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Exploring inter-subject anatomic variability using a population of patient-specific femurs and a statistical shape and intensity model

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ABSTRACT

This paper is motivated by the need to accurately and efficiently measure key periosteal and endosteal parameters of the femur, known to critically influence hip biomechanics following arthroplasty. The proposed approach uses statistical shape and intensity models (SSIMs) to represent the variability across a wide range of patients, in terms of femoral shape and bone density. The approach feasibility is demonstrated by using a training dataset of computer tomography scans from British subjects aged 25–106 years (75 male and 34 female). For each gender, a thousand new virtual femur geometries were generated using a subset of principal components required to capture 95% of the variance in both female and male training datasets. Significant differences were found in basic anatomic parameters between females and males: anteversion, CCD angle, femur and neck lengths, head offsets and radius, cortical thickness, densities in both Gruen and neck zones. The measured anteversion for female subjects was found to be twice as high as that for male subjects: 13 ± 6.4° vs. 6.3 ± 7.8° using the training datasets compared to 12.96 ± 6.68 vs. 5.83 ± 9.2 using the thousand virtual femurs. No significant differences were found in canal flare indexes. The proposed methodology is a valuable tool for automatically generating a large specific population of femurs, targeting specific patients, supporting implant design and femoral reconstructive surgery.

1. Introduction

Inter-subject anatomic variability is an important consideration in hip arthroplasty and in the design of implants. The development of computational platforms to automatically assess key anatomic parameters and bone quality measures can serve as pre-operative planning tools with the potential to identify risks and guide implant selection and placement for optimal patient outcomes. Image-based modelling, along with statistical shape analysis, can facilitate the development of such tools for improving our understanding of the human anatomy and capturing the variability across the population. High-fidelity computer models that represent the femur and knee joint geometries for example can now be generated, ready for simulation and for the interrogation of designs and scenarios that would be impossible or infeasible in live patients or in laboratory testing. As a result, given a set of training images of variable resolution for the human body, the main goal is to model the geometric variability of the anatomic structures. The detail available in specimen-specific models can then be harnessed while leveraging the power of the parameterisation techniques common in generic models [7–9,11,13,15,20,22,28,31,35].

The measurement of image-based anatomy parameters is often a manual process [19] and can be labour intensive and time consuming. The reliability and accuracy of parameter measurements depend on the experience of users, their knowledge of the studied anatomy but also on the available software. Important parameters such as the hip offset, typically derived from 2D X-rays (frontal plane) or the anteversion (characterising the anatomy in the transverse plane of the hip) are not only known to critically influence the hip mechanics but their influence is not well understood [16]. Failure to adequately consider the full 3D anatomy and its variation across gender and age may not only limit the patient's function but can also compromise the long-term success of the surgery [18,41]. Whilst tomographic imaging modalities such as CT and MRI provide an opportunity to assess the anatomy three-dimensionally, there is no consensus on which specific reference axes and coordinate systems are best suited to accurately and reliably determine 3D measures of femoral

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Table 1
Meshing parameters.

Meshing parameters	Value
Target minimum edge length (mm)	0.8
Target maximum error (mm)	0.5
Maximum edge length (mm)	10
Surface change rate (1 = slow, 100 = fast)	8
Target number of elements across a layer	30
Element internal change rate (1 = slow, 100 = fast)	30
Mesh quality optimisation cycles	5
In-out target ratio	0.1
Tetrahedron volume skew	0.9
Tetrahedron minimum dihedral angle (°)	10
Jacobian	0.1

anatomy [16,19]. A pre-operative estimate of the version still depends on the accuracy of these axes either using CT scan images [38], standard radiographs, CAD or finite element (FE) mesh-based measurements. Therefore, as a critical first step towards understanding the role of 3D femoral anatomy for hip mechanics, a comprehensive measurement of shape and density-based parameters must be conducted.

The present study focuses on the development of a novel computational tool that enables to fully represent the possible variations in bone shape and density for patients using a statistical shape and intensity model (SSIM), based on a library of patient CT scans. Key anatomic parameters are accurately and automatically measured and results between females and males are compared. The rationale behind this was to represent the variability in anatomic parameters across gender and reveal any significant differences in both shape and density. The ultimate goal is to define a strategy that can help to better classify types of femoral canal shape using a wide range of patients and bone quality but also to aid in the selection of the most appropriate hip replacement.

2. Materials and methods

In this study approved by the local ethics committee and executed in accordance with the respective regulations, CT scan images were used to generate 75 male (47 left, 28 right) and 34 female (19 left and 15 right) femurs for analysis (voxel size: 0.488 × 0.488 × 1.5–0.7422 × 0.7422 × 0.97 mm). Patients were aged 25–106 years with a mean average age of 64.61 ± 19.69 years, 33 being less than 60 years old. The average weight, height and body mass index (BMI) for females (males) was 73.02 ± 11.93 kg (88.06 ± 16.07 kg), 1611 ± 65.83 mm (1773.5 ± 98.29 mm) and 28.19 ± 4.78 kg m^2 (27.89 ± 3.92 kg m^2), respectively.

2.1. Femur model generation

A total of 109 femur models were segmented using ScanIP software ([36], UK). CT image thresholds were interactively defined to select the desired tissue and identify trabecular and cortical bone. A “floodfill” capability was used to remove non-connected artefacts; blood vessels, cartilage and any anomalies were removed by using the “unpainting” option available within the software. Any detected gaps were manually reconnected before filling the cavities and generating femur masks (Fig. 1a). The segmented femurs were converted into high-quality 3D tetrahedral finite element (FE) meshes in ScanIP which provides detailed control over the number of elements and further indicators of mesh quality mesh density transition speed (Table 1). For each mesh, the bone apparent density (ρ) was automatically assigned, assuming a linear relation to the Hounsfield unit from the CT scan; no calibration phantom was available for the CT images. For the calibration between bone elastic modulus E and ρ, the relationship $E = 6850\rho^{1.49}$ was used [24], based on the combined numerical–experimental study by Schileo et al. [33] on the effects of density–elasticity relationship on strain levels in long bones. Elements within the medullary canal had a density of 0 g/cm^3 while a peak value of 1.73 g/cm^3 was assigned to the densest cortical bone of the femoral shaft.

2.2. Mesh registration and morphing

The FE meshes resulting from segmented femurs were used to form a dataset of training samples. First, each femur shape was described by a dense cloud of points located on the external surface and an element connectivity matrix. Next, a source mesh of a segmented left femur (25580 nodes, 51156 triangles) from the visible human dataset [37] was used for elastic surface registration of each considered target male and female subjects. The voxel size from the visible human dataset is 0.9375 × 0.9375 × 1 mm. The rationale behind the choice of this model was to use a medium size femur model that guarantees a minimum mesh distortion when elements are either stretched or distorted [9]. All models were initially aligned to a unique orientation with the same centre of mass using the iterative closest point (ICP) algorithm [6]. This allowed eliminating the effects of variability in patient positioning during scanning procedures.

The registration scheme initially proposed by Moshfeghi et al. [25] and modified by Bryan et al. [9] uses the *k-d* trees (Samet [34]) to find the nearest neighbour and iteratively applies a Laplacian smoothing technique (Vollmer et al. [40]) to minimise mesh distortion. Note that for the right femurs considered in this study (28 males and 15 females), the models were mirrored through the mid-sagittal plane to make them “virtually left.” This was followed by applying a volume mesh morphing strategy [2,9] to achieve a 3D correspondence between the source and target femur models. This allowed each target femur mesh to be matched to the source mesh and to convert it into a 3D solid 4-noded tetrahedral mesh (304,638 elements, 65,031 nodes). Finally, the CT-based nodal material properties were directly mapped from each target femur model to each morphed mesh using a nearest point 3D interpolation. Then, for each finite element, the material properties were averaged over its 4 nodes (Bah et al. [3]).

2.3. Principal component analysis (PCA)-based statistical shape intensity model (SSIM)

A training dataset of femur nodal coordinates and Young moduli was first assembled into a matrix **TD** that can be written as follow:

$$\mathbf{TD} = [\mathrm{X}_1, \mathrm{X}_2, \ldots, \mathrm{X}_N]^{\mathrm{T}} \in \mathbb{R}^{Nx4n}, \tag{1}$$

where X_i is a single vector of length $4n$ that defines the ith femur and contains both the nodal coordinates (x, y, z) and elastic Young moduli E;

$$\mathrm{X}_i = \{x_{i,1}, x_{i,2}, \ldots, x_{i,n}, y_{i,1}, y_{i,2}, \ldots, y_{i,n}, z_{i,1}, z_{i,2}, \ldots, z_{i,n}, E_{i,1}, E_{i,2}, \ldots, E_{i,n}\}^T, \tag{2}$$

n is the total number of nodes in each femur mesh and N is the total number of femur models. **TD** was first modified into a standardised training dataset **TD**′. This was achieved by removing the average femur denoted $\bar{\mathrm{X}}$ from each femur candidate X_i and dividing by the standard deviation along each column of **TD**. A PCA-eigenanalysis of the resulting covariance matrix was then performed that projects it to the first few eigenvectors, the eigenvalues highlighting the directions of the highest variances. This led to the selection of the first principal components that account for 95% of the total cumulative variance, i.e. those that best decomposed the training dataset in terms of shape and bone density [9,15,26].

Using this approach, it is possible to approximate each new femur model as follows:

$$X = \bar{\mathrm{X}} + \sum_{i=1}^{m} c_i \Phi^i, \tag{3}$$