of 0.5 degree on one of the faces ($\theta = 0$) are prescribed. This comparison is used to evaluate the influence of Young modulus representation together with the influence of errors in the surface representation.

![Models 2A to 2F](image)

**Fig. A.2. Cylinder comparisons:** Models A-D are voxel-based. Models E-F are p-meshed with a continuous function for the Young modulus.

**Bone slice dataset**

A realistic bone slice 36 mm long from a part of the proximal femur with both cortical and trabecular regions was considered. Four models are created according to the data extracted from the clinical CT scan (Figure A.3). The first two (3A, 3B) are voxel-based models with element sizes of 3.2 mm and 2.4 mm respectively. Models 3C-3D are constructed according to the suggested method. They are formed by tetrahedral p-elements with two distinct regions separated by a surface - the outer region is the cortical region in which for simplicity we used a constant Young modulus $E = 16$ GPa, whereas in the trabecular region a spatial field is obtained and $E$ is assigned according to (t.4). The bone slice was subjected to two different load cases: 1) an axial force of 70 kgf distributed uniformly on the upper surface and clamped at the bottom surface, and; 2) an axial uniform displacement of the top surface generating a 0.1% strain in the $z$ direction over the whole model. The difference between models 3C-3D is in the surface representation. The surfaces in model 3C are represented by a second-order polynomial, whereas in model 3D blending functions are used for an exact surface representation. This comparison serves for evaluating a realistic geometry with the influence of Young modulus representation together with the influence of errors in surface representation, and the two distinct regions of the bone.

![Bone slice comparison](image)

**Fig. A.3. “Bone slice comparison”:** Models A-B are constructed by voxel based method. Models C-D are p-meshed with a continuous function describing the Young modulus in the trabecular region. Model D represents exactly the surfaces.
A.1 Results of the comparison

Comparison of the displacements and strains at several points in the cube show only small differences (of up to 3%) between the voxel-based and the suggested methods. In the FE analysis of models 1A-1D, the polynomial degree in each hexahedral was increased from 1 to 3 (typical h-FE methods use polynomial degrees 1 or 2), whereas models 1E-1F are based on p-FEM in which the polynomial degree of each element is increased from 1 to 8 (obtaining 8 consecutive solutions and an estimate of the numerical error). The new suggested method demonstrates a faster convergence rate (Figure A.4). However a typical difference of 10%-20% is obtained between the various cylindrical models. Figure A.5 shows that for the voxel-based models the surface influence on the solution is evident at two elements away from the surface, while in the models using spatial field (2E-2F), minor surface influence is observed. These results are consistent with analyses performed using the same mesh but with constant homogeneous material (not shown herein).

![Figure A.4. Strains ($\varepsilon_{zz}$) at the cube center point vs. number of DOF.](image)

In the bone slice models, we have compared the results along an ellipse inside the trabecular region of the bone slice and along a medial-lateral line across the center of the bone (see Figure A.6). Figure A.7 shows the Young modulus distribution in the plane of the two shown curves.

Results of the four models show qualitative agreement. The same trends are seen in the graphs describing displacements and strains. The results of models 3C and 3D are almost identical, so only model 3C is mentioned in comparison with models 3A-3B. Models 3C-3D show almost constantly lower displacements and strains compared to the voxel-based models. For example, the maximum displacement ($u_z$) of model 3C was 0.019 mm compared to 0.022 mm according to models 3A and 3B (the overall displacement pattern in the three different models is presented in Figure A.8). This trend is also observed in the displacements along the medial-lateral line and in the strain $\varepsilon_{zz}$ along the ellipse (Figure A.9). These results are consistent with [7], in which all structure based models investigated show 15% stiffer response compared to the voxel based model.
Fig. A.5. Tangential strain $\varepsilon_{\theta\theta}$ along the radius at $\theta = 90^\circ$ for the cylindrical models under displacement boundary conditions.

Fig. A.6. Curves (ellipse and center-line) inside the bone slice along which the results are compared.

References


Fig. A.7. Young modulus distribution across the bone slice at the curves plane. First row: trabecular region, Second row: cortical region.

Fig. A.8. Axial displacement ($u_z$) for the three different bone slice models. Model 3C shows a stiffer behavior.


Fig. A.9. Results along the curves inside the trabecular region at the mid-height of the slice for the different bone-slice FE models. Left: axial displacement ($u_z$) along the medial-lateral line. Right: $\mu$-strain in axial direction ($\varepsilon_{zz}$) along the ellipse.

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