HOW MANY DIFFERENT TYPES OF FEMORA ARE THERE IN PRIMARY HIP OSTEOARTHRITIS? AN ACTIVE SHAPE MODELLING STUDY

Merle C[1,2], Waldstein W[1,2], Gregory JS[3], Goodyear SR[3],
Aspden RM[3], Aldinger PR[4], Murray DW[1], Gill HS[5]

[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK
[2]Department of Orthopaedic and Trauma Surgery, University Hospital Heidelberg, Germany
[3]Musculoskeletal Research Programme, Division of Applied Medicine, University of Aberdeen, UK
[4]Department of Orthopaedic Surgery, Paulinenhilfe, Diakonieklinikum Stuttgart, Germany
[5]Department of Mechanical Engineering, University of Bath, UK

For Editorial Correspondence:

Christian Merle, MD, MSc, Research Fellow
Department of Orthopaedic and Trauma Surgery
University Hospital Heidelberg
Schlierbacher Landstr. 200 A
69118 Heidelberg
Germany
Phone:+49 6221 56 25000
christian.merle@med.uni-heidelberg.de

Wenzel Waldstein, MD, Research Fellow
wenzel.waldstein@project-e.eu

Jennifer S. Gregory, PhD, BSc, Research Fellow
j.gregory@abdn.ac.uk

Simon R. Goodyear, PhD, Research Fellow
s.goodyear@abdn.ac.uk

Richard M. Aspden, BA (Hons), PhD, DSc, FIPEM, Professor in Orthopaedic Science
r.aspden@abdn.ac.uk

Peter R. Aldinger, MD, Professor of Orthopaedic Surgery
peter.aldinger@diak-stuttgart.de

David W. Murray, MA, MD, FRCS (Orth), Professor of Orthopaedic Surgery
david.murray@ndorms.ox.ac.uk

Harinderjit S. Gill, B.Eng, DPhil, Professor
r.gill@bath.ac.uk

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Abstract

PURPOSE

To assess the variation in proximal femoral canal shape and its association with geometric and demographic parameters in primary hip OA.

METHODS

In a retrospective cohort study, the joint geometry of the proximal femur was evaluated on radiographs and corresponding CT scans of 345 consecutive patients with end-stage hip OA. Active shape modelling (ASM) was performed to assess the variation in endosteal shape of the proximal femur. To identify natural groupings of patients, hierarchical cluster analysis of the shape modes was used.

RESULTS

ASM identified 10 independent shape modes accounting for >96% of the variation in proximal femoral canal shape within the dataset. Cluster analysis revealed 10 specific shape clusters. Significant differences in geometric and demographic parameters between the clusters were observed.

CONCLUSIONS

ASM and subsequent cluster analysis have the potential to identify specific morphological patterns of the proximal femur despite the variability in proximal femoral anatomy. The study identified 10 distinct patterns of proximal femoral canal shape in hip OA which allow a comprehensive classification of variation in proximal femoral shape and its association with joint geometry. The present data may improve future stem designs that will optimise stem fit and simultaneously allow individual restoration of hip biomechanics.

Introduction

In cementless total hip arthroplasty (THA), the optimal femoral component should allow both accurate endosteal stem fit and individual restoration of physiologic joint mechanics. This poses a major surgical challenge as the osseous anatomy of the proximal femur is highly variable(1-3) and most contemporary stem designs are limited in their potential to adjust femoral offset, version, and limb length intraoperatively. Moreover, due to the variability in the size and shape of the proximal femoral canal, surgeons may be forced to compromise between the endosteal stem fit, which is critical to achieve stable fixation and proximal load transfer(4; 5), and accurate restoration of joint geometry, i.e. the centre of rotation.

Several studies over the last three decades have described the variation in femoral anatomy. However, most reported values were obtained from cadaveric specimens or individuals with non-arthritic hip joints(1; 2; 6), or from cohorts with limited patient numbers. Differences in femoral morphology between males and females have been described(7; 8), but there continues to be limited data on gender differences in patients with primary OA. Furthermore, it is not clear whether the shape of the proximal femoral canal is associated with geometric measures of the proximal femur such as femoral offset, version or neck-shaft angle.

The hypothesis of the present study was that distinct patterns of canal shape and joint geometry can be identified which allow a comprehensive classification of femoral morphology in primary hip OA. The current study aims were (I) to investigate the variation in proximal femoral anatomy and (II) to determine specific associations of proximal femoral canal shape and underlying joint geometry in a cohort of patients with primary, end-stage hip OA.

Materials and Methods

Study Cohort

For the present retrospective cohort study, we reviewed a consecutive series of 597 patients who had undergone primary THA for end-stage hip osteoarthritis (OA) with a custom-made cementless femoral component between June 2008 and December 2009(9). Each patient received standardised radiographs and a CT scan of the affected hip preoperatively, and all images were retrieved in generic DICOM format.

In order to obtain normative values for the variation in femoral shape and geometry, we only included patients with primary hip osteoarthritis. Patients with a history of trauma, infection, rheumatic disease, developmental dysplasia of the hip (DDH), previous pelvic and/or femoral osteotomy, avascular necrosis (AVN) of the femoral head, Legg–Calvé–Perthes disease, or symptomatic slipped capital femoral epiphysis were excluded from the present study. To quantitatively identify patients with acetabular undercoverage, radiographic exclusion criteria were defined as a center-edge angle < 20 degrees(10), an acetabular angle > 42 degrees(11) and an acetabular index < 38(12). When THA was performed bilaterally during the study period, we only included the side of the first procedure.

According to the criteria stated above, 252 patients were excluded from the initial cohort, leaving 345 patients (146 males, 199 females, mean age 60 (range: 40-79) years, mean body- mass- index (BMI) 27 (range: 19-57) kg/m², Table 1) that were included in the present study. The study was approved by the institutional review board (reference S-272/2009).

Imaging Protocols

For all patients, low-centered AP hip radiographs were obtained in a supine position according to a standardised protocol in order to achieve a reproducible radiographic projection. To correct for effects of magnification, a metal calibration sphere of 25 mm diameter was positioned on the inner thigh at the anterior-posterior level of the femoral head.

The crosshair of the beam was directed to the midpoint between the anterior superior iliac spine and the symphysis in order to centre the beam on the centre of the femoral head of the diseased hip. In order to position the femoral neck in the coronal plane, the affected leg was internally rotated and retained so that the greatest prominence of the greater trochanter was palpated at its most lateral position. When internal rotation of the leg was not sufficient due to external rotation contracture, the affected hip was additionally elevated on the AP hip view using a wedge. During the study period, two x-ray tubes were in use: Canon CXDI series [Canon Inc., Tokyo, Japan] and Philips Bucky Diagnost VE VT [Royal Philips Electronics Inc., Amsterdam, Netherlands]. The tube-to-film distance was 1150 mm, with the tube orientation perpendicular to the table.

For all CT scans, patients were positioned supine, with legs retained in neutral rotation as shown by scout views. The scans were obtained in three sets: from the cranial aspect of the acetabulum to below the lesser trochanter, from below the lesser trochanter to 50 mm distal to the femoral isthmus and 4 slices of the femoral condyles. **Slice spacing of 4 mm, 8 mm and 2 mm was used, respectively. Slice thickness was 2 mm. All hip CT scans were performed using a Toshiba Aquilion 16 CT scanner [Toshiba Corp., Tokyo, Japan] with gantry tilt 0°, 120 kV, 436 mAs and a field of view (FOV) of 250 mm.**

Radiographic Measurements

A previously validated custom MATLAB program [version 7.10, The MathWorks Inc., MA, USA] was used to determine the centre of the femoral head, the head diameter (HD), the femoral shaft axis, and the femoral neck axis (FNA) on AP hip radiographs. Details of the measurement protocol have been previously reported(9). In brief, the neck-shaft-angle (NSA) was calculated as the angle between the femoral shaft axis and the femoral neck axis. FO was calculated as the perpendicular distance from the centre of the femoral head to the femoral shaft axis.

To quantify differences in shape between clusters, we calculated the radiographic canal flare index (CFI) as described by Noble(2), and performed separate calculations of the medial cortical flare (CFI_{med}) and the lateral cortical flare (CFI_{lat}) with reference to the femoral shaft axis, respectively. The canal-to-calcar ratio (CCR) and the cortical thickness index (CTI) were determined as described by Dorr(13). For comparison of the medial and lateral cortical flare with regard to gender and cluster membership, points on the endosteal surface were depicted as scatter plots (x: femoral shaft axis (FSA), y: perpendicular distance from FSA). Endosteal dimensions and point locations were derived from the ASM template perpendicular to the femoral shaft axis and scaled with reference to the calibration marker. We performed a least squares curve fit to quantify variation and differences in canal flare (Figure 4).

CT Measurements

In addition to the 2-D measurements, a validated MATLAB programme was used to measure femoral offset and femoral anteversion on the corresponding CT data. The program enabled the user to select points from pre-selected axial CT slices (s1-s5) and performed calculations in the 3-D co-ordinate system of the CT scanner(9) (Figure 2).

For the 3-D calculation of FO (FO_{CT}) and head diameter (HD_{CT}), three axial slices were selected (s1, s3, s4). HD_{CT} and the centre of the femoral head were determined on the slice with the femoral head at its largest diameter (s1) using a least squares circle fit tool. The femoral shaft axis was defined by the centroid(14; 15) (s3) and the centre of the isthmus (s4); FO_{CT} was then calculated as the perpendicular distance from the femoral shaft axis to the centre of the femoral head.

For the calculation of femoral anteversion (FA_{CT}), two axial slices were selected (s2, s5). On s2, the femoral neck axis was defined using the single slice method according to Sugano(16), and on s5 the posterior condylar axis was defined by the most

posterior aspects of the lateral and medial condyles. FA_{CT} was calculated as angle between the femoral neck axis and the posterior condylar axis.

Active Shape Modelling

The present study used Active Shape Modelling (ASM), a statistical method to represent shape, to describe the variation in shape of the proximal femoral canal in the present cohort. The model was built using the freely available ASM tool kit (Manchester University, Manchester, UK)(17; 18). To define the shape of the proximal femoral canal, the ASM template used in this study contained 33 points from a 67-point model of the proximal femur (Figure 1). Key points were placed at easily identifiable features of the endosteal cortices (e.g. at the femoral isthmus, the lesser trochanter, the head neck junction), while the remaining points were spaced approximately evenly between these features. Each key point was placed on the same feature on corresponding images to allow comparison between shapes and to perform point-based measurements. **The ASM Model was initially built and trained on a subset of AP pelvis views of randomly selected hips (n=50) of the present cohort. We performed semi-automated point-based measurements using the ASM model to facilitate determination of the endosteal shape of the proximal femur. On each radiograph, the model was applied and the fit of points on the endosteal surface was visually checked and manually improved thereafter so that all key points were placed in the exact location on the endosteal surface and that all other points were evenly spaced between key points.**

ASM works by calculating the distances of an individual set of landmark points that define the outline of an object of interest from the mean position of equivalent points in a set of images. Procrustes analysis(18) is performed to align all objects as closely as possible to ensure that differences in point placement are genuinely due to variation in shape, rather than in size, position or rotation of the object. Thereafter, principal component analysis (PCA)(18), a dimension reduction technique, is used to generate modes of variation that describe the variation of shape in the given dataset. In ASM, shape is described by a series of orthogonal modes of variation, so each mode is an independent descriptor of shape. For each mode in the model, the mean and SD values for the entire dataset were calculated, and the mean value of each mode was scaled to zero. Mode scores for each radiograph were calculated and expressed how many standard deviations it lay from the mean value (zero) of that mode.

Cluster Analysis

Agglomerative hierarchical cluster analysis (Ward's method) of the mode scores (1-10) derived from ASM was performed to identify natural groupings of patients based on femoral canal shape(19). This approach defines the proximity between two clusters by the increase in the sum of the squared error that would result when two clusters are merged and attempts to minimise the sum of the squared Euclidean distance from each mode score to its cluster centroid in an n-dimensional space. The number of clusters that allowed the best separation of clusters was determined according to the Duda and Hart index(20).

Measurement reliability

Intra- and inter-observer reliabilities for 15 randomly selected corresponding radiographs and CT scans were evaluated by two independent and blinded observers using single-measure intra-class-correlation coefficients (ICC) with a two-way-random effects model for absolute agreement. For placement of keypoints on the ASM template, the mean error was determined for 2 independent observers.

Statistical analysis

For descriptive analysis, absolute mean values and differences were expressed in mm or degrees (°) with standard deviations (SD). Differences between males and females and between clusters were expressed as mean values with 95% confidence intervals (95%CI).

The distributions of all variables were examined in an exploratory data analysis, and tested for normality using Kolmogorov-Smirnov tests. As not all variables met the criteria for a normal distribution, we used non-parametric tests. Differences between males and females were compared using Mann–Whitney U tests for unpaired observations. Differences in morphologic measures of the proximal femur and demographic parameters between the clusters were evaluated using Kruskal-Wallis or Chi-square tests, as appropriate. Spearman's correlation (r) was used to evaluate associations between continuous variables. Correlation was characterised as poor (0.00-0.20), fair (0.21-0.40), moderate (0.41-0.60) good (0.61-0.80), or excellent (0.81-1.00)(21).

Coefficients of curve fits ($f(x) = ax^b+c$) were calculated with 95% confidence intervals (95%CI). The goodness of curve fit was determined using R^2 values.

Results with *P* values <0.05 were considered as significant, *P* values of <0.001 were considered as highly significant. Statistical analysis was carried out using PASW Statistics 18 [SPSS Inc. an IBM company, IL, USA], STATA 11 (Stata Corp LP, TX, USA and MATLAB [version 7.10, The MathWorks Inc., MA, USA].

Results

Measurement reliability

Intra-observer ICC was excellent and ranged from 0.80-0.99 for all measured parameters. Inter-observer ICC also showed good correlation for NSA (0.75) and excellent correlation for all other parameters (ICC range: 0.81-0.99).

The mean error for placement of keypoints on the radiographic ASM template was <1 mm for both intra- and inter-observer measurements.

Radiographic and CT measurements

FO was significantly higher in male (47.6 mm, SD: 6.3 mm) than in female patients (41.6 mm, SD: 6.3 mm, $p<0.001$). In the entire cohort, there was no significant difference between mean FO_{CT} (44.6 mm, SD: 5.6 mm) and FO on radiographs (44.1 mm, SD: 7.0 mm, $p=0.09$, Table 1). FO_{CT} and FO as measured on radiographs demonstrated a good correlation ($r_s=0.75$, $p<0.001$) indicating that the present radiographic protocol allows accurate assessment of FO.

Mean NSA was 125° for both males (SD: 5.6°) and females (SD: 6.3°, $p=0.69$). Females had a slightly higher femoral anteversion (FA: 15°, SD 10.5°) than males (FA: 13°, SD 8.3°), however, this finding was not statistically significant ($p=0.35$, Table 1).

The CFI of the medial cortex (4.45, SD: 0.54) was significantly higher than the CFI of the lateral cortex (3.50, SD: 0.51, $p<0.001$). **No significant differences in radiographic canal flare parameters (CFI, CFI_{med}, CFI_{lat}, CCR, CTI) were observed between males and females (Table 1). No significant correlations between radiographic canal flare parameters (CFI, CFI_{med}, CFI_{lat}, CCR, CTI) and measures of size (HD, height, weight, BMI) or patient age were observed.**

ASM

Principal component analysis was used as an integrated part of the applied model and has been previously shown to be an effective approach to reduce the dimensionality of the data that form a cloud in a multidimensional space(22). Applying PCA to the dataset reduced the number of parameters to 10 shape modes. In the present model, the first 10 independent shape modes accounted for 96% of the overall variation in proximal femoral canal shape within the dataset.

Modes 2, 3 and 4 depicted the variation in cortical flare which has been previously characterised as stove pipe vs. champagne flute shape(13) (Figure 3). **Distributions of mode scores between males and females were significantly different for mode 2 ($p<0.001$). Mode 3 showed a moderate correlation with FO ($r_s=0.48$, $p<0.001$), and a fair inverse correlation with NSA ($r_s=-0.38$, $p<0.001$); similarly, mode 4 showed a moderate correlation with NSA ($r_s=-0.49$, $p<0.001$) and a fair correlation with FO ($r_s=0.28$, $p<0.001$). No significant correlations between shape modes and measures of size (HD, height, weight, BMI) were observed.**

Cluster Analysis

Cluster Analysis identified 10 distinct clusters of shapes (Table 2 A and B) for which all 10 shape modes demonstrated a significantly different distribution ($p<0.001$). We observed significant differences in gender, BMI, HD, NSA, FO, $FO_{CT,}$ and FA_{CT} between the clusters (Table 2). Similarly, CFI and CCR were significantly different between clusters. No significant differences with regard to patient age were seen.

Both medial and lateral cortical flares were considerably different in each cluster (Table 3, Figure 4). The derived least squares curve fits showed that the variation in flare was greater for the medial femoral cortex than for the lateral cortex. Least squares curve fits demostrated a high goodness of fit ($R^2>0.85$); details and equation coefficients for each cluster are reported in the supplementary material (Supplement 1).

Discussion

Unlike cemented femoral hip replacement, in which a geometric mismatch between the femoral component and the medullary canal of the proximal femur is required for a sufficient cement mantle, cementless femoral reconstruction aims for a close geometric fit between the implant and the endosteal surface of the proximal femur(4; 23). Primary stability is achieved by press-fit implantation(24) and is essential for osteointegration of the implant(25; 26). Previous studies have demonstrated that close metaphyseal stem fit reduces micromotion at the implant-bone interface(4; 5), and minimises stress-shielding(27; 28). An increased risk of aseptic loosening has been reported for undersized femoral components(29) and there is still a concern that progressive periprosthetic bone loss may compromise long-term stem performance(30). This is particularly important with regard to a rising number of THAs performed in young and active patients(31).

Besides endosteal stem fit, the clinical outcome following THA is closely related to the restoration of physiologic joint mechanics. There is substantial evidence that accurate restoration of femoral offset and soft tissue tension reduce risk for post-operative complications such as impingement, dislocation or wear failure(32-35). Moreover, it is well accepted that the restoration of joint geometry provides patients with a better functional outcome in terms of improved abductor muscle strength(36; 37) and greater range of motion(32; 36; 38).

The present study describes the variation in proximal femoral anatomy in patients with primary end-stage hip osteoarthritis and has identified an association of proximal femoral canal shape and joint geometry.

We found that the native anatomy of the primary arthritic proximal femur is highly variable, which confirms previous findings of non-arthritic femora(1; 2). However, cluster analysis identified 10 shape clusters which were associated with significant differences in gender, BMI, and geometric parameters (NSA, FO, $FO_{CT,}$ and FA). This finding highlights the association of shape and geometry. Our analysis conclusively shows that distinct patterns of femoral canal shape exist and that each pattern is associated with a specific set of geometric parameters. Moreover the distribution of gender and BMI was significantly different between clusters, although we did not detect a significant difference in the distribution of NSA and FA and radiographic measures of cortical flare (CCR, CFI) between genders in the entire cohort. This may be attributed to the strict exclusion criteria we adopted that excluded all secondary forms of OA. **Table 3 provides a brief description of each cluster to highlight the most critical properties with regard to A) femoral canal shape, B) proximal femoral geometry and C) demographic parameters to facilitate interpretation of the data.**

The mean values for FO, NSA, FA and CFI in the present cohort compare well to reported values in the literature(1; 2; 39). Similarly, the observed lack of correlation between measures of size (HD, height) and shape (mode scores) is consistent with previous findings(2).

To our knowledge, the observed association between shape and geometry of the internal structure of the proximal femur has not been previously described and the present findings suggest that the native internal femoral anatomy of patients with primary OA may be different from those of healthy individuals(40).

We acknowledge the following limitations of this study:

Firstly, the present study comprised patients with primary end-stage hip OA. **In the present cohort, our definition of primary OA did neither exclude the presence of mild acetabular over- (i.e. coxa profunda) or undercoverage (i.e. mild dysplasia) nor cases of hip OA related to cam- or pincer-type impingement syndromes. Due to the retrospective nature of this study, mild morphological alterations of the acetabulum or head–neck junction as possible risk factors for OA(41) were not assessed, as these changes are frequently subtle and cannot not be reliably identified in the present cohort with end-stage OA .** Care should be taken to apply the present findings to all patients who undergo THA, as the variation in patients with secondary forms of OA, such as dysplasia or other deformity, might be even greater. However, the present cohort can be considered as representative and findings should be put into perspective as the leading diagnosis for THA is primary OA(42).

Secondly, we only assessed the shape of the proximal femur in the frontal plane and did not address the anterior-posterior bowing of the femur. However, preoperative templating of implant size and position is performed on AP radiographs as the design of most femoral components aims for endosteal fit in the frontal plane. **We have previously shown that the present radiographic protocol for AP hip views allows accurate 2D assessment of proximal femoral geometry(43). Additionally, the reported agreement between radiographic and CT-based FO values in the present cohort confirms this finding(9).**

Lastly, there are numerous clustering approaches and measures for the quality of clustering, and each approach may lead to different answers to the question of how many different shapes of the proximal femur exist. In the preliminary analysis of the data, we have evaluated different clustering approaches with varying cluster centers demonstrating that the chosen clustering method (hierarchical clustering, Ward´s method) allows best separation of shape differences as represented by conventional radiographic measures, i.e. CFI, CCR, CTI. We have also performed the clustering several times on randomly selected subsets of the present patient cohort, and for males and females separately. Interestingly, according to the measures of cluster quality (i.e. Duda and Hart Indices), the best separation was seen when 8-10 clusters were present in all trails, with 10 clusters showing the best separation as presented.

The present study used active shape modelling (ASM) to assess the overall variation of the proximal femoral canal shape on AP hip radiographs. This method enables measurement of the variation in a complex shape, such as the hip. In ASM, a mode does not just capture one aspect of variation in femoral canal shape, it is a combination of evident and/or subtle differences between femurs and identifies features that vary together in a coordinated fashion (44). Although this may make it difficult to visualize what aspect of shape variation each mode represents, this method is powerful and able to detect differences that are not necessarily evident with conventional radiographic measures (e.g. angles, distances or canal flare indices) that are often strongly correlated (18).

This study does not intend to emphasize absolute measurement values, its primary aim was to describe the variation in proximal femoral anatomy.

We observed that the greatest variation in the shape of the medullary canal occurred in the femoral metaphysis, and specifically in the medial cortical flare. When aiming for proximal load transfer, the femoral component fit has to be selected with regard to the shape of the proximal femoral metaphysis(4; 5). However, previous studies have demonstrated that proximal loading cannot be entirely achieved with the use of current stem designs that aim for a proximal intertrochanteric fixation and that fixation is more likely to occur in the meta-diaphyseal region(45).

To allow independent adjustment of stem fixation and reconstruction of geometry, modular hip stems have gained growing popularity(7; 46). However, concerns have been raised that - as with any metal-on-metal modular junction - there is an increased risk for fretting corrosion, concomitant metal ion release or implant failure(47; 48). In summary, the issue of identifying the optimal femoral component has not yet been resolved. **The question that arises from the present data is what the minimum number of different stem designs is that are needed to accommodate all shapes with a high accuracy of stem fit. This study suggests that one stem design might not be sufficient to allow high accuracy of fit and concomitant restoration of joint geometry in all patients of the present cohort. To answer the question of how many different stems we really need one would need a better understanding of how much distance between the stem and the endosteal surface of the proximal femur at different levels can be considered as "good" or even "perfect" fit. In addition, a simulation of fit and reconstructive potential for different existing stem designs is desirable. To our knowledge, there is very limited data on**

this issue in the literature but a sound answer to this question is beyond the scope of this study. However, the present identification of distinct shape clusters and the association between canal shape and hip joint geometry is clinically relevant for the development of future femoral component designs that aim to account for optimal stem fit and concomitant reconstruction of individual hip geometry.

The present study illustrates that active shape modelling and subsequent cluster analysis have the potential to identify specific patterns of proximal femoral shape and geometry despite the variability in proximal femoral anatomy. Understanding of variation and association of geometry and shape of the proximal femur is essential both for surgeons and for implant manufacturers in order to achieve the goals of accurate stem fit and restoration of individual joint mechanics.

In conclusion, the design of the femoral component should take into account both the variation in shape and its association with geometric parameters.

Our findings highlight the great variability in native proximal femoral anatomy in patients with primary hip OA and support the use of implant systems that enable independent adjustment of stem fit and reconstruction of joint geometry. We have identified 10 different types of femora in patients with primary OA, and the present data allow a comprehensive classification of variation in proximal femoral shape and geometry. This may improve future designs of femoral components that will optimise stem fit and simultaneously allow individual restoration of physiological biomechanics of the hip, regardless of individual anatomic variations.

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