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Délivré par :

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Titre :

Etude de la variabilité en fonction du sexe, de l'âge et de l'origine géographique de l'extrémité distale du fémur

Study of the sex-, age- and geography-based variability in the distal femur

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Imprimer le formulaire

Résumé en Français

La morphologie des os humains varie en fonction du sexe, de l'âge et de l'ethnie. Cette variabilité de l'anatomie humaine peut aider à déterminer le sexe, l'âge et l'ethnie. Les outils utilisés pour de telles analyses sont classiquement des méthodes ostéométriques (longueur, angle, rapport de longueur) qui peuvent être sujettes à des biais d'analyse ou d'interprétation. L'analyse morphométrique géométrique 3D (MG) permet de limiter ces biais. Elle étudie et compare la forme d'un ou plusieurs objets en éliminant les effets liés à la taille de celui-ci. Nous n'avons pas retrouvé d'analyse du dimorphisme sexuel, ethnique et lié à l'âge de l'extrémité distale du fémur à l'aide de cette méthode. Le fémur est pourtant un des plus gros os du corps et il est souvent bien conservé dans les restes humains.

L'objectif de ce travail était de montrer qu'il existe une différence de forme du fémur distal en fonction de l'âge, du sexe et de l'ethnie visualisable grâce à MG.

Nous avons réalisé une MG de 482 scanners d'extrémité distale de fémur de sujets vivant dans le sud de la France et dans la région de Chongqing (chine). Les sujets présentant une pathologie osseuse ou articulaires ont été exclus. Dix landmarks ont été positionnés sur des reconstructions tridimentionelles. Nous avons également réalisé une analyse ostéométrique « classique » en plus de MG afin d'évaluer la vraisemblance de nos résultats.

Les données ont été analysées par deux observateurs à deux temps différents. Nous avons calculé pour chaque landmark la variabilité inter et intraobservateur. Les landmarks choisis permettaient de caractériser la forme de l'extrémité distale du fémur. La première étape a consisté en la réalisation d'une analyse généralisée procrustre (GPA). Les coordonnées dans l'espace des landmarks ont été analysées en utilisant une analyse en composant principal (PCA). Une analyse discriminante a permis de vérifier le pourcentage de cas dans lequel le sexe, l'âge ou l'ethnie estimés étaient les bons.

GPA retrouve une différence de forme statistiquement significative entre les sexes, en fonction de l'âge et entre les ethnies. PCA retrouve une différence de forme en fonction de l'âge, du sexe ou de l'ethnie qui représente respectivement 54,4 ;58,6 et 61,9% de la variabilité observée. Les taux d'assignement correct avec cette méthode étaient de 80% (âge) ; 77,3% (sexe) et 82 % (l'ethnie). L'analyse ostéométrique « classique » retrouvait des valeurs comparables à celles retrouvées dans la littérature. Le pourcentage d'erreur intra et inter observateur pour l'ensemble des landmarks n'excédait jamais 2%.

Nous avons démontré que l'analyse MG du fémur distal permettait de mettre en évidence une variabilité en fonction du sexe, de l'âge et de l'ethnie de ce segment osseux. La reproductibilité élevée et la vraisemblance des résultats valident notre méthodologie.

Cette différence de forme a des retombées directes en anthropobiologie mais aussi en orthopédie. Cette méthode d'assignation ne donne pas de résultats suffisamment précis pour être utilisée seule. Cependant, elle a l'avantage de pouvoir être utilisée dans des contextes d'autopsie virtuelle ou in vivo. Par ailleurs, par la présente étude nous réactualisons les données morphométriques de population contemporaine du sud de la France et aussi de la région de Chongqing en chine. Cette méthodologie adéquate et reproductible va permettre de réaliser des comparaisons diachroniques ainsi qu'inter ethnique. La validation de l'utilisation d'examen d'imagerie médicaux ouvre un champ nouveau en anthropologie physique. En ce qui concerne l'aspect orthopédique, cette variabilité questionne sur la nécessité ou non d'implant spécifique et surtout sur la nécessité de réévaluer de manière régulière la forme des prothèses de genou.

Abstract

The shape of human bones varies based on age, sex and ethnicity. This variability in human anatomy can be used to determine a person's age, sex and ethnicity. Historically, the tools used for such analyses are osteometric methods (length, angle, length ratio) that can be plagued by analysis or interpretation biases. Three-dimensional geometric morphometric analysis (3D GM) can limit the impact of these biases. It is used to describe and compare the general shape of one or more objects by eliminating any size-related effects. To the best of our knowledge, this method has never been used to analyse the sexual dimorphism, ethnicity-related and age-related differences in the distal femur. The femur is one of the longest human bones and is often well preserved in human remains. The goal of this study was to demonstrate differences in the shape of the distal femur according to age, sex and ethnicity using GM.

We carried out 3D GM on 482 CT scans of the distal femur of adults living in the South of France and in the Chongqing region of China. Subjects with bone or joint pathologies were excluded. Ten landmarks were defined on 3D reconstructions of the distal femur. A standard osteometric analysis was performed in addition to the GM analysis to evaluate the plausibility of our results.

The data were analysed by two observers at two different times. This allowed us to calculate the inter- and intra-observer variability for each landmark. The chosen landmarks were used to characterise the shape of the distal femur. The first step consisted of a generalized Procrustes analysis (GPA). The landmarks' coordinates in space were analysed using a principal component analysis (PCA). A discriminant analysis was performed to determine the percentage of cases in which the sex, age or ethnicity was correctly estimated.

The GPA found a statistically significant difference in the distal femur shape between different sexes, ethnicity groups and age groups. The PCA found that age, sex and ethnicity

accounted for 54.4%, 58.6% and 61.9% of the observed variability in distal femur shape, respectively. Using this method, 80% of cases were assigned the correct age, 77.3% the correct sex and 82% the correct ethnic group. The results of the osteometric analysis were comparable to published values. The percentage error for the intra- and interobserver comparisons for all the landmarks was always less than 2%.

In this study, MG analysis of the distal femur revealed age-related, sex-related and ethnicity-related variability in the distal femur. The high reproducibility and plausibility of our results validate our methodology. These shape differences have direct implications for anthropobiology and also orthopaedics. Although this method is not sufficiently accurate to be used alone, it has the advantage of being usable in the context of virtual or in vivo autopsy cases. Moreover, this study has updated the morphometric data for a modern population in the south of France and the Chongqing region of China. This reliable and accurate methodology can be used to perform diachronic and interethnic comparisons. Validation of this medical imaging modality opens new avenues in physical anthropology research. In the orthopaedics field, this variability means that the shape of implants used for knee arthroplasty should be re-assessed regularly and brings into question the need for gender-specific or ethnicity-specific implants.

Il y a peu de différence entre un homme et un autre, mais c'est cette différence qui est tout

william james

Remerciements

Ce travail n’aurait pas pu voir le jour sans le Pr Norbert Telmon qui m’a guidé dans cette recherche. Je vous suis éternellement reconnaissant de tout ce que vous avez fait et que vous continuez à faire pour moi. Vous m’avez fait confiance dès notre première rencontre. Merci infiniment.

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Ce travail n’aurait pas abouti sans l’équipe de l’hôpital universitaire de Chongqing et en particulier le docteur Lee : « Chris, you are always welcome in our unit »

Je voudrais enfin remercier les professeurs Mansat, Bonnevialle(S) et Chiron ainsi que le docteur Reina pour leur soutien permanent. Je suis fier de faire parti de cette équipe.

A Marie , je t’aime pour toujours,

A Lucie et Numéro 2, (Regis me l’avait dit : « tu ne feras que des filles !!! »),

A ma famille,

A mes amis,

Sommaire

INTRODUCTION

La forme des os est variable entre les individus mais aussi entre les groupes d'individu. Cette différence d'anatomie ou variabilité peut être utilisée pour donner des caractéristiques communes en fonction du sexe, de l'âge ou du groupe ethnique.

Les analyses classiquement réalisées pour analyser ces différences reposent sur des mesures métriques entre des points remarquables (longueur, angle, rapport) [1]. Ces méthodes ostéométriques peuvent être sujettes à des biais d'analyse liés : au risque d'erreur inter et intra observateur, à l'expérience des observateurs, à des problèmes de standardisation et à des problèmes d'analyse statistiques [2].

L'analyse géometrique morphométrique permet la quantification de caractéristiques morphologiques [3]. Cette technique permet une analyse de la forme globale d'un objet dont la géométrie est préservée ce qui rend l'analyse statistique réalisable [4]. Elle a été développée pour quantifier la forme de structures rigides faites de courbes et de bombements qui ne sont pas facilement interprétables par des méthodes métriques classiques [5]. Cette méthode a déjà montré son utilité en anthropologie physique [6].

Nous n'avons pas retrouvé d'analyse du dimorphisme sexuel, ethnique et lié à l'âge de l'extrémité distale du fémur à l'aide de cette méthode. L'extrémité distale du fémur est pourtant une structure rigide faite de courbe et de bombement. Le fémur est un des os les plus gros du corps et il est souvent conservé en bon état dans les restes humains. [7] Il est donc tout à fait pertinent d'analyser son dimorphisme ethnique, sexuel et lié à l'âge. Cette analyse aura des retombées anthropobiologiques mais aussi orthopédiques.

Estimer l'âge et le sexe d'un individu dans un contexte de médecine légale représente un objectif majeur de l'anthropologie physique [8-13]. La détermination de l'âge, du sexe et de l'ethnie de restes humains repose sur un faisceau d'arguments. En déterminant les caractéristiques de l'extrémité distale du fémur, on peut obtenir des informations supplémentaires qui peuvent affiner l'analyse.

D'un point de vue anthropobiologique, l'analyse des caractéristiques de l'extrémité distale du fémur va pouvoir permettre de réaliser des comparaisons diachroniques et interethniques. La possibilité d'analyse de sujets contemporains à partir d'examen médicaux va ouvrir un champ nouveau dans les possibilités de comparaison, il s'agit d'une évolution majeure en anthropobiologie. Les variations temporelles observées avec les populations contemporaines montrent que la réévaluation de certaines mesures osseuses est nécessaire [1].

Enfin en ce qui concerne le point de vue orthopédique, le nombre de prothèse de genou qui vont être posées dans le monde va connaître une croissance exponentielle (fig 1). Il convient donc d'avoir une analyse fine des différentes anatomies et des différences d'anatomie afin d'évaluer l'adéquation avec la forme des prothèse totales de genou.

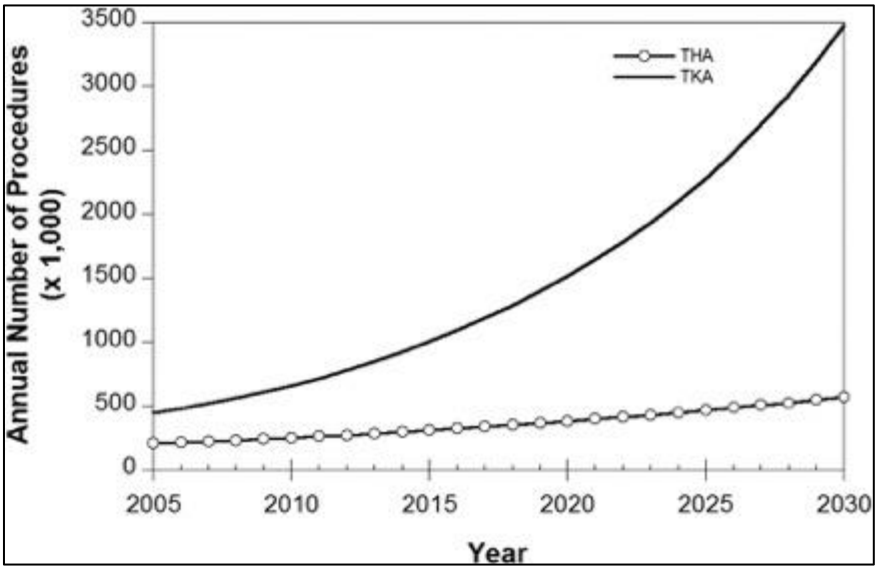

Figure 1 : Etat des lieux et prévision du nombre de prothèse totale de hanche (THA) et de genou (TKA) implantées par an au Etats Unis d'Amérique. D'après Kremers et coll [14]

HYPOTHESE

Notre hypothèse est qu’il existe un dimorphisme sexuel, ethnique et lié à l’âge de l’extrémité distale du fémur. L’analyse morphométrique géométrique va permettre de le mettre en évidence et de le quantifier.

OBJECTIF

L’objectif de ce travail était de montrer qu’il existe une différence de forme du fémur distal en fonction de l’âge, du sexe et de l’ethnie. Cette différence peut être mise en évidence, visualisée et quantifiée en utilisant l’analyse morphométrique géométrique en 3D.

Nous avons organisé notre travail de thèse en 4 articles : analyse du dimorphisme sexuel dans la population européenne, analyse du dimorphisme lié à l’âge dans la population européenne, analyse du dimorphisme ethnique entre une population européenne et une population asiatique, enfin une étude de la variabilité de la torsion fémorale épiphysaire distale. Vous trouverez également en annexe 4 un travail d’analyse du dimorphisme sexuel et lié à l’âge dans une population asiatique réalisé par le groupe avec lequel nous travaillons en chine. Nous allons débuter par un rappel sur ce qu’est l’analyse morphologique géométrique.

La Morphométrie Géométrique

La morphométrie géométrique est un concept qui vise à étudier la forme d'objet complexe. Ce type d'analyse permet d'effectuer des comparaisons en s'affranchissant du critère de taille.

Principe

L'analyse est basée sur l'utilisation et l'identification de point repères ou landmarks. Ceux-ci doivent être des points repères reconnaissables sur tous les objets comparés dans la même analyse.[15]Cet ensemble de point va définir la forme ou la configuration d'un objet. La morphométrie géométrique permet d'analyser cette configuration en préservant l'information géométrique tout au long de l'analyse menée dans un espace de conformation spécifique (l'espace de conformation de Kendall). La forme ainsi obtenue va être décomposée pour analyser la conformation. La conformation se définit comme l'ensemble de l'information géométrique qui reste lorsque la position, l'échelle et les effets de rotation sont éliminées. La morphométrie géométrique est donc l'analyse souvent comparative de cette conformation.

Des objets de même taille peuvent avoir des conformations différentes ou inversement. La morphométrie géométrique permet l'analyse d'objet par une décomposition en conformation et en taille. Cette technique permet une analyse de la forme globale d'un objet dont la géométrie est préservée ce qui rend l'analyse statistique réalisable. [4] L'objet n'est plus analysé avec des critères de jugement linéaires ou angulaires mais par les coordonnées cartésiennes dans un repère normé des différents landmarks. Elle a été développée pour quantifier la forme de structures rigides faites de courbes et de bombements qui ne sont pas facilement interprétables par des méthodes métriques classiques. [5] Cette méthode a déjà montré son utilité en anthropologie physique. [6]

Méthode

Calcul de la taille centroïde (décomposition de la taille)

Les coordonnées tridimensionnelles des points repères homologues sont ramenés à la même échelle. Durant cette étape, la distance entre chaque point est inchangée respectant le principe d'isométrie. C'est durant cette étape que le paramètre de taille est extrait, il s'agit de la taille centroïde tel que définie par Gower.

Cette mesure est indépendante de la conformation, il s'agit d'une mesure de la taille.

Superposition Procruste (décomposition de la conformation)

L'analyse Procruste Généralisée ou superposition procruste est la technique qui permet de se concentrer sur l'étude de la conformation des spécimens

Elle se décompose en trois étapes (fig2)

La première élimine les différences de position par translation

La deuxième élimine les différences de taille par mise à l'échelle

La troisième élimine les différences d'orientation par rotation

La conformation moyenne est calculée après superposition procruste. La conformation de chaque objet est définie par ses « résidus Procrustes » : distance de chacun des points repères par rapport aux points repères de la forme moyenne.

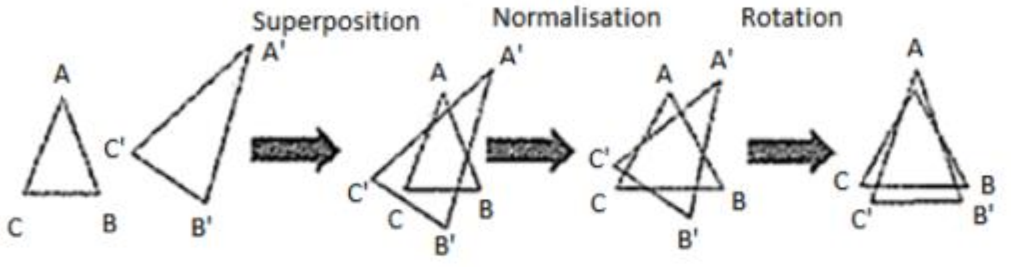

Figure 2 : Etapes de l'Analyse Procruste Généralisée (AGP), suppression des différences de formes autres que la différence due à la conformation. d'après Evin et al

A la fin de ce procédé, les différences de position existant entre chaque point repère homologue représentent la différence de conformation entre les deux objets. Ces différences peuvent être visualisées et sont ensuite analysées statistiquement.

Analyse statistique

Analyse en composant Principale

Il s'agit d'analyser la variabilité de la conformation sans tenir compte de la valeur de la taille centroïde.

Elle est une méthode descriptive multidimensionnelle. Il est réalisé des représentations géométriques de X variables quantitatives pour Y unité. L'analyse de la représentation graphique permettra de voir s'il existe des groupes distincts les uns des autres et de déterminer ce qui les rapproche et la force de ce lien (% variabilité retrouvée).

En quelque sorte, ACP permet de déterminer des groupes au sein du collectif étudié. Les analyses statistiques détaillées ci-dessous permettent de quantifier les différences entre les groupes mises en évidence.

Analyse discriminante

Elle est aussi nommée Canonical Variate Analysis (CVA). Il s'agit d'une fonction mathématique qui détermine les différences maximales entre des groupes définis à priori en prenant en compte les variations intragroupes. On mesure la valeur F du test ainsi que la valeur de p(F) qui correspond à la probabilité.

En tenant compte de l'ensemble de la variance, CVA permet l'analyse des différences globales de forme.

CVA nécessite la détermination des variables de mesures à priori à la différence de ACP qui permet de déterminer les groupes d'intérêts une fois l'analyse réalisée.

Cette méthodologie va nous servir à analyser les différences selon le sexe et l'ethnie.

La distance de Mahalanobis et les distances procrustes

Il s'agit d'une mesure de distance introduite par Mahalanobis (1936). Elle permet de déterminer la similarité entre une série de données connues et inconnus. Nous avons pu ainsi étudier les distances procrustes entre les sous-groupes.

L'analyse multivariée de la variance MANOVA

Elle permet de déterminer si la différence de variance observée est liée au hasard. Elle permet de donner la valeur de la probabilité p.

Les validations croisées

Elles servent à conforter le modèle statistique en évaluant la performance de la méthode statistique. Dans la mesure où était connue la répartition de la population en fonction du sexe, de l'âge et de l'ethnie, nous avons pu vérifier si l'appartenance déterminée par le modèle statistique était correcte. Elle mesure ainsi la fiabilité de la reproductibilité d'une fonction discriminante.

Représentation graphique des résultats des analyses statistiques.

Elles sont de deux ordres (figure 3) : superpositions procrustes pour déterminer la différence de forme moyenne et représentation graphique de type ACP ou CVA (fig 3)

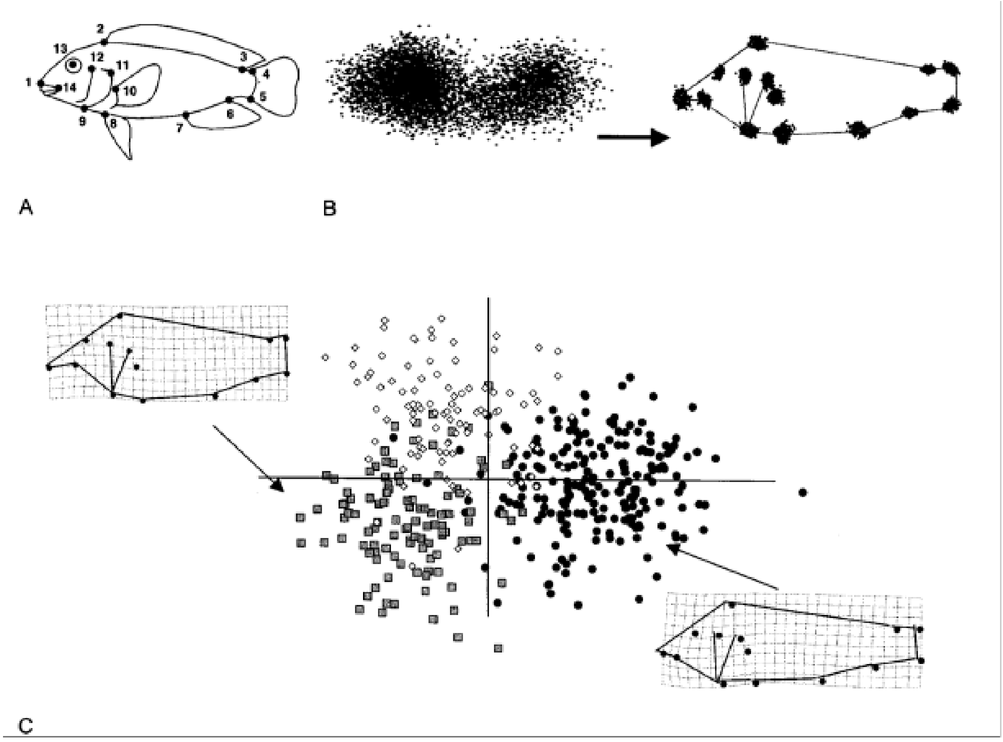

Figure 3 : Représentation graphique des étapes de la géométrie morphométrique d'après Adam et coll (2001). A : mise en place des landmarks, B : analyse procruste généralisé (élimine effet taille, position et orientation, C : analyse statistique et représentation graphique

Geometric morphometric analysis reveals sexual dimorphism in the distal femur

Publié dans la revue Forensic Science International (cf annexes)

ABSTRACT

An individual's sex can be determined by the shape of their distal femur. The goal of this study was to show that differences in distal femur shape related to sexual dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis.

Geometric morphometric analysis was carried out on CT scans of the distal femur of 256 subjects living in the south of France. Ten landmarks were defined on 3D reconstructions of the distal femur. Both traditional metric and geometric morphometric analyses were carried out on these bone reconstructions; these analyses identified trends in bone shape in sex-based subgroups.

Sex-related differences in shape were statistically significant. The subject's sex was correctly assigned in 77.3% of cases using geometric morphometric analysis.

This study has shown that geometric morphometric analysis of the distal femur is feasible and has revealed sexual dimorphism differences in this bone segment. This reliable, accurate method could be used for virtual autopsy and be used to perform diachronic and interethnic comparisons. Moreover, this study provides updated morphometric data for a modern population in the south of France.

KEYWORDS

- distal femur dimorphism
- principal component analysis
- Procrustes analysis
- geometric morphometric analysis
- forensic anthropology population data

HIGHLIGHTS

- Distal femur shape varies based on sex.
- Three-dimensional analysis of the distal femur can be used to predict sex.
- geometric morphometric analysis can predict sex

INTRODUCTION

The morphology of human bones differs between men and women; these differences can be used to determine the sex of human remains [16 9 10]. Several studies have shown that sex can be determined using femoral dimorphism [16 9 10 11 12 13 7 1 17 18]. An individual's sex can be determined by the shape of their distal femur [1 17 19 18]. This determination is based on metric measurements between distinct points on the femur [1 18 20 21 22]. However, these metric methods suffer from analysis bias related to inter- and intra-observer errors, rater experience, standardization challenges and problems related to statistical analysis [2 23].

Geometric morphometric analysis can be used to quantify morphological features [3 24 25 24 26]. This technique allows the overall shape of an object to be analyzed with its geometry intact, making statistical analysis possible [24]. It was developed to quantify the shape of rigid structures consisting of curves and bulges that are not easy to interpret using traditional metric methods [5]. This method has demonstrated its usefulness in physical anthropology [19 25 26 6 27]. To the best of our knowledge, this method has not been used to analyze the sexual dimorphism in the distal femur. And yet, the distal femur lends itself well to this type of analysis as it is a rigid structure with curves and bulges.

We hypothesized that three-dimensional (3D) geometric morphometric analysis of the distal femur would reveal sexual dimorphism. The goal of this study was to show that differences in distal femur shape related to sexual dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis.

MATERIAL AND METHODS

This was a retrospective descriptive analytical study. The research ethics committee at our healthcare facility approved this study (No. 01-0415).

The analysis was carried out on the CT images of 256 distal femurs residing in our facility's imaging database. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) were retained. Any CT scans performed to assess disease conditions in the distal femur were excluded. The included CT scans had mainly been performed to assess leg vasculature (CT angiogram) or to evaluate a tibial plateau fracture. The CT scans were taken on a Sensation 16 Scanner (Siemens, Erlangen, Germany). Between June 1, 2014 and December 31, 2014, 256 CT scans of the distal femur met our inclusion criteria. There were 134 women and 122 men. The average age was 58 ± 15.2 years. The right side was analyzed 122 times and the left side 134 times. The groups were statistically similar (Table 1). The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA).

		Age	***P***
Sex	Male (n=134)	56.7 ± 14.42	0.445
	Female (n=122)	58.14 ± 15.5	
Side	Right (n=122)	57.36 ± 15.3	0.885
	Left (n=134)	57.43 ± 14.7	

Table 1 : Mean age of the various subgroups relative to sex and side. Comparisons were performed with Student's *t*-test.

Ten osteometric landmarks were defined based on standard bone landmarks used in anthropometry (Fig 4 and Table 2) [11] [18] [20]. By using points typically associated with osteometric techniques, comparisons could be made with published studies on this subject to determine the plausibility of our results. The metric variables measured were the epicondylar breadth (EB), which is the distance between the two epicondyles [9,10,12,13,7,1,17,19,28], anterior posterior diameter of the medial condyle (APDMC), which is the largest anteroposterior dimension of the medial condyle [11,21], and anterior posterior diameter of the lateral condyle (APDLC), which is the largest anteroposterior dimension of the lateral condyle [11,21] (Figure 5). All of these were Type I landmarks [5]. Once these landmarks had been located with 3D in vivo imaging software (Amira®, Visualization Sciences Group, Bordeaux, France), the coordinates of each landmark in space (x,y,z) were recorded.

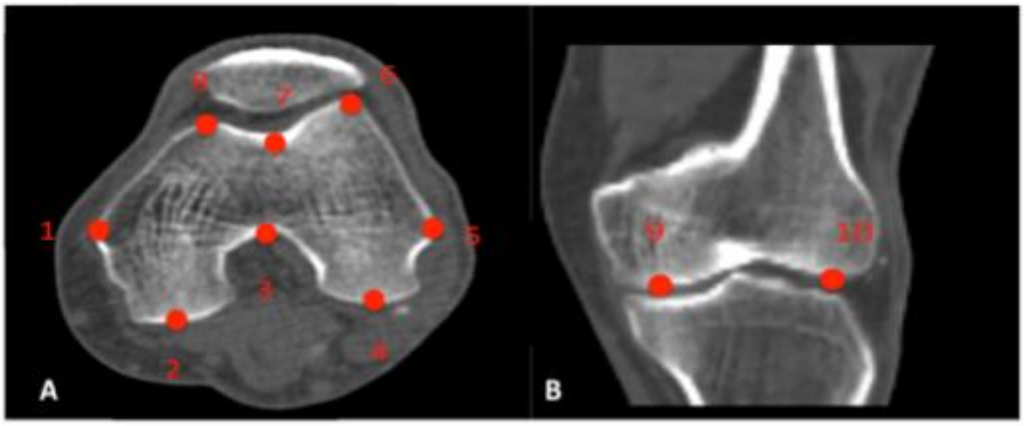

Figure 4 : Location of landmarks on axial (A) and frontal (B) CT scan slices: 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) top of intercondylar notch, 4) most dorsal point on lateral condyle, 5) lateral epicondyle, 6) most ventral point on lateral edge of trochlear groove, 7) most distal point at bottom of the trochlear groove, 8) most ventral point on the medial edge of the trochlear groove, 9) most distal point on medial condyle, 10) most distal point on lateral condyle.

Landmark	Location	Intra-observer Variability	Inter-observer Variability
1	Medial epicondyle	1.64	1.63
2	Most dorsal point on medial condyle	1.64	1.64
3	Top of intercondylar notch	1.64	1.64
4	Most dorsal point on lateral condyle	1.64	1.64
5	Lateral epicondyle	1.63	1.64
6	Most outside point on trochlear groove	1.63	1.65
7	Most distal point at bottom of trochlear groove	1.64	1.65
8	Most ventral point on margin of trochlear groove	1.64	1.65
9	Most distal point on medial condyle	1.53	1.51
10	Most distal point on lateral condyle	1.52	1.49

Table 2 : Anatomical description of the various landmarks used, with the intra- and interobserver variability for each. The error is given as a percentage.

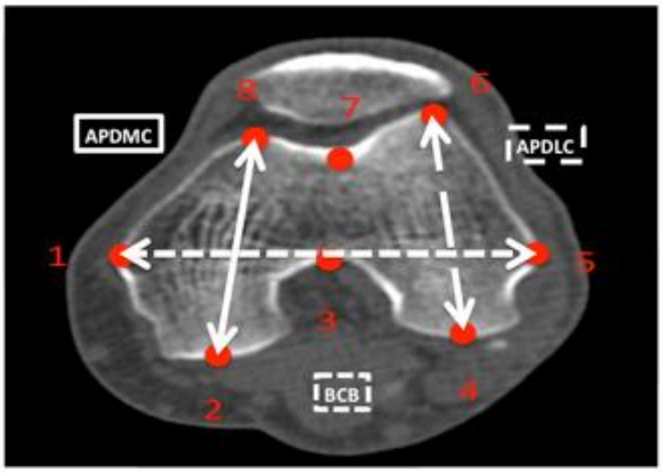

Figure 5 : Osteometric data used to measure the plausibility of the study's methodology. EB: epicondylar breadth, distance between the two epicondyles, APDMC: anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial condyle [11 21] and APDLC: anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle [11 21].

The analyzed data was taken from the same database and analyzed twice on separate occasions by two observers. This made it possible to calculate the intra- and interobserver variability for each landmark. For each observer, landmark deviations were calculated relative to the landmark's mean value. The percentage error for each landmark was calculated, as described previously [29] [30] (Table 2). The results were deemed acceptable if this error was less than 5% [29] [31] [30] [32].

All morphometric geometric analyses were carried out with Morpho J software [33] and R 2.2.0 software. The chosen landmarks made it possible to characterize the shape of the distal femur (Fig. 4). The first step consisted of a generalized Procrustes analysis (GPA) [26] [33] [34]. As described previously [25] [26], this strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. A comparative analysis was performed with all the variables based on sex (male, female). The landmark coordinates were analyzed using principal component analysis (PCA) [34] and canonical variate analysis (CVA) to identify shape trends in the various subgroups [25] [26].

A discriminant analysis was performed to determine the percentage of cases in which the sex was correctly estimated. Pearson's Chi-square test was used to determine if this analysis was statistically significant. To determine if the difference between shapes was statistically significant, a *P*-value was also calculated using Goodall's F-test and Mahalanobis D2 matrices [35] [36]. The length variables (EB, ADPLC and ADPMC) were compared using an analysis of variance (ANOVA).

RESULTS

The percentage errors for the intra- and interobserver comparisons for all the landmarks are given in Table 2. None exceeded 2%. The mean EB value was greater in men (85.1 ± 4.9 mm) than women (75.5 ± 3.7) ($P < 0.005$). Similar results were found for the APDMC (men: 66.7± 4.2, women: 60.4 ± 3.9; $P < 0.005$) and the APDLC (men: 65.3 ± 4.3, women: 60 ± 3.8, $P < 0.005$) (Table 3).

Sex	Female	Male	*P*
EB	75.5 ± 3.7	85.1 ± 4.9	< 0.005
APDMC	60.4 ± 3.9	66.7 ± 4.2	< 0.005
APDLC	60 ± 3.8	65.3 ± 4.3	< 0.005

EB: epicondylar breadth. APDMC: Anterior posterior diameter of the medial condyle. APDLC: Anterior posterior diameter of the lateral condyle

Table 3 : Mean values (± standard deviation) of the osteometric data for each subgroup based on sex. Comparisons were performed with an ANOVA.

The shape of the male and female distal femur differed significantly (Figure 6) (Goodall's F = 0.048, $P < 0.001$ and Mahalanobis D2 distance = 1.52, $P < 0.001$). PCA identified a difference in distal femur shape between males and females; PC1 and PC2 accounted for 58.6% of the variance measured (Figure 7). The CVA revealed that the correct sex was assigned in 77.3% of cases and the cross-validation revealed a 68.7% rate of correct sex estimation (Table 4).

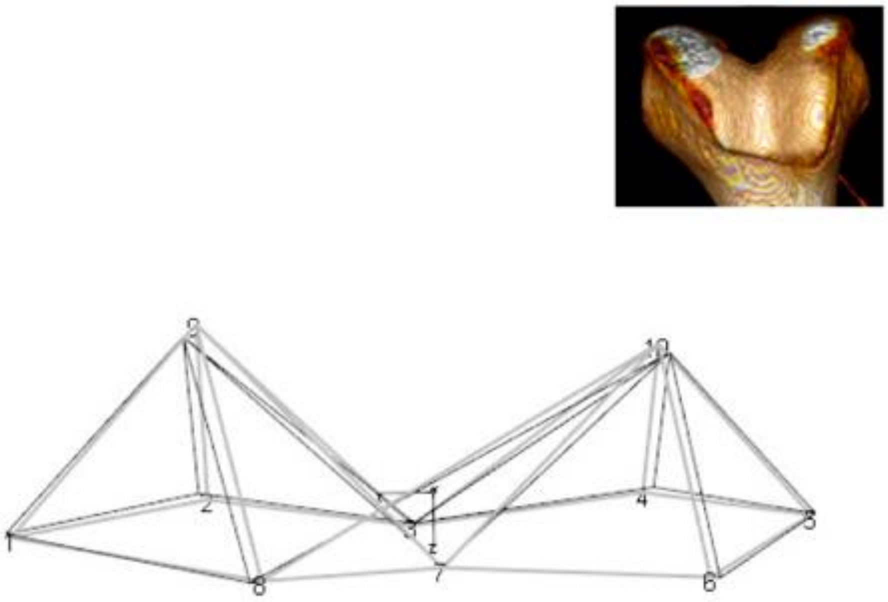

Figure 6 : Shape variation based on sex (male: black line, female: gray line). A: 3D view obtained of the inferior end, B: view on an axial plane containing the first eight landmarks. The 3D reconstructions are shown to make it easier to understand the two planes.

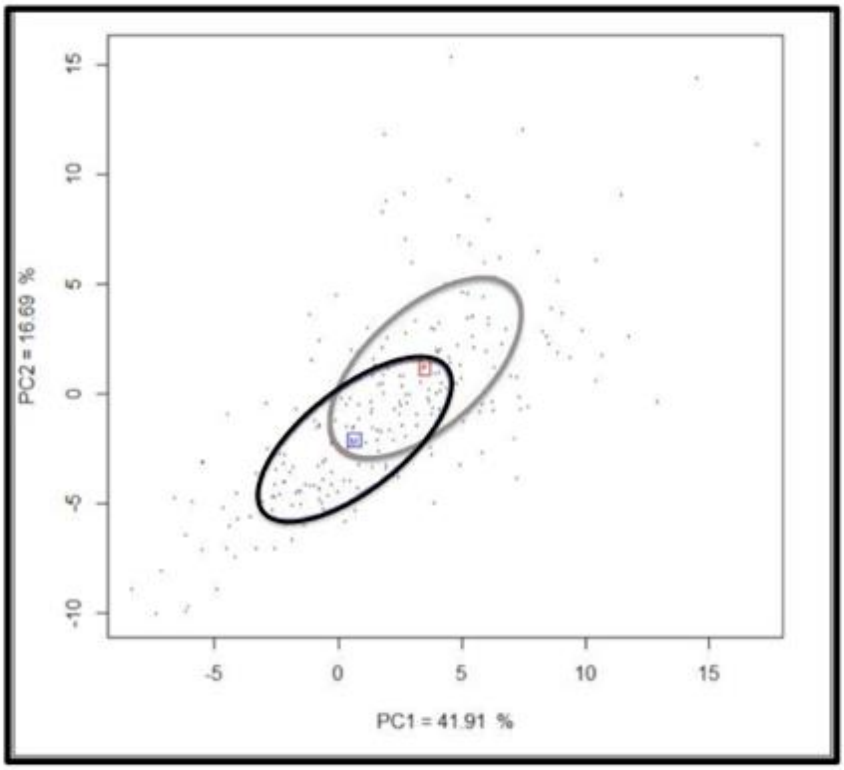

Figure 7 : PCA obtained for the shape of the distal femur based on sex (male: black line, female: gray line). The ellipses correspond to 68% confidence intervals.

	Original CVA			Cross-Validated		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
Female	93	29	76.2	78	44	63.9
Male	105	29	78.4	98	36	73.1
Total	198	58	77.3	176	80	68.7

Table 4 : Results of the CVA and cross-validation for the sex estimation

When using the EB threshold (79.6 mm) defined by Alunni-Perret et al. [1] in a comparable French population, 87% of women, 88% of men and 88% overall were correctly assigned.

DISCUSSION

Our hypothesis was confirmed: the shape of the distal femur significantly differs on the basis of sex (Figure 6). Geometric morphometric analysis revealed sexual dimorphism in the distal femur.

One of the main objectives of physical anthropology is to estimate a person's sex in the forensic or anthropology context [9 10 11 12 13 37 38 8]. Most of the postcranial bones have been used to determine the sex of human remains through various statistical models [18]. The femur is the longest bone and it is often well preserved [9 12 13]. But anthropologists must have different algorithms in their diagnostic arsenal for cases where the skeletons are fragmented or when specific populations are analyzed [16 9 10 11 13 17]. The shape of the two condyles of the distal femur differs between men and women [39 40]. The large number of subjects (n = 256) included in this study has provided osteometric references related to sexual dimorphism in a modern population.

This study is the most extensive up to now to evaluate sexual dimorphism of the distal femur. The data were derived from a modern population, contrary to most of the published studies on this topic [9 10 1 19 30 41]. This data set can be used as a current reference when virtual or in vivo autopsy is performed [37 42 43]. Temporal changes observed in modern populations mean that certain bone measurements must be re-evaluated over time [1].

In this study, osteometric analyses were carried out in addition to the 3D analyses. By placing easily identifiable points on the apex of the bone contours, we were able to obtain data in the traditional manner, which allowed us to verify that the data obtained were in agreement with published values (Table 5). Origin-based variability [10] must be taken into account in the literature comparison, but the results of these three reference measurements are consistent. Furthermore, the intra- and interobserver error rates were very low in the current study (Table 2). These two aspects (reproducibility and plausibility) validate our methodology.

Nationality	**EB**			**ADPMC**		**ADPLC**		**N**
	Female	Male	Ac.	Female	Male	Female	Male	
Spanish [13]	70.8 ± 2.3	80.6 ± 2.9	97.5	NA	NA	NA	NA	132
French [1]	74.8 ± 2.5	84.3 ± 3.6	95.4	NA	NA	NA	NA	88
Chinese [7]	70.6 ± 3.2	80.3 ± 4.2	94.9	NA	NA	NA	NA	87
Thai [12]	75.4 ± 5.4	83.7 ± 4.7	93.3	NA	NA	NA	NA	104
North Indians [11]	68.3 ± 4	76.8 ± 4.2	85.1 (M) 78.6 (F)	54 ± 3.2	59.4 ± 3.3	55.6 ± 3.4	60.3 ± 3	122
Croatian [9]	75.1 ± 3.3	86.7 ± 4.3	91.3	NA	NA	NA	NA	195
White South African [19]	75.1 ± 3.3	84.6 ± 4.6	90.5	NA	NA	NA	NA	106
Indian [10]	66.8 ± 4.2	78.7 ± 4.5	90.3	NA	NA	NA	NA	124
Chinese [28]	69.3 ± 3	77.8 ± 5.8	83.7	NA	NA	NA	NA	141
German [17]	77 ± 5	84.0 ± 10	81.4	NA	NA	NA	NA	170
Czech [21]	78.2	88.8	NA	65.6	71.8	63.4	69.9	200
Korean [18]	NA	NA	NA	55.3 ± 3	61.2 ± 3	58.4 ± 2.8	64.6 ± 3	202
Our STUDY	75.5 ± 3.7	85.1 ± 4.9	88	60.4 ± 3.9	66.7 ± 4.2	60.4 ± 3.8	65.3 ± 4	255

EB: epicondylar breadth, APDMC: Anterior posterior diameter of the medial condyle, APDLC: Anterior posterior diameter of the lateral condyle, Ac: Accuracy is the percentage of correct assignment. N: number of subjects in the study

Table 5 : Published osteometric data. Mean values with standard deviation.

It is worth noting that the rate of correct sex estimation was higher with the traditional metric values than with classic morphometric analysis (EB 88%, CVA: 77.3%). Geometric morphometric analysis, particularly GPA, minimizes effects related to a stocky or slender build; only allometric differences are retained and observable [25 34]. Geometric morphological analysis effectively minimizes differences related to general somatotype and keeps only the shape differences. Bellemans et al [44] have shown that differences in femur shape were related to the individual's sex and somatotype. The somatotype concept was introduced by Sheldon in the 1940s. Carter and Heath refined it into three somatotypes: endomorph, mesomorph, ectomorph [45 46 47]. Skeletal structure and body composition are used to classify individuals into these three groups. Although the somatotype concept has been criticized in the past for being too simplistic and for being used by behavioral specialist to correlate somatotype to certain psychological features, it is an accepted method for studying physical characteristics [48 49 50 51]. Osteometric analysis is able to correctly assign sex, but is subject to the somatotype effect. Geometric morphometric analysis discounts somatotype-related differences, reducing the accuracy of this analysis. Osteometric analysis is subject to two variables (sex and somatotype), while geometric morphometric analysis is subject to only one variable (sex). We believe that the relatively low rate of correct sex estimation is due to this factor. However, we were able to show that sexual dimorphism exists in the distal femur, independent of somatotype.

The current study has certain limitations. Skeletally immature subjects were not included. In younger persons, the bone contours of the distal femoral epiphysis are not completely ossified. This would have increased the possibility of errors during landmark placement by the observers. Diseases that do not affect the distal femur but may require a CT scan that includes the distal femur, such as vascular conditions and tibial plateau fracture, are more common in older subjects.

In summary, the distal femur exhibits sexual dimorphism. Three-dimensional geometric morphometric analysis made it possible to show these differences. The large number of subjects studied made it possible to modernize the references for certain bone measurements. This reliable and accurate methodology can be used to perform diachronic and interethnic comparisons.

Geometric morphometric analysis reveals age-related differences in the distal femur of Europeans

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ABSTRACT

Background: Few studies have looked into age-related variations in femur shape. We hypothesized that three-dimensional (3D) geometric morphometric analysis of the distal femur would reveal age-related differences. The purpose of this study was to show that differences in distal femur shape related to age could be identified, visualized, and quantified using three-dimensional (3D) geometric morphometric analysis.

Methods: Geometric morphometric analysis was carried out on CT scans of the distal femur of 256 subjects living in the south of France. Ten landmarks were defined on 3D reconstructions of the distal femur. Both traditional metric and geometric morphometric analyses were carried out on these bone reconstructions. These analyses were used to identify trends in bone shape in various age-based subgroups (<40, 40–60, >60).

Results: Only the average bone shape of the < 40-year subgroup was statistically different from that of the other two groups. When the population was divided into two subgroups using 40 years of age as a threshold, the subject's age was correctly assigned 80% of the time.

Discussion: Age-related differences are present in this bone segment. This reliable, accurate method could be used for virtual autopsy and to perform diachronic and interethnic comparisons. Moreover, this study provides updated morphometric data for a modern population in the south of France.

Conclusion Manufacturers of knee replacement implants will have to adapt their prosthesis models as the population evolves over time.

KEYWORDS

distal femur dimorphism; principal component analysis; Procrustes analysis; geometric morphometric analysis; biological anthropology

INTRODUCTION

The sex of human remains can be determined by analyzing human bones. [16] The review of literature by Ozer et al has shown that sex can be estimated using femoral dimorphism. [16] However, few studies have looked into age-related variations in femur shape. [37] [52] Age is typically determined using metric measurements between distinct points on the femur. [52] However, these metric methods suffer from analysis bias related to inter- and intra-observer errors, observer experience, standardization challenges and problems related to statistical analysis. [2]

Geometric morphometric analysis can be used to quantify morphological features. [53] This technique allows the overall shape of an object to be analyzed with its geometry intact, making statistical analysis possible. [24] It was developed to quantify the shape of rigid structures consisting of curves and bulges that are not easy to interpret using traditional metric methods. [5] This method has demonstrated its usefulness in physical anthropology. [6] To the best of our knowledge, this method has not been used to analyze the age-related differences in the distal femur. The distal femur is a rigid structure with curves and bulges so geometric morphometric analysis seems to be an appropriate method to explore it. With this method, the shape of two or more objects can be compared while disregarding the volume of these objects. [25] Since the size is normalized, the analysis can focus on the shape.

Age determination is a critical element of anthropology and forensic medicine. [37] [54] Several statistical models have been developed to determine person's age using various bone fragments. [18] The femur is the longest bone and it is often well preserved [12] [{Slaus, 2003 #99]. We believe it is relevant to analyze age variations in this bone with a method that can be used in both living and deceased subjects.

Bone shapes changes as a person ages.[55] We believe it is important to describe these changes in the shape of the distal femur, as the shape of the distal femur has a direct impact on the design of total knee replacement implants.

We hypothesized that three-dimensional (3D) geometric morphometric analysis of the distal femur would reveal age-related differences. The goal of this study was to show that differences in distal femur shape related age could be identified, visualized, and quantified using 3D geometric morphometric analysis.

MATERIALS AND METHODS

This was a retrospective descriptive analytical study. The research ethics committee at our healthcare facility approved this study (number 01-0415).

Materials

Study population: Between June 1, 2014 and December 31, 2014, 256 CT scans of the distal femur met our inclusion criteria (Figure 8). There were 134 women and 122 men. The average age was 58 ± 15.2 years. The right side was analyzed 122 times and the left side 134 times. The groups were comparable (Table 6). The analysis was carried out on the CT images of 256 distal femurs stored in our facility's imaging database. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) without signs of disease conditions or osteoarthritis were retained. The included CT scans had mainly been performed to assess leg vasculature (CT angiogram) or to evaluate a tibial plateau fracture without previous history of knee problem and without lesions in the distal femur.

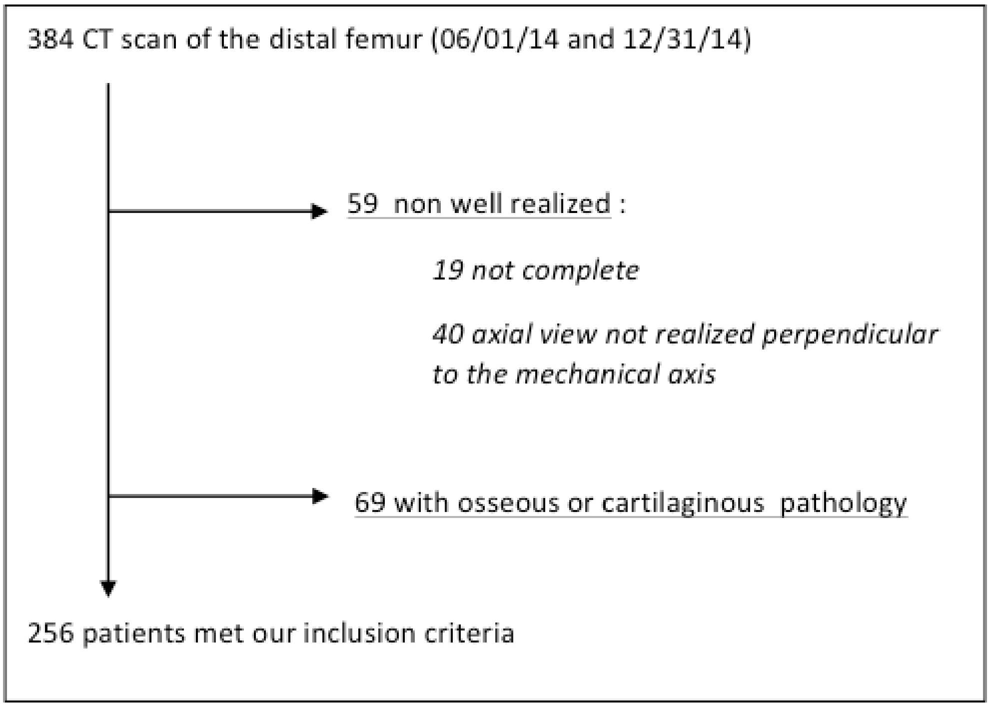

Figure 8 : Flow chart of our studied population

		Age	*P*
Sex	Male (n=134)	56.7 ± 14.42	0.445
	Female (n=122)	58.14 ± 15.5	
Side	Right (n=122)	57.36 ± 15.3	0.885
	Left (n=134)	57.43 ± 14.7	

Table 6 : Mean age of the various subgroups relative to sex and side. Comparisons were performed with Student's *t*-test.

The CT scans were taken on a Sensation 16 Scanner (Siemens, Erlangen, Germany). Scanning was performed with the following parameters: 80 kV, 70 mA, gantry rotation time of 2 seconds, 144-mm table height, and axial scanning mode. The thickness of the reconstructed sections was kept constant at 2 mm every 1 mm. The image matrix was 512*512 pixels. A bone filter and a soft tissue filter were used.

The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA).

Methods

3D morphological analysis: Ten osteometric landmarks were defined based on standard bone landmarks used in anthropometry (Figure 9 and Table 7). [44] By using points typically associated with osteometric techniques, comparisons could be made with published studies to determine the plausibility of our results. The metric variables measured were the bicondylar breadth (BCB), which is the distance between the two epicondyles [7],anterior posterior diameter of the medial condyle (APDMC), which is the largest anteroposterior dimension of the medial condyle [11], and anterior posterior diameter of the lateral condyle (APDLC), which is the largest anteroposterior dimension of the lateral condyle [21] (Figure 10). Once these landmarks had been located with 3D in vivo imaging software (Amira®, Visualization Sciences Group, Bordeaux, France), the coordinates of each landmark in space (x,y,z) were recorded.

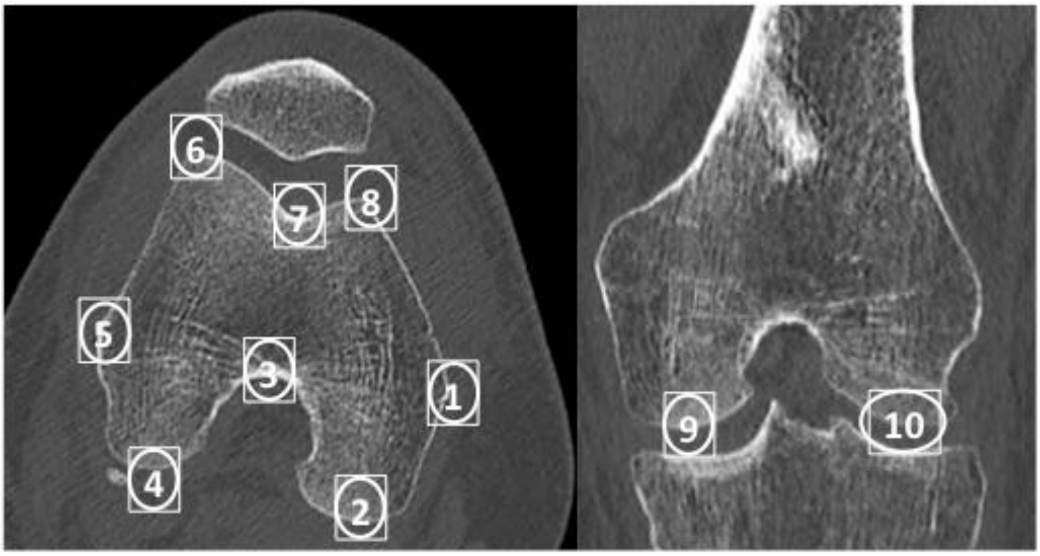

Figure 9 : Location of landmarks on axial (left) and frontal (right) CT scan slices: 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) top of intercondylar notch, 4) most dorsal point on lateral condyle, 5) lateral epicondyle, 6) most ventral point on lateral edge of trochlear groove, 7) most distal point at bottom of the trochlear groove, 8) most ventral point on the medial edge of the trochlear groove, 9) most distal point on medial condyle, 10) most distal point on lateral condyle.

Landmark	Location	Intra-observer Variability	Inter-observer Variability
1	Medial epicondyle	1.64	1.63
2	Most dorsal point on medial condyle	1.64	1.64
3	Top of intercondylar notch	1.64	1.64
4	Most dorsal point on lateral condyle	1.64	1.64
5	Lateral epicondyle	1.63	1.64
6	Most outside point on trochlear groove	1.63	1.65
7	Most distal point at bottom of trochlear groove	1.64	1.65
8	Most ventral point on margin of trochlear groove	1.64	1.65
9	Most distal point on medial condyle	1.53	1.51
10	Most distal point on lateral condyle	1.52	1.49

Table 7 : Anatomical description of the various landmarks used, with the intra- and interobserver variability for each. The error is given as a percentage.

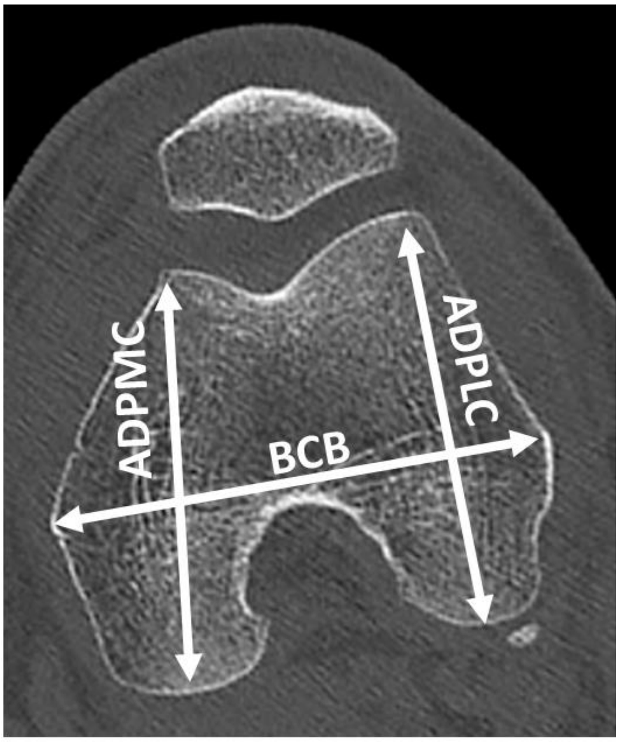

Figure 10 : Osteometric data used to measure the plausibility of the study's methodology. EB: Epicondylar breadth, distance between the two epicondyles, APDMC: Anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial condyle and APDLC: Anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle

Axial slice where the epicondyles are more prominent were selected to place points 1–10. Oblique slices were created by resampling the images stack in order to be orthogonal to the axial plane (Figure 11).

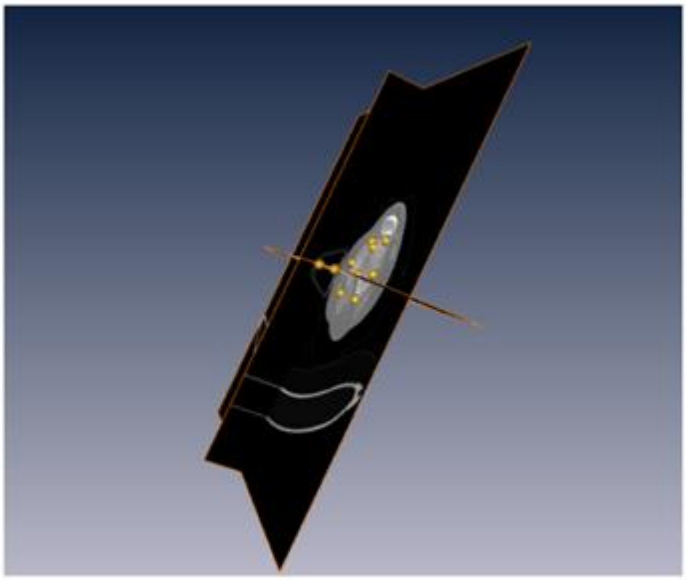

Figure 11 : Creation of 3D reconstructions using the Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA). First, the axial plane in which the epicondyles were most prominent was identified. Reconstructions in the orthogonal planes were generated to position the landmarks.

Reliability studies: The analyzed data were taken from the same database and analyzed twice on separate occasions by two observers. This made it possible to calculate the intra- and inter-observer variability for each landmark. For each observer, landmark deviations were calculated relative to the landmark mean value. The percentage error for each landmark was calculated, as described previously (Table 7). The results were deemed acceptable if this error was less than 5%. [29]

Procrustes analysis: All morphometric geometric analyses were carried out with Morpho J software and R 2.2.0 software. The chosen landmarks made it possible to characterize the shape of the distal femur (Fig. 9). The first step consisted of a generalized Procrustes analysis

(GPA). [33] As described previously [26], this strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

Statistical analysis

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. A comparative analysis was performed with all the variables based on age (< 40, 40–60, > 60 years).

The landmark coordinates were analyzed using principal component analysis (PCA) and canonical variate analysis (CVA) to identify shape trends in the various subgroups. [26]

A discriminant analysis was performed to determine the percentage of cases in which the age was estimated correctly. Pearson's Chi-square test was used to determine if this analysis was statistically significant [34]. To determine if the difference between shapes was statistically significant, a *P*-value was also calculated using Goodall's F-test and Mahalanobis D2 matrices [35]. The length variable (BCB) was compared using an analysis of variance (ANOVA).

RESULTS

Reliability analysis

The percentage errors for the intra- and inter-observer comparisons for all the landmarks are given in Table 7 – none exceeded 2%.

Age differences

The osteometric analysis (BCB, APDMC and APDLC) revealed no significant differences between the three subgroups of subjects (<40, 40–60, >60 years) (Table 8). Only the average bone shape of the < 40-year subgroup was statistically different from that of the other two groups (Table 9, Figure 12). For the same femur size, < 40-year femurs are significantly longer in the frontal plane, i.e. the distance between the axial plane containing the epicondyles and the two most distal points on the condyles is greater in the < 40-year group. In the axial plane through the epicondyles, < 40-year femurs are shorter along the anteroposterior axis than > 40 year femurs, while the mediolateral distance is the same. The PCA based on age is shown in Figure 13; principal component (PC)1 and PC2 accounted for 54.42% of the variance measured. When the population was divided into two subgroups using 40 years of age as a threshold, the subject's age was correctly assigned in 80% of the cases (original CVA) and in 74% of cases by cross-validated classification (table 10).

Age	**< 40**	**40–60**	**> 60**	***P***
BCB	80.3 ± 7.7	80.7 ± 6.6	80.4 ± 5.9	0.9
APDMC	62.8 ± 5.5	64.2 ± 5.4	63.5 ± 4.8	0.3
APDLC	62.7 ± 5.9	63 ± 4.9	62.6 ± 4.5	0.8

BCB: BiCondylar breadth. APDMC: Anterior posterior diameter of the medial condyle. APDLC: Anterior posterior diameter of the lateral condyle

Table 8 : Mean values (± standard deviation) of the osteometric data for each subgroup based on age and sex. Comparisons were performed with an analysis of variance (ANOVA).

Comparison	**Mahalanobis D2 distance**	**Goodall's F test**	***P***
< 40 vs. > 60	1.73	0.04	0.001
40–60 vs. > 60	0.68	0.019	0.78
< 40 vs. 40–60	1.8	0.056	0.0002

Table 9 : Values of Goodall's F and Mahalanobis D2 distance for the comparisons performed.

	Original CVA			**Cross-validated**		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
< 40	24	13	64.9	14	23	60.9
> 40	182	37	83.1	176	43	80.4
Total	206	50	80	190	66	74

Table 10 : Results of the canonical variate analysis (CVA) and cross-validation for the age determination

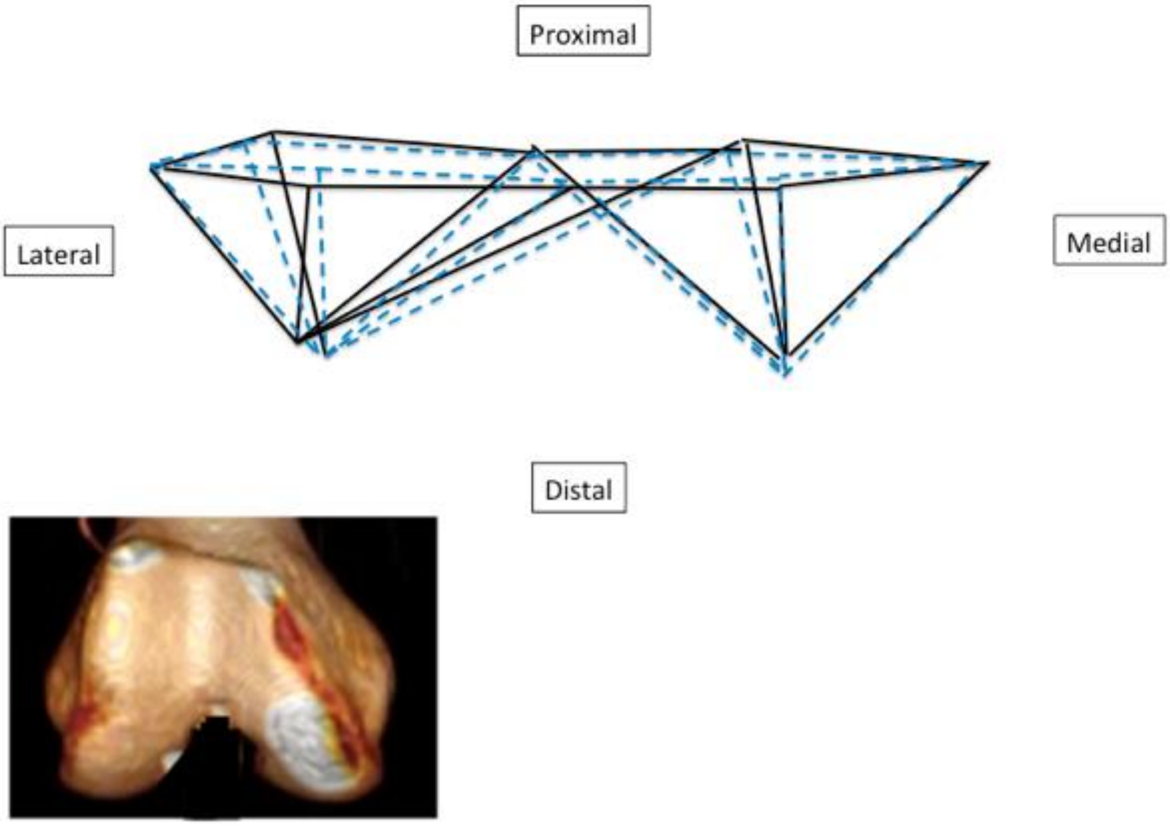

Figure 12 : Shape variation based on age (> 40: black solid line, < 40: blue dotted line). A 3D reconstruction is shown to make it easier to understand the data.

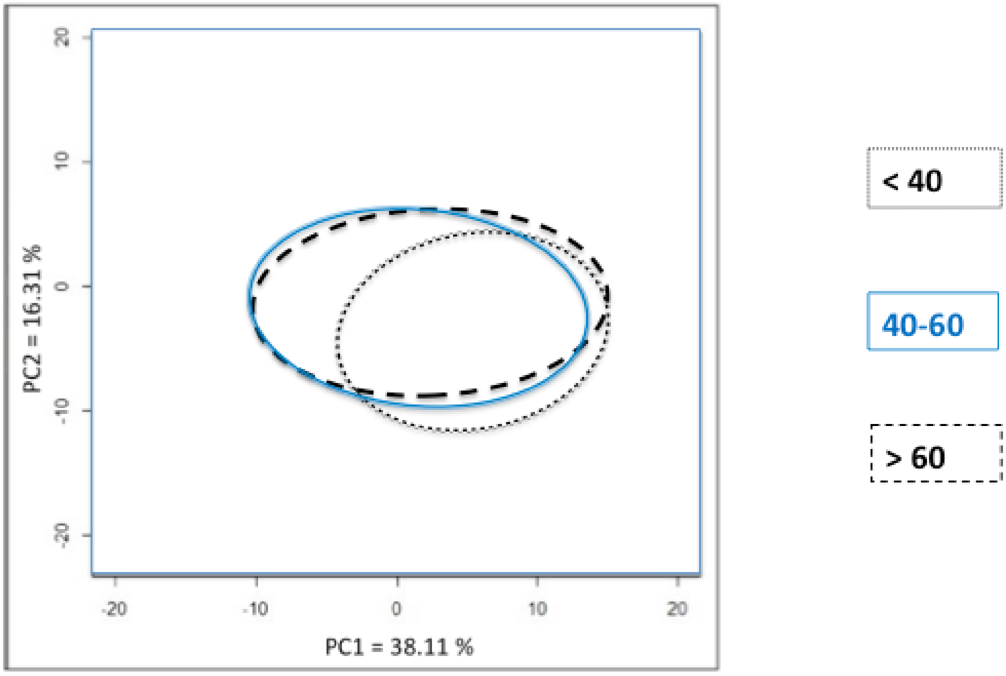

Figure 13: PCA obtained for the shape of the distal femur based on age. The ellipses correspond to 68% confidence intervals.

DISCUSSION

Our hypothesis is confirmed: 3D geometric morphometric analysis of the distal femur revealed differences between age groups (Figure 12). Geometric morphometric analysis revealed age-related differences in the shape of the distal femur (Table 9). The shape of the femur in subjects under 40 years of age was different than the shape of the femur in older subjects. Classic osteometric analysis did not reveal age-related differences in the distal femur (Table 8). This means there are no differences in femur size between the three age groups, but for the same size of femur, the shape differs.

One of the main objectives of physical anthropology is to estimate a person's age and sex in the forensic or anthropology context. [37] [38] Most of the postcranial bones have been used to determine anthropological data of human remains through various statistical models. [18] The femur is the longest bone and it is often well preserved. As a consequence, we feel it is relevant to develop a method that can be used to determine a person’s age based on this bone [13] [12] [9] The large number of subjects (n = 256) included in this study has provided osteometric references related to age differences in a modern European population. Moreover, since this methodology can be used in living and deceased persons, it can be used in forensic medicine to determine age of a person in a legal context.

This is the first 3D study to show age-related differences in the overall shape of the distal femur, as the shape was different in subjects under 40 years of age and those over 40 years of age (Fig. 12). Discriminant analysis showed that 80% of subjects were correctly classified (original CVA). Although this method is not sufficiently accurate to be used alone, it can be used in the context of virtual or in vivo autopsy. [42] [43]

The age-related variations observed in the shape of the distal femur have consequences for orthopedic surgery, particularly for total knee arthroplasty (TKA). A better grasp of knee morphology and its variations can improve the design of TKA implants [52]. The same kind of implants are not suitable for different populations [56]. Differences in shape have been reported by gender and ethnic groups [44]. We are the first group to show differences in distal femur shape relative to age that are independent of the difference in size. In our study, we analyzed the differences in shape, not size. For these reasons, only adjusting the implant size does not solve the problem – the shape must be taken into account. Our study is the first to show age-related differences (< 40 years and > 40 years) in a Caucasian population. The design of total knee arthroplasty implants is based on the anatomy of a Caucasian population. [57] Successful component placement in knee arthroplasty includes minimal overhang and good bone coverage. [58] As a consequence, the age-related variations in a Caucasian population have to be take into account by manufacturers to modify the implant design over time.

Han et al studied age-related anthropometric differences in Asians by analyzing MRI images of 535 knees. They used 20-year bands to evaluate successive generations. They found statistically significant differences in the classic anthropometric data between all the age bands. Although we also split our study population into 20-year segments, only the < 40-year population was significantly different to the others. This disparity can be explained by interethnic variability [9]. In addition, we performed a 3D analysis of the shape of the entire distal femur, while Han et al. performed two-dimensional analyses in various planes.

Our study is the most extensive up to now to evaluate age dimorphism of the distal femur in a modern European population. This data set can be used as a current reference when virtual or in vivo autopsy is performed. [43] [42] Temporal changes observed in modern populations mean that certain bone measurements must be re-evaluated over time [1]. Moreover, intergenerational variability must be taken into account when comparing populations. [52] Bias will be introduced into the analysis if the populations being compared are not from the same generation.

In our study, osteometric analyses were carried out in addition to the 3D analyses. By placing easily identifiable points on the apex of the bone contours, we obtained data in the traditional manner, which allowed us to verify that these data were consistent with published values (Table 11). The EB values reported by Han et al [52] were comparable to ours (Table 8) : group < 40 years, EB = 74.2 ± 2.1; group 40–60 years, EB= 73.4 ±2.99 and group > 60 years, EB= 74.12 ± 3.24. Origin-based variability [10] and sex-related variability must be taken into account when performing comparisons with published data, but the results of EB measurement are consistent (Table 11). Furthermore, the intra- and inter-observer error rates were very low in our study (Table 7). These two aspects (reproducibility and plausibility) validate our methodology. In addition, we only used femurs with no signs of bone pathology or osteoarthritis; any patients with osteoarthritis were excluded because this disease can alter the shape of the distal femur. [59] Contrary to previous OA studies, we found that older patients had a smaller femur. [60] Murshed et al reported similar findings when analyzing femurs free of bone pathology. [54]

Nationality	**BCB**			**ADPMC**		**ADPLC**		**n**
	Female	Male	Ac.	Female	Male	Female	Male	
Spanish [13]	70.8 ± 2.3	80.6 ± 2.9	97.5	NA	NA	NA	NA	132
French [1]	74.8 ±	84.3 ±	95.4	NA	NA	NA	NA	88

	2.5	3.6						
Chinese [7]	70.6 ± 3.2	80.3 ± 4.2	94.9	NA	NA	NA	NA	87
Thai [12]	75.4 ± 5.4	83.7 ± 4.7	93.3	NA	NA	NA	NA	104
North Indians [11]	68.3 ± 4	76.8 ± 4.2	85.1 (M) 78.6 (F)	54 ± 3.2	59.4 ± 3.3	55.6 ± 3.4	60.3 ± 3	122
Croatian [9]	75.1 ± 3.3	86.7 ± 4.3	91.3	NA	NA	NA	NA	195
White South African [19]	75.1 ± 3.3	84.6 ± 4.6	90.5	NA	NA	NA	NA	106
Indian [10]	66.8 ± 4.2	78.7 ± 4.5	90.3	NA	NA	NA	NA	124
Chinese [28]	69.3 ± 3	77.8 ± 5.8	83.7	NA	NA	NA	NA	141
German [17]	77 ± 5	84.0 ± 10	81.4	NA	NA	NA	NA	170
Czech [21]	78.2	88.8	NA	65.6	71.8	63.4	69.9	200
Korean [18]	NA	NA	NA	55.3 ± 3	61.2 ± 3	58.4 ± 2.8	64.6 ± 3	202
Our STUDY	75.5 ± 3.7	85.1 ± 4.9	88	60.4 ± 3.9	66.7 ± 4.2	60.4 ± 3.8	65.3 ± 4	255

BCB: Bicondylar breadth, APDMC: Anterior posterior diameter of the medial condyle, APDLC: Anterior posterior diameter of the lateral condyle, Ac: Accuracy is the percentage of correct assignment. n: number of subjects in the study

Table 11 : Published osteometric data. Mean values with standard deviation.

Anthropometric data varies not only as a function of ethnicity, but also genetic, environmental, socioeconomic and nutritional factors [52]. Age-related variations may be related to the differences in height and weight between generations [61].

The current study has certain limitations. Skeletally immature subjects were not included. In younger persons, the bone contours of the distal femoral epiphysis are not completely ossified. This would have increased the possibility of errors during landmark placement by the observers. In addition, very few subjects were under 40 years of age. Diseases that do not affect the distal femur but may require a CT scan that includes the distal femur, such as vascular conditions and tibial plateau fracture, are more common in older subjects. Furthermore, the age cut-off for the subgroups was chosen arbitrarily and not based on validated data, although we used previously described age brackets [52]. We analyzed the relationship between age and femur shape, not the changes during aging. A longitudinal study would be needed to measure changes in anthropological measurements as a person ages. While only the distal femur was analyzed in this study, it would be interesting to pair our analysis with data on the patients' morphotype or other femur anatomy data. However, additional analyses could not be performed since the records were anonymized and the patients had no complaints related to their knee joint.

CONCLUSION

The distal femur exhibits age-related differences. Three-dimensional geometric morphometric analysis made it possible to show these differences. Based on our findings, we feel that changes in bone anatomy over time cannot be ignored. It would be too simplistic to say that patients under 40 years of age require a different knee implant design because their distal femur differs in shape from older adults. TKA indications in patients under 40 years of age are extremely rare. Implant manufacturers must recognize that patient anatomy changes and that implant design should be reevaluated regularly.

Three-dimensional geometric morphometric analysis reveals ethnic dimorphism in the shape of the femur

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ABSTRACT

Background: Ethnic dimorphism in the distal femur has never been studied in a three-dimensional analysis focused on shape instead of size. Yet, this dimorphism has direct implications in orthopedic surgery and in anthropology. The goal of this study was to show that differences in distal femur shape related to ethnic dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis.

Methods: CT scans of the distal femur were taken from 482 patients who were free of any bone-related pathology: 240 patients were European (E) and 242 were Asian (A). Ten osteometric landmarks based on standard bone landmarks used in anthropometry were placed on these scans. Geometric morphometric analysis, principal component analysis (PCA), canonical variates analysis (CVA), and other discriminant analyses (Goodall's F-test and Mahalanobis distance) were performed. A cross-validation analysis was carried out to determine the percentage of cases in which the ethnicity was correctly estimated.

Results: The shape of the E and A distal femur differed significantly (Goodall's F = 94.43, $P < 0.001$ and Mahalanobis D2 distance = 1.85, $P < 0.001$). PCA identified a difference in distal femur shape between A and E. The CVA revealed that correct ethnicity was assigned in 82% of cases and the cross-validation revealed a 75% rate of correct ethnic group estimation.

Discussion: The distal femur exhibits ethnic dimorphism. 3D geometric morphometric analysis made it possible to demonstrate these differences. The large number of subjects studied has helped modernize the references for certain bone measurements, with direct implication for orthopedic surgery and anthropology.

KEYWORDS

distal femur dimorphism; principal component analysis; Procrustes analysis; geometric morphometric analysis; biological anthropology

INTRODUCTION

Ethnic diversity is always an important element that may affect anthropometric data. It has shown that the anatomy of the distal femur varies by ethnic group. [37 44 25 26 5 53 62 63 34 2 56] These comparisons were based on metric measurements between distinct points on the femur, but not true three-dimensional (3D) analysis. [56 62]However, these metric methods suffer from analysis bias related to inter- and intra-observer errors, rater experience, standardization challenges and problems related to statistical analysis. [2]

Geometric morphometric analysis is a useful tool that allows quantification of morphological features. The primary advantage of geometric morphometric analysis over traditional morphological tools is that it uses powerful multivariate statistics tools to investigate morphological variations in the anatomical context of the structure studied. [25] It provides valuable visual information that can be used to study differences between skeletal features. It was developed to quantify the shape of rigid structures consisting of curves and bulges that are not easy to interpret using traditional metric methods [5]. Geometric morphometric analysis has been used since the 1980s, but has only become popular in anthropology recently [27]. This method can be used to perform diachronic and interethnic comparisons [53]. This method allows the shape of two or more objects to be compared while disregarding the volume of these objects. [25] Since the size is normalized, the analysis can focus on the shape.

To the best of our knowledge, this method has not been used to analyze ethnic dimorphism in the distal femur. Measurement of this dimorphism has direct implication for orthopedics. The shape of the distal femur has a direct impact on the design of total knee replacement implants. Kim et al. recently published a systematic review that looked into the anatomical differences in the knee of patients of various races. [64] All the comparisons reviewed by Kim et al used classic osteometric methods. [64] Although some of the osteometric analyses were done in various planes in space, they were not truly three-dimensional. In addition, these classic osteometric parameters are affected by the size of the objects being compared. It is widely known that the anatomical profiles of Asian knees are smaller and narrower than those of Caucasian. [65] However, we were not interested in analyzing size variations, as size variations can be compensated for by using a different size implant. Instead, we were interested in shape differences, which may bring into question the design of the implant itself. Geometric morphometric analysis studies the shape by disregarding size-related effects.

We hypothesized that 3D geometric morphometric analysis of the distal femur would reveal differences between ethnic groups. The primary goal of this study was to show that differences in distal femur shape related to ethnic dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis. The secondary goal was to quantify the differences observed in the 3D anatomy of the distal femur relative to ethnic group and sex.

MATERIALS AND METHODS

This was a retrospective descriptive analytical study. The research ethics committee at our respective healthcare facilities approved this study (No. 01-0415 and No. 2016-94).

Materials

Study population: The analysis was carried out on the CT images of 482 distal femurs. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) were retained. Any CT scans with signs of pathology or osteoarthritis in the distal femur were excluded. The included CT scans had been performed to assess leg vasculature (CT angiogram). Between June 1, 2014 and December 31, 2014, 482 CT scans of the distal femur met our inclusion criteria: 240 patients were European (E) (from southwest France) and 242 were Asian (A) (Huan from Chongqing, China). There were 228 women (122 Asian and 106 European and 254 men (137 Asian and 117 European). The average age was 55.3 ± 15.2 years. The right side was analyzed 235 times and the left side 247 times. The two groups were comparable in terms of their demographics (Table 12).

		Age
Sex	Male (n=254)	55.24 ± 15.20
	Female (n=228)	55.45 ± 16.47
Side	Right (n=235)	55.14 ± 6.24
	Left (n=247)	55.53 ± 15.59
Ethnicity	European (n=240)	56.47 ± 14.85
	Asian (n=242)	54.22 ± 16.80

Table 12 : Mean age of the various subgroups relative to sex, side and ethnicity. Comparisons were performed with Student's *t*-test – $P > 0.05$ for all comparisons

The CT scans were taken on a Sensation 16 (120 kV, 80 mA; light speed 16) Scanner (Siemens, Erlangen, Germany) with 16*1.5 mm collimation. The image matrix was 512*512 pixels. A bone filter and a soft tissue filter were used. The scanning protocol was carried out to acquire axial 2-mm reconstructions every 1 mm.

The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira® software (version 4.1.1, FEI Visualization Sciences Group, Bordeaux, France).

Methods

3D morphological analysis: Ten osteometric landmarks were defined based on standard bone landmarks used in anthropometry [44]. These landmarks were located at the 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) top of intercondylar notch, 4) most dorsal point on lateral condyle, 5) lateral epicondyle, 6) most ventral point on lateral edge of trochlear groove, 7) most distal point at bottom of trochlear groove, 8) most ventral point on medial edge of trochlear groove, 9) most distal point on medial condyle, and 10) most distal point on lateral condyle. By using points typically associated with osteometric techniques, comparisons could be made with published studies to determine the plausibility of our results. Three metric parameters were measured: the bicondylar breadth (BCB), which is the distance between the two epicondyles [9], the anterior posterior diameter of the medial condyle (APDMC), which is the largest anteroposterior dimension of the medial condyle [11], and the anterior posterior diameter of the lateral condyle (APDLC), which is the largest anteroposterior dimension of the lateral condyle [11] (Fig. 14). The landmarks were positioned using 3D *in vivo* imaging software (Amira®) using the volume rendering technique (VRT) mode and the multi-planar reconstruction (MPR) mode. Once these landmarks had been defined, the coordinates of each landmark in space (x,y,z) were recorded.

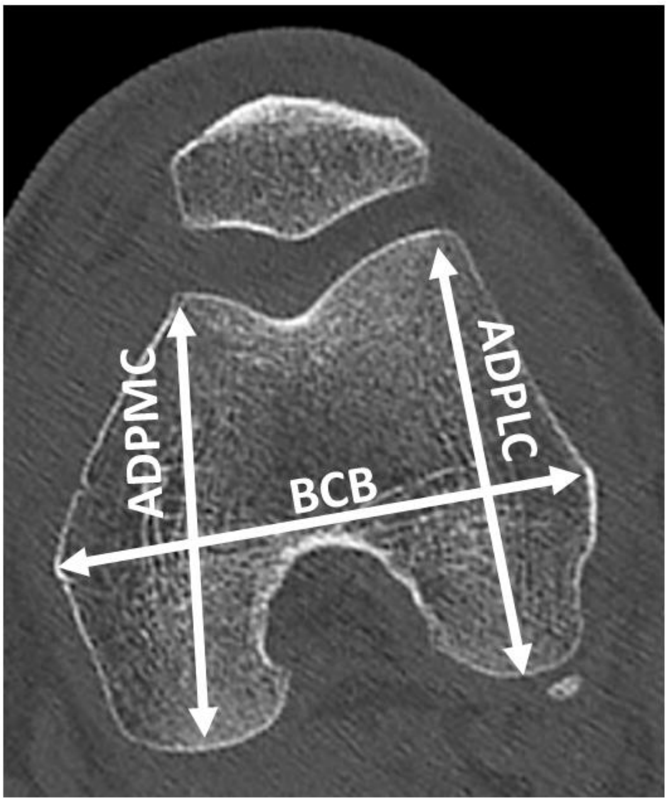

Figure 14 : Osteometric data used to measure the plausibility of the study's methodology. BCB: bicondylar breadth, distance between the two epicondyles, APDMC: anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial condyle and APDLC: anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle

During the scan, the subject was placed in a supine position with their knee in a relaxed and extended position. Axial slices perpendicular to the femoral long axis in which the epicondyles were the most prominent were used to place points 1 to 8. Oblique slices were created by resampling the image stack in order to be orthogonal to the axial plane; points 9 and 10 were placed on these images.

Reliability studies: The analyzed data were taken from the same database and analyzed twice on separate occasions by two observers. This made it possible to calculate the intra- and inter-observer variability for each landmark. The percentage error for each landmark was calculated, as described previously (Table 13). The results were deemed acceptable if this error was less than 5%.

Landmark	**Location**	**Intra-observer Variability**	**Inter-observer Variability**
1	Medial epicondyle	1.77	1.82
2	Most dorsal point on medial condyle	1.45	1.46
3	Top of intercondylar notch	1.52	1.60
4	Most dorsal point on lateral condyle	1.77	1.89
5	Lateral epicondyle	1.68	1.64
6	Most outside point on trochlear groove	1.59	1.62
7	Most distal point at bottom of trochlear groove	1.66	1.69
8	Most ventral point on margin of trochlear groove	1.62	1.72
9	Most distal point on medial condyle	1.73	1.69
10	Most distal point on lateral condyle	1.62	1.52

Table 13 : Anatomical description of the various landmarks used, with the intra- and inter-observer variability for each. The error is given as a percentage.

Procrustes analysis: All morphometric geometric analyses were carried out with Morpho J software and R 2.2.0 software. The chosen landmarks made it possible to characterize the shape of the distal femur. The first step consisted of a generalized Procrustes analysis (GPA). With GPA, size effects related to isometry were removed, but allometric size differences were retained and visible. This strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

Statistical analysis

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. Normal distribution of continuous variables was verified using the Shapiro-Wilk test and homogeneity of variances was determined using Fisher's F-test and Levene’s test to ensure the assumptions were met for use of parametric tests. Comparisons of subgroup demographics were performed with Student’s *t*-test. The length variables (BCB, APDLC and APDMC) in the various subgroups were compared using an analysis of variance (ANOVA).

The landmark coordinates were analyzed using principal component analysis (PCA) and canonical variate analysis (CVA) to identify shape trends in the various subgroups.

To determine if the difference between shapes was statistically significant, a *P*-value was also calculated using Goodall’s F-test and Mahalanobis D2 matrices. [16] [27] Goodall’s F-test allows testing for overall shape differences between groups while taking all sample variables into account.

A discriminant analysis with leave-one-out cross-validation was performed to determine the percentage of cases in which the ethnic group was correctly estimated. Pearson’s Chi-square test was also performed to compare the percentages of correct ethnic group classification in order to determine if this analysis was statistically significant. [34]

RESULTS

Reliability analysis

The percentage errors for the intra- and inter-observer comparisons for all the landmarks are given in the Appendix. None exceeded 2% (Table13).

Ethnic dimorphism

The mean BCB value was greater in Europeans (80.5 ± 6.5 mm) than Asians (76.3 ± 5.2) ($P < 0.001$). Similar results were found for the APDMC (E: 63.7± 5.1, A: 58.5 ± 4.2; $P < 0.005$) and the APDLC (E: 62.8 ± 4.9, A: 58.9 ± 3.8, $P < 0.001$) (Table 14).

	Asian		**European**	
BCB	76.3 ± 5.2		80.5 ± 6.5	
APDMC	58.5 ± 4.2		63.7 ± 5.1	
APDLC	58.9 ± 3.8		62.8 ± 4.9	
	ASF	ASM	EUF	EUM
BCB	72.1 ± 3.2	80.0 ± 3.6	75.5 ± 3.7	85.0 ± 4.9
APDMC	55.8 ± 3.3	60.9 ± 3.3	60.3 ± 4.0	66.7 ± 4.2
APDLC	56.9 ± 3	60.7 ± 3.6	60.2 ± 3.9	65.2 ± 4.4

Table 14 : Mean values (± standard deviation) of the osteometric data for each subgroup based on ethnicity and sex. Comparisons were performed with an ANOVA – $P < 0.001$ for all comparisons. ASF: Asian Female, ASM: Asian Male, EUF: European Female and EUM: European Male

The shape of the E and A distal femur differed significantly (Figure 15) (Goodall's F = 94.43, $P < 0.001$ and Mahalanobis D2 distance = 1.85, $P < 0.001$). For the same femur size, Asian femurs are significantly longer in the frontal plane, i.e. the distance between the axial plane containing the epicondyles and the two most distal points on the condyles is greater in the Asian group. In the axial plane through the epicondyles, Asian femurs are shorter along the anteroposterior axis than European femurs, while the mediolateral distance is the same. The graphical PCA representation that provided the best discrimination in terms of ethnic dimorphism was PC1 against PC2. PCA identified a difference in distal femur shape between A and E; PC1 and PC2 accounted for 71.9% of the variance measured (Figure 16). CVA revealed that the correct ethnic group was assigned in 82% of cases and the cross-validation revealed a 75% rate of correct ethnic estimation (table 15).

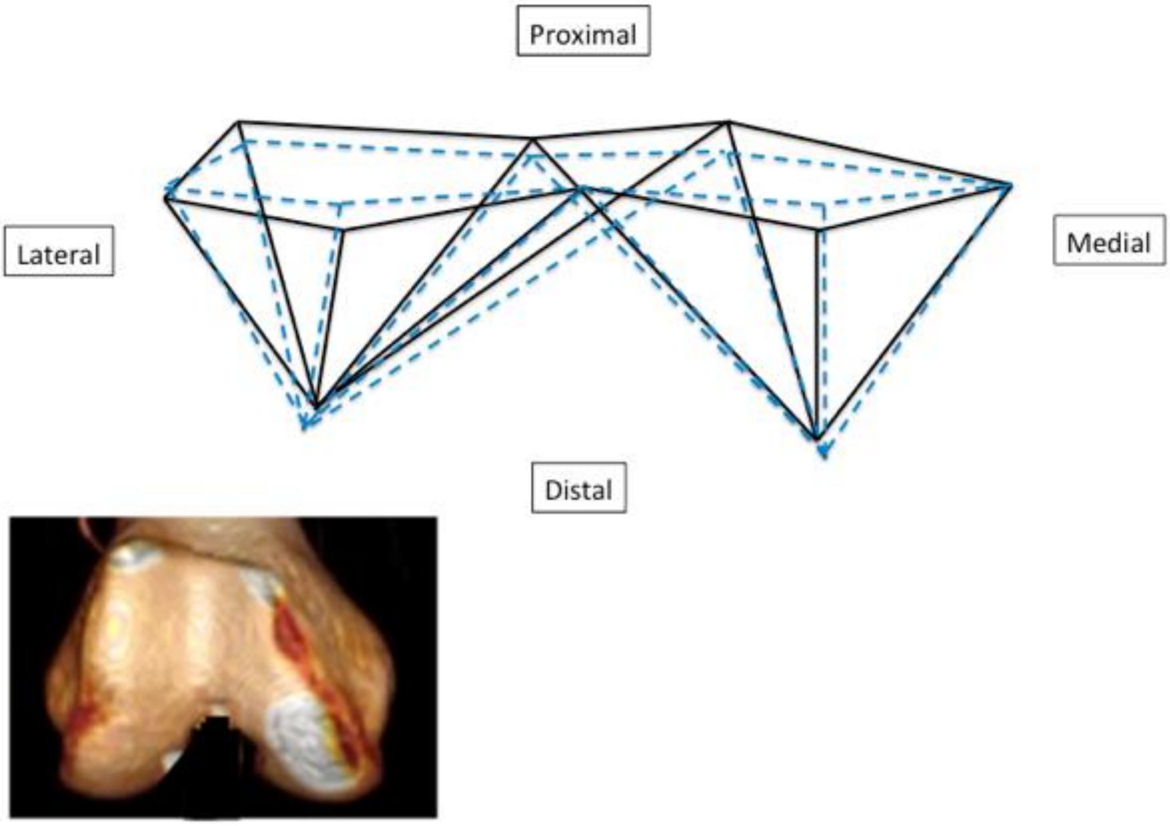

Figure 15 : Shape variation based on ethnicity. A 3D reconstruction is shown to make it easier to understand the data (Asian in blue, European in black).

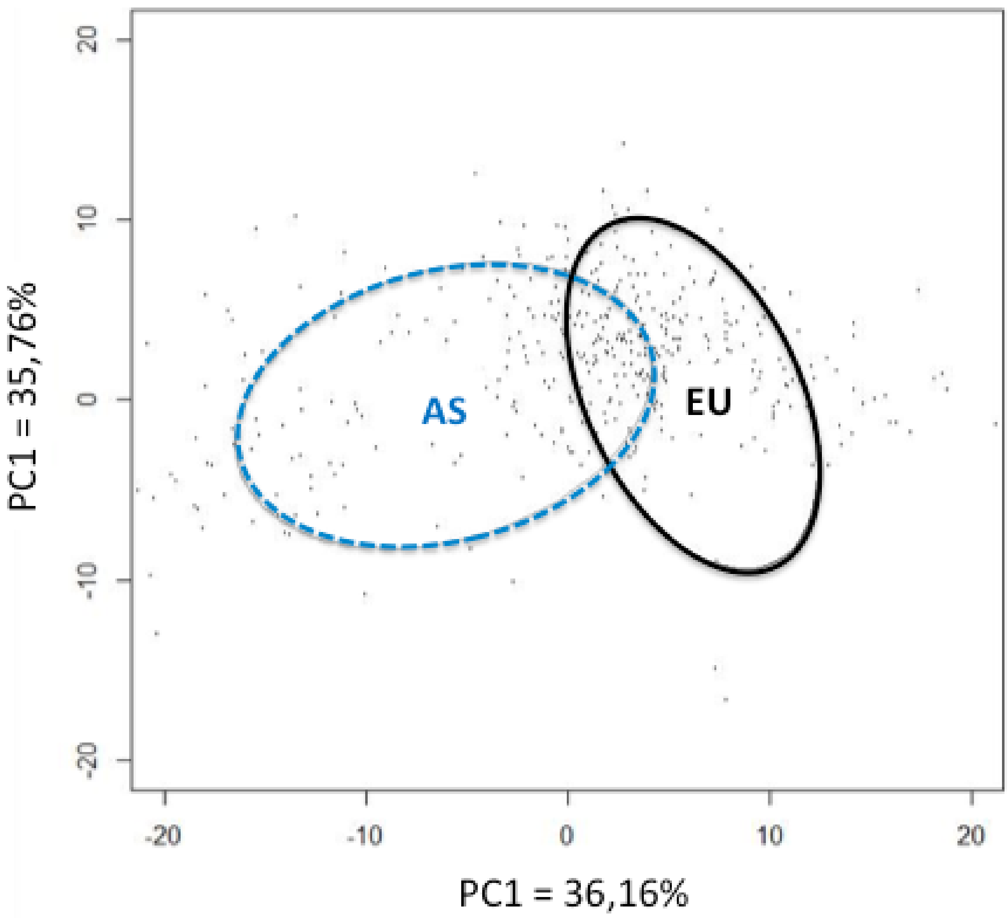

Figure 16 : PCA obtained for the shape of the distal femur based on ethnicity. The ellipses correspond to 68% confidence intervals (Asian (AS) in blue, European (EU) in black).

	Original CVA			Cross-Validated		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
A	203	39	83	187	53	77
E	195	45	81	179	63	73
Total	398	84	82	366	116	75

Table 15: Results of the CVA and cross-validation for the ethnic estimation.

Ethnic and sex differences

The osteometric analysis (BCB, APDMC and APDLC) revealed significant differences between subgroups of subjects (Table 14). The PCA based on ethnicity and sex is shown in Figure 16; PC1 and PC2 accounted for 61.9% of the variance measured.

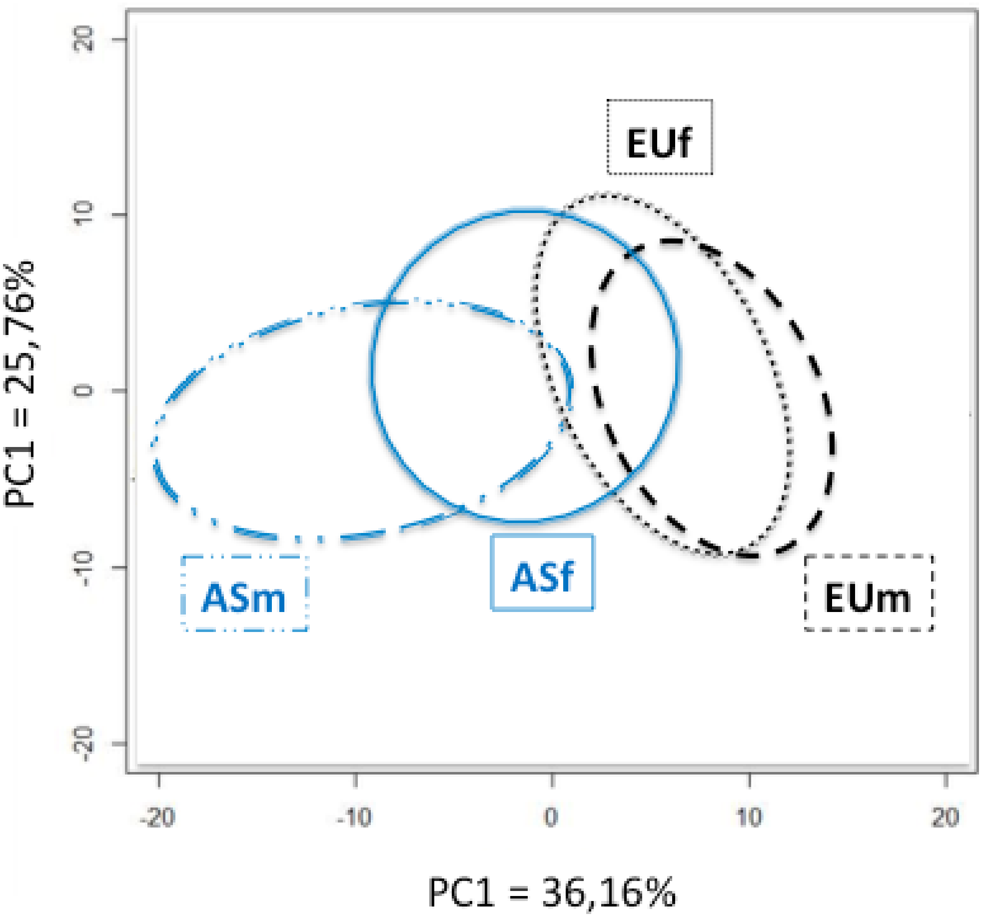

Figure 17/: PCA obtained for the shape of the distal femur based on sex and ethnicity. The ellipses correspond to 68% confidence intervals (Asian males (ASM) in blue dotted line, Asian females (ASF) in blue continuous line, European males (EUM) in black dashed line, European females (EUF) in black dotted line).

DISCUSSION

Our hypothesis is confirmed: 3D geometric morphometric analysis of the distal femur revealed differences between ethnic groups. There are ethnic and ethnic–sexual dimorphisms in the distal femur. All the comparisons performed in this study were statistically significant. The 3D analysis and osteometric data revealed dimorphisms related to ethnicity. Moreover, the PCA analysis (Figures 15 and 16) and comparative analysis of metric data (Table 14) revealed dimorphisms related to ethnicity, but also sex and ethnicity. The greatest dimorphism was found between Asian men and European men (Figure 16).

To our knowledge, this is the first study comparing the 3D anatomy of the distal femur between two ethnic groups. We are the first group to show differences in distal femur shape that are independent of the difference in size. It is well-known that the anatomical profiles of Asian knees are smaller and narrower than those of Caucasian knees. [65] However, in our study, we analyzed the differences in shape, not size. We performed a true 3D analysis because the location of each landmark was analyzed relative to the others. This differs from the analysis of two osteometric data points in two planes in space that is often used for comparisons between ethnic groups. [64]

Geometric morphological analysis effectively minimizes differences related to general somatotype and keeps only the shape differences. Bellemans et al. [44] have shown that differences in femur shape were related to an individual's sex and somatotype. Carter and Heath refined it into three somatotypes: endomorph, mesomorph, ectomorph [45]. Skeletal structure and body composition are used to classify individuals into these three groups. Osteometric analysis helps to assign ethnicity, but is subject to the somatotype effect. Geometric morphometric analysis discounts somatotype-related differences, reducing the accuracy of this analysis. Osteometric analysis is subject to two variables (ethnicity and somatotype), while geometric morphometric analysis is subject to only one variable (ethnicity).

One of the main objectives of physical anthropology is to estimate a person's sex and ethnicity in the forensic or anthropology context. [9] Most of the postcranial bones have been used to determine the sex of human remains through various statistical models [18]. The femur is the longest bone and it is often well preserved. [12] But anthropologists must have different algorithms in their diagnostic arsenal for cases where the skeletons are fragmented or when specific populations are analyzed. [16] The large number of subjects (n = 482) included in our study provides osteometric references related to sexual dimorphism in a modern population.

Determining ethnicity based on a bone fragment could improve identification of a specimen, particularly when it is not fully intact. This method made it possible to correctly assign ethnicity in 82% of subjects (original CVA) (table15). But this is not sufficient to allow the ethnic origin of a specimen to be determined without a doubt. Anthropologists have different algorithms in their diagnostic arsenal for cases where the skeletons are fragmented or when specific populations are analyzed. [16 9 11 13 10]This data may be used as a current reference when virtual or in vivo autopsy is performed [37].

In this study, osteometric analyses were carried out in addition to the 3D analyses. By placing easily identifiable points on the apex of the bone contours, we were able to obtain data in the traditional manner, which allowed us to verify that our data were in agreement with published values [53]. Origin-based variability [10] must be taken into account in literature comparisons, but the results of these three reference measurements are consistent with published results. [53] Furthermore, the intra- and inter-observer error rates were very low in our study—none exceed 2%. These two aspects (reproducibility and plausibility) validate our methodology. If we had wanted to carry out an analysis based only on classic osteometric variables (EB, ADPMS, ADPLC), we would have had to consider the patients' morphotype, hence their biometric data (height, weight, frontal plane morphotype, etc.). However, these variables (EC, ADPMS, ADPLC) were secondary outcome measures used to validate our measurement method by comparing it to existing data. We felt it was not necessary to weight these results with the biometric data, especially that our data were consistent with published values. [53] Geometric morphometric analysis eliminates differences related to object size.

The anatomical profiles of Asian knees are smaller and narrower than those of Caucasian knees. [65] Most of the commercially available total knee arthroplasty (TKA) implants were designed based on anthropometric data of Caucasian knees, thus they may not be suitable for Asian patients. [25 2 56 65] In a comparative study of the outcomes following

TKA, Asian patients had significantly less postoperative range of motion and a higher rate of revision [66]. As the number of TKA procedures is expected to increase in Asia [67], it is essential to analyze the morphological characteristics of Asian knees to provide validated references for Asian TKA implants. We performed a shape-based analysis that removed size effects. This is a crucial issue for us, as the anatomical difference is not only related to differences in size. The simplistic solution that Chinese patients need smaller implants will only solve part of the problem. Not only do these implants need to be smaller, they need to have a different shape. Only the concept of anteroposterior length, mediolateral width and/or aspect ratio provide some insight into interethnic differences [64]. Like Kim et al [64], we believe that these data create uncertainty around variability but do not answer the question itself.

Geometric morphometric analysis is a global 3D analysis that takes into account the location of each landmark in space relative to the others. Our analysis confirms that this dimorphism exists even when the size effect is removed. Furthermore, doing an analysis based on ratios or lengths over-simplifies the problem. It has been shown that soft tissue impingement due to overhang leads to postoperative pain and worse functional outcomes [56 63 68]. Reducing the size of the femoral component increases the risk of instability during knee flexion. If the femoral implant is shifted proximally to compensate for downsizing, the height of the joint line will be altered. For these reasons, only adjusting the size does not solve the problem – the shape must be taken into account.

The primary finding of our study is that ethnic dimorphism is present in the distal femur. The sex differences in distal femur from a Chinese population have been evaluated by Yang and colleagues [67]. However, their study used classic osteometric methods and measured distances, angles and ratios in three dimensions without connecting these dimensions. In our study, the coordinates of each target point were analyzed in three dimensions and were related to the location of other points. Thus our study should be more properly called 3D analysis [27].

It is also interesting to note that sexual dimorphism was more prevalent in the Asian population than the European one (Fig 16). We chose to quantify sex-related differences in the context of both orthopedics and anthropology. The impact of gender is hotly debated in orthopedics; it appears that the size difference between men and women explains part of the differences. [44] However, these differences are in part related to shape, independently of size . Geometric morphometric analysis have revealed these shape-related differences. In the anthropology context, sex determination contributes to identifying human remains. [16] [10] [9]

The current study has certain limitations. Only skeletally mature subjects were included. In younger persons, the bone contours of the distal femoral epiphysis are not completely ossified. This would have increased the possibility of error during landmark placement by the observers. Moreover, diseases that do not affect the distal femur but may require a CT scan that includes the distal femur, such as vascular conditions, are more common in older subjects. We were not able to determine the number of subjects needed for this study, as this was the first time that morphometric geometry methods were used to analyze distal femur anatomy. We initially based our sample size calculation on data from the Yang study [69] (measuring BCB in an Asian population) and the Cavaignac study [53] (measuring BCB in a European population). This calculation pointed to 35 subjects being needed in each group to reveal a difference of more than 4 mm between two ethnic groups using the BCB (common standard deviation of 6 mm, alpha risk of 0.05 and 90% power). But we felt it was timely to include a much larger number of subjects, making this the largest study to compare distal femur anatomy between two ethnic groups.

It is important to point out that our analysis of shape differences resulted in an average shape for each sub-group (Fig 15). Although the average shapes differ, they do not capture all the variability within a population. The shape of Asian and European distal femurs differs, while the extremes of each group can have similar components. The APC circles in Figures

16 and 17 are have some overlap become there are similarities between the populations. This is a drawback of “grouped” analysis, which suppresses individual characteristics. Most of the differences in shape in the orthopedic context occur in the axial plane (distal femoral twist, aspect ratio of distal femurs) [64 57 70]. We were somewhat surprised to found notable dimorphism in the frontal plane in our study (Fig 15) – Asian femurs were longer from cranial to caudal than the European femurs. To our knowledge, this frontal dimorphism has never been shown. This may be one of the reasons why Asian TKA patients have worse range of motion results. [66]

This study is the first step in an effort to classify the variability in femur shape suggested by Mahfouz [57] but in the three planes in space. We will add data from other ethnic groups to enrich our database.

The use of clinical investigations for anthropological purposes, after validation of the methods applied, also opens new fields for anthropology. The number of subjects who could be studied for anthropological purposes is greater than those in classic osteological collections.

In summary, the distal femur exhibits ethnic and ethnic–sexual dimorphism. Three-dimensional geometric morphometric analysis made it possible to show these shape differences. The large number of subjects studied may help to modernize the references for certain bone measurements.

Interethnic variability in distal femoral torsion

Multicentre study of 515 CT scans

of the distal femur

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Travail soumis à la revue Bone and Joint Journal

Abstract

Purpose

Distal femoral torsion (DFT) is defined as the angle between the posterior condyle line and the transepicondylar axis. This angle must be taken into consideration when performing total knee arthroplasty (TKA) as it affects the gap balance and patellar tracking. To our knowledge, no studies have been done to compare DFT between ethnic groups. We hypothesised that DFT displays interethnic variability. The purpose of this study was to study how the DFT varies as a function of ethnicity, age and sex.

Methods

We carried out a retrospective analysis of 515 CT scans of the femur from Asian and European patients. These CT scans had been performed to assess the vascular condition of the lower limbs. Subjects with bone and joint diseases (including osteoarthritis) were excluded. Four osteometric landmarks were defined based on standard bone landmarks used to measure DFT with Amira 3D imaging software. Descriptive statistics (mean, median and standard deviation values) were calculated. The Mann-Whitney test was used to compare the DFT in the two ethnic groups. The effects of age and side were assessed using Spearman's correlation coefficient. We also determined the number of cases with more than 3° difference (outliers) that would have occurred by choosing a fixed distal femoral rotation value (median in each group).

Results

We analysed scans from 259 Asians and 256 Europeans (53% male). The mean age was 55.3 ± 15.2 years. The mean DFT was 5.9° ± 2.5 (0–14°). The mean DFT angle in Asians was 1.1° larger than that in Europeans ($p < 0.0001$). Using the median DFT value in each group as the reference value, 33% of the Asians and 27% of the Europeans could be considered outliers. Age and side had no effect on the DFT value ($R = 0.03$; $p = 0.43$).

Conclusion

There are significant interethnic differences in the DFT angle. Using a fixed distal femur rotation value during TKA could lead to rotational malalignment that alters the balance between the flexion and extension gaps.

Keywords :distal femoral torsion, variability, posterior condyle line, trans epicondylar axis

Level of evidence : IV

INTRODUCTION

Total knee arthroplasty (TKA) is a standard treatment for various disabling disorders of the knee and has proven long-term success [71]. Positioning of the femoral implant in the axial plane is referred to as “rotational alignment” and is crucial for long-term survival of TKA [72]. Axial alignment of the femoral component will impact flexion stability, tibiofemoral and patellofemoral kinematics, and knee alignment in flexion. Commonly described distal femoral references include the posterior condylar line (PCL) [73] and two transepicondylar axes (TEA): the anatomical or clinical TEA (cTEA) (line connecting most prominent point on both epicondyles) [74] and the surgical TEA (sTEA) (line connecting the lateral epicondylar prominence and the medial sulcus) [75 76].

Published data show that rotational alignment of the femur parallel to the TEA leads to correct alignment in TKA [77 78]. The TEA is considered the functional axis of the knee around which flexion/extension kinematics occur [79]. The cTEA is the most reasonable landmark for kinematics, but can be difficult to identify during surgery [74 80]. The PCL is the easiest reference axis to find consistently during surgery, but it is internally rotated relative to the TEA. Hence, some degree of external rotation of the femoral component must be applied during TKA procedure [77 81]. In general, 3° has been measured between the PCL and sTEA [74 75]. For this reason, some surgeons always place the femoral component in 3° of external rotation, no matter the patient characteristics.

There are conflicting suggestions as to whether there is a need for distinct designs of femoral components for men and women based on morphologic and size differences between genders but also between ethnic groups [82-84]. It is reasonable to ask whether gender-based or ethnic-based modifications exist in anatomical landmarks used to implant a TKA.

Distal femoral torsion (DFT) is defined as the angle between the PCL and the TEA [85]. We hypothesised that DFT displays interethnic variability. The purpose of this study was to study how the DFT varies as a function of ethnicity, age and sex.

METHODS

This was a multicentre, retrospective, descriptive, analytical study. The research ethics committee at our respective healthcare facilities approved this study (No. 01-0415 and No. 2016-94).

Materials

Study population: The analysis was carried out on the computed tomography (CT) images of distal femurs. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) were retained. The included CT scans had been performed to assess leg vasculature (CT angiogram). Any CT scans with signs of bone or joint pathology or osteoarthritis in the distal femur were excluded.

Between 1 June 2014 and 31 December 2014, 515 unpaired CT scans of the distal femur met our inclusion criteria: 256 patients were European (from southwest France) and 259 were Asian (Huan from Chongqing, China). There were 244 women and 271 men. The average age was 55 ± 16.2 years (20–87). The right side was analysed 251 times and the left side 264 times. The two groups were comparable in terms of their demographics (Table 16).

		Age
Sex	Male (n=254)	55.24 ± 15.20
	Female (n=228)	55.45 ± 16.47
Side	Right (n=235)	55.14 ± 6.24
	Left (n=247)	55.53 ± 15.59
Ethnicity	European (n=240)	56.47 ± 14.85
	Asian (n=242)	54.22 ± 16.80

Table 16 : Mean age of the various subgroups relative to sex, side and ethnicity; Comparisons were performed with Student's t-test – $P > 0.05$ for all comparisons

The CT scans were taken on a Sensation 16 (120 kV, 80 mA; light speed 16) Scanner (Siemens, Erlangen, Germany) with 16*1.5 mm collimation. The image matrix was 512*512 pixels. A bone filter and a soft tissue filter were used. During the scan, the subject was supine with his or her knee in a relaxed and extended position. Axial slices perpendicular to the femoral long axis in which the epicondyles were the most prominent were used.

The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira® software (version 4.1.1, FEI Visualization Sciences Group, Bordeaux, France).

Methods

Four osteometric landmarks were defined based on standard bone landmarks used to measure DFT [86] and placed by two observers twice on separate occasions. These landmarks were located at the 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) most dorsal point on lateral condyle, 4) lateral epicondyle (Fig18).

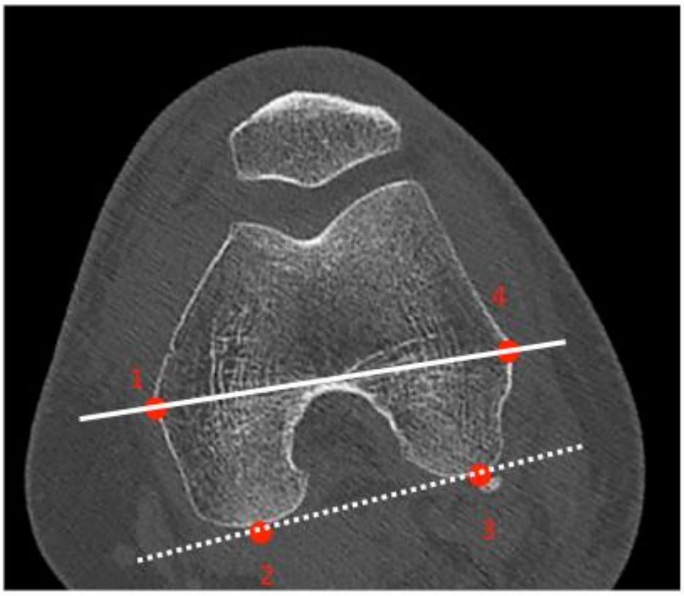


Figure 18 : Location of landmarks placed on the CT scans :1) medial epicondyle, 2) most dorsal point on medial condyle, 3) most dorsal point on lateral condyle, 4) lateral epicondyle. The solid line joining landmarks 1 and 4 is the cTEA. The dashed line joining landmarks 2 and 3 is the PCL.

The landmarks were positioned using 3D imaging software (Amira®) using the volume rendering technique mode and the multi-planar reconstruction mode. Once these landmarks had been defined, the coordinates of each landmark in space (x,y,z) were recorded. The software used automatically calculated the DFT value using the cTEA as described in the literature [74 76].

Statistical analysis

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. Normal distribution of continuous variables was verified using the Shapiro-Wilk test and homogeneity of variances was determined using Fisher's F-test and Levene's test to ensure the assumptions were met for use of parametric tests.

Comparisons of subgroup demographics were performed with Student's *t*-test. DFT in both groups was compared using Mann-Whitney test. The effects of age and side were assessed using Spearman's correlation coefficient. We also determined the number of cases with more than 3° difference (outliers) that would have occurred by choosing a fixed distal femoral rotation value (median in each group).

The analysed data were taken from the same database and analysed twice on separate occasions by two observers. This made it possible to calculate the intra- and inter-observer variability for each landmark. For each observer, landmark deviations were calculated relative to the landmark's mean value. For each point placed by an observer, the deviation is relative to the mean value of the position calculated from all the observers for this point. The percentage error for each landmark was calculated, as described previously [29] (Table 17). The results were deemed acceptable if this error was less than 5% [29].

RESULTS

The percentage errors for the intra- and inter-observer comparisons for all the landmarks never exceeded 2%, making this analysis reliable (Table 2).

Landmark	**Location**	**Intra-observer Variability**	**Inter-observer Variability**
1	Medial epicondyle	1.77	1.82
2	Most dorsal point on medial condyle	1.45	1.46
3	Most dorsal point on lateral condyle	1.77	1.89
4	Lateral epicondyle	1.68	1.64

Table 17 : Anatomical description of the various landmarks used, with the intra- and inter-observer variability for each. The error is given as a percentage.

The mean DFT for the entire study population was 5.9° ± 2.5 (0–14°). The mean DFT angle in Asians was 1.1° larger than the mean value in Europeans ($p < 0.0001$) (Table 18). Subgroup analysis found no significant difference between the four ethnicity–sex combinations ($p = 0.17$) (Fig. 19).

Ethnicity	**Median**	**Min**	**Max**	**Mean**	**SD**
Asian	6.37	0.31	14.1	6.51	2.59
European	5.52	0.00	13.1	5.43	2.36
Total	5.99	0.00	14.1	5.97	2.54

Table 18 : Comparison of the values of the angle between the TEA and the PCA between the Asian population and the European population. For all the comparisons, the **p-value was < 0.0001.** SD: standard deviation

Using the median DFT value in each ethnic group as the reference value, 33% of the Asians and 27% of the Europeans could be considered outliers, as the difference from the median value was more than 3° (Fig. 20). Age and side had no effect on the DFT value (R = 0.03; p = 0.43).

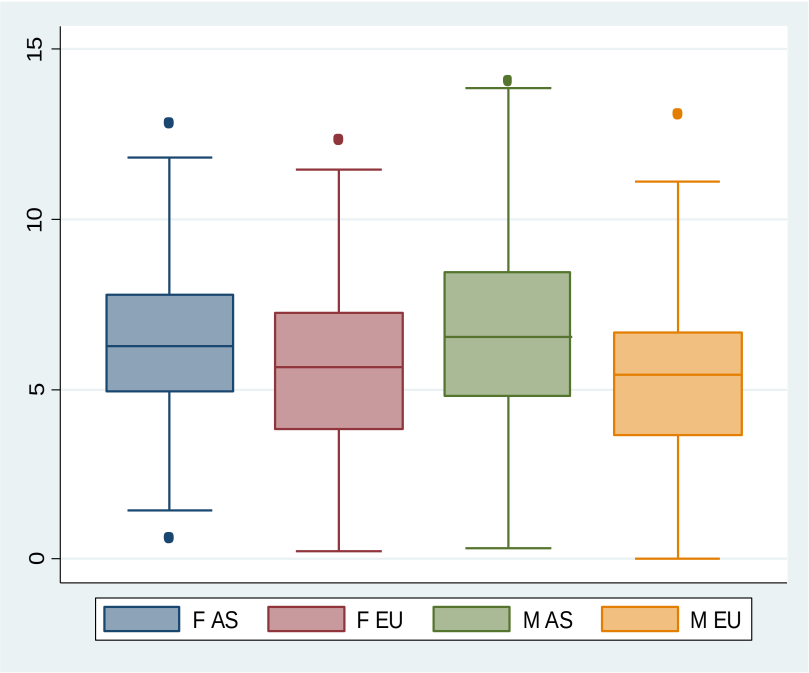


Figure 19 : Box plot summarising the DFT values in the four ethnicity–sex subgroups
FAS – Female Asian, FEU – Female European, MAS – Male Asian, FAS – Female Asian.
The difference in the median value for each subgroup is not significant (p = 0.17).

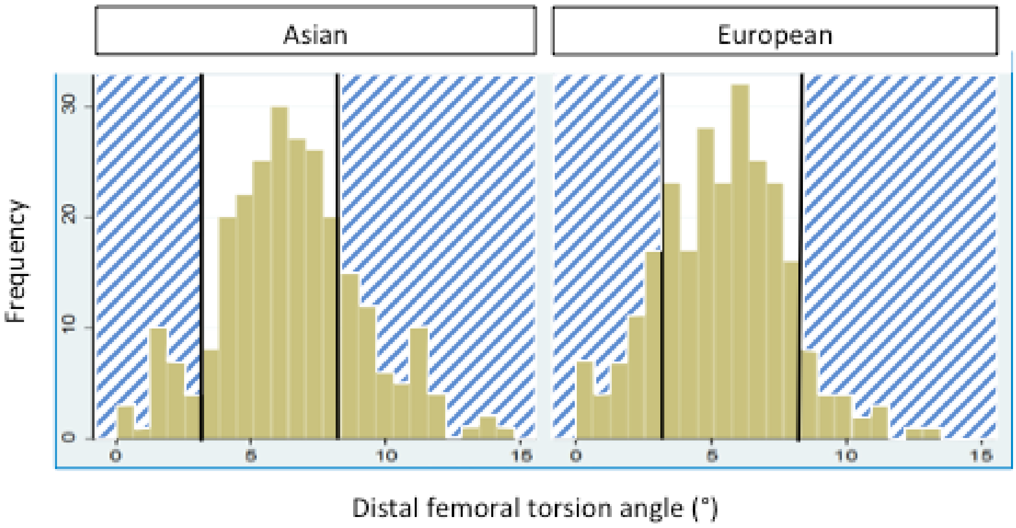


Figure 20 : Frequency distribution of the DFT values in the Asian and European populations. The hatched areas correspond to greater than 3° difference from the median value. Note that the DFT has a Gaussian distribution within each population.

DISCUSSION

Our hypothesis is confirmed. There are interethnic differences in the DFT. The mean value in both groups was statistically different; the mean difference was 1.1°. The central finding of this study is the number of outliers if a fixed rotation angle relative to the PCL had been applied during TKA in these patients. About one-third of Asians and one-quarter of Europeans would have too much or too little rotation (> 3°) (Fig 20).

Several published studies have shown differences in alignment of knees between Caucasians and Asians [87-89]. A recent systematic review showed differences in the size (anterior–posterior height and medial–lateral width of the femur and tibia) and shape (tibial and femoral aspect ratios) of knees from Caucasian and East Asian populations [64]. Our results are consistent with published results. Furthermore, the intra- and inter-observer error rates were very low in our study – none exceed 2%. These two aspects (reproducibility and plausibility) validate our methodology.

The femurs in the Chinese population are substantially more externally rotated than the traditionally accepted 3° in Western patients. Using sTEA, Yip et al. showed that Chinese femurs are significantly more externally rotated [90]. They recommend planning 6° of external rotation for Chinese women and 5° for Chinese men during TKA [90].

Urabe et al showed that morphological measurement of the distal femur was significantly greater in Caucasian women [91]. In a study of 32 Japanese cadaveric femoral bones, Yoshioka et al. found a condylar twist angle of 5° in males and 6° degrees in females [74]. Moghtadaei's study of an Iranian population using sTEA and cTEA also found a greater angle than that applied during surgery, which is comparable to the value of the angle of the Asian population in our study and published data [92].

Several studies have pointed out differences of knee morphology between Caucasian and Asian populations. We conducted a large study (515 patients) comparing the DFT between both populations. We found a significant difference in the value of the angle between PCL and cTEA. The DFT angle is greater in the Asian population (6.5° vs 5.4°, $p < 0.001$). We found no gender differences in this study. Bellemans et al showed that both gender and morphotype influence the knee shape of patients undergoing TKA [86].

By measuring the distribution of the DFT angle, not only the mean value, we found large variability in the DFT angle. Ollivier et al. had previously reported large variability in the DFT angle measured with MRI in a cohort of 54 Europeans [93]. The large variability in PCL was also documented by Thienpont et al. in a cohort of more than 2000 cases, but ethnic dimorphism was not taken into consideration [94]. As the number of TKA procedures increases in Asia [95 96], it has become essential to analyse the morphological characteristic of Asian knees in order to provide references for Asian TKA surgeons.

Rotational malalignment still accounts for an unacceptable number of TKA failures and is one of the main causes of persisting anterior knee pain after knee replacement [97].

Interethnic differences can no longer be ignored during surgery, because of the risk of implant malpositioning and its functional consequences. Based on our study's findings, an appreciable percentage of patients are at risk for femoral implant malpositioning when a fixed distal femoral rotation value is used to perform TKA: about one-third of Asians and one-quarter of Europeans. Preoperative CT or MRI scans are the only reliable means for measuring DFT and adjusting the femoral component's rotation to the anatomy of the knee [72 76].

Our study has limitations. Since this was a retrospective study in a population undergoing vascular disease assessment, we could not analyse our findings based on other anatomical parameters such as morphotype, which may have provided further insight into the differences. Also, the patients analysed in this study were younger than those who typically undergo TKA. This was required because the goal of the study was to analyse interethnic variability in a population without bone or joint diseases. The number of outliers was determined using a median DFT value of 3°. We believe this actually under-estimated the number of outliers given the Gaussian distribution of the DFT values in both populations. An outlier was defined as a subject with more than 3° difference from the target value based on recommended definition for outliers [98].

CONCLUSION

There is ethnic dimorphism in the femoral distal torsion value. This dimorphism and the variability have to be taken into account when TKA is performed. An appreciable percentage of patients are at risk for femoral implant malpositioning when a fixed distal femoral rotation value is used to perform TKA.

DISCUSSION GENERALE

Notre objectif est atteint. Nous avons pu mettre en évidence la variabilité de l'anatomie du fémur distal en fonction du sexe, de l'âge et de l'ethnie à l'aide d'une analyse morphométrique géométrique. Nous avons analysé environ 500 TDM de fémur distal de population ne présentant pas de pathologie osseuse ou articulaire. Cette analyse reflète donc l'anatomie non pathologique de populations contemporaines. Il s'agit à notre connaissance de la première étude internationale utilisant une analyse tridimentionnelle vraie pour caractériser la forme du fémur distal. Nous rapportons ici des données issues d'une population contemporaine contrairement à la majorité des études sur le sujet [1 9 10 19 99]. Nos données peuvent donc servir de référentiels actuels pour la réalisation d'autopsies virtuelles ou in vivo[42 43]. Les variations temporelles observées avec les populations contemporaines montre que la réévaluation de certaines mesures osseuses est nécessaire [1].

Nous avons choisi une méthodologie adaptée à l'analyse de la conformation pour éliminer les effets de taille. Nous avons tout de même réalisé pour chaque étape une analyse ostéométrique classique afin de pouvoir analyser la vraisemblance de notre méthodologie. La précision de positionnement des points était excellente, en témoignent les chiffres de reproductibilité bien qu'il y ait eu plusieurs observateurs. L'association précision de mesure et vraisemblance valide notre méthodologie.

Cette méthode ne donne pas de résultat suffisamment précis pour être utilisée seule. Cependant, elle a l'avantage de pouvoir être utilisée dans des contextes d'autopsie virtuelle ou in vivo[42 43].

Quelques points méritent d'être évoqués plus en détails dans ce travail : la mise en évidence d'un dimorphisme sexuel dans le contexte orthopédique, le dimorphisme lié à l'âge et ses conséquences et enfin un chapitre sur le dimorphisme ethnique et ces conséquences.

Dimorphisme sexuel

Il s’agit d’un sujet qui a été très médiatisé il y a quelques années en orthopédie. Par l’utilisation de mesures ostéométriques classiques, certains auteurs ont essayé de classifier les genoux en féminin ou masculin. Certains fabricants de prothèses ont profité de l’occasion pour proposer d’augmenter leur gamme d’implants en utilisant des implants dit « gender » en fonction du sexe. A longueur antéro-postérieure égale les implants féminins étaient plus étroits en médio-latéral. En effet dans certains cas les pièces fémorales de prothèse de genou étaient trop large par rapport à la longueur antéro-postérieure nécessaire ce qui pouvait entrainer des conflits avec les parties molles. Si l’opérateur choisit de diminuer la taille, alors la prothèse peut ne pas être assez grande en antéro-postérieur et donc la stabilité peut en être perturbée. Il a donc été proposé ces implants gender.

Bellemans et al [44] ont notamment montré que ces différences initialement évaluées comme liées au sexe étaient principalement liées aux morphotypes des patients. Les hommes généralement plus grands et massifs avaient des genoux plus larges et massifs. Ils ont réalisé leur analyse à l’aide de données ostéométriques classiques.

Nous avons mis en évidence un dimorphisme lié au sexe de la conformation du fémur distal. Par ailleurs notre analyse est réellement tridimentionnelle. On peut noter à la figure 15 que le dimorphisme est surtout dans le plan frontal. Les autres auteurs n’ont pas réalisé d’analyses dans le plan frontal. En effet, le problème expliqué au chapitre précédent concernant la différence de forme des prothèses en fonction du sexe est une analyse simplement dans le plan axial. Il existe donc un dimorphisme de la forme lié au sexe qui est tridimentionnel pour lequel une analyse uniplanaire simple n’est probablement pas suffisante.

Dimorphisme lié à l'âge

Nous avons mis en évidence une différence de la forme des extrémités distales de fémur des européens en fonction de l'âge. Nous avons déterminé de façon arbitraire des limites à 40 et 60 ans. Il n'y avait pas à notre avis de limite pouvant avoir une logique clinique. Nous avons donc choisi de manière arbitraire des tranches d'âge.

Nous avons exclu de l'analyse les sujets présentants des lésions osseuses ou des signes d'atteinte dégénérative. Nous avons voulu limiter les signes de sénescence avec ces critères stricts d'exclusion. Notre étude portait donc sur une anatomie non pathologique.

Nous avons pu mettre en évidence un dimorphisme lié à l'âge avec une différence de forme des sujets < 40 ans pour les européens. Cela a deux conséquences : une orthopédique et une anthropologique. En ce qui concerne l'orthopédie, il nous semble évident que le dessin des prothèses de genou doit être ré évaluer de manière fréquente pour s'adapter aux variations d'anatomie de la population. En ce qui concerne la conséquence anthropologique, pour expliquer cette variabilité il convient de savoir si elle est liée à l'évolution séculaire de la population. Nous avons pour cela analysé 32 pièces anatomiques provenant du museum d'histoire naturelle de Toulouse. Il s'agissait de sujets décédés il y 150 ans. Nous avons mis en évidence une différence en ce qui concerne les mesures ostéométriques classiques (fémur ancien plus petit) probablement lié à l'évolution du morphotype des habitants de la région (plus grand et plus lourd). Nous n'avons pas pu mettre en évidence de résultats probants en ce qui concerne l'analyse de la forme. Une fois l'effet de taille éliminé, nous ne possédions pas assez de sujets pour pouvoir donner une interprétation fiable et cohérente. L'analyse en composant principal ci-dessous ne donnait aucune tendance (fig 22), elle était ininterprétable.

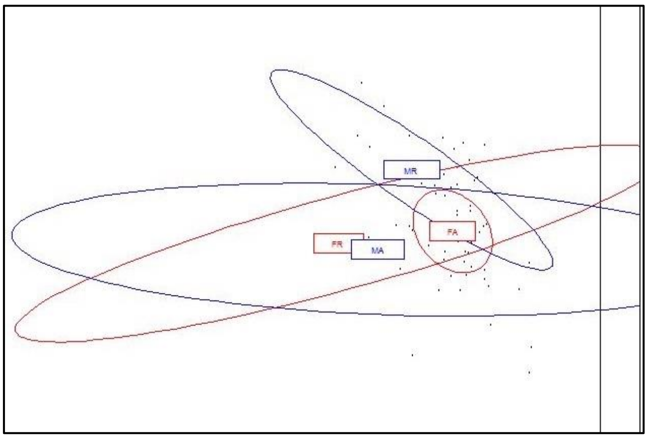


Figure 21 : Analyse en composant principal de la comparaison fémur ancien et fémur contemporain. Aucun groupe distinct ne se dégage.MR : male Récent, MA : male ancien, FR : female recent, FA : Female Ancient.

L'analyse procruste met en évidence une différence de forme sans que celle-ci ne soit statistiquement significative. Le condyle latéral reste sensiblement identique alors que le condyle médial semble montrer des différences entre les fémurs contemporains et les fémurs anciens (fig 22). Le condyle médial semble s'être allongé dans le plan frontal. Nous n'avons pas trouvé d'explications à ce phénomène qui devrait nécessiter plus de sujets pour permettre une analyse pertinente.

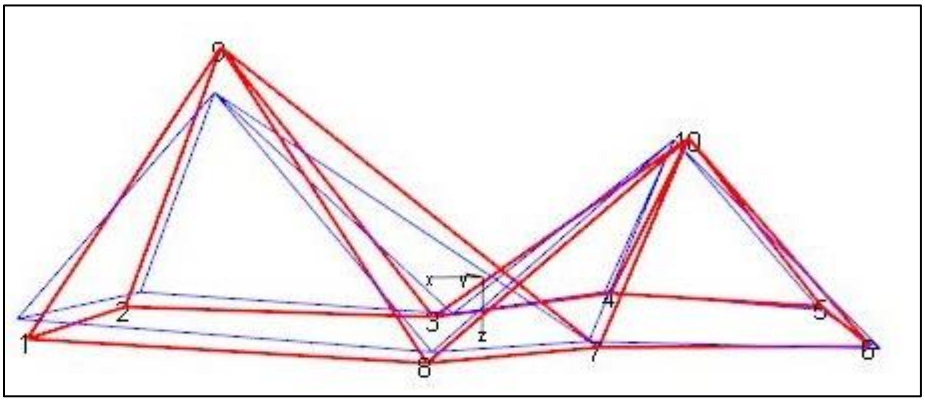


Figure 22 : Analyse procruste de la comparaison fémur ancien (bleu) et fémur contemporain (rouge). A gauche il s'agit d'un condyle médial et à droite du condyle latéral.

Dimorphisme lié à l'origine géographique

Nous sommes en train de poursuivre notre analyse avec l'étude d'une population venant d'Afrique Sub Saharienne. Nous avons obtenu 50 TDM remplissant nos critères d'inclusion venant de l'hôpital universitaire de Pretoria (Afrique du sud).

Bien entendu ce travail ne permet pas une analyse globale de l'ensemble des ethnies. Il ne sera jamais possible de réaliser un « catalogue » de telle forme en fonction de telle ethnie d'une part car il existe une variabilité importante au sein même d'une ethnie et que par ailleurs les ethnies ne sont pas des populations fermées dans lesquelles aucun contact n'est possible.

Toute fois nous soulignons la variabilité importante de l'anatomie du fémur distal notamment interethnique. Cette variabilité doit être prise en compte dans l'analyse des résultats anthropobiologiques, anatomiques et orthopédiques. Les populations ne doivent pas être jugées comparables seulement par l'analyse de données biométriques classiques (poids, taille, BMI, âge,..) . La variabilité interethnique peut expliquer une partie des différences de résultats obtenus mais elle peut aussi devenir un biais d'analyse en étant un facteur de confusion. En effet si l'ethnie de deux groupes de patients n'est pas la même il va être problématique de statuer si la différence est liée au procédé tester ou à l'ethnie. Il s'agit d'un sujet sensible, il est interdit en France d'établir des recherches en précisant l'origine ethnique des patients.

On note en effet des différences de résultats pour un même type d'implants entre différentes populations [25] [2] [56] [65]. La place de la variabilité interethnique est à notre avis primordiale pour comprendre ces différences.

Cette variabilité n'est pourtant pas prise en compte dans notre prise en charge quotidienne en ce qui concerne la réalisation de prothèse totale de genou. En effet, une prothèse totale de genou a plusieurs tailles qui permettent « d'adapter » le femur et la prothèse cependant il n'y a aucune variation de la forme proposée.

Nous avons donc décidé d'analyser la forme des fémurs et de la comparer avec la forme des prothèses totales de genou commercialisées. Il s'agit d'un travail en cours de réalisation, nous allons vous présenter des résultats partiels.

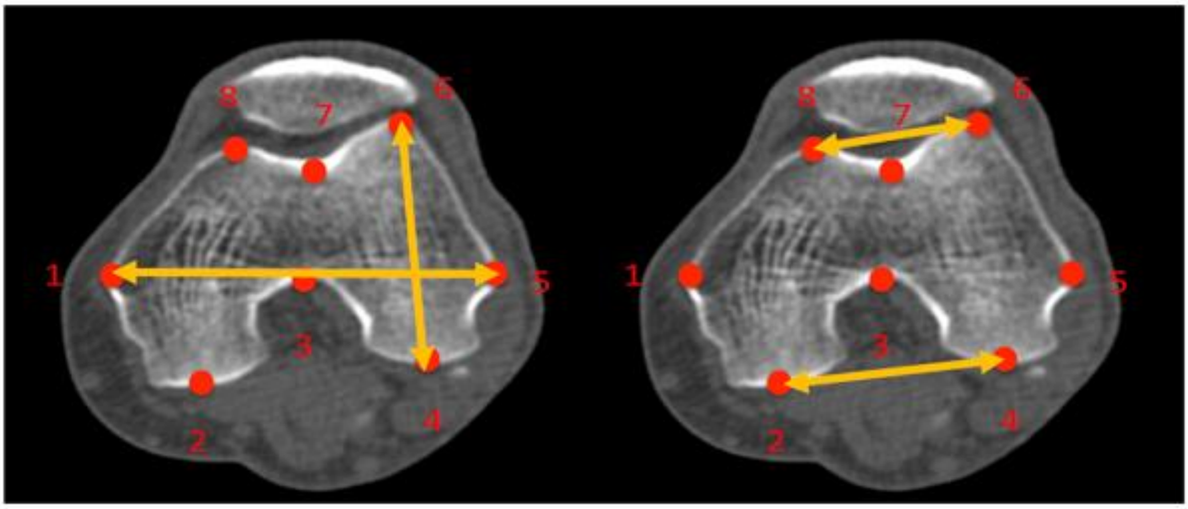
Nous avons donc décider d'analyser dans le plan axial la forme des fémurs que nous avions colligés en la comparant à la forme des prothèses commercialisées. Pour cela nous avons utilisé les rapports proposés par Mahfouz et al :[57] (Fig 23)

« Aspect ratio » correspond au rapport entre la plus grande distance médio latérale et la plus grande longueur antéro-postérieure.

« Trapezoidicity ratio » correspond au rapport entre la plus grande longueur medio-latérale antérieure au niveau de la trochlée et la distance entre les deux points condyliens postérieurs.

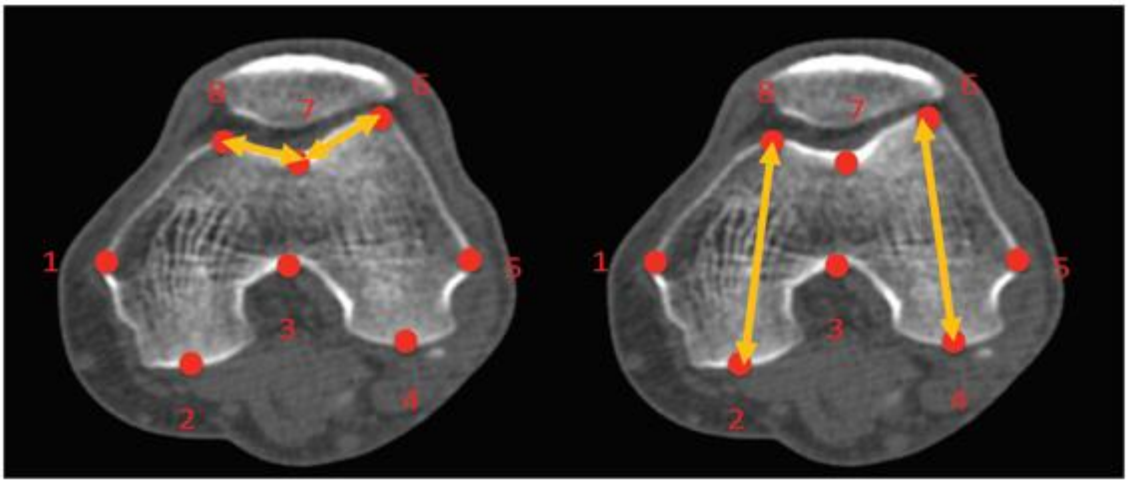
« Assymetrical ratio » correspond au rapport entre la plus grande longueur antéro-posterieure du condyle latéral sur la plus grande longueur antéro-posterieure du condyle médial.

« Trochlear ratio » correspond au rapport entre la berge latérale et la berge médiale de la trochlée.



Aspect Ratio
ML/AP

Trapezoidicity Ratio
ML_A/ML_p



Trochlear Ratio

Assymetry Ratio
AP_L/AP_M

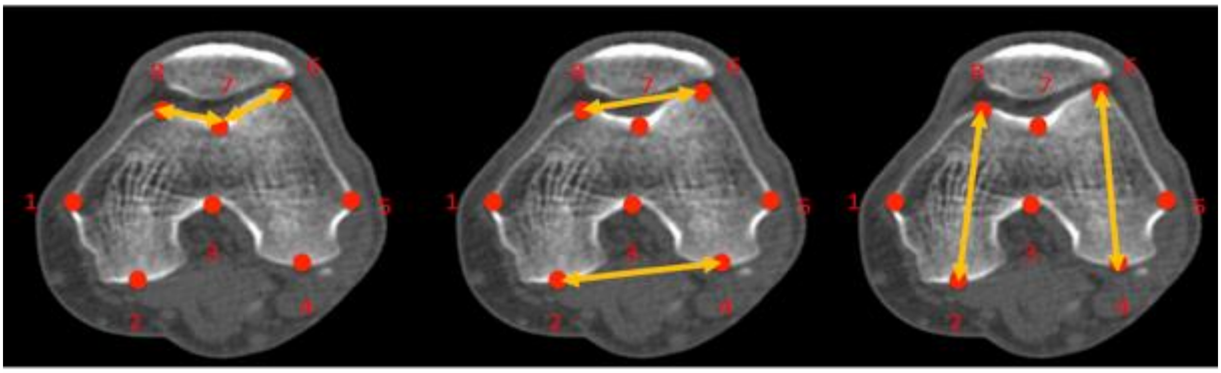
Figure 23 : schéma des différents critères de jugement utilisés pour caractériser l'anatomie dans le plan axial du fémur distal.

Par ailleurs, nous avons mesuré des valeurs angulaires qui nous semblaient caractéristiques de la forme du fémur distal.

« Narrowing angle » qui correspond à l'angle entre le grand axe du condyle externe et le grand axe du condyle interne.

« Trochlear rotation » qui correspond à l'angle entre l'axe condylien postérieur et une droite joignant le point le plus médial et le point le plus latéral de la trochlée fémorale.

Angle de creusement de la trochlée ou sulcus angle.



Sulcus angle Trochlear rotation Narrowing angle

Figure 24 : Représentation des différentes données angulaires mesurées.

Vous pouvez noter sur les figures ci-dessous la grande variabilité des valeurs obtenues au sein des populations. Il y a une distribution gaussienne de l'ensemble de ces éléments pour chaque ethnie et en fonction du sexe (fig 25 et 26). La variabilité est assez importante pour tous les critères mais aussi pour toutes les composantes de la population. Il est difficile de mettre en évidence une différence de distribution entre les différents groupes.

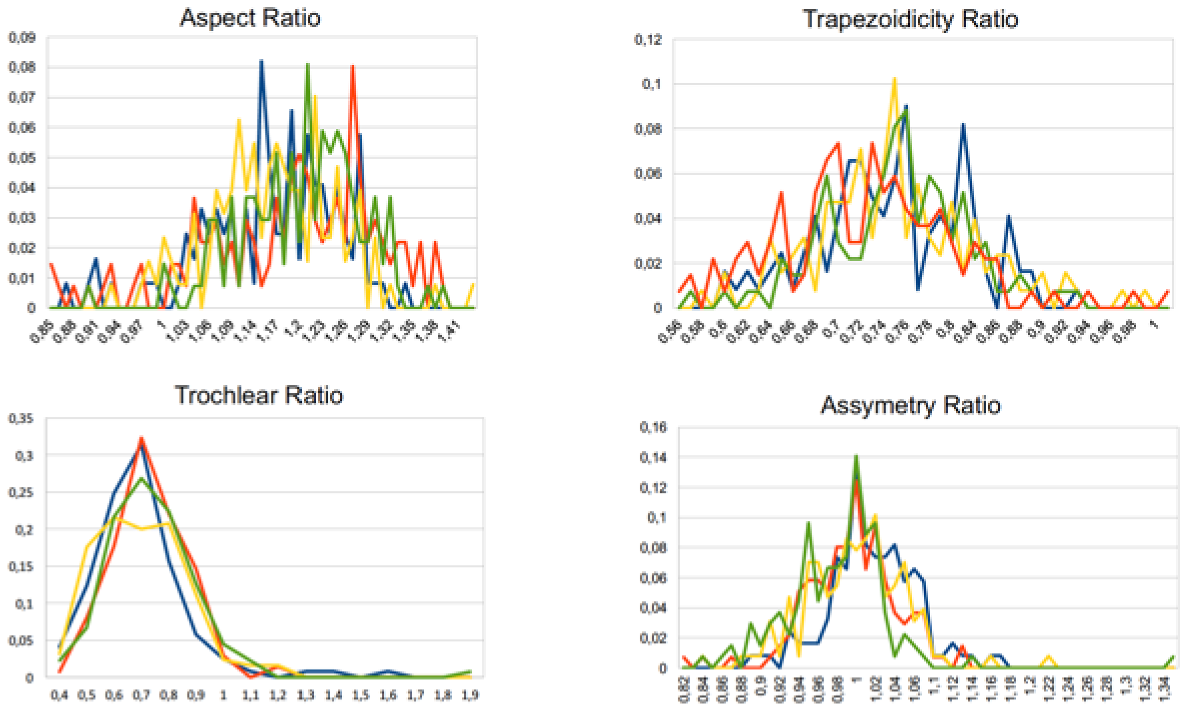


Figure 25 : Distribution des différents ratios dans la population. En ordonnée le pourcentage de population pour chaque valeur, en abscisse la valeur du ratio. En rouge les hommes asiatiques, en bleu les femmes asiatiques, en vert les hommes européens, en jaune les femmes européennes.

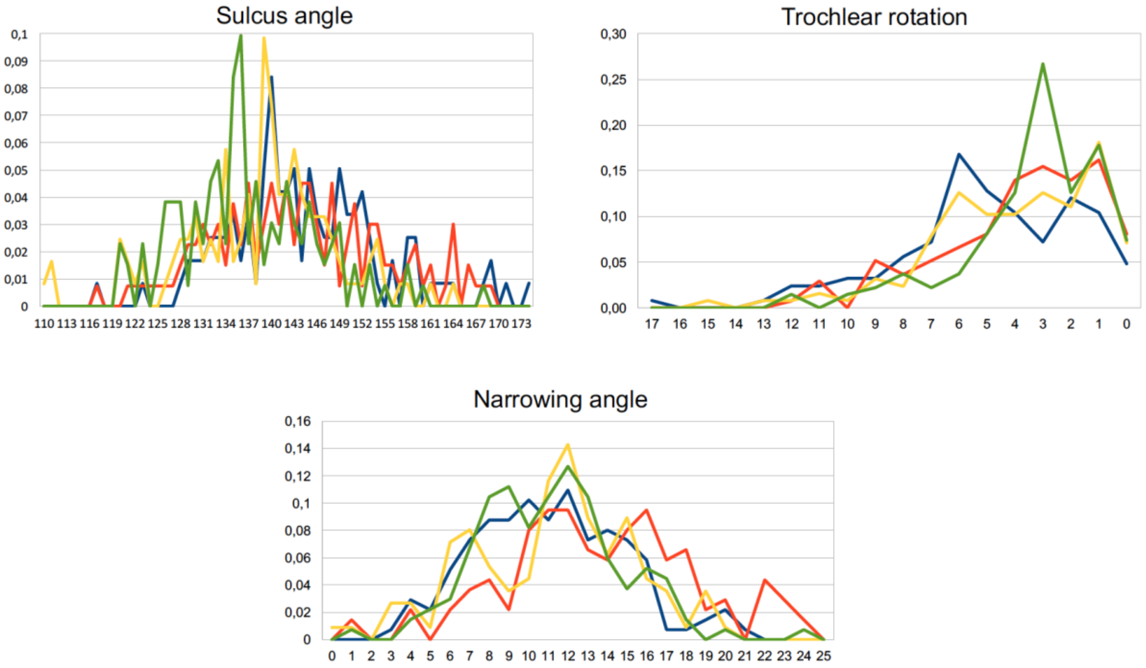


Figure 26 : Distribution des différentes valeurs angulaires dans la population. En ordonnée le pourcentage de population pour chaque valeur angulaire, en abscisse la valeur de l'angle. En rouge les hommes asiatiques, en bleu les femmes asiatiques, en vert les hommes européens, en jaune les femmes européennes.

Par ailleurs, sur le tableau 19, nous vous présentons les résultats comparatifs entre européens et chinois pour les critères de jugement utilisés. La plupart des différences sont statistiquement significatives mais sont en général peu importantes mis à part le sulcus angle. Il est à noter que nous avons déjà montré que la torsion épiphysaire distale était différente entre les deux populations (cf article spécifique chapitre 3).

	European	**Asian**	**p**
Aspect ratio ***ML/AP***	1.18 + /- 0.1	1.17 + /- 0.1	0.27
Assymetry ratio AP_L/AP_M	0.99 + /- 0.1	1.01 + /- 0.1	p<0.01
Narrowing angle AP_L/AP_M	11.02 + /- 3.2	12.68 + /- 2.8	p<0.01
Trapezoidicity ratio ML_A/ML_P	0.77 + /- 0.1	0.76 + /- 0.1	p<0.01
Trochlear rotation ML_A/ML_P	3.65 + /- 3.3	4.4+ /- 2.7	p<0.01
Trochlear ratio	0.72 + /- 0.2	0.72 + /- 0.2	0.85
Sulcus angle	137.19 + /- 8.8	143.65 + /- 10.2	p<0.01

Table 19 : Analyse comparative par test T student des valeurs retrouvées chez les européens et chez les chinois exprimées par la moyenne +/- déviation standard. p : probability.

Il est intéressant de noter qu'il existe une différence de forme du fémur distal mais que ce dimorphisme interethnique ne peut être mis en évidence de manière franche que par l'analyse du plan axial même avec des rapports et des angles qui annihilent l'effet de taille. Il semble que la majeure partie du dimorphisme soit visible dans le plan frontal c'est à dire la distance entre le plan Bi-épidoncylien et le point le plus distal de chaque condyle (fig 15). Ceci a un impact direct sur le rayon de courbure. Il s'agit d'un élément difficile à quantifier. Pour cela, une analyse de surface de l'ensemble du fémur distal et pas seulement les points remarquables est nécessaire. Nous sommes en train de travailler à l'analyse de ce rayon de courbure par intégration automatique des TDM. Nous pourrons ainsi proposer une analyse complète des populations et comparative avec la forme des prothèses de genou disponibles dans le commerce. En effet la comparaison avec les valeurs des critères de jugement retrouvés sur la mesure des prothèses montre une inadéquation entre les constatations anatomiques et ce qui est retrouvé sur les prothèses de genou (table 20).

Manufacturer			**Zimmer**		**Smith and Nephew**	**Depuy**			**Biomet**	**Stryker**	
Model	European	Asian	Persona*	Nexgen	Journey	Attune*	PFC*	LCS	Vanguard	Scorpio	Triathlon
Aspect ratio ***ML/AP***	1.18 + /- 0.1	1.17 + /- 0.1	1.28	1.31	1.26	1.38	1.56	1.25	1.47	2.04	1.19
Assymetry ratio ***AP_L/AP_M***	0.99 + /- 0.1	1.01 + /- 0.1	0.98	1	0.99	0.98	0.98	1.03	1.01	0.96	1
Narrowing angle ***AP_L/AP_M***	11.02 + /- 3.2	12.68 + /- 2.8	22.2	15.8	17.6	15.9	10.5	12.5	6.1	-2.2	13
Trapezoidicity ratio ***ML_A/ML_P***	0.77 + /- 0.1	0.76 + /- 0.1	0.49	0.63	0.61	0.62	0.77	0.73	0.85	1.08	0.74
Trochlear rotation ***ML_A/ML_P***	3.65 + /- 3.3	4.4+ /- 2.7	3.2	1.5	4.9	0	0	4.1	1.9	4.2	1.4
Trochlear ratio	0.72 + /- 0.2	0.72 + /- 0.2									
Sulcus angle	137.19 + /- 8.8	143.65 + /- 10.2									

* identical values for both standard and narrow versions of these implant models.

Table 20 : Critères de jugement de la forme dans le plan axial du fémur distal dans la population ainsi que sur les prothèses les plus commercialisées.

CONCLUSION

Nous faisons partis d'une équipe qui a beaucoup oeuvrée à l'utilisation des techniques d'imagerie en anthropobiologie. [43] [42] [25] [6] Ces techniques ont l'avantage de pouvoir être utilisées chez le sujet vivant et le sujet mort. L'utilisation de données médicales ouvre un champ nouveau en anthropologie physique.

Nous avons mis en évidence un dymorphisme sexuel, ethnique et lié à l'âge de l'extrémité distale du fémur. La méthodologie utilisée pourra rentrer en ligne de compte pour aider à l'identification de restes humains. De même, les données obtenues permettent de réactualiser les données existantes et permettront des analyses diachroniques et inter ethniques. Il semble qu'il y ait une réflexion à avoir concernant le design des prothèses totales de genou qui n'est pas toujours superposable aux caractéristiques morphologiques de population contemporaines.

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Forensic Anthropology Population Data

Geometric morphometric analysis reveals sexual dimorphism in the distal femur

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ABSTRACT

An individual's sex can be determined by the shape of their distal femur. The goal of this study was to show that differences in distal femur shape related to sexual dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis.

Geometric morphometric analysis was carried out on CT scans of the distal femur of 256 subjects living in the south of France. Ten landmarks were defined on 3D reconstructions of the distal femur. Both traditional metric and geometric morphometric analyses were carried out on these bone reconstructions; these analyses identified trends in bone shape in sex-based subgroups.

Sex-related differences in shape were statistically significant. The subject's sex was correctly assigned in 77.3% of cases using geometric morphometric analysis.

This study has shown that geometric morphometric analysis of the distal femur is feasible and has revealed sexual dimorphism differences in this bone segment. This reliable, accurate method could be used for virtual autopsy and be used to perform diachronic and interethnic comparisons. Moreover, this study provides updated morphometric data for a modern population in the south of France.

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2. Materials and methods

This was a retrospective descriptive analytical study. The research ethics committee at our healthcare facility approved this study (No. 01-0415).

The analysis was carried out on the CT images of 256 distal femurs residing in our facility's imaging database. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) were retained. Any CT scans performed to assess disease conditions in the distal femur were excluded. The included CT scans had mainly been performed to assess leg vasculature (CT angiogram) or to evaluate a tibial plateau fracture. The CT scans were taken on a Sensation 16 Scanner (Siemens, Erlangen, Germany). Between June 1, 2014 and December 31, 2014, 256 CT scans of the distal femur met our inclusion criteria. There were 134 women and 122 men. The average age was 58 ± 15.2 years. The right side was analyzed 122 times and the left side 134 times. The groups were statistically similar (Table 1). The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA).

Ten osteometric landmarks were defined based on standard bone landmarks used in anthropometry (Fig. 1 and Table 2) [4,11–13,24,25]. By using points typically associated with osteometric techniques, comparisons could be made with published studies on this subject to determine the plausibility of our results. The metric variables measured were the epicondylar breadth (EB), which is the distance between the two epicondyles [2,3,5–10,26], anterior posterior diameter of the medial condyle (APDMC), which is the largest anteroposterior dimension of the medial condyle [4,13], and anterior posterior diameter of the lateral condyle (APDLC), which is the largest anteroposterior dimension of the lateral condyle [4,13] (Fig. 2). All of these were Type I landmarks [21]. Once these landmarks had been located with 3D in vivo imaging software (Amira®, Visualization Sciences Group, Bordeaux, France), the coordinates of each landmark in space (x,y,z) were recorded.

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Table 1
Mean age of the various subgroups relative to sex and side. Comparisons were performed with Student's *t*-test.

		Age	*P*
Sex	Male (n = 134)	56.7 ± 14.42	0.445
	Female (n = 122)	58.14 ± 15.5	
Side	Right (n = 122)	57.36 ± 15.3	0.885
	Left (n = 134)	57.43 ± 14.7	

Table 2
Anatomical description of the various landmarks used, with the intra- and inter-observer variability for each. The error is given as a percentage.

Landmark	Location	Intra-observer variability	Inter-observer variability
1	Medial epicondyle	1.64	1.63
2	Most dorsal point on medial condyle	1.64	1.64
3	Top of intercondylar notch	1.64	1.64
4	Most dorsal point on lateral condyle	1.64	1.64
5	Lateral epicondyle	1.63	1.64
6	Most outside point on trochlear groove	1.63	1.65
7	Most distal point at bottom of trochlear groove	1.64	1.65
8	Most ventral point on margin of trochlear groove	1.64	1.65
9	Most distal point on medial condyle	1.53	1.51
10	Most distal point on lateral condyle	1.52	1.49

The analyzed data was taken from the same database and analyzed twice on separate occasions by two observers. This made it possible to calculate the intra- and inter-observer variability for each landmark. For each observer, landmark deviations were calculated relative to the landmark's mean value. The percentage error for each landmark was calculated, as described previously [32,34] (Table 2). The results were deemed acceptable if this error was less than 5% [32–35].

All morphometric geometric analyses were carried out with Morpho J software [27] and R 2.2.0 software [28]. The chosen landmarks made it possible to characterize the shape of the distal femur (Fig. 1). The first step consisted of a generalized Procrustes analysis (GPA) [20,29–31]. As described previously [19,20], this strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

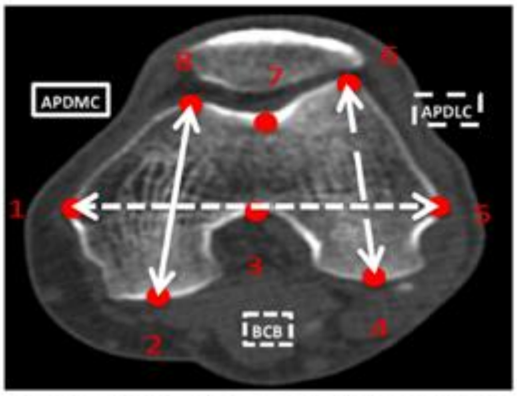

Fig. 2. Osteometric data used to measure the plausibility of the study's methodology. EB: epicondylar breadth, distance between the two epicondyles, APDMC: anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial condyle [4,13] and APDLC: anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle [4,13].

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. A comparative analysis was performed with all the variables based on sex (male, female). The landmark coordinates were analyzed using principal component analysis (PCA) [30,31] and canonical variate analysis (CVA) to identify shape trends in the various subgroups [19,20].

A discriminant analysis was performed to determine the percentage of cases in which the sex was correctly estimated. Pearson's Chi-square test was used to determine if this analysis was statistically significant [30]. To determine if the difference between shapes was statistically significant, a *P*-value was also calculated using Goodall's *F*-test and Mahalanobis D2 matrices [36,37]. The length variables (EB, ADPLC and ADPMC) were compared using an analysis of variance (ANOVA).

3. Results

The percentage errors for the intra- and inter-observer comparisons for all the landmarks are given in Table 2. None

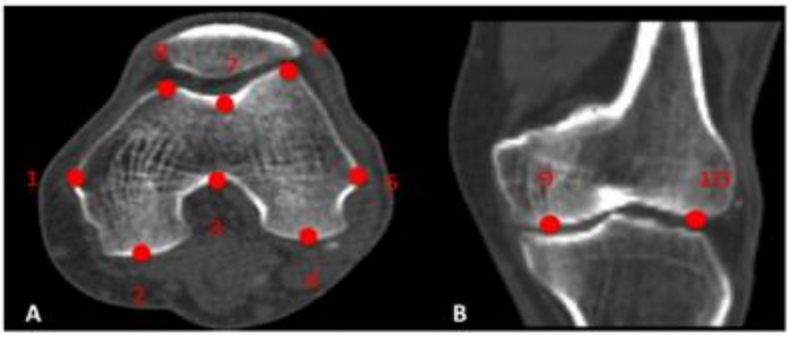

Fig. 1. Location of landmarks on axial (A) and frontal (B) CT scan slices: (1) medial epicondyle, (2) most dorsal point on medial condyle, (3) top of intercondylar notch, (4) most dorsal point on lateral condyle, (5) lateral epicondyle, (6) most ventral point on lateral edge of trochlear groove, (7) most distal point at bottom of the trochlear groove, (8) most ventral point on the medial edge of the trochlear groove, (9) most distal point on medial condyle, (10) most distal point on lateral condyle.

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Table 3
Mean values (±standard deviation) of the osteometric data for each subgroup based on sex. Comparisons were performed with an ANOVA.

Sex	Female	Male	*P*
EB	75.5 ± 3.7	85.1 ± 4.9	<0.005
APDMC	60.4 ± 3.9	66.7 ± 4.2	<0.005
APDLC	60 ± 3.8	65.3 ± 4.3	<0.005

EB: epicondylar breadth, APDMC: anterior posterior diameter of the medial condyle, APDLC: anterior posterior diameter of the lateral condyle.

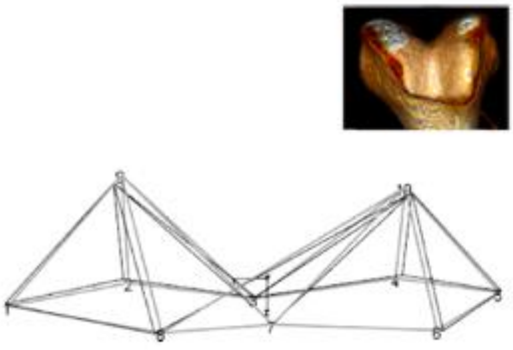

Fig. 3. Shape variation based on sex (male: black line, female: gray line). (A) 3D view obtained of the inferior end, (B) view on an axial plane containing the first eight landmarks. The 3D reconstructions are shown to make it easier to understand the two planes.

exceeded 2%. The mean EB value was greater in men (85.1 ± 4.9 mm) than women (75.5 ± 3.7) ($P < 0.005$). Similar results were found for the APDMC (men: 66.7 ± 4.2, women: 60.4 ± 3.9; $P < 0.005$) and the APDLC (men: 65.3 ± 4.3, women: 60 ± 3.8, $P < 0.005$) (Table 3).

The shape of the male and female distal femur differed significantly (Fig. 3) (Goodall's $F = 0.048$, $P < 0.001$ and Mahalanobis D2 distance = 1.52, $P < 0.001$). PCA identified a difference in distal femur shape between males and females; PC1 and PC2 accounted for 58.6% of the variance measured (Fig. 4). The CVA revealed that the correct sex was assigned in 77.3% of cases and the cross-validation revealed a 68.7% rate of correct sex estimation (Table 4).

4. Discussion

Our hypothesis was confirmed: the shape of the distal femur significantly differs on the basis of sex (Fig. 3). Geometric morphometric analysis revealed sexual dimorphism in the distal femur.

One of the main objectives of physical anthropology is to estimate a person's sex in the forensic or anthropology context [2–6,38–40]. Most of the postcranial bones have been used to determine the sex of human remains through various statistical models [11]. The femur is the longest bone and it is often well preserved [2,5,6]. But anthropologists must have different algorithms in their diagnostic arsenal for cases where the skeletons are fragmented or when specific populations are analyzed [1–4,6,7,9]. The shape of the two condyles of the distal femur differs between men and women [41,42]. The large number of subjects ($n = 256$) included in this study has provided osteometric references related to sexual dimorphism in a modern population.

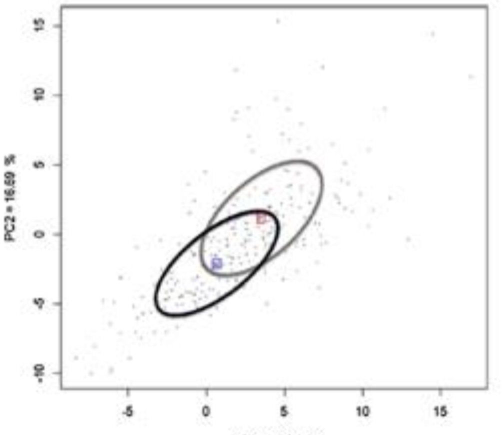

Fig. 4. PCA obtained for the shape of the distal femur based on sex (male: black line, female: gray line). The ellipses correspond to 68% confidence intervals.

This study is the most extensive up to now to evaluate sexual dimorphism of the distal femur. The data were derived from a modern population, contrary to most of the published studies on this topic [2,3,8,10,25,45]. This data set can be used as a current reference when virtual or in vivo autopsy is performed [38,43,44]. Temporal changes observed in modern populations mean that certain bone measurements must be re-evaluated over time [8].

In this study, osteometric analyses were carried out in addition to the 3D analyses. By placing easily identifiable points on the apex of the bone contours, we were able to obtain data in the traditional manner, which allowed us to verify that the data obtained were in agreement with published values (Table 5). Origin-based variability [3] must be taken into account in the literature comparison, but the results of these three reference measurements are consistent. Furthermore, the intra- and inter-observer error rates were very low in the current study (Table 2). These two aspects (reproducibility and plausibility) validate our methodology.

It is worth noting that the rate of correct sex estimation was higher with the traditional metric values than with classic morphometric analysis (EB 88%, CVA: 77.3%). Geometric morphometric analysis, particularly GPA, minimizes effects related to a

Table 4
Results of the CVA and cross-validation for the sex estimation When using the EB threshold (79.6 mm) defined by Alunni-Perret et al. [8] in a comparable French population, 87% of women, 88% of men and 88% overall were correctly assigned.

	Original CVA			Cross-validated		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
Female	93	29	76.2	78	44	63.9
Male	105	29	78.4	98	36	73.1
Total	198	58	77.3	176	80	68.7

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Table 5
Published osteometric data. Mean values with standard deviation.

Nationality	EB			ADPMC		ADPLC		*N*
	Female	Male	Ac.	Female	Male	Female	Male	
Spanish [6]	70.8 ± 2.3	80.6 ± 2.9	97.5	NA	NA	NA	NA	132
French [8]	74.8 ± 2.5	84.3 ± 3.6	95.4	NA	NA	NA	NA	88
Chinese [7]	70.6 ± 3.2	80.3 ± 4.2	94.9	NA	NA	NA	NA	87
Thai [5]	75.4 ± 5.4	83.7 ± 4.7	93.3	NA	NA	NA	NA	104
North Indians [4]	68.3 ± 4	76.8 ± 4.2	85.1 (M) 78.6 (F)	54 ± 3.2	59.4 ± 3.3	55.6 ± 3.4	60.3 ± 3	122
Croatian [2]	75.1 ± 3.3	86.7 ± 4.3	91.3	NA	NA	NA	NA	195
White South African [10]	75.1 ± 3.3	84.6 ± 4.6	90.5	NA	NA	NA	NA	106
Indian [3]	66.8 ± 4.2	78.7 ± 4.5	90.3	NA	NA	NA	NA	124
Chinese [26]	69.3 ± 3	77.8 ± 5.8	83.7	NA	NA	NA	NA	141
German [9]	77 ± 5	84.0 ± 10	81.4	NA	NA	NA	NA	170
Czech [13]	78.2	88.8	NA	65.6	71.8	63.4	69.9	200
Korean [11]	NA	NA	NA	55.3 ± 3	61.2 ± 3	58.4 ± 2.8	64.6 ± 3	202
Our study	75.5 ± 3.7	85.1 ± 4.9	88	60.4 ± 3.9	66.7 ± 4.2	60.4 ± 3.8	65.3 ± 4	255

EB: epicondylar breadth, APDMC: anterior posterior diameter of the medial condyle, APDLC: anterior posterior diameter of the lateral condyle, Ac.: accuracy is the percentage of correct assignment. *N*: number of subjects in the study.

stocky or slender build; only allometric differences are retained and observable [19,30]. Geometric morphological analysis effectively minimizes differences related to general somatotype and keeps only the shape differences. Bellemans et al. [24] have shown that differences in femur shape were related to the individual's sex and somatotype. The somatotype concept was introduced by Sheldon in the 1940s. Carter and Heath refined it into three somatotypes: endomorph, mesomorph, ectomorph [46–48]. Skeletal structure and body composition are used to classify individuals into these three groups. Although the somatotype concept has been criticized in the past for being too simplistic and for being used by behavioral specialist to correlate somatotype to certain psychological features, it is an accepted method for studying physical characteristics [49–52]. Osteometric analysis is able to correctly assign sex, but is subject to the somatotype effect. Geometric morphometric analysis discounts somatotype-related differences, reducing the accuracy of this analysis. Osteometric analysis is subject to two variables (sex and somatotype), while geometric morphometric analysis is subject to only one variable (sex). We believe that the relatively low rate of correct sex estimation is due to this factor. However, we were able to show that sexual dimorphism exists in the distal femur, independent of somatotype. The current study has certain limitations. Skeletally immature subjects were not included. In younger persons, the bone contours of the distal femoral epiphysis are not completely ossified. This would have increased the possibility of errors during landmark placement by the observers. Diseases that do not affect the distal femur but may require a CT scan that includes the distal femur, such as vascular conditions and tibial plateau fracture, are more common in older subjects.

In summary, the distal femur exhibits sexual dimorphism. Three-dimensional geometric morphometric analysis made it possible to show these differences. The large number of subjects studied made it possible to modernize the references for certain bone measurements. This reliable and accurate methodology can be used to perform diachronic and interethnic comparisons.

Disclosure

No conflict of interest to declare.

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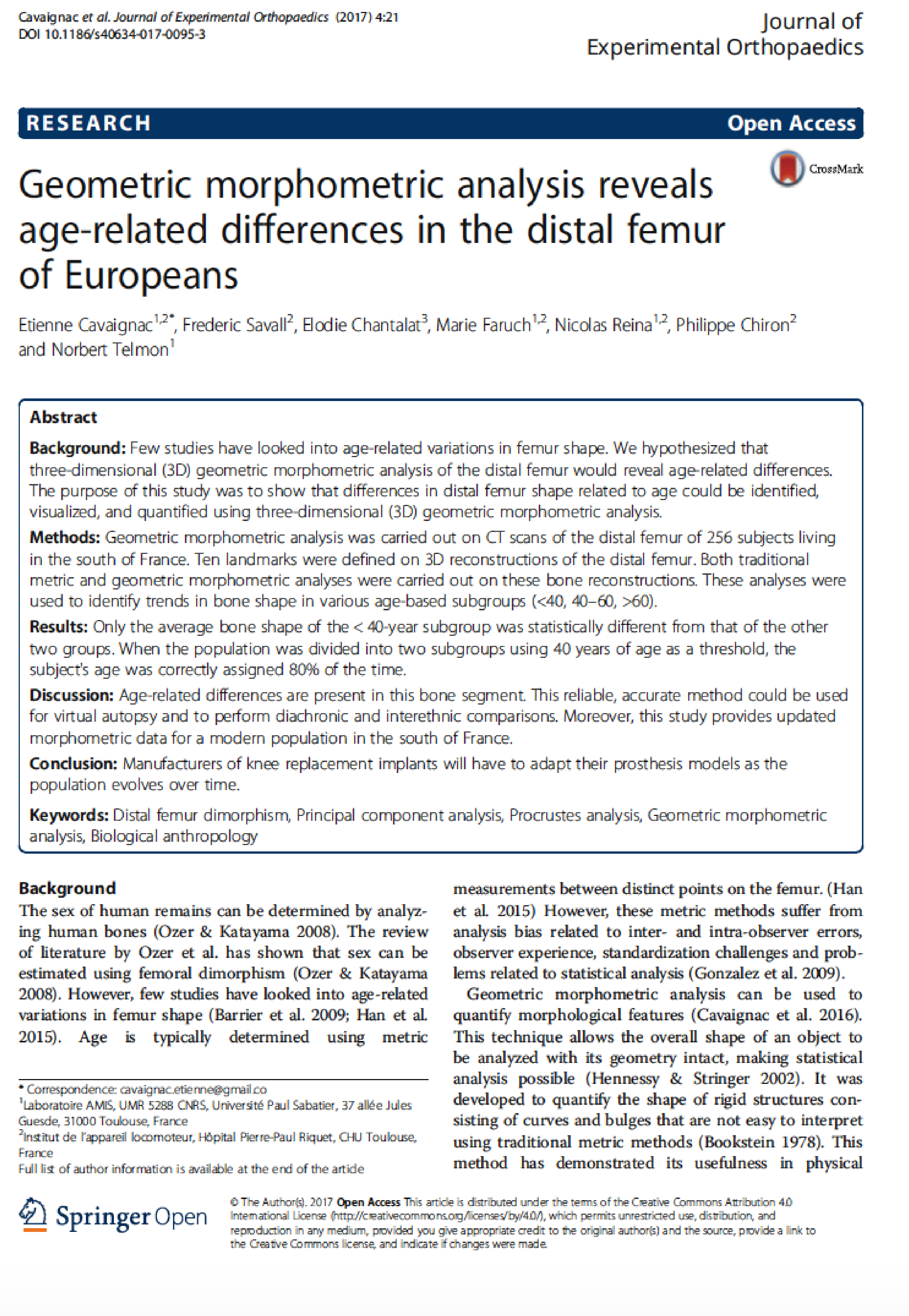
Annexe 2 : Article publié dans JEO concernant le dimorphisme lié à l'âge.



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RESEARCH **Open Access**

Geometric morphometric analysis reveals age-related differences in the distal femur of Europeans

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Abstract

Background: Few studies have looked into age-related variations in femur shape. We hypothesized that three-dimensional (3D) geometric morphometric analysis of the distal femur would reveal age-related differences. The purpose of this study was to show that differences in distal femur shape related to age could be identified, visualized, and quantified using three-dimensional (3D) geometric morphometric analysis.

Methods: Geometric morphometric analysis was carried out on CT scans of the distal femur of 256 subjects living in the south of France. Ten landmarks were defined on 3D reconstructions of the distal femur. Both traditional metric and geometric morphometric analyses were carried out on these bone reconstructions. These analyses were used to identify trends in bone shape in various age-based subgroups (<40, 40–60, >60).

Results: Only the average bone shape of the < 40-year subgroup was statistically different from that of the other two groups. When the population was divided into two subgroups using 40 years of age as a threshold, the subject's age was correctly assigned 80% of the time.

Discussion: Age-related differences are present in this bone segment. This reliable, accurate method could be used for virtual autopsy and to perform diachronic and interethnic comparisons. Moreover, this study provides updated morphometric data for a modern population in the south of France.

Conclusion: Manufacturers of knee replacement implants will have to adapt their prosthesis models as the population evolves over time.

Keywords: Distal femur dimorphism, Principal component analysis, Procrustes analysis, Geometric morphometric analysis, Biological anthropology

Background

The sex of human remains can be determined by analyzing human bones (Ozer & Katayama 2008). The review of literature by Ozer et al. has shown that sex can be estimated using femoral dimorphism (Ozer & Katayama 2008). However, few studies have looked into age-related variations in femur shape (Barrier et al. 2009; Han et al. 2015). Age is typically determined using metric measurements between distinct points on the femur. (Han et al. 2015) However, these metric methods suffer from analysis bias related to inter- and intra-observer errors, observer experience, standardization challenges and problems related to statistical analysis (Gonzalez et al. 2009).

Geometric morphometric analysis can be used to quantify morphological features (Cavaignac et al. 2016). This technique allows the overall shape of an object to be analyzed with its geometry intact, making statistical analysis possible (Hennessy & Stringer 2002). It was developed to quantify the shape of rigid structures consisting of curves and bulges that are not easy to interpret using traditional metric methods (Bookstein 1978). This method has demonstrated its usefulness in physical

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anthropology (Bilfeld et al. 2015). To the best of our knowledge, this method has not been used to analyze the age-related differences in the distal femur. The distal femur is a rigid structure with curves and bulges so geometric morphometric analysis seems to be an appropriate method to explore it. With this method, the shape of two or more objects can be compared while disregarding the volume of these objects (Bilfeld et al. 2012). Since the size is normalized, the analysis can focus on the shape.

Age determination is a critical element of anthropology and forensic medicine (Barrier et al. 2009; Martrille et al. 2007). Several statistical models have been developed to determine person's age using various bone fragments (Kim et al. 2013b). The femur is the longest bone and it is often well preserved (King et al. 1998; Slaus et al. 2003; Trancho et al. 1997). We believe it is relevant to analyze age variations in this bone with a method that can be used in both living and deceased subjects.

Bone shapes changes as a person ages (MacLatchy et al. 2000). We believe it is important to describe these changes in the shape of the distal femur, as the shape of the distal femur has a direct impact on the design of total knee replacement implants.

We hypothesized that three-dimensional (3D) geometric morphometric analysis of the distal femur would reveal age-related differences. The goal of this study was to show that differences in distal femur shape related age could be identified, visualized, and quantified using 3D geometric morphometric analysis.

Methods

This was a retrospective descriptive analytical study. The research ethics committee at our healthcare facility approved this study (number 01–0415).

Materials

Study population

Between June 1, 2014 and December 31, 2014, 256 CT scans of the distal femur met our inclusion criteria (Fig. 1). There were 134 women and 122 men. The average age was 58 ± 15.2 years. The right side was analyzed 122 times and the left side 134 times. The groups were comparable (Table 1). The analysis was carried out on the CT images of 256 distal femurs stored in our facility's imaging database. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) without signs of disease conditions or osteoarthritis were retained. The included CT scans had mainly been performed to assess leg vasculature (CT angiogram) or to evaluate a tibial plateau fracture without previous history of knee problem and without lesions in the distal femur.

The CT scans were taken on a Sensation 16 Scanner (Siemens, Erlangen, Germany). Scanning was performed with the following parameters: 80 kV, 70 mA, gantry rotation time of 2 s, 144-mm table height, and axial scanning mode. The thickness of the reconstructed sections was kept constant at 2 mm every 1 mm. The image matrix was 512*512 pixels. A bone filter and a soft tissue filter were used.

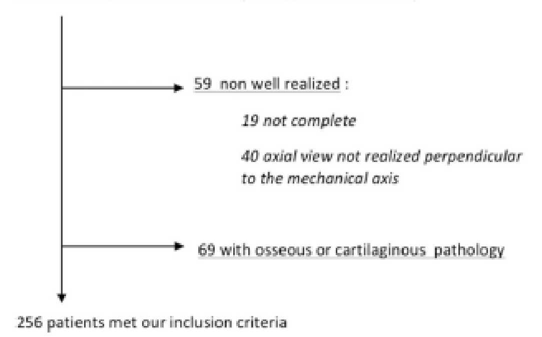

Fig. 1 Flow chart of our studied population

The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA).

Methods

3D morphological analysis

Ten osteometric landmarks were defined based on standard bone landmarks used in anthropometry (Fig. 2 and Table 2) (Bellemans et al. 2010). By using points typically associated with osteometric techniques, comparisons could be made with published studies to determine the plausibility of our results. The metric variables measured were the bicondylar breadth (BCB), which is the distance between the two epicondyles (Iscan & Shihai 1995),anterior posterior diameter of the medial condyle (APDMC), which is the largest anteroposterior dimension of the medial condyle (Srivastava et al. 2012), and anterior posterior diameter of the lateral condyle (APDLC), which is the largest anteroposterior dimension of the lateral condyle (Pinskerova et al. 2014) (Fig. 3). Once these landmarks had been located with 3D in vivo imaging software (Amira®,

Table 1 Mean age of the various subgroups relative to sex and side. Comparisons were performed with student's *t*-test

		Age	*P*
Sex	Male (*n* = 134)	56.7 ± 14.42	0.445
	Female (*n* = 122)	58.14 ± 15.5	
Side	Right (*n* = 122)	57.36 ± 15.3	0.885
	Left (*n* = 134)	57.43 ± 14.7	

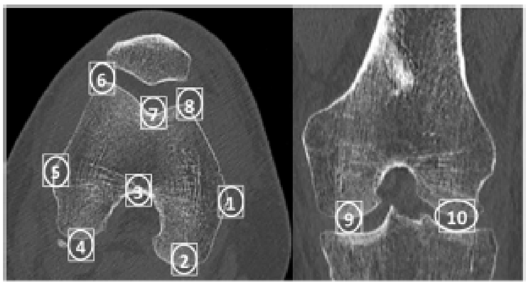

Fig. 2 Location of landmarks on axial (left) and frontal (right) CT scan slices: 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) top of intercondylar notch, 4) most dorsal point on lateral condyle, 5) lateral epicondyle, 6) most ventral point on lateral edge of trochlear groove, 7) most distal point at bottom of the trochlear groove, 8) most ventral point on the medial edge of the trochlear groove, 9) most distal point on medial condyle, 10) most distal point on lateral condyle

Visualization Sciences Group, Bordeaux, France), the coordinates of each landmark in space (x,y,z) were recorded.

Axial slice where the epicondyles are more prominent were selected to place points 1–10. Oblique slices were created by resampling the images stack in order to be orthogonal to the axial plane (Fig. 4).

Reliability studies

The analyzed data were taken from the same database and analyzed twice on separate occasions by two observers. This made it possible to calculate the intra- and inter-observer variability for each landmark. For each observer, landmark deviations were calculated relative to the landmark mean value. The percentage error for each landmark was calculated, as described previously (von Cramon-Taubadel et al. 2007) (Table 2). The results were deemed acceptable if this error was less than 5% (von Cramon-Taubadel et al. 2007).

Procrustes analysis

All morphometric geometric analyses were carried out with Morpho J software (CP 2008) and R 2.2.0 software (Team 2014). The chosen landmarks made it possible to characterize the shape of the distal femur (Fig. 1). The first step consisted of a generalized Procrustes analysis (GPA) (Klingenberg 2002). As described previously (Bilfeld et al. 2013), this strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

Statistical analysis

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. A comparative analysis was performed with all the variables based on age (<40, 40–60, > 60 years).

The landmark coordinates were analyzed using principal component analysis (PCA) (M Z 2004) and canonical variate analysis (CVA) to identify shape trends in the various subgroups (Bilfeld et al. 2013).

A discriminant analysis was performed to determine the percentage of cases in which the age was estimated correctly. Pearson's Chi-square test was used to determine if this analysis was statistically significant (Elewa 2010). To determine if the difference between shapes was statistically significant, a *P*-value was also calculated using Goodall's F-test and Mahalanobis D2 matrices (Oettle et al. 2009). The length variable (BCB) was compared using an analysis of variance (ANOVA).

Results

Reliability analysis

The percentage errors for the intra- and inter-observer comparisons for all the landmarks are given in Table 2 – none exceeded 2%.

Table 2 Anatomical description of the various landmarks used, with the intra- and interobserver variability for each. The error is given as a percentage

Landmark	Location	Intra-observer Variability	Inter-observer Variability
1	Medial epicondyle	1.64	1.63
2	Most dorsal point on medial condyle	1.64	1.64
3	Top of intercondylar notch	1.64	1.64
4	Most dorsal point on lateral condyle	1.64	1.64
5	Lateral epicondyle	1.63	1.64
6	Most outside point on trochlear groove	1.63	1.65
7	Most distal point at bottom of trochlear groove	1.64	1.65
8	Most ventral point on margin of trochlear groove	1.64	1.65
9	Most distal point on medial condyle	1.53	1.51
10	Most distal point on lateral condyle	1.52	1.49

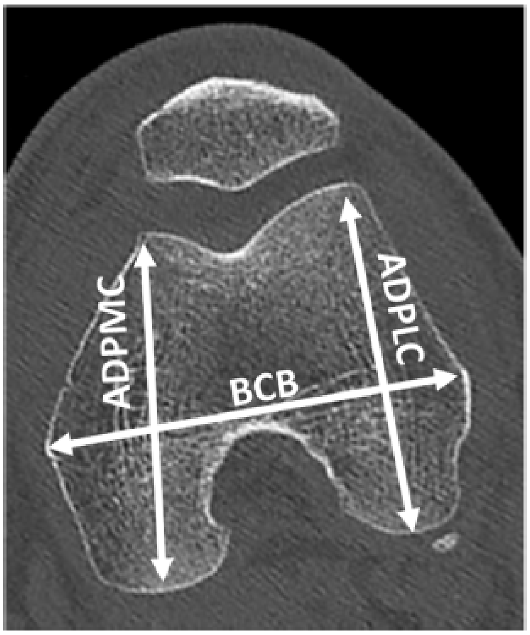

Fig. 3 Osteometric data used to measure the plausibility of the study's methodology. EB: Epicondylar breadth, distance between the two epicondyles, APDMC: Anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial condyle (Srivastava et al. 2012) and APDLC: Anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle

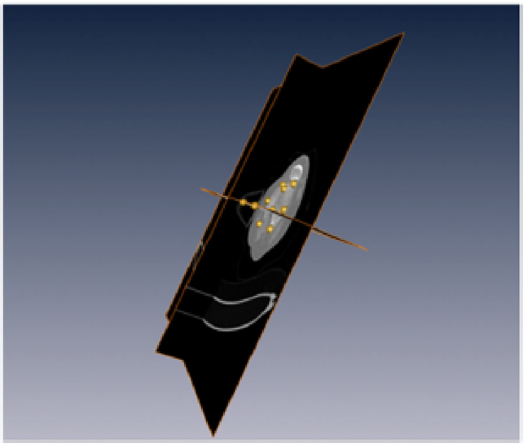

Fig. 4 Creation of 3D reconstructions using the Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA). First, the axial plane in which the epicondyles were most prominent was identified. Reconstructions in the orthogonal planes were generated to position the landmarks

Age differences

The osteometric analysis (BCB, APDMC and APDLC) revealed no significant differences between the three subgroups of subjects (<40, 40–60, >60 years) (Table 3). Only the average bone shape of the < 40-year subgroup was statistically different from that of the other two groups (Table 4, Fig. 5). For the same femur size, < 40-year femurs are significantly longer in the frontal plane, i.e. the distance between the axial plane containing the epicondyles and the two most distal points on the condyles is greater in the < 40-year group. In the axial plane through the epicondyles, < 40-year femurs are shorter along the anteroposterior axis than > 40 year femurs, while the mediolateral distance is the same. The PCA based on age is shown in Fig. 6; principal component (PC)1 and PC2 accounted for 54.42% of the variance measured. When the population was divided into two subgroups using 40 years of age as a threshold, the subject's age was correctly assigned in 80% of the cases (original CVA) and in 74% of cases by cross-validated classification (Table 5).

Discussion

Our hypothesis is confirmed: 3D geometric morphometric analysis of the distal femur revealed differences between age groups (Fig. 5). Geometric morphometric analysis revealed age-related differences in the shape of the distal femur (Table 4). The shape of the femur in subjects under 40 years of age was different than the shape of the femur in older subjects. Classic osteometric analysis did not reveal age-related differences in the distal femur (Table 3). This means there are no differences in femur size between the three age groups, but for the same size of femur, the shape differs.

One of the main objectives of physical anthropology is to estimate a person's age and sex in the forensic or anthropology context (Barrier et al. 2009; Martrille et al. 2007). Most of the postcranial bones have been used to determine anthropological data of human remains through various statistical models (Kim et al. 2013b). The femur is the longest bone and it is often well preserved. As a consequence, we feel it is relevant to develop a method that can be used to determine a person's age based on this bone (King et al. 1998;

Table 3 Mean values (± standard deviation) of the osteometric data for each subgroup based on age and sex. Comparisons were performed with an analysis of variance (ANOVA)

Age	<40	40–60	>60	*P*
BCB	80.3 ± 7.7	80.7 ± 6.6	80.4 ± 5.9	0.9
APDMC	62.8 ± 5.5	64.2 ± 5.4	63.5 ± 4.8	0.3
APDLC	62.7 ± 5.9	63 ± 4.9	62.6 ± 4.5	0.8

BCB BiCondylar breadth. *APDMC* Anterior posterior diameter of the medial condyle, *APDLC* Anterior posterior diameter of the lateral condyle

Table 4 Values of Goodall's F and Mahalanobis D2 distance for the comparisons performed

Comparison	Mahalanobis D2 distance	Goodall's F test	*P*
<40 vs. > 60	1.73	0.04	0.001
40–60 vs. > 60	0.68	0.019	0.78
<40 vs. 40–60	1.8	0.056	0.0002

Slaus et al. 2003; Trancho et al. 1997) The large number of subjects ($n = 256$) included in this study has provided osteometric references related to age differences in a modern European population. Moreover, since this methodology can be used in living and deceased persons, it can be used in forensic medicine to determine age of a person in a legal context.

This is the first 3D study to show age-related differences in the overall shape of the distal femur, as the shape was different in subjects under 40 years of age and those over 40 years of age (Fig. 3). Discriminant analysis showed that 80% of subjects were correctly classified (original CVA). Although this method is not sufficiently accurate to be used alone, it can be used in the context of virtual or in vivo autopsy (Dedouit et al. 2015; Dedouit et al. 2014).

The age-related variations observed in the shape of the distal femur have consequences for orthopedic surgery, particularly for total knee arthroplasty (TKA). A better grasp of knee morphology and its variations can improve the design of TKA implants (Han et al. 2015). The same kind of implants are not suitable for different populations (Ho et al. 2006). Differences in shape have been reported by gender and ethnic groups (Bellemans et al. 2010). We are the first group to show differences in distal femur shape relative to age that are independent of the difference in size. In our study, we analyzed the differences in shape, not size. For these reasons, only adjusting the implant size does not solve the problem – the shape must be taken into account. Our study is the first to show age-related differences (<40 years and > 40 years) in a Caucasian population. The design of total knee arthroplasty implants is based on the anatomy of a Caucasian population (Mahfouz et al. 2012). Successful component placement in knee arthroplasty includes minimal overhang and good bone coverage (Bonnin et al. 2013). As a consequence, the age-related variations in a Caucasian population have to be take into account by manufacturers to modify the implant design over time.

Han et al. studied age-related anthropometric differences in Asians by analyzing MRI images of 535 knees. They used 20-year bands to evaluate successive generations. They found statistically significant differences in the classic anthropometric data between all the age bands. Although we also split our study population into 20-year segments, only the < 40-year population was significantly different to the others. This disparity can be explained by interethnic variability (Purkait & Chandra 2004). In addition, we performed a 3D analysis of the shape of the entire distal femur, while Han et al. performed two-dimensional analyses in various planes.

Our study is the most extensive up to now to evaluate age dimorphism of the distal femur in a modern European population. This data set can be used as a current reference when virtual or in vivo autopsy is performed (Dedouit et al. 2015; Dedouit et al. 2014). Temporal changes observed in modern populations mean that certain bone measurements must be re-evaluated over time (Alunni-Perret et al. 2008). Moreover, intergenerational

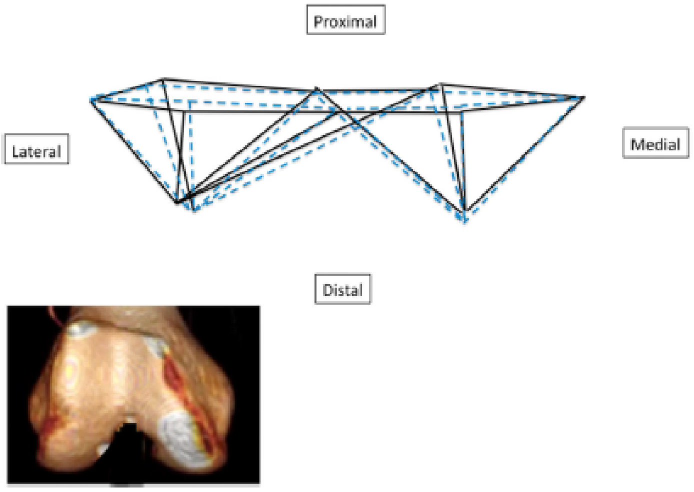

Fig. 5 Shape variation based on age (>40: black solid line, < 40: blue dotted line). A 3D reconstruction is shown to make it easier to understand the data

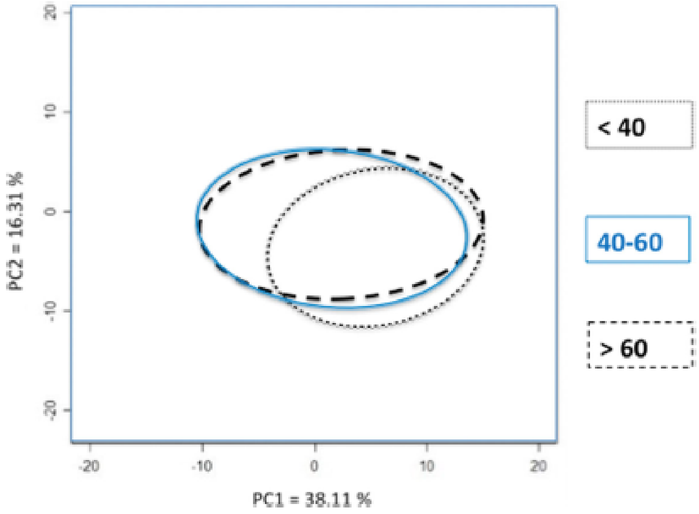

Fig. 6 PCA obtained for the shape of the distal femur based on age. The ellipses correspond to 68% confidence intervals

variability must be taken into account when comparing populations (Han et al. 2015). Bias will be introduced into the analysis if the populations being compared are not from the same generation.

In our study, osteometric analyses were carried out in addition to the 3D analyses. By placing easily identifiable points on the apex of the bone contours, we obtained data in the traditional manner, which allowed us to verify that these data were consistent with published values (Table 6). The EB values reported by Han et al. (Han et al. 2015) were comparable to ours (Table 3) : group < 40 years, EB = 74.2 ± 2.1; group 40–60 years, EB = 73.4 ± 2.99 and group > 60 years, EB = 74.12 ± 3.24. Origin-based variability (Purkait & Chandra 2004) and sex-related variability must be taken into account when performing comparisons with published data, but the results of EB measurement are consistent (Table 6). Furthermore, the intra- and inter-observer error rates were very low in our study (Table 2). These two aspects (reproducibility and plausibility) validate our methodology. In addition, we only used femurs with no signs of bone pathology or osteoarthritis; any patients with osteoarthritis were excluded because this disease can alter the shape of the distal femur (Yip et al. 2004). Contrary to previous OA studies, we found that older patients had a smaller femur (Ding et al. 2005). Murshed et al. reported similar findings when analyzing femurs free of bone pathology (Murshed et al. 2005).

Anthropometric data varies not only as a function of ethnicity, but also genetic, environmental, socioeconomic and nutritional factors (Han et al. 2015). Age-related variations may be related to the differences in height and weight between generations (Yoshiike et al. 2002).

The current study has certain limitations. Skeletally immature subjects were not included. In younger persons, the bone contours of the distal femoral epiphysis are not completely ossified. This would have increased the possibility of errors during landmark placement by the observers. In addition, very few subjects were under 40 years of age. Diseases that do not affect the distal femur but may require a CT scan that includes the distal femur, such as vascular conditions and tibial plateau fracture, are more common in older subjects. Furthermore, the age cut-off for the subgroups was chosen arbitrarily and not based on validated data, although we used previously described age brackets (Han et al. 2015). We analyzed the relationship between age and femur shape, not the changes during aging. A longitudinal study would be needed to measure changes in anthropological measurements as a person ages. While only the distal femur was analyzed in this study, it would be interesting to pair our analysis with data

Table 5 Results of the canonical variate analysis (CVA) and cross-validation for the age determination

	Original CVA			Cross-validated		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
<40	24	13	64.9	14	23	60.9
>40	182	37	83.1	176	43	80.4
Total	206	50	80	190	66	74

Table 6 Published osteometric data. Mean values with standard deviation

Nationality	BCB			ADPMC		ADPLC		n
	Female	Male	Ac.	Female	Male	Female	Male	
Spanish(Trancho et al. 1997)	70.8 ± 2.3	80.6 ± 2.9	97.5	NA	NA	NA	NA	132
French(Alunni-Perret et al. 2008)	74.8 ± 2.5	84.3 ± 3.6	95.4	NA	NA	NA	NA	88
Chinese(Iscan & Shihai 1995)	70.6 ± 3.2	80.3 ± 4.2	94.9	NA	NA	NA	NA	87
Thai (King et al. 1998)	75.4 ± 5.4	83.7 ± 4.7	93.3	NA	NA	NA	NA	104
North Indians(Srivastava et al. 2012)	68.3 ± 4	76.8 ± 4.2	85.1 (M) 78.6 (F)	54 ± 3.2	59.4 ± 3.3	55.6 ± 3.4	60.3 ± 3	122
Croatian(Slaus et al. 2003)	75.1 ± 3.3	86.7 ± 4.3	91.3	NA	NA	NA	NA	195
White South African (Steyn & Iscan 1997)	75.1 ± 3.3	84.6 ± 4.6	90.5	NA	NA	NA	NA	106
Indian(Purkait & Chandra 2004)	66.8 ± 4.2	78.7 ± 4.5	90.3	NA	NA	NA	NA	124
Chinese(Wu 1989)	69.3 ± 3	77.8 ± 5.8	83.7	NA	NA	NA	NA	141
German (Mall et al. 2000)	77 ± 5	84.0 ± 10	81.4	NA	NA	NA	NA	170
Czech (Pinskerova et al. 2014)	78.2	88.8	NA	65.6	71.8	63.4	69.9	200
Korean (Kim et al. 2013a)	NA	NA	NA	55.3 ± 3	61.2 ± 3	58.4 ± 2.8	64.6 ± 3	202
Our STUDY	75.5 ± 3.7	85.1 ± 4.9	88	60.4 ± 3.9	66.7 ± 4.2	60.4 ± 3.8	65.3 ± 4	255

BCB Bicondylar breadth, *APDMC* Anterior posterior diameter of the medial condyle, *APDLC* Anterior posterior diameter of the lateral condyle, *Ac* Accuracy is the percentage of correct assignment. *n* number of subjects in the study

on the patients' morphotype or other femur anatomy data. However, additional analyses could not be performed since the records were anonymized and the patients had no complaints related to their knee joint.

Conclusion

The distal femur exhibits age-related differences. Three-dimensional geometric morphometric analysis made it possible to show these differences. Based on our findings, we feel that changes in bone anatomy over time cannot be ignored. It would be too simplistic to say that patients under 40 years of age require a different knee implant design because their distal femur differs in shape from older adults. TKA indications in patients under 40 years of age are extremely rare. Implant manufacturers must recognize that patient anatomy changes and that implant design should be reevaluated regularly.

Authors' contributions

All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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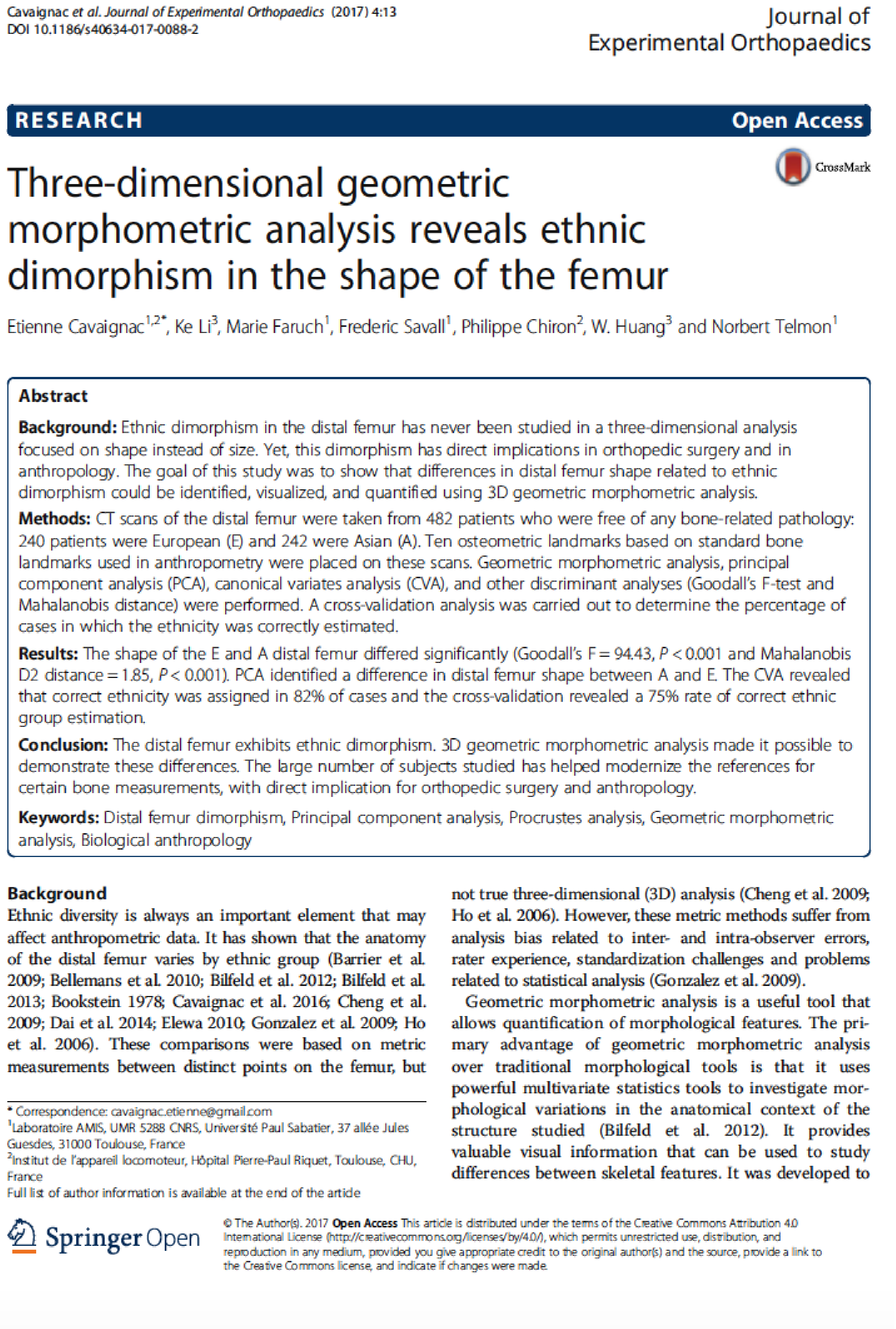
Annexe 3 : article publié dans JEO relatif au dimorphisme interethnique



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RESEARCH Open Access

Three-dimensional geometric morphometric analysis reveals ethnic dimorphism in the shape of the femur

Etienne Cavaignac[1,2*], Ke Li[3], Marie Faruch[1], Frederic Savall[1], Philippe Chiron[2], W. Huang[3] and Norbert Telmon[1]

Abstract

Background: Ethnic dimorphism in the distal femur has never been studied in a three-dimensional analysis focused on shape instead of size. Yet, this dimorphism has direct implications in orthopedic surgery and in anthropology. The goal of this study was to show that differences in distal femur shape related to ethnic dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis.

Methods: CT scans of the distal femur were taken from 482 patients who were free of any bone-related pathology: 240 patients were European (E) and 242 were Asian (A). Ten osteometric landmarks based on standard bone landmarks used in anthropometry were placed on these scans. Geometric morphometric analysis, principal component analysis (PCA), canonical variates analysis (CVA), and other discriminant analyses (Goodall's F-test and Mahalanobis distance) were performed. A cross-validation analysis was carried out to determine the percentage of cases in which the ethnicity was correctly estimated.

Results: The shape of the E and A distal femur differed significantly (Goodall's $F = 94.43$, $P < 0.001$ and Mahalanobis D2 distance $= 1.85$, $P < 0.001$). PCA identified a difference in distal femur shape between A and E. The CVA revealed that correct ethnicity was assigned in 82% of cases and the cross-validation revealed a 75% rate of correct ethnic group estimation.

Conclusion: The distal femur exhibits ethnic dimorphism. 3D geometric morphometric analysis made it possible to demonstrate these differences. The large number of subjects studied has helped modernize the references for certain bone measurements, with direct implication for orthopedic surgery and anthropology.

Keywords: Distal femur dimorphism, Principal component analysis, Procrustes analysis, Geometric morphometric analysis, Biological anthropology

Background

Ethnic diversity is always an important element that may affect anthropometric data. It has shown that the anatomy of the distal femur varies by ethnic group (Barrier et al. 2009; Bellemans et al. 2010; Bilfeld et al. 2012; Bilfeld et al. 2013; Bookstein 1978; Cavaignac et al. 2016; Cheng et al. 2009; Dai et al. 2014; Elewa 2010; Gonzalez et al. 2009; Ho et al. 2006). These comparisons were based on metric measurements between distinct points on the femur, but not true three-dimensional (3D) analysis (Cheng et al. 2009; Ho et al. 2006). However, these metric methods suffer from analysis bias related to inter- and intra-observer errors, rater experience, standardization challenges and problems related to statistical analysis (Gonzalez et al. 2009).

Geometric morphometric analysis is a useful tool that allows quantification of morphological features. The primary advantage of geometric morphometric analysis over traditional morphological tools is that it uses powerful multivariate statistics tools to investigate morphological variations in the anatomical context of the structure studied (Bilfeld et al. 2012). It provides valuable visual information that can be used to study differences between skeletal features. It was developed to

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quantify the shape of rigid structures consisting of curves and bulges that are not easy to interpret using traditional metric methods (Bookstein 1978). Geometric morphometric analysis has been used since the 1980s, but has only become popular in anthropology recently (Pretorius et al. 2006). This method can be used to perform diachronic and interethnic comparisons (Cavaignac et al. 2016). This method allows the shape of two or more objects to be compared while disregarding the volume of these objects (Bilfeld et al. 2012). Since the size is normalized, the analysis can focus on the shape.

To the best of our knowledge, this method has not been used to analyze ethnic dimorphism in the distal femur. Measurement of this dimorphism has direct implication for orthopedics. The shape of the distal femur has a direct impact on the design of total knee replacement implants. Kim et al. recently published a systematic review that looked into the anatomical differences in the knee of patients of various races (Kim et al. 2017). All the comparisons reviewed by Kim et al used classic osteometric methods. Although some of the osteometric analyses were done in various planes in space, they were not truly three-dimensional. In addition, these classic osteometric parameters are affected by the size of the objects being compared. It is widely known that the anatomical profiles of Asian knees are smaller and narrower than those of Caucasian (Yue et al. 2011). However, we were not interested in analyzing size variations, as size variations can be compensated for by using a different size implant. Instead, we were interested in shape differences, which may bring into question the design of the implant itself. Geometric morphometric analysis studies the shape by disregarding size-related effects.

We hypothesized that 3D geometric morphometric analysis of the distal femur would reveal differences between ethnic groups. The primary goal of this study was to show that differences in distal femur shape related to ethnic dimorphism could be identified, visualized, and quantified using 3D geometric morphometric analysis. The secondary goal was to quantify the differences observed in the 3D anatomy of the distal femur relative to ethnic group and sex.

Methods

This was a retrospective descriptive analytical study. The research ethics committee at our respective healthcare facilities approved this study (No. 01-0415 and No. 2016-94).

Materials

Study population

The analysis was carried out on the CT images of 482 distal femurs. Only scans showing the entire distal femur (tip of femoral groove to most distal aspect of femur) were retained. Any CT scans with signs of pathology or osteoarthritis in the distal femur were excluded. The included CT scans had been performed to assess leg vasculature (CT angiogram). Between June 1, 2014 and December 31, 2014, 482 CT scans of the distal femur met our inclusion criteria: 240 patients were European (E) (from southwest France) and 242 were Asian (A) (Huan from Chongqing, China). There were 228 women (122 Asian and 106 European and 254 men (137 Asian and 117 European). The average age was 55.3 ± 15.2 years. The right side was analyzed 235 times and the left side 247 times. The two groups were comparable in terms of their demographics (Table 1).

The CT scans were taken on a Sensation 16 (120 kV, 80 mA; light speed 16) Scanner (Siemens, Erlangen, Germany) with 16*1.5 mm collimation. The image matrix was 512*512 pixels. A bone filter and a soft tissue filter were used. The scanning protocol was carried out to acquire axial 2-mm reconstructions every 1 mm.

The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira® software (version 4.1.1, FEI Visualization Sciences Group, Bordeaux, France).

Methods

3D morphological analysis

Ten osteometric landmarks were defined based on standard bone landmarks used in anthropometry (Bellemans et al. 2010). These landmarks were located at the 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) top of intercondylar notch, 4) most dorsal point on lateral condyle, 5) lateral epicondyle, 6) most ventral point on lateral edge of trochlear groove, 7) most distal point at bottom of trochlear groove, 8) most ventral point on medial edge of trochlear groove, 9) most distal point on medial condyle, and 10) most distal point on lateral condyle. By using points typically associated with osteometric techniques, comparisons could be made with published studies to determine the plausibility of our results. Three metric parameters were measured: the bicondylar breadth (BCB), which is the distance between the two epicondyles (Slaus et al. 2003), the anterior posterior diameter of the

Table 1 Mean age of the various subgroups relative to sex, side and ethnicity

		Age
Sex	Male (*n* = 254)	55.24 ± 15.20
	Female (*n* = 228)	55.45 ± 16.47
Side	Right (*n* = 235)	55.14 ± 6.24
	Left (*n* = 247)	55.53 ± 15.59
Ethnicity	European (*n* = 240)	56.47 ± 14.85
	Asian (*n* = 242)	54.22 ± 16.80

Comparisons were performed with Student's *t*-test – $P > 0.05$ for all comparisons medial condyle (APDMC), which is the largest anteroposterior dimension of the medial condyle, (Srivastava et al. 2012) and the anterior posterior diameter of the lateral condyle (APDLC), which is the largest anteroposterior dimension of the lateral condyle (Srivastava et al. 2012) (Fig. 1). The landmarks were positioned using 3D in vivo imaging software (Amira®) using the volume rendering technique (VRT) mode and the multi-planar reconstruction (MPR) mode. Once these landmarks had been defined, the coordinates of each landmark in space (x,y,z) were recorded.

During the scan, the subject was placed in a supine position with their knee in a relaxed and extended position. Axial slices perpendicular to the femoral long axis in which the epicondyles were the most prominent were used to place points 1–8. Oblique slices were created by resampling the image stack in order to be orthogonal to the axial plane; points 9 and 10 were placed on these images.

Reliability studies

The analyzed data were taken from the same database and analyzed twice on separate occasions by two observers. This made it possible to calculate the intra- and inter-observer variability for each landmark. The percentage error for each landmark was calculated, as described previously (Table 2). The results were deemed acceptable if this error was less than 5%.

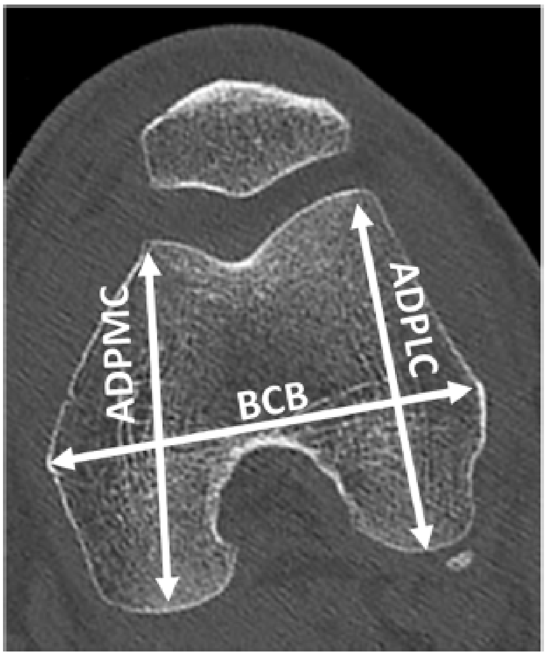

Fig. 1 Osteometric data used to measure the plausibility of the study's methodology. BCB: bicondylar breadth, distance between the two epicondyles, APDMC: anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial condyle and APDLC: anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle

Procrustes analysis

All morphometric geometric analyses were carried out with Morpho J software and R 2.2.0 software. The chosen landmarks made it possible to characterize the shape of the distal femur (Fig. 2). The first step consisted of a generalized Procrustes analysis (GPA) (Klingenberg 2002). With GPA, size effects related to isometry were removed, but allometric size differences were retained and visible. This strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

Statistical analysis

The descriptive analysis consisted of calculating the mean, median and standard deviation values for each subgroup. Normal distribution of continuous variables was verified using the Shapiro-Wilk test and homogeneity of variances was determined using Fisher's F-test and Levene's test to ensure the assumptions were met for use of parametric tests. Comparisons of subgroup demographics were performed with Student's *t*-test. The length variables (BCB, APDLC and APDMC) in the various subgroups were compared using an analysis of variance (ANOVA).

The landmark coordinates were analyzed using principal component analysis (PCA) (Miriam 2004) and canonical variate analysis (CVA) to identify shape trends in the various subgroups (Bilfeld et al. 2013).

To determine if the difference between shapes was statistically significant, a *P*-value was also calculated using Goodall's F-test and Mahalanobis D2 matrices (Ozer & Katayama 2008; Pretorius et al. 2006). Goodall's F-test allows testing for overall shape differences between groups while taking all sample variables into account.

A discriminant analysis with leave-one-out cross-validation was performed to determine the percentage of cases in which the ethnic group was correctly estimated. Pearson's Chi-square test was also performed to compare the percentages of correct ethnic group classification in order to determine if this analysis was statistically significant (Elewa 2010).

Results

Reliability analysis

The percentage errors for the intra- and inter-observer comparisons for all the landmarks are given in the Appendix. None exceeded 2% (Table 2).

Table 2 Anatomical description of the various landmarks used, with the intra- and inter-observer variability for each. The error is given as a percentage

Landmark	Location	Intra-observer Variability	Inter-observer Variability
1	Medial epicondyle	1.77	1.82
2	Most dorsal point on medial condyle	1.45	1.46
3	Top of intercondylar notch	1.52	1.60
4	Most dorsal point on lateral condyle	1.77	1.89
5	Lateral epicondyle	1.68	1.64
6	Most outside point on trochlear groove	1.59	1.62
7	Most distal point at bottom of trochlear groove	1.66	1.69
8	Most ventral point on margin of trochlear groove	1.62	1.72
9	Most distal point on medial condyle	1.73	1.69
10	Most distal point on lateral condyle	1.62	1.52

Ethnic dimorphism

The mean BCB value was greater in Europeans (80.5 ± 6.5 mm) than Asians (76.3 ± 5.2) ($P < 0.001$). Similar results were found for the APDMC (E: 63.7 ± 5.1, A: 58.5 ± 4.2; $P < 0.005$) and the APDLC (E: 62.8 ± 4.9, A: 58.9 ± 3.8, $P < 0.001$) (Table 3).

The shape of the E and A distal femur differed significantly (Fig. 2) (Goodall's F = 94.43, $P < 0.001$ and Mahalanobis D2 distance = 1.85, $P < 0.001$). For the same femur size, Asian femurs are significantly longer in the frontal plane, i.e. the distance between the axial plane containing the epicondyles and the two most distal points on the condyles is greater in the Asian group. In the axial plane through the epicondyles, Asian femurs are shorter along the anteroposterior axis than European femurs, while the mediolateral distance is the same. The graphical PCA representation that provided the best discrimination in terms of ethnic dimorphism was PC1 against PC2. PCA identified a difference in distal femur shape between A and E; PC1 and PC2 accounted for 71.9% of the variance measured (Fig. 3). CVA revealed that the correct ethnic group was assigned in 82% of cases and the cross-validation revealed a 75% rate of correct ethnic estimation (Table 4).

Ethnic and sex differences

The osteometric analysis (BCB, APDMC and APDLC) revealed significant differences between subgroups of subjects (Table 3). The PCA based on ethnicity and sex is shown in Fig. 4; PC1 and PC2 accounted for 61.9% of the variance measured.

Discussion

Our hypothesis is confirmed: 3D geometric morphometric analysis of the distal femur revealed differences

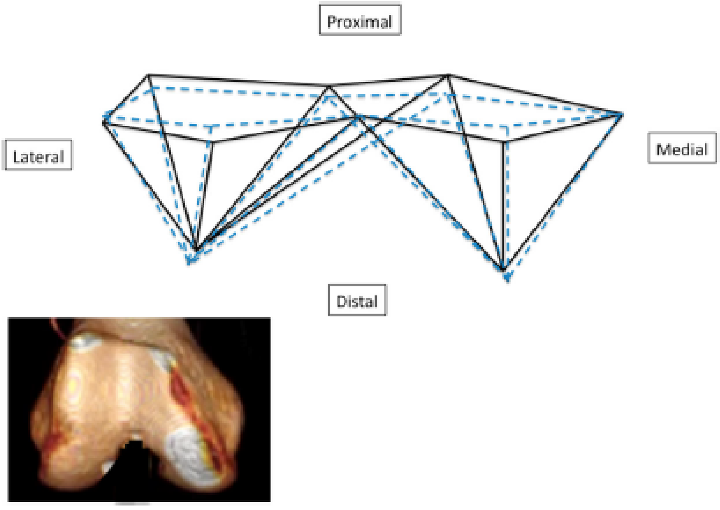

Fig. 2 Shape variation based on ethnicity. A 3D reconstruction is shown to make it easier to understand the data (Asian in *blue*, European in *black*)

Table 3 Mean values (± standard deviation) of the osteometric data for each subgroup based on ethnicity and sex

	Asian		European	
BCB	76.3 ± 5.2		80.5 ± 6.5	
APDMC	58.5 ± 4.2		63.7 ± 5.1	
APDLC	58.9 ± 3.8		62.8 ± 4.9	
	ASF	ASM	EUF	EUM
BCB	72.1 ± 3.2	80.0 ± 3.6	75.5 ± 3.7	85.0 ± 4.9
APDMC	55.8 ± 3.3	60.9 ± 3.3	60.3 ± 4.0	66.7 ± 4.2
APDLC	56.9 ± 3	60.7 ± 3.6	60.2 ± 3.9	65.2 ± 4.4

Comparisons were performed with an ANOVA – $P < 0.001$ for all comparisons. *ASF* Asian Female, *ASM* Asian Male, *EUF* European Female and *EUM* European Male

between ethnic groups (Figs. 2 and 3). There are ethnic and ethnic–sexual dimorphisms in the distal femur. All the comparisons performed in this study were statistically significant. The 3D analysis and osteometric data revealed dimorphisms related to ethnicity. Moreover, the PCA analysis (Figs. 3 and 4) and comparative analysis of metric data (Table 3) revealed dimorphisms related to ethnicity, but also sex and ethnicity. The greatest dimorphism was found between Asian men and European men (Fig. 3).

To our knowledge, this is the first study comparing the 3D anatomy of the distal femur between two ethnic groups. We are the first group to show differences in distal femur shape that are independent of the difference in size. It is well-known that the anatomical profiles of Asian knees are smaller and narrower than those of Caucasian knees (Yue et al. 2011). However, in our study, we analyzed the differences in shape, not size. We performed a true 3D analysis because the location of each landmark was analyzed relative to the others. This differs from the analysis of two osteometric data points in two planes in space that is often used for comparisons between ethnic groups (Kim et al. 2017).

Geometric morphological analysis effectively minimizes differences related to general somatotype and keeps only the shape differences. Bellemans et al. (Bellemans et al. 2010) have shown that differences in femur shape were related to an individual's sex and somatotype. Carter and Heath refined it into three somatotypes: endomorph, mesomorph, ectomorph (Sheldon 1950). Skeletal structure and body composition are used to classify individuals into these three groups. Osteometric analysis helps to assign ethnicity, but is subject to the somatotype effect. Geometric morphometric analysis discounts somatotype-related differences, reducing the accuracy of this analysis. Osteometric analysis is subject to two variables (ethnicity and somatotype), while geometric morphometric analysis is subject to only one variable (ethnicity).

One of the main objectives of physical anthropology is to estimate a person's sex and ethnicity in the forensic or anthropology context (Slaus et al. 2003). Most of the

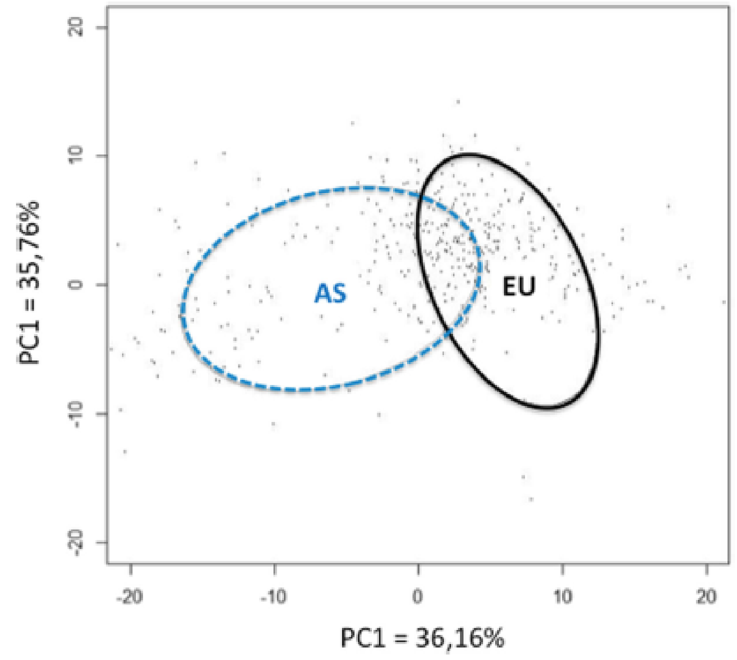

Fig. 3 PCA obtained for the shape of the distal femur based on ethnicity. The ellipses correspond to 68% confidence intervals (Asian (AS) in *blue*, European (EU) in *black*)

Table 4 Results of the CVA and cross-validation for the ethnic estimation

	Original CVA			Cross-Validated		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
A	203	39	83	187	53	77
E	195	45	81	179	63	73
Total	398	84	82	366	116	75

postcranial bones have been used to determine the sex of human remains through various statistical models (Kim et al. 2013). The femur is the longest bone and it is often well preserved (King et al. 1998). But anthropologists must have different algorithms in their diagnostic arsenal for cases where the skeletons are fragmented or when specific populations are analyzed (Iscan & Shihai 1995). The large number of subjects ($n = 482$) included in our study provides osteometric references related to sexual dimorphism in a modern population. Determining ethnicity based on a bone fragment could improve identification of a specimen, particularly when it is not fully intact. This method made it possible to correctly assign ethnicity in 82% of subjects (original CVA) (Table 4). But this is not sufficient to allow the ethnic origin of a specimen to be determined without a doubt. Anthropologists have different algorithms in their diagnostic arsenal for cases where the skeletons are fragmented or when specific populations are analyzed (Mall et al. 2000; Ozer & Katayama 2008; Purkait & Chandra 2004; Slaus et al. 2003; Srivastava et al. 2012; Trancho et al. 1997). This data may be used as a current reference when virtual or in vivo autopsy is performed (Barrier et al. 2009).

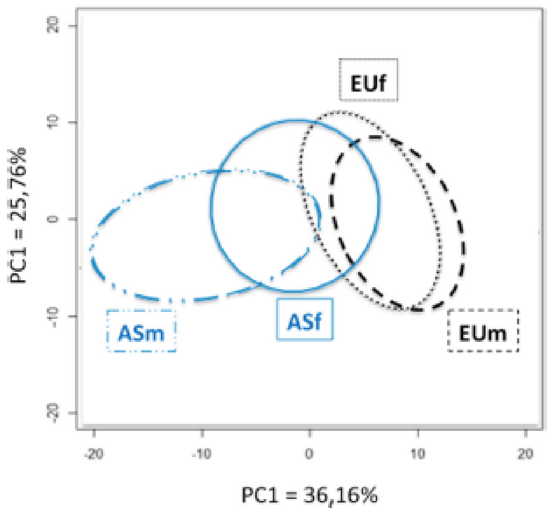

Fig. 4 PCA obtained for the shape of the distal femur based on sex and ethnicity. The ellipses correspond to 68% confidence intervals (Asian males (ASM) in *blue dotted line*, Asian females (ASF) in *blue* continuous line, European males (EUM) in *black dashed line*, European females (EUF) in *black dotted line*)

In this study, osteometric analyses were carried out in addition to the 3D analyses. By placing easily identifiable points on the apex of the bone contours, we were able to obtain data in the traditional manner, which allowed us to verify that our data were in agreement with published values (Cavaignac et al. 2016). Origin-based variability (Purkait & Chandra 2004) must be taken into account in literature comparisons, but the results of these three reference measurements are consistent with published results (Cavaignac et al. 2016). Furthermore, the intra- and inter-observer error rates were very low in our study—none exceed 2%. These two aspects (reproducibility and plausibility) validate our methodology. If we had wanted to carry out an analysis based only on classic osteometric variables (EB, ADPMS, ADPLC), we would have had to consider the patients' morphotype, hence their biometric data (height, weight, frontal plane morphotype, etc.). However, these variables (EC, ADPMS, ADPLC) were secondary outcome measures used to validate our measurement method by comparing it to existing data. We felt it was not necessary to weight these results with the biometric data, especially that our data were consistent with published values (Cavaignac et al. 2016). Geometric morphometric analysis eliminates differences related to object size.

The anatomical profiles of Asian knees are smaller and narrower than those of Caucasian knees (Yue et al. 2011). Most of the commercially available total knee arthroplasty (TKA) implants were designed based on anthropometric data of Caucasian knees, thus they may not be suitable for Asian patients (Bilfeld et al. 2012; Gonzalez et al. 2009; Ho et al. 2006; Yue et al. 2011). In a comparative study of the outcomes following TKA, Asian patients had significantly less postoperative range of motion and a higher rate of revision (Iorio et al. 2007). As the number of TKA procedures is expected to increase in Asia (Yang et al. 2012), it is essential to analyze the morphological characteristics of Asian knees to provide validated references for Asian TKA implants. We performed a shape-based analysis that removed size effects. This is a crucial issue for us, as the anatomical difference is not only related to differences in size. The simplistic solution that Chinese patients need smaller implants will only solve part of the problem. Not only do these implants need to be smaller, they need to have a different shape. Only the concept of anteroposterior length, mediolateral width and/or aspect ratio provide some insight into inter-ethnic differences (Kim et al. 2017). Like Kim et al (Kim et al. 2017), we believe that these data create uncertainty around variability but do not answer the question itself.

Geometric morphometric analysis is a global 3D analysis that takes into account the location of each landmark in space relative to the others. Our analysis confirms that this dimorphism exists even when the size effect is removed. Furthermore, doing an analysis based on ratios or lengths over-simplifies the problem. It has been shown that soft tissue impingement due to overhang leads to postoperative pain and worse functional outcomes (Dai et al. 2014; Ho et al. 2006; Mahoney & Kinsey 2010). Reducing the size of the femoral component increases the risk of instability during knee flexion. If the femoral implant is shifted proximally to compensate for downsizing, the height of the joint line will be altered. For these reasons, only adjusting the size does not solve the problem – the shape must be taken into account.

The primary finding of our study is that ethnic dimorphism is present in the distal femur. The sex differences in distal femur from a Chinese population have been evaluated by Yang and colleagues (Yang et al. 2012). However, their study used classic osteometric methods and measured distances, angles and ratios in three dimensions without connecting these dimensions. In our study, the coordinates of each target point were analyzed in three dimensions and were related to the location of other points. Thus our study should be more properly called 3D analysis (Pretorius et al. 2006). It is also interesting to note that sexual dimorphism was more prevalent in the Asian population than the European one (Fig. 4). We chose to quantify sex-related differences in the context of both orthopedics and anthropology. The impact of gender is hotly debated in orthopedics; it appears that the size difference between men and women explains part of the differences (Bellemans et al. 2010). However, these differences are in part related to shape, independently of size (Fig. 4). Geometric morphometric analysis have revealed these shape-related differences. In the anthropology context, sex determination contributes to identifying human remains (Ozer & Katayama 2008; Purkait & Chandra 2004; Slaus et al. 2003).

The current study has certain limitations. Only skeletally mature subjects were included. In younger persons, the bone contours of the distal femoral epiphysis are not completely ossified. This would have increased the possibility of error during landmark placement by the observers. Moreover, diseases that do not affect the distal femur but may require a CT scan that includes the distal femur, such as vascular conditions, are more common in older subjects. We were not able to determine the number of subjects needed for this study, as this was the first time that morphometric geometry methods were used to analyze distal femur anatomy. We initially based our sample size calculation on data from the Yang study (Yang et al. 2014) (measuring BCB in an Asian population) and the Cavaignac study (Cavaignac et al. 2016) (measuring BCB in a European population). This calculation pointed to 35 subjects being needed in each group to reveal a difference of more than 4 mm between two ethnic groups using the BCB (common standard deviation of 6 mm, alpha risk of 0.05 and 90% power). But we felt it was timely to include a much larger number of subjects, making this the largest study to compare distal femur anatomy between two ethnic groups.

It is important to point out that our analysis of shape differences resulted in an average shape for each subgroup (Fig. 2). Although the average shapes differ, they do not capture all the variability within a population. The shape of Asian and European distal femurs differs, while the extremes of each group can have similar components. The APC circles in Figs. 3 and 4 are have some overlap become there are similarities between the populations. This is a drawback of “grouped” analysis, which suppresses individual characteristics. Most of the differences in shape in the orthopedic context occur in the axial plane (distal femoral twist, aspect ratio of distal femurs) (Kim et al. 2017; Mahfouz et al. 2012; Yip et al. 2004). We were somewhat surprised to found notable dimorphism in the frontal plane in our study (Fig. 2) – Asian femurs were longer from cranial to caudal than the European femurs. To our knowledge, this frontal dimorphism has never been shown. This may be one of the reasons why Asian TKA patients have worse range of motion results (Iorio et al. 2007).

This study is the first step in an effort to classify the variability in femur shape suggested by Mahfouz (Mahfouz et al. 2012) but in the three planes in space. We will add data from other ethnic groups to enrich our database.

The use of clinical investigations for anthropological purposes, after validation of the methods applied, also opens new fields for anthropology. The number of subjects who could be studied for anthropological purposes is greater than those in classic osteological collections.

Conclusions

In summary, the distal femur exhibits ethnic and ethnic–sexual dimorphism. Three-dimensional geometric morphometric analysis made it possible to show these shape differences. The large number of subjects studied may help to modernize the references for certain bone measurements.

Authors' contributions
All authors read and approved the final manuscript.

Competing interests
The authors dadare that they have no competing interests.

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Annexe 4 : Travail sur le dimorphisme sexuel et lié à l'âge dans une population chinoise.

3D geometric morphometric analysis of the distal femur reveals sexual dimorphism and age-related differences in Chinese population

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Abstract

Background: Accurately morphologic data of the knee is crucial in the design of total knee prostheses. Generally, the design of the total knee prostheses are based on the knee anatomy of Caucasian population. Moreover, in forensic medicine, an individual's sex and age might be estimated by the shape of their distal femur. The goal of this study was to firstly utilize 3D geometric morphometric analysis of the distal femur in Chinese population to reveal sexual dimorphism and age-related differences.

Methods: Sexually dimorphic differences and age-related differences of the distal femur were studied using geometric morphometric analysis of 10 osteometric landmarks on three-dimensional reconstructions of 259 knees in Chinese population. General Procrustes Analysis (GPA), Principal Component Analysis (PCA), Canonical Variates Analysis (CVA), and other discriminant analysis (Goodall's F-test and Mahalanobis distance) were performed for the distal femur. These analyses were used to identify trends in bone shape in sex-based subgroups and various age-based subgroups (<40, 40–60, >60 years).

Results: The shape of distal femur between the male and female are significantly different. PCA identified a difference in distal femur shape between males and females; PC1 and PC2 accounted for 61.63% of the variance measured. The CVA revealed that the correct sex was assigned in 84.9% of cases and the cross-validation revealed a 81.1% rate of correct sex estimation. The osteometric analysis also showed significant differences between the three age-based subgroups (<40, 40–60, >60 years, P<0.005).

Conclusion: This study showed both sex-related difference and age-related difference in the distal femur in Chinese population by 3D geometric morphometric analysis. Our bone measurements and geometric morphometric analysis suggest that population characteristics should be taken into account and may provide references for design of total knee prostheses in a Chinese population. Moreover, this reliable, accurate method could be used to perform diachronic and interethnic comparisons.

Key words: distal femur dimorphism, principal component analysis, Procrustes analysis geometric morphometric analysis, biological anthropology

Background

In the surgery of total knee arthroplasty (TKA), proper prosthetic selection, accurate sizing and proper placement of the components are important factors for achieving a long-term survivorship[1]. A properly shaped prosthesis which matches the resected surface of the knee could provide adequate balancing of the soft tissue and best coverage[2]. There has been increasing interests in the concept of gender specific replacement[3, 4], previous studies have indicated that female knee was narrower than the male knee regardless of the size[5, 6]. However, some new designed TKA prostheses accounting for gender-specific implants were suspected to be driven by commercial interests since there was evidence that women had better clinical outcomes than men regardless of the prosthesis[7, 8].

Ethnic diversity is always an important factor that might affect the anthropometric data, some studies have suggested that anatomical profiles of Asian knees were smaller and narrower than those of Caucasion[9-11]. To date, owing to shortage of data on distal femur and proximal tibial of Asian population, most of the commercially available TKA prostheses were designed according to anthropometric data of Caucasian knees and may not be suitable for Asian patients[12]. It seems that traditional “western” implants used in Asian population tend to overhang[13-15], Iorio et al reported that the clinical results are poorer in Asian patient group, which had a significantly less postoperative range of motion and a higher rate of revision[16]. As the TKA has been more and more widely used in Asia[17, 18], it has become essential to analyze the morphological characteristic of Asian knees in order to provide references for Asian TKA.

Moreover, in a forensic point of view, The morphology of human bones differs between men and women; these differences can be used to determine the sex of human remains[19]. Several studies have shown that sex can be estemated using distal femur dimorphism[19]. Also, Ethnic specific morphology has to be measured to perform diachronic and interethnic comparisons[20].

In previous studies, the anthropometric data of the knee was mainly evaluated by 2 dimensional osteometric analysis[4, 6, 10, 13, 15]. Geometric morphometric analysis is a useful tool that permits quantification of morphological characters. The most important advantage of geometric morphometric analysis over traditional morphological tools is that it combines powerful tools of multivariate statistics and makes possible investigation of morphological variations with direct reference to the anatomical context of the structure studied[20, 21]. It provides quite useful visual information when applied to the study of differences between skeletal features. Geometric morphometric analysis has been used since the 1980s, but has only become popular in anthropology recently[22, 23]. We hypothesized that three-dimensional (3D) geometric morphometric analysis of the distal femur would reveal sexual dimorphism and age-related differences. The goal of this study was to show that differences in distal femur shape related to sexual dimorphism and age could be identified, visualized, and quantified using 3D geometric morphometric analysis in a Chinese Han population. To our knowledge, this is the first study that utilize 3D geometric morphometric analysis of the distal femur to reveal sexual dimorphism and age-related differences in a Chinese Han population.

Methods

We carried out a retrospective study of distal femur from patients undergoing lower limb CT scan in our institution between January 2013 to June 2014 (Chongqing, China). Patients included in our study must meet our inclusion criterion including a fully shown distal femur (tip of femoral groove to most distal aspect of femur) on CT scan and those with a known history of diseases related to distal femur were excluded from our study. The patients were of single ethnic origin (Chinese Han population) and could be representative of the population in most part of China. A total of 259 distal femurs met our inclusion criteria consisting of 137 men and 122 women. The right side was analyzed 123 times and left side 136 times. The mean age of subgroups relative to sex and side was shown in **Table 1**. The CT scans were saved as digital imaging and communications in medicine (DICOM) files and then processed with Amira 4.1.1® software (Mercury Computer System, Inc., Chelmsford, MA, USA).

		Age	***P***
Sex	Male (n=137)	52,04 +/- 17,6	0.472
	Female (n=122)	53,5 ± 16,9	
Side	Right (n=123)	52,7 ± 17.3	0.962
	Left (n=136)	52,8 ± 17.1	

Table 1: Mean age of the various subgroups relative to sex and side. Comparisons were performed with Student's *t*-test.

3D morphological analysis

We have chosen ten osteometric landmarks based on standard bone landmarks used in anthropometry including medial/lateral epicondyle, most dorsal/ventral point on medial/lateral condyle, top of intercondylar notch, most distal point at bottom at trochlear groove and most distal point on medial/lateral condyle (**Fig 1 and Table 2**)

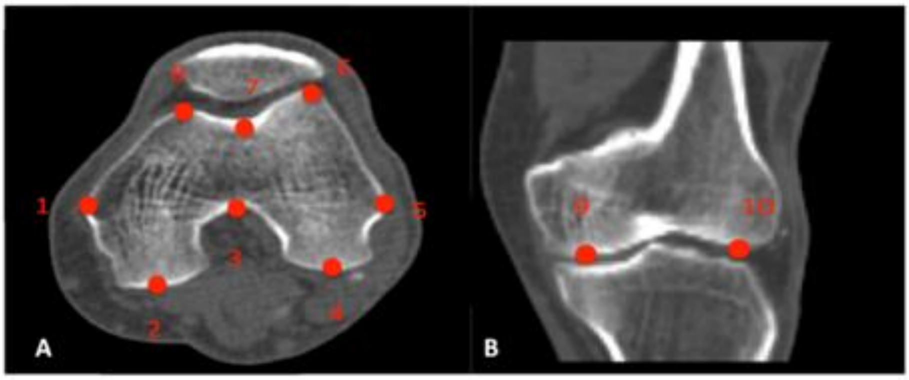

Figure 1: Location of landmarks on axial (A) and frontal (B) CT scan slices: 1) medial epicondyle, 2) most dorsal point on medial condyle, 3) top of intercondylar notch, 4) most dorsal point on lateral condyle, 5) lateral epicondyle, 6) most ventral point on lateral edge of trochlear groove, 7) most distal point at bottom of the trochlear groove, 8) most ventral point on the medial edge of the trochlear groove, 9) most distal point on medial condyle, 10) most distal point on lateral condyle. [24-27]. With these points as well as osteometric techniques, our results could be evaluated and compared with the already published articles. Several variables were measured including the epicondylar breadth (EB), which is the distance between the two epicondyles [28, 29], anterior posterior diameter of the medial condyle (APDMC), which is the largest anterior-posterior distance of the medial condyle [24], and anterior-posterior diameter of the lateral condyle (APDLC), which is the largest anterior-posterior dimension of the lateral condyle [24] (**Figure 2**).

Landmark	Location	Intra-observer Variability	Inter-observer Variability
1	Medial epicondyle	1.64	1.63
2	Most dorsal point on medial condyle	1.64	1.64
3	Top of intercondylar notch	1.64	1.64
4	Most dorsal point on lateral condyle	1.64	1.64
5	Lateral epicondyle	1.63	1.64
6	Most outside point on trochlear groove	1.63	1.65
7	Most distal point at bottom of trochlear groove	1.64	1.65
8	Most ventral point on margin of trochlear groove	1.64	1.65
9	Most distal point on medial condyle	1.53	1.51
10	Most distal point on lateral condyle	1.52	1.49

Table 2: Anatomical description of the various landmarks used, with the intra- and interobserver variability for each. The error is given as a percentage.

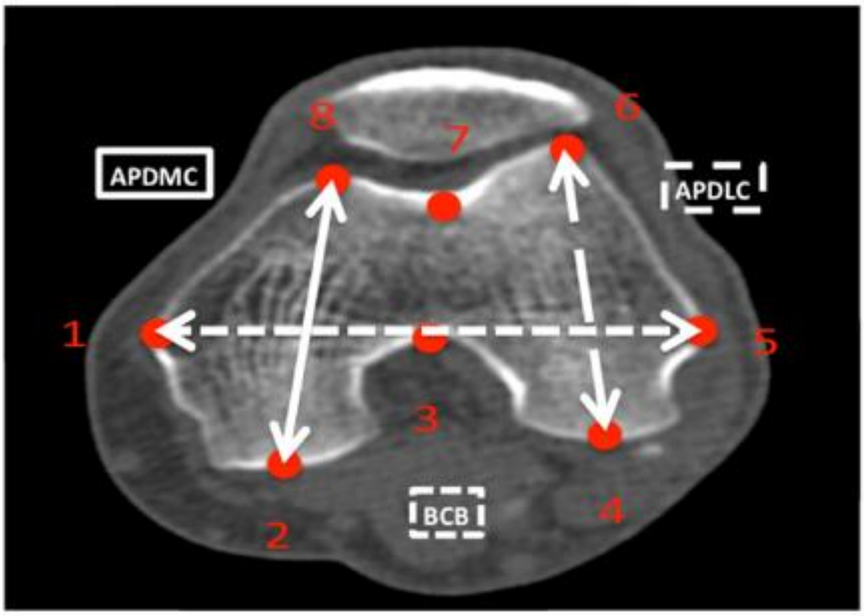

Figure 2 : Osteometric data used to measure the plausibility of the study's methodology. EB: Epicondylar breadth, distance between the two epicondyles, APDMC: Anterior posterior diameter of the medial condyle, which is largest anteroposterior dimension of the medial

condyle and APDLC: Anterior posterior diameter of the lateral condyle, which is largest anteroposterior dimension of the lateral condyle

The coordinates of each landmark in space (x,y,z) were recorded once these landmarks had been located with 3D in vivo imaging software (Amira®, Visualization Sciences Group, Bordeaux, France).

Reliability studies

The 3D morphological data was analyzed separately by two observers to calculate the intra- and inter-observer variability for each landmark. For each observer, landmark deviations were calculated relative to the landmark's mean value. As previously described[30-32], the percentage error for each landmark was calculated (Table 2). The results were regarded acceptable if this error was less than 5%[30-32].

Procrustes analysis

The Morpho J software[33] and R 2.2.0 software were utilized to conduct the morphometric geometric analyses. The shape of each distal femur was characterized with those recorded landmarks (**Figure 1**).

A generalized Procrustes analysis (GPA) was firstly performed[34]. As described previously[21, 34], this strategy expresses the results in graphical format by showing the average shape of the subgroups of interest.

Statistical Analysis

The descriptive analysis included the calculation of the mean, median and standard deviation values for each subgroup. A comparative analysis was performed with all the variables based on sex (male, female) and then age (< 40, 40–60, > 60 years). The principal component analysis (PCA) and canonical variate analysis (CVA) were utilized to analyze the landmark coordinates to identify shape trends in the various subgroups[21].

The percentage of cases in which the sex was correctly estimated was analyzed by a discriminant analysis. Pearson's Chi-square test was used to determine if this analysis was statistically significant. A P-value was also calculated using Goodall's F-test and Mahalanobis D2 matrices to determine if the difference between shapes was statistically significant[35, 36]. The length variables (EB, ADPLC and ADPMC) were compared using an analysis of variance (ANOVA).

Results

The percentage errors for the intra- and inter-observer comparisons for all the landmarks are given in **Table 2**, none exceeded 2%. The mean EB value was not significantly different from each age group (<40: 76.6±5.5mm, 40-60: 75.6±5mm, >60: 76.5±5mm; p=0.453), neither did APDMC (<40: 58.6±4mm, 40-60: 58.2±4.7mm, >60: 58.4±3.9mm; p=0.837) nor APDLC (<40: 59.1±3.7mm, 40-60: 59.0±4.1mm, >60: 58.6±3.6mm; p=0.716). However, the mean EB value was found greater in male (79.9±3.58mm) than in female (72.1±3.2mm) (p<0.005), so did APDMC (male:60.7±3.3mm, female: 55.8±3.5mm; p<0.005) and APDLC (male: 60.7±3.5mm, female: 56.8±3.0mm; p<0.005) (**Table 3**).

Age	**< 40**	**40–60**	**> 60**	***p***
EB	76.6 ± 5.5	75.6 ± 5	76.5 ± 5	0.453
APDMC	58.6 ± 4	58.2 ± 4.7	58.4 ± 3.9	0.837
APDLC	59.1 ± 3.7	59.0 ± 4.1	58.6 ± 3.6	0.716

Sex	Female	Male	*p*
EB	72.1 ± 3.2	79,9 ± 3.58	< 0.005
APDMC	55.8 ± 3.5	60.7 ± 3.3	< 0.005
APDLC	56.8 ± 3.	60.7 ± 3.5	< 0.005

Table 3: Mean values (± standard deviation) of the osteometric data for each subgroup based on age and sex. Comparisons were performed with an ANOVA.
EB: epicondylar breadth. APDMC: Anterior posterior diameter of the medial condyle. APDLC: Anterior posterior diameter of the lateral condyle

The 3D shape of the distal femur differed significantly between the age groups (**Figure 3**) by Goodall's F-test and Mahalanobis D2 matrices (p<0.005) (**Table 4**). Similar results were identified between men and women (Goodall's F=24.65 and Mahalanobis D2 distance=1.74; p<0.005) (**Figure 5**). A difference was identified by PCA in distal femur shape between men and women as well as age groups; PC1 and PC2 accounted for 61.63% of the variance measured. (**Figure 4**) (**Figure 6**). The correct sex was assigned in 84.9% according to the original CVA and a 81.1% rate of correct sex estimation was obtained by the cross validation. (**Table 5**)

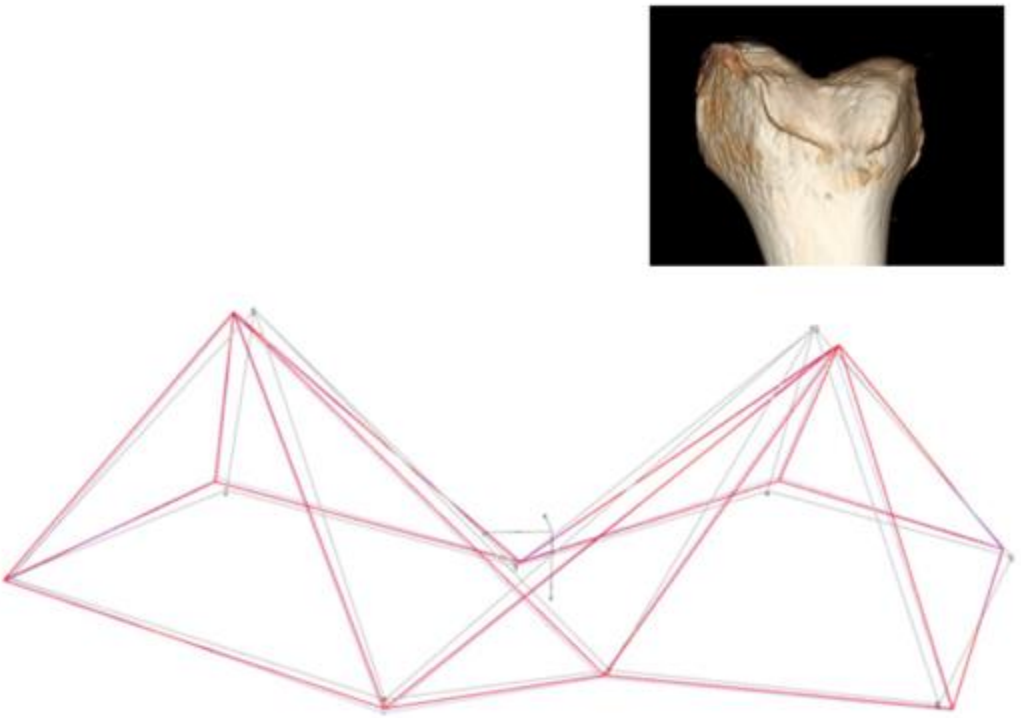

Figure 3: Shape variation based on age (< 40: gray line, 40-60: blue, >60 : red). A 3D reconstruction is shown to make it easier to understand the data.

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Comparison	Mahalanobis D2 Distance	Goodall's F test	p
< 40 / > 60	1,34	10,27	<0.005
40–60 / > 60	1,49	9,68	<0.005
< 40/ 40–60	1,43	9,53	<0.005
Male / Female	1.7437	24,65	<0.005

Table 4: Values of Goodall's F and Mahalanobis D2 distance for the comparisons performed

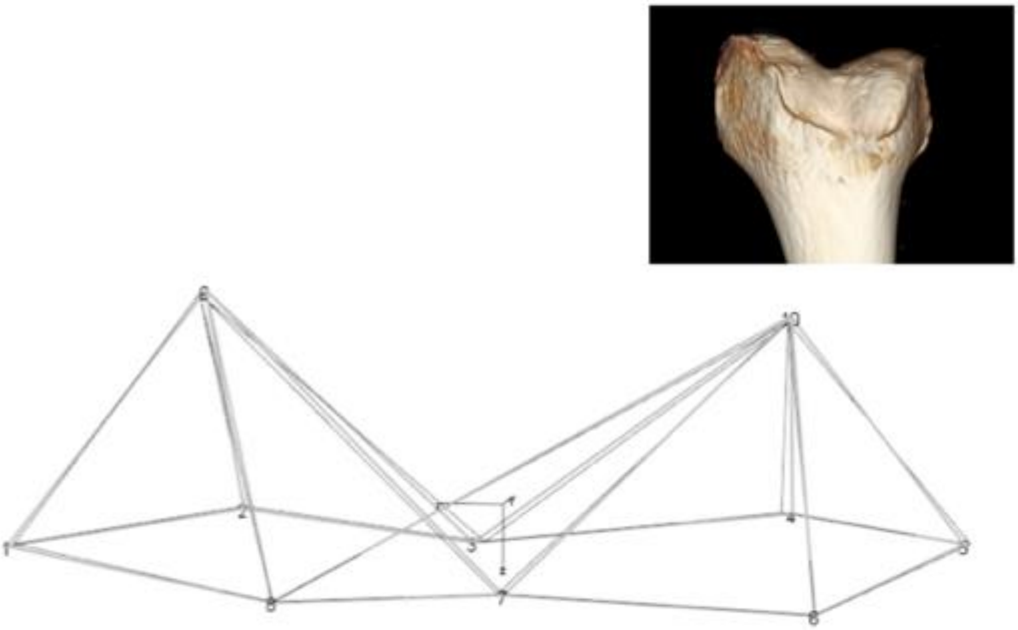

Figure 4: Shape variation based on sex (male: black line, female: gray line). A: 3D view obtained of the inferior end, B: view on an axial plane containing the first eight landmarks. The 3D reconstructions are shown to make it easier to understand the two planes.

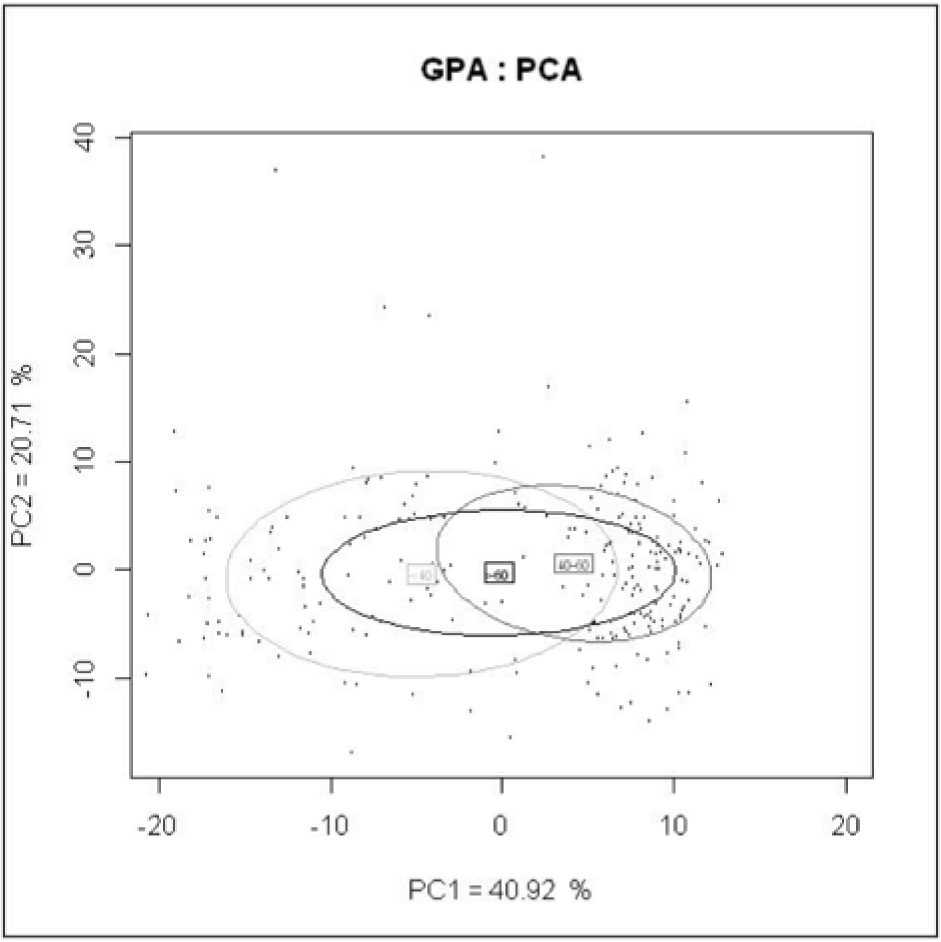

Figure 5: PCA obtained for the shape of the distal femur based on age. The ellipses correspond to 62% confidence intervals.

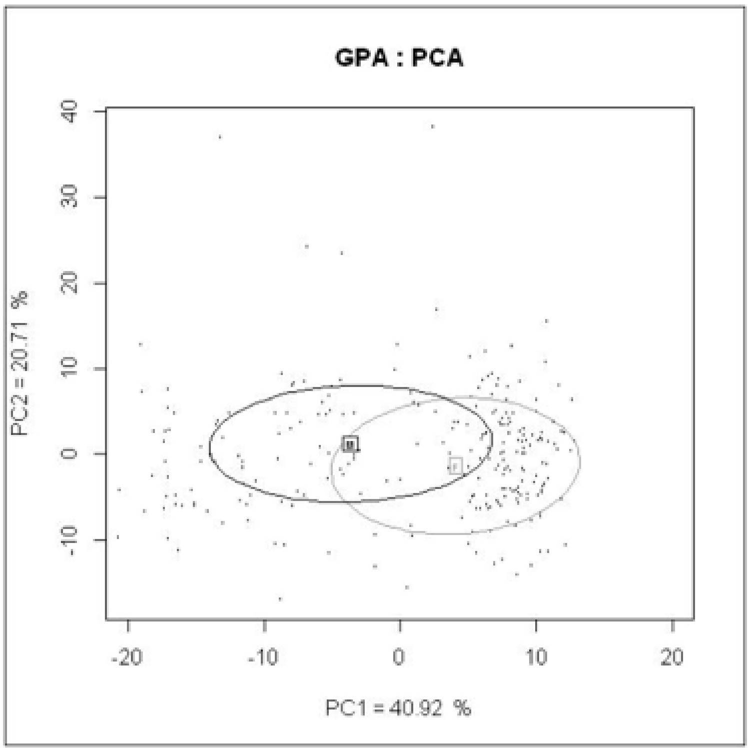

Figure 6: PCA obtained for the shape of the distal femur based on sex (male: black line, female: gray line). The ellipses correspond to 62% confidence intervals.

	Original CVA			Cross-Validated		
	Correctly assigned	Incorrectly assigned	% Correctly assigned	Correctly assigned	Incorrectly assigned	% Correctly assigned
Female	103	19	84,4	97	25	79,5
Male	117	20	85,5	114	23	84
Total	220	39	84,9	211	48	81,1

Table 5: Results of the CVA and cross-validation for the sex estimation

Discussion

The most important finding of this study was that our hypothesis was confirmed: distal femur shape related to sexual dimorphism and age-related differences could be identified, visualized, and quantified using 3D geometric morphometric analysis in a Chinese Han population. Moreover, based on our results, the distal femur in Chinese Han population presented an even more notable sexual dimorphism (Goodall's F=24.65 and Mahalanobis D2 distance=1.74; p<0.005) and age-related differences (p values of Goodall's F-test and Mahalanobis D2 distances <0.005). Our results showed that intra- and inter-observer variabilities were less than 2%, attesting of the accuracy and reproducibility of the technique, which is acceptable[30, 32, 35, 36].

Some studies have indicated that Asian knees are generally smaller than the Caucasian population[9, 11, 12, 37]. In order to achieve successful outcome, the TKA prostheses are required to properly cover the resected surface of the knee[1].It is necessary to evaluate the morphology of Asian knees and compare with Caucasian knees to provide reference for the design of prostheses suitable to Asian population. This is the first study of shape comparison that looked at the distal femur as a whole, the differences inside an ethnic group (European[20] and Chinese population) was firstly evaluated, then we will measure the differences between populations in the further study. The most important result here is to show that Chinese population presents sex and age related dimorphism. Several studies have already shown sex differences in the distal femur in an Asian population [38] or in a western population [39, 40]. It’s still not known whether using sex-specific implants results in better clinical outcomes or not[40-43]. Our previous study have revealed sexual dimorphism in the distal femur of French population by using geometric morphometric analysis[20]. To date, this is the first study that utilize 3D geometric morphometric analysis of the distal femur to reveal sexual dimorphism and age-related differences in a Chinese Han population.

Yang et al[38] have also evaluated the sex differences in distal femur from a Chinese population. However, their study utilizing classic osteometric methods only measured distances, angles and ratios in three dimensions but without connections between dimensions. In our study, the coordinates of each target point was analyzed in three dimensions and was relative to the location of other points. Moreover, by using geometric morphometric analysis, the three-dimensional morphology of the distal femur was evaluated as a whole. Thus our study should be more properly called 3D analysis[22, 43].

Geometric morphometric analysis can be used to quantify morphological features[44]. This technique allows the overall shape of an object to be analyzed with its intact geometry, making statistical analysis possible[45]. It was developed to quantify the shape of rigid structures consisting of curves and bulges that are not easy to interpret using traditional metric methods[46]. This method has demonstrated its usefulness in physical anthropology[47]. As the results shown in our study, geometric morphometric analysis could identify an age related difference between groups. With the same samples, classic metrics couldn’t show any differences using EB, ADPMC, ADPLC. For a complex object as the distal part of the femur consisting of curves and bulges, classic osteometric tools are not adapted because the measurements were always separately conducted and curves or bulges could not be taken into account. 3D geometric morphometric analysis takes into account everything in one analysis.

In addition, our study could help estimate a person's sex and age in the forensic or anthropology context[28, 48-53]. Generally, the postcranial bones were utilized to estimate the sex and age[26], however, besides postcranial bones, the anthropologists should have other methods to diagnose, the distal femur is often well preserved in human and might serve as a good target to help differentiate the sex and age for cases where the skeletons are fragmented or when specific populations are analyzed[25, 28, 48, 54]. Our study has provided osteometric references related to sexual dimorphism and age-related differences in Chinese Han population.

This study is the most extensive up to now to evaluate sexual dimorphism of the distal femur in Chinese Han population. The data were derived from a modern population, contrary to most of the published studies on this topic. This data set can be used as a current reference when virtual or in vivo autopsy is performed. Temporal changes observed in modern populations mean that certain bone measurements must be reevaluated over time.

The age-related variations observed in the shape of the distal femur have consequences for orthopedic surgery, particularly for total knee arthroplasty (TKA). A better grasp of knee morphology and its variations can improve the design of TKA implants[55]. Our study is the first to show age-related differences in an Asian population. As a consequence, the age-related variations have to be take into account by the manufacturer in order to modify the implant design over time or at least to reevaluate the implant's design regularly. This is the first 3D study to show age-related differences in the overall shape of the distal femur (Fig 3). Discriminant analysis showed that 80% of subjects were correctly classified (original CVA). Although this method is not sufficiently accurate to be used alone, it can be used in the context of virtual or in vivo autopsy[56, 57].

General osteometric analysis that previous studies have utilized is capable to correctly assign sex and age, but their results could be confounded by differences related to general somatotype. Sheldon firstly described the concept of somatotype[58], then it's refined by Carter and Heath into three subtypes: endomorph, mesomorph and ectomorph[59, 60]. Geometric morphometric analysis minimizes somatotype-related differences and makes it possible to show the sexual dimorphism and age-related differences in the distal femur independent of somatotype.

Our study had several limitations, most of the patients included in our study were patients with vascular diseases due to availability of 3D reconstruction of CT scan, and the morphology of knees in patients with osteoarthritis may differ from normal knees. However, we have analyzed the age-related differences between several subgroups (<40, 40–60, >60 years) and this might give us suggestions on morphological differences related to osteoarthritis. In addition, the results of geometric morphometric analysis on age-related differences would have been more convincing if skeletally immature subjects were also included.

Conclusion

In summary, a 3D geometric morphometric analysis of distal femur was firstly utilized in a Chinese Han population, our study showed both sex dimorphism and age-related differences in the distal femur in Chinese population and might give us references on prostheses for Asian population. Interethnic comparisons are needed by this reliable and accurate methodology in the future.

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CAVAIGNAC Etienne

TITRE : Etude de la variabilité en fonction du sexe, de l'âge et de l'origine géographique de l'extrémité distale du fémur

Soutenue à Toulouse, le 10 Novembre 2017

DISCIPLINE : ANTHROPOBIOLOGIE

Titre en anglais :

Study of the sex-, age- and geography-based variability in the distal femur

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MOTS CLES : analyse morphométrique géométrique, variabilité, dimorphisme.

Directeur de Thèse : Professeur N. Telmon

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