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Variability of the femoral mechanical-anatomical axis angle and its implications in primary and revision total knee arthroplasty

An analysis of 2,156 knees using a deep learning tool

Cite this article:
Bone Jt Open 2024;5(2):
101–108.

DOI: 10.1302/2633-1462.
52.BJO-2023-0056.R1

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Aims
Distal femoral resection in conventional total knee arthroplasty (TKA) utilizes an intramedullary guide to determine coronal alignment, commonly planned for 5° of valgus. However, a standard 5° resection angle may contribute to malalignment in patients with variability in the femoral anatomical and mechanical axis angle. The purpose of the study was to leverage deep learning (DL) to measure the femoral mechanical-anatomical axis angle (FMAA) in a heterogeneous cohort.

Methods
Patients with full-limb radiographs from the Osteoarthritis Initiative were included. A DL workflow was created to measure the FMAA and validated against human measurements. To reflect potential intramedullary guide placement during manual TKA, two different FMAAs were calculated either using a line approximating the entire diaphyseal shaft, and a line connecting the apex of the femoral intercondylar sulcus to the centre of the diaphysis. The proportion of FMAAs outside a range of 5.0° (SD 2.0°) was calculated for both definitions, and FMAA was compared using univariate analyses across sex, BMI, knee alignment, and femur length.

Results
The algorithm measured 1,078 radiographs at a rate of 12.6 s/image (2,156 unique measurements in 3.8 hours). There was no significant difference or bias between reader and algorithm measurements for the FMAA ($p = 0.130$ to 0.563). The FMAA was 6.3° (SD 1.0°; 25% outside range of 5.0° (SD 2.0°)) using definition one and 4.6° (SD 1.3°; 13% outside range of 5.0° (SD 2.0°)) using definition two. Differences between males and females were observed using definition two (males more valgus; $p < 0.001$).

Conclusion
We developed a rapid and accurate DL tool to quantify the FMAA. Considerable variation with different measurement approaches for the FMAA supports that patient-specific anatomy and surgeon-dependent technique must be accounted for when correcting for the FMAA using an intramedullary guide. The angle between the mechanical and anatomical axes of the femur fell outside the range of 5.0° (SD 2.0°) for nearly a quarter of patients.

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Take home message

- A standard 5° resection angle may be sub-optimal for certain patients undergoing manual total knee arthroplasty (TKA) with almost a fourth of patients falling outside 2° of error.
- Both the surgical approach and patient-specific alignment must be considered to minimize error in defining the distal femoral resection during manual TKA.

Introduction

Coronal mechanical axis restoration within a neutral alignment is sought during mechanical alignment total knee arthroplasty (TKA). This accurate coronal plane alignment is associated with long-term prosthesis survival, improved lower limb function, and improved patient reported outcomes after TKA. Malalignment results in excessive mechanical and shear forces across the bearing surfaces and component-osseous interfaces, which may jeopardize implant longevity through accelerated polyethylene wear, aseptic component loosening, or catastrophic failure.[1-4] Therefore, TKA is performed with attention to coronal plane alignment during preoperative planning and intraoperative technique to ensure its proper restoration.

An intramedullary (IM) alignment guide is used in conventional TKA for the distal femoral resection as it allows surgeons to adjust resection angularity based on the femoral joint line, although IM alignment guides can introduce error and result in femoral component malalignment.[5] While 5° for the femoral mechanical-anatomical axis angle (FMAA), or valgus correction angle, is often assumed for all patients,[6,7] recent literature demonstrates variability in the relationship between the mechanical and anatomical axes of the femur.[8-10] Authors report average FMAA values ranging from 7.3° (standard deviation (SD) 1.6°) in patients with varus osteoarthritis to 5.7° (SD 2.3°) in patients with both varus and valgus osteoarthritis.[8] [8,9] Up to 19% of patients in these cohorts had FMAAs greater than 9°,[8] ranging up to 16° in valgus.[9] Furthermore, up to 29% of patients have been reported to have FMAA values outside the range of 5° (SD 2°; range 2.0° to 9.6°).[10] A meta-analysis that examined TKA outcomes following procedures performed using conventional methods versus computer-assisted surgery (CAS) found that there was mechanical axis malalignment greater than 3° in 32% and 9% of patients, respectively.[11] Although CAS is a step toward reduction in error, it can be associated with more cost and a learning curve.[11,12]

The mechanical axis of the femur is reliably defined as a line connecting the centre of the femoral head to the apex of the intercondylar notch. However, some studies define the femoral anatomical axis as a line connecting the midpoint of the femur at a proximal and distal portion to approximate the diaphysis,[10,13] whereas other studies define the anatomical axis via a line connecting the midpoint of the femur at 50% of the femoral length to the apex of the intercondylar sulcus of the distal femur.[8,9]

Thus, differences exist in how the FMAA is defned. It is critical to develop methods to objectively measure the FMAA to reduce variability across measurers and institutions, and to accurately restore coronal plane alignment. Moreso, this is imperative to ensure appropriate alignment and targets for individuals undergoing TKA.

Given the differences in FMAA measurement methods in the current literature and in patient anatomy, the purpose of the current study was to leverage a validated deep learning (DL) algorithm to measure the FMAA in a large, heterogeneous patient cohort. The authors hypothesized that there would exist substantial variability in the FMAA across patients and that utilizing different definitions would yield significantly different measurements.

Methods

Patient and image selection

Patient radiographs were acquired from the Osteoarthritis Initiative (OAI), a public online database for studying knee osteoarthritis in a large population. Patients were enrolled from 2004 to 2015, and Institutional Review Board (IRB) approval was obtained at each institution involved in the database creation. IRB review was exempt from the authors' institution as this study was a secondary analysis of de-identified data. Inclusion criterion was any patient who had a full-limb radiograph available at the 12-month annual visit after enrolment. Patients with extra-articular deformities or pre-existing knee or hip implants were excluded from the analysis (Figure 1).

Femoral mechanical-anatomical axis angle

The femoral mechanical-anatomical axis angle (FMAA) was measured as the angle between the femoral mechanical and anatomical axes. The femoral mechanical and anatomical axes have been previously described.[10] The femoral mechanical axis was defined as a line from the femoral head centre to the most proximal and central point of the intercondylar sulcus of the distal femur.[10] To reflect potential intramedullary guide placement during manual primary and revision TKA, the anatomical axis of the femur was defined in two different ways based on literature (Figure 2).[9,10]

The femoral anatomical axis was defined as the defined as the line connecting the midpoint of the femoral diaphysis at 25% and 75% of the femur from the lesser trochanter to the femoral condyles, thus approximating the diaphyseal shaft. The distal femoral anatomical axis was defined as the tine connecting the midpoint of the femur at 50% of the femoral length and the most proximal and central point of the intercondylar sulcus of the distal femur.

These two definitions resulted in the FMAA, and the distal FMAA (dFMAA). The FMAA canal entry point is more medial, similar to the entry point in primary TKA. The dFMAA more closely represents the femoral distal cut angle achieved with manual instrumentation during revision TKA with a central entry point and when the mid-diaphysis is tightly engaged with an IM reamer and often a press-fit stem.

Deep learning automated measurements: U-Nets

A DL workflow with a U-Net, a form of convolutional neural network, was created to automate the measurements of the FMAA on patient radiographs. U-Nets are DL neural network models capable of taking image inputs and classifying each pixel as belonging to an object. U-Nets can be trained to achieve high accuracy in this computer vision task with smaller training data.[14] They have been used in various orthopaedic studies for the measurement of arthroplasty-relevant parameters including acetabular component inclination

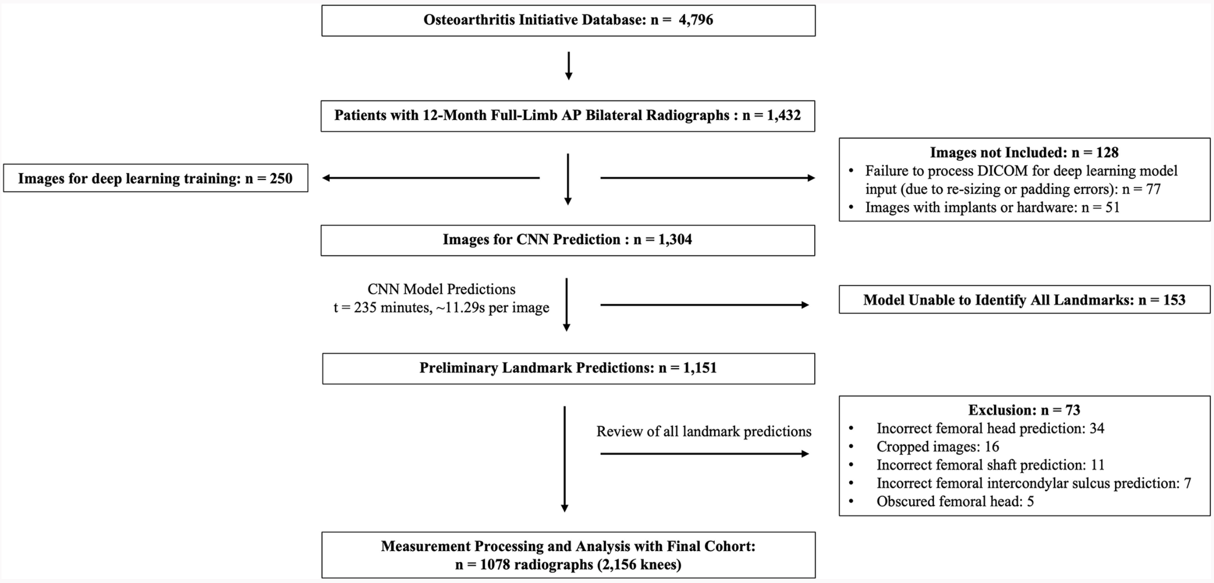

Fig. 1

Patient selection.

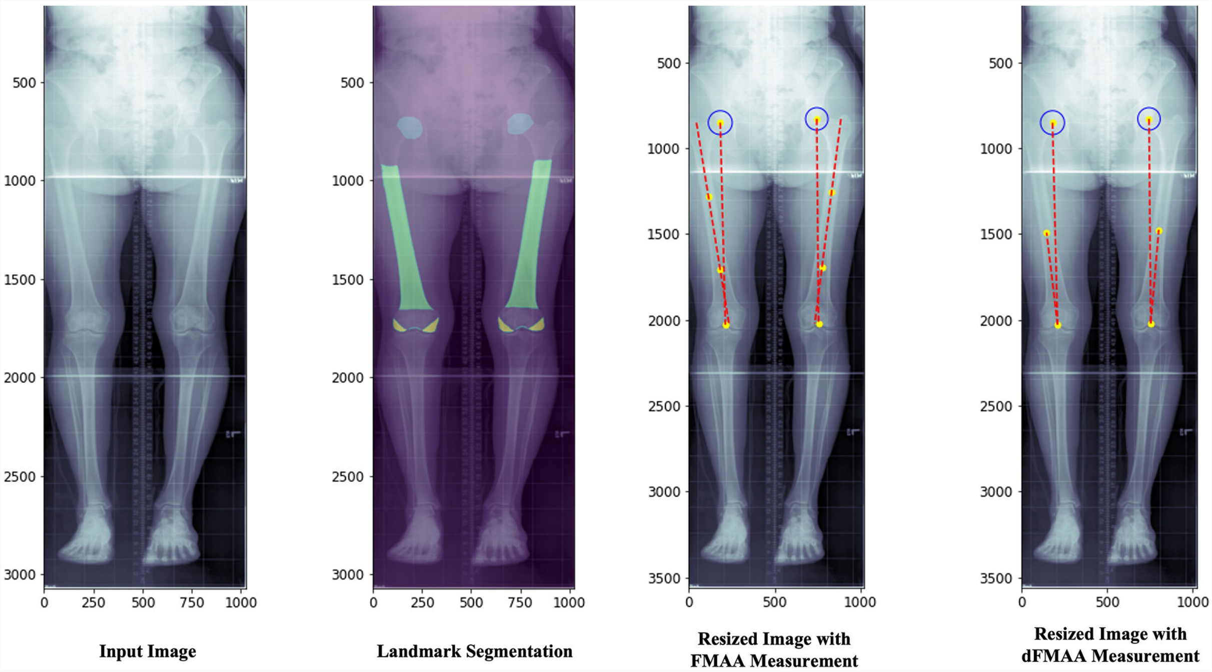

Fig. 2

Femoral mechanical-anatomical axis angle definitions.

and version or hip joint centre.[15,16] In this study, we used a U-Net to identify bony landmarks necessary to measure the FMAA and dFMAA, including the femoral head, femoral shaft, femoral condyles, and intercondylar sulcus.

All training and validation data were manually annotated to establish ground truths. After model training, the algorithm was deployed on the entire cohort of radiographs to predict bony landmarks on each image. Each image was further processed to measure the FMAA and dFMAA for both limbs. For algorithm training and segmentation performance, see the Supplementary figures a and b.

Ground truth measurements

To ensure the accuracy of the DL-produced measurements, the FMAA and dFMAA were compared against that of two trained readers (SJJ, JRS), including an adult reconstruction fellowship-trained orthopaedic surgeon (JRS). A power analysis with 0.80 power and an α of 0.05 for a clinically relevant difference of 1° indicated a sample size of 39 measurements for the FMAA and dFMAA. The two trained readers measured the FMAA and dFMAA on 60 knees in an independent testing sample separate from model creation. The readers were blinded to the algorithm-produced measurements.

Statistical analysis

All images were reviewed to ensure accurate landmark prediction by the DL algorithm to produce the FMAA and dFMAA. The FMAA and dFMAA measurements were first compared between the two readers to establish an accurate ground truth using the interclass coefficient (ICC). Then, the measurements produced by the DL algorithm were compared against human readers using a Bland-Altman plot analysis to assess for bias, and an independent *t*-test to determine significant differences. The absolute mean difference and the root mean square error were also calculated. All measurements were first tested for normality using the Shapiro-Wilk test.

After validation of the DL model, the DL produced FMAA and dFMAA were compared in the entire population cohort. Pearson's R correlation analyses were conducted to determine if age, BMI, femur length, or the hip-knee-ankle angle (i.e. knee alignment, positive as valgus, negative as varus) correlated to measured parameters. Independent *t*-tests were conducted to determine differences in measurements based on patient-reported sex, and chi-squared tests were conducted to determine differences in number of outliers outside of 3° and 7°. DL models were trained and optimized using the fast.ai library (V2.3.0).[17] All statistical analyses were conducted on a Jupyter notebook (Python).

Results

A total of 1,078 radiographs (2,156 knees) were included for final analysis. Of the included radiographs, 53% were from female patients. The mean age was 61.4 years (SD 9.1; range 46 to 80). The DL algorithm calculated measurements for all 1,078 knees at a rate of 12.6 seconds per image (3.8 hours; 4,312 unique FMAA and dFMAA measurements (Figure 1)).

Deep learning comparison against surgeon measurements

On an independent cohort of 60 knees, the accuracy of the DL algorithm is depicted in Table I. The ICC between the two readers were 0.88 to 0.94 with no significant difference in either FMAA measurements ($p = 0.209$ to 0.762, independent *t*-test). For the FMAA, the absolute mean paired difference between the DL algorithm and reader's average (ground truth) was 0.5° (SD 0.4°) with a root mean square error (RMSE) of 0.61 and ICC of 0.84 (95% confidence interval (CI) 0.74 to 0.90). For the dFMAA, the mean paired difference was 0.5° (SD 0.4°) with an RMSE of 0.64 and ICC of 0.89 (95% CI 0.82 to 0.93). There was no significant difference between the DL algorithm or the reader measurements for either the FMAA ($p = 0.563$, independent *t*-test) or dFMAA ($p = 0.130$, independent *t*-test). Bland-Altman analyses for measurement bias of the model against both readers and their means are depicted in Figure 3.

Femoral mechanical-anatomical axis angle (FMAA)

Using definition one for the anatomical axis, the FMAA was 6.3° (SD 1.0°; range 2.3° to 12.4°) in the full cohort of 2,156 knees. In this cohort, 25% of knees were outside the range of 5.0° *(*SD 2.0°*)*. For males, the FMAA was 6.3° (SD 1.0°; range 2.4° to 12.4°, 25% outside 3° and 7°), and for females, the FMAA was 6.3° (SD 1.0°; range 2.3° to 10.0°, 25% outside 3° and 7°). (Figure 4). There was no significant difference in FMAA or proportion of outliers outside 3° and 7° based on sex, and there was no correlation ($r < 0.3$) between FMAA and age, BMI, femur length, or knee alignment (hip-knee-ankle angle).

Distal femoral mechanical-anatomical axis angle (dFMAA)

Using definition two for the anatomical axis, the dFMAA was 4.6° (SD 1.3°; range 0.4° to 11.9°) in the full cohort of 2,156 knees. In this cohort, 13% of knees were outside the range of 3° and 7°. For males, the dFMAA was 4.8° (SD 1.2°; range 0.8° to 10.8°, 11% outside 3° and 7°) and for females, the dFMAA was 4.4° (SD 1.3°; range 0.4°–11.9°, 15% outside 3° and 7°) (Figure 5). Males had greater (more valgus) dFMAAs ($p < 0.001$, independent *t*-test) compared to females and had fewer outliers outside 3° and 7° ($p = 0.042$, chi-squared test). The dFMAA was weakly correlated with the hip-knee-ankle angle ($r = -0.33$; $p < 0.001$) (i.e. more valgus dFMAA with more varus knees). There was no correlation ($-0.3 < r < 0.3$) between dFMAA and age, BMI, or femur length. When considering a target correction angle of 6°, 39% of female knees were outside 4° and 8° compared to 25% of male knees.

dFMAA vs FMAA

The mean difference between the FMAA and dFMAA was 1.7° (SD 1.2°; range 0.9° to 7.7°), indicating that the FMAA approximates a greater distal resection valgus angle than the dFMAA (Figure 6). Differences were greater in females (1.8° (SD 1.2°)) than males (1.5° (SD 1.2°)) ($p < 0.001$, independent *t*-test). There was no correlation ($-0.3 < r < 0.3$) between the difference and age, BMI, femur length, or knee alignment.

Discussion

The principle findings of the current study were as follows: 1) a DL algorithm was developed to accurately and objectively measure the angle between the mechanical and anatomical axes of the femur at a rate of 12.6 seconds per image with fellowship-trained orthopaedic surgeon-level accuracy; 2) approximately one in four patients fell outside of the acceptable range of measurement variability using the FMAA and one-in-eight for the dFMAA using a range of 5.0° (SD 2.0°); 3) statistically significant variation was observed between two commonly implicated measurement methods for finding the angle between the femoral anatomical and mechanical axes, with use of the FMAA resulting in greater valgus angulation compared with the dFMAA; and 4) the dFMAA was influenced by patient sex, with males demonstrating significantly more valgus dFMAA compared with females.

A novel DL algorithm was successfully applied to a heterogeneous patient sample to perform accurate, objective, and rapid predictions on patient images. The DL measurements were not significantly different for either FMAA definitions in this study compared to a fellowship-trained arthroplasty surgeon (JRS) in a powered sub-cohort of images. This DL algorithm withholds clinical utility to this end in that it may aide the surgical planning process and minimize subjectivity inherent in both human measurement and imaging qualities (such as rotation and image resolution). For conventional primary and revision TKA, the imaging-based algorithm in this study could provide an augmented method of patient-specific coronal alignment estimations.

In a large patient cohort, approximately 25% of patients fell outside the range of 5.0° (SD 2.0°) using the FMAA, whereas 13% of patients fell out of this range when using the

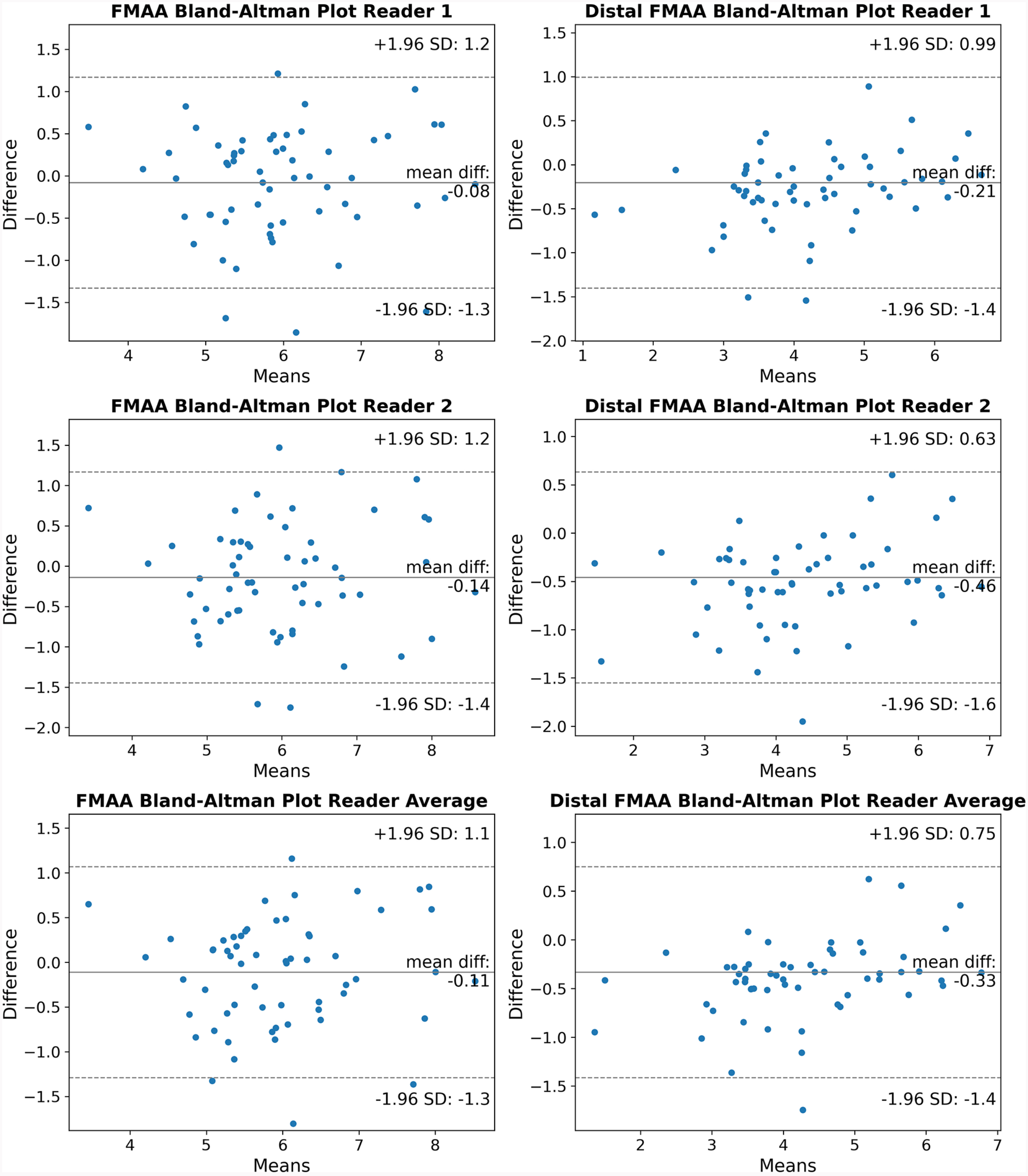

Fig. 3
Bland-altman analysis of deep learning measurements against readers.

Table I. Comparison of deep learning measurements against reader measurements.

Measurement (n = 60)	Mean DL (SD)	Mean reader 1 (SD)	Mean reader 2 (SD)	Mean reader 1/reader 2 absolute difference (range)	Reader 1/reader 2 ICC (95% CI)	Reader 1/ reader 2 p-value*	Mean DL vs reader, absolute difference (range)	Average RMSE, L vs reader	DL vs reader, average ICC (95% CI)	DL vs reader, average p-value
FMAA	5.9° (1.1°)	6.0° (1.1°)	6.1° (1.0°)	0.4° (0.0° to 1.4°)	0.88 (0.81 to 0.93)	0.762	0.5° (0.0° to 1.8°)	0.61	0.84 (0.74 to 0.90)	0.563
Distal FMAA	4.1° (1.3°)	4.4° (1.1°)	4.6° (1.1°)	0.3° (0.0° to 1.2°)	0.94 (0.90 to 0.96)	0.209	0.5° (0.2° to 2.0°)	0.64	0.89 (0.82 to 0.93)	0.130

P-values generated from t-tests
*Independent *t*-test.

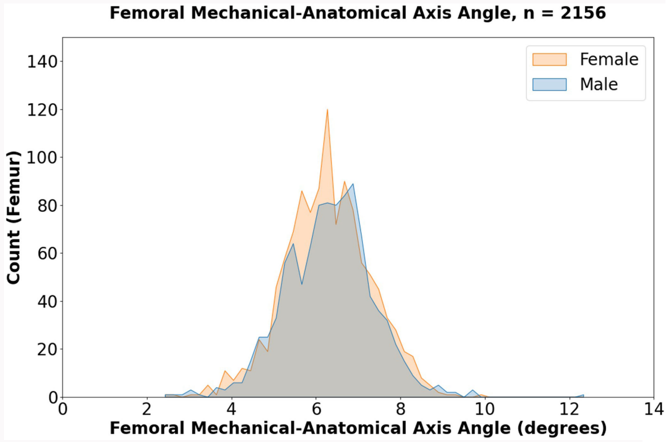

Fig. 4
Femoral mechanical-anatomical axis angle distribution in patient cohort

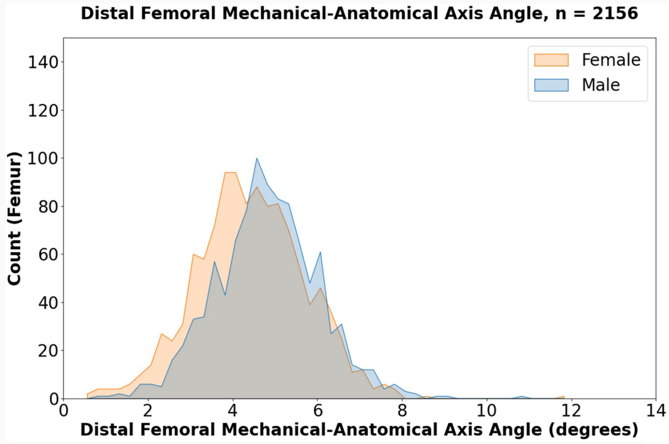

Fig. 5
Distal femoral mechanical-anatomical axis angle distribution in patient cohort.

dFMAA. Similarly, Nam et al[10] found that 29% of patients had an FMAA value outside the range of 5.0° (SD 2.0°; range 2.0° to 9.6°) when defining the anatomical axis as a line through the centre of the femoral diaphysis. Rather, a range of 6.0° (SD 2.0°), compared to 5.0° (SD 2.0°), resulted in only 8% of female and 7% of male patients to be considered outliers using the FMAA. Thus, for surgeons placing the IM rod in a manner that approximates the entire diaphyseal shaft regardless of entry point, such as in primary TKA, a fixed target angle of 6.0° may yield less error in most cases. For surgeons placing the IM rod with the central sulcus as the entry point, such as in revision TKA, a fixed target angle of 5.0° may yield less error. It is important to consider the substantial variability that exists across patients and surgeon technique as to minimize the risk of malalignment during conventional TKA, which our results support.

In line with these previous studies, the difference in the FMAA (mean 6.3° (SD 1.1°)) and dFMAA (mean 4.8° (SD 1.2°)) values in our study were solely due to how the anatomical axis of the femur was defined. The FMAA (definition one) may reflect measurements of the valgus correction angle based on placing the IM rod to approximate the entire femoral diaphysis trajectory as in primary TKA whereas the dFMAA (definition two) may reflect measurements based on only the IM rod entry point on the distal femur to the proximal end of the rod after insertion as in revision TKA. The average FMAA and dFMAA in the present study align with prior literature findings. Mullaji et al[8] used a dFMAA definition of the femoral anatomical axis and reported a mean dFMAA in healthy control patients of 5.5° (SD 0.8°). Meric et al's[9] anatomical axis of the femur approximation also resembled that of the dFMAA. In the osteoarthritic population, they reported an average dFMAA of 5.7° (SD 2.3°; range 1° to 16°) with 14% of patients as outliers. Kobayashi et al [13] defined the anatomical axis as a line through the femoral midpoints at the level of the lesser trochanter and femoral condyles (i.e., FMAA) and found mean FMAAs to be 7.3° to 7.4° for patients undergoing conventional and navigation TKA. Discrepancies in the mean FMAA value in previous studies may be attributed to differences in measurement definitions. In this study, an average coronal plane alignment discrepancy of 1.7° was observed between the FMAA and dFMAA, representing a statistically significant difference.

Though the clinical relevance of this finding remains unknown, a difference of 1.7° approximates the boundary of an acceptable amount of variation as defined in prior literature.[10] Therefore, this variability may be too high in patients whose preoperative alignment is already more valgus. Yazdi et al reported significant differences between the FMAA and dFMAA based on defining the femoral anatomical axis using the entire femur diaphysis or only the distal half of the femoral diaphysis.[18] Reed and Gollish[5] determined that the femoral anatomical axis exits the femur distally at an average of 6.6 mm medial to the centre of the femoral notch, and used a mathematical model to show that lateral deviation and medial deviation of the point of IM guide entry into the femoral canal relative to the anatomical axis exit point would result in valgus and varus femoral component malalignment, respectively. This finding aligns with our finding that the dFMAA, which exits the distal femoral canal lateral to the FMAA exit point, has a lower valgus correction angle than the FMAA. These findings emphasize the importance of accurately defining the valgus correction angles based on the entry point of the IM reamer, as using different definitions can lead to malalignment.

The angle between the femoral mechanical and anatomical axes varied based on patient sex when quantifying the dFMAA, with males demonstrating greater valgus correction angles. Deakin et al[19] report similar findings in an osteoarthritic population of more valgus values in males, although their measurements more closely resemble the FMAA definition. Using both the FMAA and dFMAA definitions to study a non-osteoarthritic population of Chinese adults, Tang et al[6] found larger dFMAA values in males than females but no difference using the FMAA, similar to our results. The FMAA measurement in our study was not influenced by patient sex or other patient-specific characteristics. This study cannot comment on the clinical implications of differences in measurement methods or sex-based differences as it pertains to implant survivorship or clinical outcomes. However, previous studies have demonstrated that using patient-specific FMAA angles to define the valgus

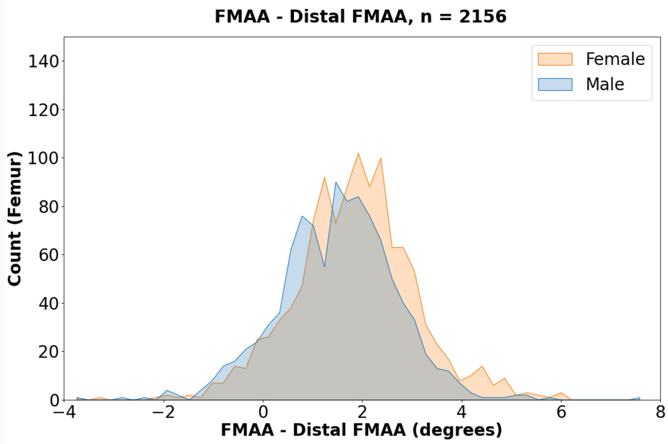

Fig. 6
Distal femoral mechanical-anatomical axis angle (FMAA) and FMAA difference (positive = more valgus FMAA).

correction angles improved the accuracy of postoperative alignment targets after TKA compared to a fixed valgus correction angle.[20] Patient-specific adjustments provide the best alignment targets and valgus correction angle for the manual TKA procedure, yet the accuracy of computer-assisted surgical techniques has been reported to be significantly higher. A meta-analysis of 29 studies that compared traditional techniques to computer-assisted found that femoral component alignment was within 2° of perpendicular to the mechanical axis 65.9% and 90.4% of the time, respectively.[11] Despite this, traditional techniques remain popular which warrants continued investigation into ways of optimizing the accuracy of manual procedures. Our findings support preoperative planning for patients with lower limb alignment deviations due to deformity or joint degeneration. Furthermore, differences in procedural technique may be considered based on variables such as sex when using the FMAA to measure coronal plane alignment. Future studies are warranted to determine if these differences correlate with clinically important metrics such as complication rates and patient-reported outcomes. Future studies could also investigate the use of postoperative DL measurement models to determine if having patient-specific preoperative alignment targets results in a more accurately aligned knee.

Limitations

This study had several limitations. First, the population of the OAI cohort represents those with or at risk of osteoarthritis at the time of enrolment. Osteoarthritis grade or assessment were not available at the one-year timepoint at which radiographs were measured. Thus, sub-analyses were not performed to determine differences in FMAA in patients with or without osteoarthritis at time of measurements. Furthermore, the relationship between the FMAA and other radiological parameters such as the neck-shaft angle and femoral offset were not investigated in the current study. Second, we acknowledge that X-rays with extra-articular deformities or previous implants or hardware may affect axis measurements and these were excluded from this study. Radiological data is also 2D in form, and future research to develop and deploy similar tools for 3D imaging, such as CT, would be beneficial. Finally, all images with incorrect landmark predictions by the DL were excluded from analysis as the purpose of this study was to compare FMAA values using different anatomical definitions. This, however, required human review of the DL tool outputs to ensure both accuracy and precision of measurements on all images.

In conclusion, using DL, we determined that up to a quarter of patients in a large cohort fall outside the range of 5.0° (SD 2.0°) for the angle between the mechanical and anatomical axes of the femur. Furthermore, using the proximal and distal portion of the femur to define the anatomical axis results in a more valgus FMAA compared to just using the distal portion of the femur. We believe that the FMAA is representative of what we achieve during primary TKA (more medial starting point in the sulcus), while the dFMAA is reflective of the revision TKA scenario with a central sulcus starting point. Regardless, a fixed valgus angle for either intramedullary primary or revision TKA systems may create clinically relevant malalignment. This tool may provide clinical value when considering preoperative planning for the estimated valgus correction angle utilizing an intramedullary guide in conventional TKA.

Supplementary material

Supplementary methods and results, and figures showing deep learning algorithm training, and excluded images for final analysis.

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Funding statement

The author(s) received no financial or material support for the research, authorship, and/or publication of this article.

ICMJE COI statement

The following authors have disclosures, all of which are unrelated to this work: S. J. Jang declares stock or stock options with Ortho.AI. S. A. Jerabek reports royalties or licenses, consulting fees, and payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational from Stryker. K. N. Kunze declares being on the editorial board of Arthroscopy. D. J. Mayman discloses royalties or licenses from Smith & Nephew, consulting fees from Stryker, and a leadership or fiduciary role for the Hip Society and the Knee Society; and stock or stock options from Cymedica, Imagen, MiCare, OrthAlign, and Wishbone. P. K. Sculco reports consulting fees for Depuy, EOS, Intellijoint, Lima, and Zimmer Biomet, payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Depuy, EOS, and Intellijoint, and stock or stock options from Intellijoint and Parvizi Surgical Innovation. J. M. Vigdorchik declares royalties or licenses from Corin and Depuy Synthes, consulting fees from Stryker, Depuy Synthes, Orchard Medical, and Intellijoint, patents (planned, issued, or pending) with Ortho AI, and a leadership or fiduciary role with the American Association of Hip and Knee Surgeons Program Committee.

Data sharing

All data generated or analyzed during this study are included in the published article and/or in the supplementary material.

Acknowledgements

Data and/or research tools used in the preparation of this manuscript were obtained and analyzed from the controlled access datasets distributed from the Osteoarthritis Initiative (OAI), a data repository housed within the NIMH Data Archive (NDA). OAI is a collaborative informatics system created by the National Institute of Mental Health and the National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) to provide a worldwide resource to quicken the pace of biomarker identification, scientific investigation and OA drug development. Dataset identifier(s): 10.15154/1524216 This manuscript was prepared using the OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners.

Ethical review statement

This study was conducted using a public online database (Osteoarthritis Initiative), which was approved by the institutional review board at the respective institutions involved in the creation of the database.

Open access funding

The authors report that they received open access funding for this manuscript from Hospital for Special Surgery, New York, New York, USA.