



High variability exists in 3D leg alignment analysis, but underlying principles that might lead to agreement on a universal framework could be identified: A systematic review

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Abstract

Purpose: To (1) investigate the hypothesis that there is high variability in the reported methods to derive axes and joint orientations from three-dimensional (3D) bone models to (a) perform 3D knee-related leg alignment analysis and (b) define coordinate systems for the femur, tibia and leg and (2) identify underlying principles that might lead to agreement on a universal 3D leg alignment analysis framework.

Methods: A systematic review of the literature between January 2006 and June 2024 was performed. Articles explicitly reporting methods to derive axes and joint orientations from CT-based 3D bone models for alignment parameters and/or coordinate systems of the femur, tibia and leg were included. Study characteristics and reported methods were extracted and presented as a qualitative synthesis.

Results: A total of 93 studies were included. There was high variability in the reported methods to derive axes and joint orientations from 3D bone models. Nevertheless, the reported methods could be categorized into four groups, and several underlying principles of the four groups could be identified. Furthermore, the definitions of femoral and tibial coordinate systems were most frequently based on the mechanical axis (femoral, 13/19 [68%]; tibial, 13/26 [50%]) and a central medial-lateral axis (femoral, 16/19 [84%]; tibial, 12/26 [46%]); no leg coordinate system was reported. Interestingly, of the included studies that reported on leg alignment parameters (76/93, 82%), only a minority reported expressing these in a complete coordinate system (25/76, 33%).

Conclusion: There is high variability in 3D knee-related leg alignment analysis. Therefore, universal 3D reference values for alignment

Abbreviations: 2D, two-dimensional; 3D, three-dimensional; CA, critical appraisal; CT, computed tomography; FCA, femoral condylar axis; ICC, intraclass correlation coefficient; ISB, International Society of Biomechanics; LOE, level of evidence; mFA, mechanical femoral axis; MRI, magnetic resonance imaging; mTA, mechanical tibial axis; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta Analyses; PTJ ML, proximal medial-lateral tibial joint orientation.

Quinten W.T. Veerman and Romy M. ten Heggeler contributed equally to this study.

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parameters cannot yet be defined, and comparison of alignment parameter values between different studies is impossible. However, several underlying principles to the reported methods were identified, which could serve to reach more agreement on a future universal 3D framework for leg alignment analysis.

Level of Evidence: Level I (1).

KEYWORDS

alignment parameters, coordinate systems, knee, osteotomy, TKA

INTRODUCTION

In recent years, both for osteotomies around the knee and total knee arthroplasty, there is an increasing interest in leg alignment analysis not only in the coronal plane but also in the sagittal and axial planes [27, 46, 89, 92, 103].

For the current gold standard two-dimensional (2D) framework for leg alignment analysis, a high degree of consensus exists on how to derive axes and joint orientations that are necessary to define joint alignment and joint orientation angles from the radiographs and torsion/version angles from the 2D computed tomography (CT) slices [65, 81]. However, the 2D framework simplifies the complex 3D shapes of bones and articular surfaces; it introduces errors due to inadequate leg and knee positioning and image distortion [38, 73, 76]; and moreover, it prevents accurate analysis of three-dimensional (3D) multiplanar deformities in their separate (not necessarily orthogonal) coronal, sagittal and axial 2D radiographic projections [93].

By contrast, through the generation of 3D bone models, 3D imaging modalities allow for a more accurate assessment of leg malalignment without further simplifications of reality [31]. It was even proposed that 'the time has come' [17] to transfer completely from a 2D to a 3D framework for malalignment analysis and correction planning of osteotomies around the knee. This indicates the need for a universal 3D framework on how to accurately and reliably derive axes and joint orientations from 3D bone models. However, since this is an emerging field of interest, and (in contrast to the 2D framework) the surface data on a 3D bone model from which to derive axes and joint orientations is abundant, it is hypothesized that consensus on such a 3D framework for leg alignment analysis is absent [22]. This lack of consensus could hinder the establishment of 3D reference values for alignment parameters, which, from a clinical point of view, would render the comparability between alignment parameter values of different studies impossible, and might lead to an inappropriate correction in osteotomy around the knee [22] or positioning of a total knee prosthesis.

Therefore, the purpose of this systematic review was to critically appraise, summarize, and compare literature on 3D frameworks for knee-related leg alignment analysis. Our aims were to (1) investigate the hypotheses that there is a high variability in the reported methods to derive axes and joint orientations from 3D bone models to (a) perform 3D knee-related leg alignment analysis and (b) define coordinate systems for the femur, tibia, and leg and (2) identify underlying principles that might lead to agreement on a universal 3D leg alignment analysis framework.

METHODS

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines were followed, and a PRISMA 2020 flow diagram was used (PROSPERO ID:[CRD42022303250]).

Search strategy

On 7 June 2024, one author (QV) performed a comprehensive literature search in the Scopus, MEDLINE/PubMed and Embase databases. Search strings were used to screen for studies that reported on methods to derive axes and/or joint orientations from 3D bone models for alignment parameters and/or coordinate systems of the femur, tibia, and leg (Supporting Information S1: Table 1). Considering the technical progress of 3D imaging techniques, the search was limited to studies published since 1 January 2006.

Inclusion and exclusion criteria

The inclusion and exclusion criteria are reported in Table 1. Only papers that used CT-based 3D models were included since this is the preferred imaging modality for segmentation purposes due to its relative homogeneous bone signal intensities [53]. Furthermore, the axes and joint orientations of alignment

TABLE 1 Inclusion and exclusion criteria applied to eligible articles.

Inclusion	<ol style="list-style-type: none"> 1) Human subjects with closed epiphysis (≥ 18 years of age); 2) Original and peer-reviewed; 3) Focused on the knee joint; 4) Investigated native and intact bone; 5) Reported their analysis on CT-based 3D bone models; 6) Reported a method to derive one or more axes or joint orientations for relevant knee-related alignment parameters, and/or 7) Reported a method to derive one or more axes that define a Cartesian coordinate system of the femur, tibia and/or leg.
Exclusion	<ol style="list-style-type: none"> 1) Languages other than English, Dutch, or German

Abbreviations: 3D, three-dimensional; CT, computed tomography.

parameters that were deemed relevant for the planning of an osteotomy around the knee [14, 82] are reported in Figure 1.

Review process

After removal of duplicates, two reviewers (QV and Rth) independently screened titles and abstracts of the identified studies for potential eligibility [80] and evaluated the full texts of studies eligible for inclusion. Disagreement on in- or exclusion was resolved by a third reviewer (RH). The references of included studies were cross-checked for in- and exclusion criteria (Table 1) independently by two authors (QV and Rth) to find studies that were not identified in the original search.

Data extraction

Two reviewers (QV and Rth) independently extracted, summarized and tabulated the study characteristics and the reported methods to derive axes or joint orientations from 3D bone models for knee-related alignment parameters and/or coordinate systems for the femur, tibia and leg and the reliability of the derived alignment parameters (if reported).

Coordinate systems were categorized as 'complete' if implicitly or explicitly a coordinate system with three orthogonal axes and an origin could be derived. Extracted data were tabulated in Excel version nr. 2203 (Microsoft Corporation).

Quality assessment

Two reviewers (QV and Rth) independently rated the level of evidence (LOE) and performed a critical appraisal (CA). The LOE and study design were rated according to the Oxford Centre of Evidence-Based Medicine [34]. The CA was performed with the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies from the National Institutes of Health [13, 77]. This tool [77] consists of fourteen questions to assess the internal validity and methodological quality

of each study, including potential bias and confounders [13]. With this tool, exposure of interest was defined as leg alignment assessed in 2D, and outcomes were defined as leg alignment assessed on 3D bone models.

Statistical analysis

The results of the reported methods to derive axes or joint orientations from 3D bone models are presented as a qualitative synthesis. First, the reported methods were categorized per segment (tibia, femur or leg). Then, per segment, the methods were categorized under one of the axes or joint orientations of interest (Figure 1). Finally, to obtain a higher level of abstraction, all reported methods were investigated to find a common approach or principle and were grouped accordingly. The results of the intraclass correlation coefficients (ICCs) of the reported methods within the included studies are presented with their 95% confidence intervals. Categorical data were reported as frequencies and percentages.

RESULTS

Search results

The search of the Scopus, MEDLINE/PubMed and Embase databases provided 5034 citations, of which 2266 duplicates were removed. After exclusion, a total of 93 studies were included in this review (Figure 2).

Study characteristics, LOE and critical appraisal

The study characteristics are presented in Supporting Information S1: Table 2. The majority of included studies were Oxford LOE III ($n = 75$ studies) [3–11, 15, 16, 18–21, 23, 25, 28–33, 35–37, 39, 41, 44, 47–52, 54–64, 66, 68–70, 78, 79, 83–85, 87, 88, 90, 91, 94, 96–102, 105, 110–116], and 18 studies were rated Oxford LOE IV [1, 2, 12, 22, 24, 42, 43, 45, 71, 72, 74, 75, 86, 95, 104, 106, 107, 109] (Supporting Information S1: Table 2). Of the

included studies, 16 were human cadaver studies [2, 5, 7, 10, 12, 15, 16, 20, 22, 24, 30, 39, 71, 75, 104, 106], 48 were retrospective cohort studies [3, 4, 6, 8, 9, 11, 19, 21, 23, 25, 28, 29, 31–33, 35, 37, 41, 43, 44, 48–52, 59–64,

68–70, 83, 85–88, 94, 96–99, 102, 107, 112, 115], 23 were prospective cohort studies [18, 36, 42, 45, 47, 54–58, 74, 79, 84, 90, 91, 100, 101, 105, 110, 111, 113, 114, 116], 2 were case-control studies [72, 78], 2 were

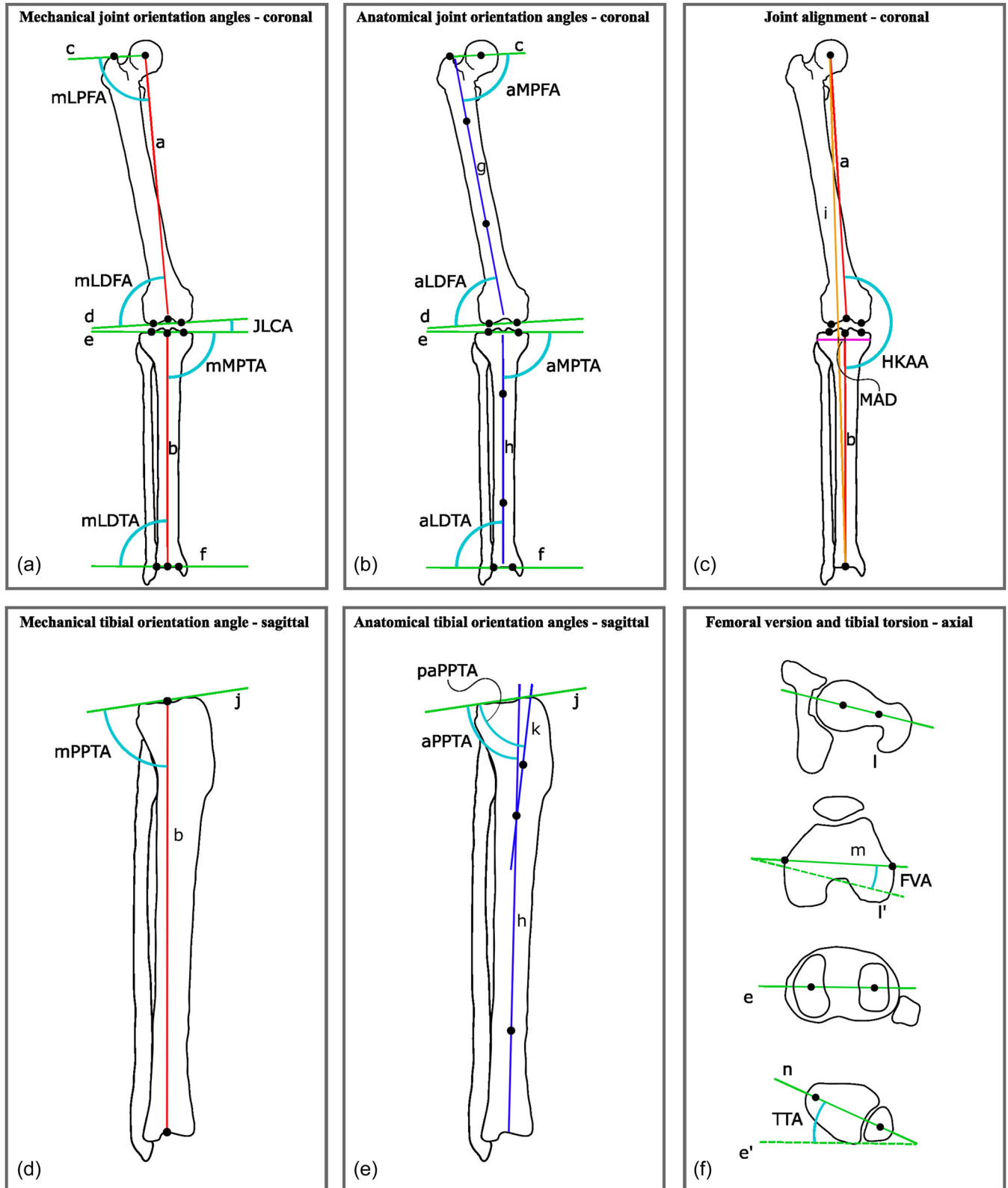


FIGURE 1 (See caption on next page).

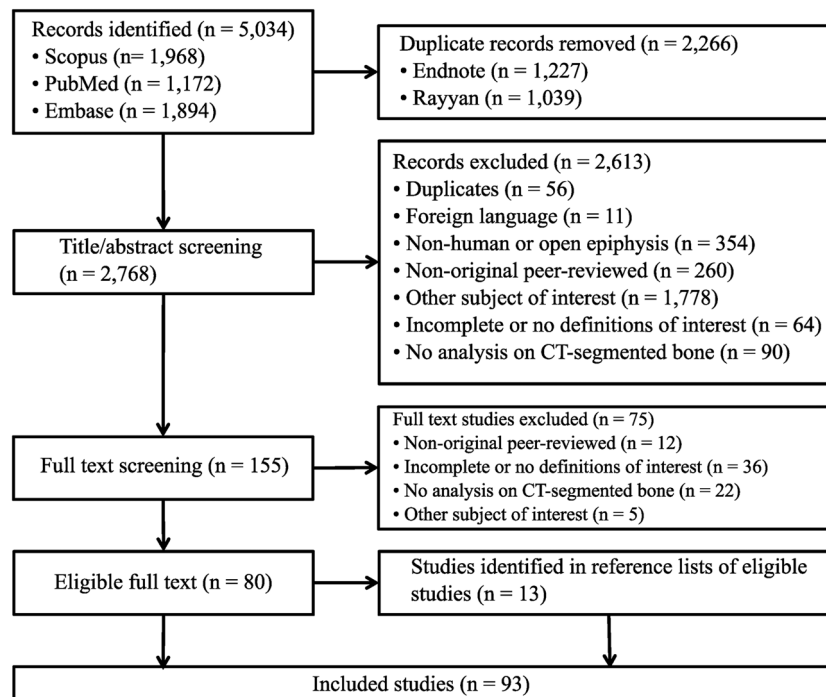


FIGURE 2 PRISMA 2020 flow chart for screening and inclusion of studies. Studies could have been excluded on the basis of multiple criteria, with the first reason for exclusion reported. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

case studies [95, 109], 1 investigated a mixed retrospective cohort of human cadavers and subjects [66] and 1 used a knee joint model [1] (Supporting Information S1: Table 3). The critical appraisal is presented in Supporting Information S1: Table 3.

Outcomes

Reported methods on how to derive axes and joint orientations from 3D bone models

Overall, there was high variability in the reported methods on how to derive axes and joint orientations from 3D bone models for knee-related leg alignment

parameters and femoral and tibial/fibular coordinate systems (Supporting Information S1: Tables 4–6, respectively). This ranged from the use of a line through two arbitrary points on the 3D bone model's surface to the use of all available relevant surface data on a 3D bone model (Figures 3 and 4).

Nevertheless, the reported methods could be categorized into four groups: (1) a 'Landmark method' [3–10, 12, 15, 16, 18–25, 28–30, 32, 33, 35, 37, 39, 41–44, 47, 49, 51, 52, 54–64, 66, 68–70, 78, 79, 83, 87, 88, 91, 94–102, 104, 106, 107, 109, 110, 112–116], (2) a 'Calculated line method' [5, 10, 19, 20, 31, 35, 41, 44, 66, 74, 87, 95, 97, 109, 113], (3) a 'Calculated plane method' [2, 4, 18, 28, 29, 31, 33, 37, 41, 44, 70, 83, 87, 88, 94, 96] or (4) a 'Best-fit

FIGURE 1 Schematic representation of axes and joint orientations from relevant knee-related alignment parameters [82] on one of three anatomical reference planes. (a) Projections of joint orientations and mechanical axes of the femur and tibia on the coronal plane, and resulting mechanical joint orientation angles in the coronal plane. (b) Projections of joint orientation and anatomical axes of the femur and tibia on the coronal plane, and anatomical joint orientation angles in the coronal plane. (c) Projections of mechanical axes of the femur, tibia and leg on the coronal plane, and leg joint alignment in the coronal plane. (d) Projection of joint orientation and mechanical axes of the tibia on the sagittal plane, and mechanical joint orientation angle in the sagittal plane. (e) Projection of joint orientation and anatomical axes of the tibia on the sagittal plane, and anatomical joint orientation angles of the tibia in the sagittal plane [14]. (f) Projection of joint orientation on the femoral and tibial axial plane, as well as femoral version and tibial torsion angles in the femoral and tibial axial plane. Joint orientation and axes: (a, mechanical femoral axis; b, mechanical tibial axis; c, hip joint orientation; d, distal femoral joint orientation; e, proximal medial-lateral tibial joint orientation; f, distal medial-lateral tibial joint orientation; g, anatomical femoral axis; h, anatomical tibial axis; i, mechanical leg axis; j, proximal anterior-posterior tibial joint orientation; k, anatomical proximal tibial axis; l, femoral neck axis; m, femoral (epi)condylar axis; n, tibial intermalleolar axis. aLDFA, anatomical lateral distal femoral angle; aLDTA, anatomical lateral distal tibial angle; aMPFA, anatomical medial proximal femoral angle; aMPTA, anatomical medial proximal tibial angle; aPPTA, anatomical posterior proximal tibial angle; FVA, femoral version angle; HKAA, hip-knee-ankle-angle; JLCA, joint-line convergence angle; MAD, mechanical axis deviation; mLDFa, mechanical lateral distal femoral angle; mLDTA, mechanical lateral distal tibial angle; mLPFA, mechanical lateral proximal femoral angle; mMPPTA, mechanical medial proximal tibial angle; mPPTA, mechanical posterior proximal tibial angle; paPPTA, proximal anatomical posterior proximal tibial angle; TTA, tibial torsion angle.

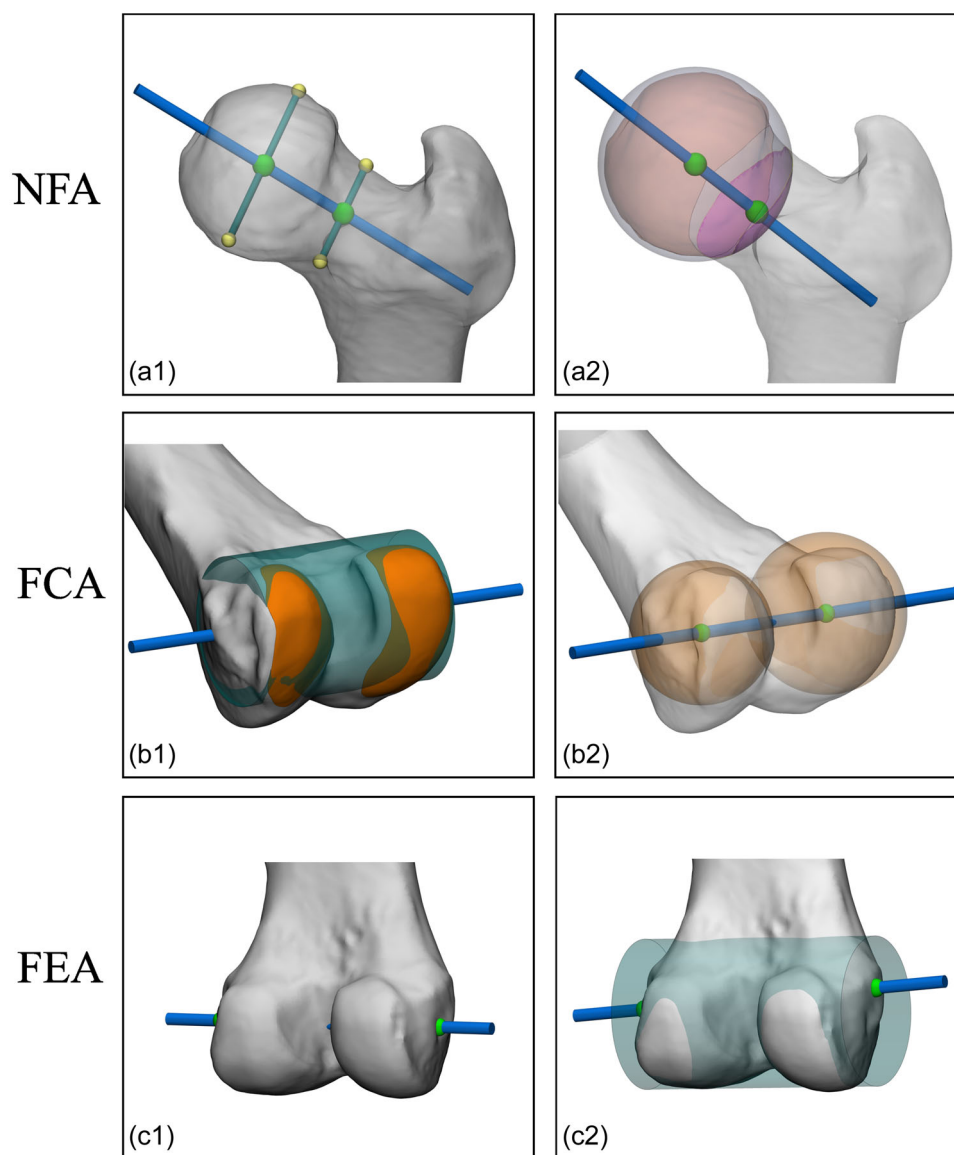


FIGURE 3 Examples of the variability of reported methods to derive femoral axes and joint orientations from 3D bone models (used for knee-related femoral alignment parameters and coordinate systems). (a1) Axis connecting midpoints of manually selected anterior and posterior points of (1) femoral head and (2) femoral neck [22]. (a2) Axis connecting the centre of the sphere fitted to the femoral head with the centre of the intersection at the base of the femoral neck, using a 2 mm radius-increased sphere fitted to the femoral head [115]. (b1) Axis of the cylinder fitted to the marked flexion-extension surfaces of the distal femur [84]. (b2) Axis connecting midpoints of sphere-fit medial and lateral femoral condyles [9]. (c1) Axis connecting the manually selected most concave point medial femoral epicondyle with the most prominent point lateral femoral epicondyle [52, 64, 69, 99, 106, 112]. (c2) Axis connecting the spot of the bone visible on medial and lateral condyles after extension of the cylinder used in B3 [16]. FCA, femoral condylar axis; FEA, femoral epicondylar axis; NFA, neck femur axis.

geometrical shape method' [8, 16, 20, 24, 47, 84] (Figure 5).

Moreover, although the Landmark method was used to derive all 3D axes and joint orientations reported in the included studies [5, 6, 8–10, 12, 15, 16, 18, 20–25, 28–30, 37, 39, 41–43, 47, 49, 51, 52, 54–58, 61, 63, 64, 66, 68–70, 78, 79, 83, 87, 91, 94–96, 98–102, 104, 106, 109, 110, 112–116], for the other groups it could be distinguished that (1) the calculated line method was more specifically used to derive anatomical femoral and tibial axes [5, 10, 18, 20, 31, 41, 66, 74, 87, 95, 109], (2) the calculated plane method

was more specifically used to derive all joint orientations that originate from the proximal tibial joint surfaces [2, 28, 29, 31, 37, 41, 70, 83, 87, 94, 96], and (3) the best-fit geometrical shape method was more specifically used to derive the femoral condylar axis [16, 24, 84] and neck femur axis [47].

Coordinate systems

Complete femoral and/or tibial coordinate systems (Supporting Information S1: Tables 7 and 8,

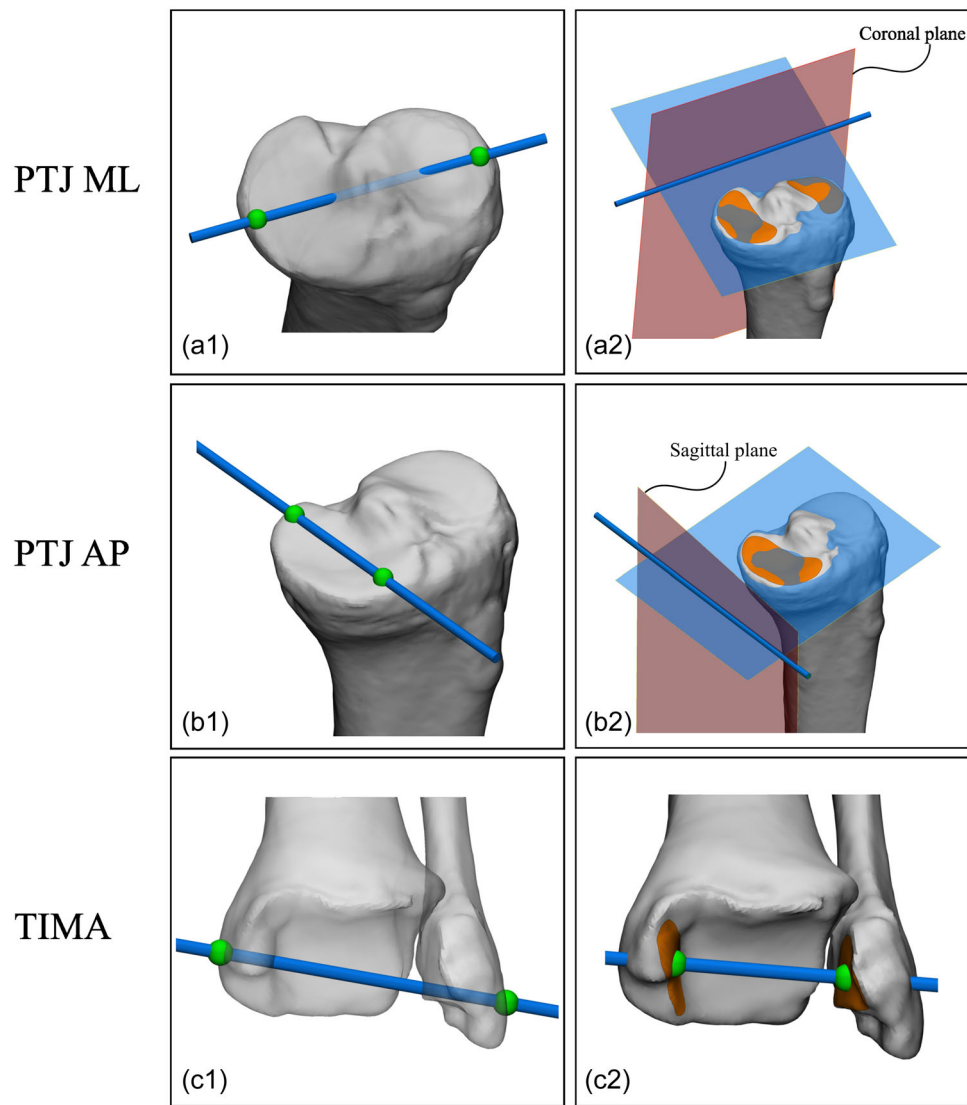


FIGURE 4 Examples of the variability of reported methods to derive tibial axes and joint orientations from 3D bone models (used for knee-related tibial alignment parameters and coordinate systems). (a1) Axis connecting manually selected single most medial and most lateral tibial plateau points [6, 22, 95, 99]. (a2) Best-fit plane through the marked articular surfaces of the medial and lateral tibial plateau indicates proximal tibial plateau 3D joint orientation; the intersecting line between this plane and the tibial coronal plane indicates the medial-lateral orientation of the tibial plateau joint surface [28]. (b1) Axis connecting the manually selected single most cranial and anterior point with the most cranial and posterior point of the medial tibia plateau [22, 39, 68]. (b2) Best-fit plane through the marked articular surface of the medial tibial plateau indicates proximal tibial plateau 3D joint orientation; the intersecting line between this plane and the tibial sagittal plane indicates the anterior-posterior orientation of the medial tibial plateau joint surface [29, 96]. (c1) Axis connecting manually selected most medial and lateral points of medial and lateral malleoli, respectively [22]. (c2) Axis connecting midpoints of articular surfaces of the medial and lateral malleoli [42]. PTJ AP, proximal tibial joint orientation anterior-posterior; PTJ ML, proximal tibial joint orientation medial-lateral; TIMA, tibial intermalleolar axis.

respectively) were reported in 38/93 (41%) [1–3, 6, 8, 11, 18, 20, 35, 36, 42, 44, 45, 48, 50, 52, 57, 60, 62–64, 66, 71, 72, 74, 75, 79, 86, 90, 91, 98, 104, 105, 110, 111, 113] of the included studies ($n = 19$ femoral and $n = 26$ tibial); for the leg, no complete coordinate system was reported.

The definition of both the femoral and tibial coordinate systems was most frequently based on their respective mechanical axes (femoral, 13/19 [68%] [1, 6, 45, 52, 57, 60, 63, 64, 72, 79, 86, 91, 104], tibial, 13/26 (50%) [3, 8, 18, 44, 62, 66, 72, 86, 90, 98, 104, 110,

111]) and central medial-lateral axis (femoral, 16/19 [84%] [1, 6, 20, 35, 36, 45, 52, 57, 60, 63, 64, 71, 72, 79, 86, 104] and tibial, 12/26 [46%] [2, 3, 8, 11, 36, 44, 45, 71, 86, 104, 111, 113]). Additionally, for the tibial coordinate system, a relevant minority of the reported studies based the longitudinal axis on the normal to a best-fit plane of (the articular surface of) the tibial plateau (4/26 [15%]) [11, 48, 50, 74].

Interestingly, while 76/93 (82%) of the included studies [2, 5–10, 12, 15, 16, 18–25, 28–33, 37, 40–44, 47–52, 54–57, 59–64, 66, 68–70, 74, 78, 79, 83, 87,

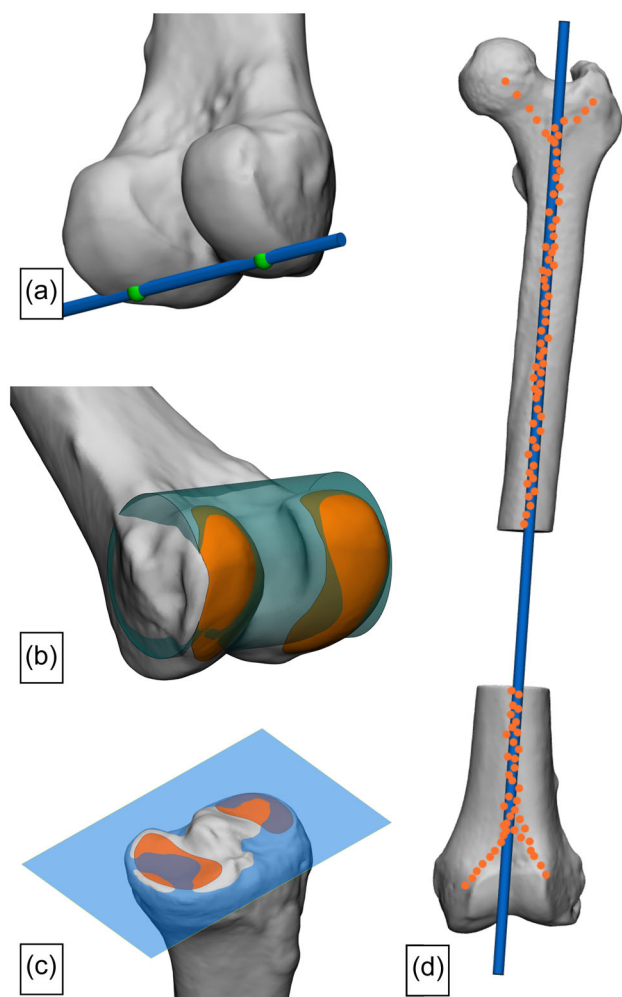


FIGURE 5 Four groups in which the reported methods to derive axes or joint orientations from 3D bone models could be categorized, with examples per group. (a) Line between two landmark points (Landmark method; for example, distal femoral joint orientation). (b) Geometrical shape (e.g., cylinder) with the best fit to a multitude of points on the round articular surface (best-fit geometrical shape method, e.g., femoral condylar axis) from which a central axis can be extracted. (c) A plane fitting a multitude of points on a flat articular surface (blue; calculated plane method; e.g., proximal tibial joint orientation) from which either the normal or the intersecting line with an anatomical reference plane can be extracted. (d) Line calculated from a multitude of points (calculated line method, e.g., anatomical femoral axis).

88, 90, 91, 94–98, 100–102, 104, 106, 109–116] reported alignment parameters, only 25 of these 76 studies (33%) [2, 6, 8, 18, 20, 42, 44, 48, 50, 52, 57, 60, 62–64, 66, 74, 79, 90, 91, 98, 104, 110, 111, 113] reported to express these in (an anatomical reference plane of) a complete coordinate system.

Reliability of the reported methods to derive alignment parameters from 3D bone models

The ICC for alignment parameters was reported in 22/93 (24%) of the included studies [2, 8, 22, 24, 28, 29,

31, 41–43, 49, 54, 59, 60, 63, 74, 87, 90, 98, 110, 114, 116], and all but three studies [22, 24, 110] reported good to excellent reliability for both manual and (semi-) automatic methods to derive alignment parameters from 3D bone models (Supporting Information S1: Table 9).

DISCUSSION

The most important findings of this study are (1) that overall, there is high variability in reported methods on how to derive axes and joint orientations from CT-based 3D bone models to (a) perform 3D knee-related leg alignment analysis and (b) define coordinate systems with their resulting anatomical reference planes in which alignment parameters are expressed, for the femur and tibia; (2) that only a minority (33%) of the studies that reported on leg alignment also reported complete coordinate systems with their corresponding anatomical reference plane in which alignment parameters are to be expressed; and (3) that despite these findings several underlying principles to the reported methods could be identified. These findings are largely in line with our hypothesis.

In order to transition from 2D to 3D leg alignment analysis and correction planning, one would expect agreement on a universal framework on how to derive axes and joint orientations from a 3D bone model. But as the results of the present study clearly show, this is not the case. One implication of this is that it renders the comparability between studies with a 3D framework for leg alignment analysis nearly impossible. The variability in reported methods to derive axes and joint orientations from 3D bone models for leg alignment parameters could lead to different values per alignment parameter between studies, even if projected on identical coordinate systems. Additionally, the variability in methods to derive axes from 3D bone models for complete coordinate systems could lead to different alignment-parameter values when calculating the same alignment parameters on anatomical reference planes of coordinate systems that have a different orientation in 3D space [28, 29]. Other implications are that although some of the included studies did report ‘normal values’ for 3D alignment parameters, these ‘normal values’ are only valid within the context of that particular study and cannot be broadly adopted; and that the normal alignment parameter values of the gold standard 2D framework for leg alignment analysis cannot be blindly adopted in 3D, as this might lead to an inappropriate correction in case of an osteotomy around the knee in clinical practice. Therefore, the 3D workflow is a promising improvement over the current gold standard 2D workflow, but a universal 3D framework for leg alignment analysis is necessary.

Despite the high variability, several underlying principles to the four groups in which the reported methods were categorized can be identified: (1) joint orientation of flatter articular surfaces might be acquired by a calculated plane through marked articular surface data (Figure 4a2); (2) joint orientation of rounder articular surfaces might be acquired by a best fit of a geometrical shape to marked articular surface data (Figure 3b1); (3) joint centres and mechanical axes might be acquired with centroids of marked articular surface data (e.g., the midpoint between acquired centroids of the marked posterior medial and lateral femoral condyles; Figure 3b2); and (4) non-linear femoral and tibial anatomical axes might be acquired by a calculated line from cortical or endosteal bone data (Figure 5d). One other identified principle might be fundamental to all of the ones mentioned above: the selection of all available relevant surface data on a 3D bone model. In contrast to the current gold standard 2D framework and some of the reported 3D frameworks for leg alignment analysis, which use one single or a few data point(s) only to derive landmarks for basic line drawing, this principle uses all available relevant surface data of the 3D bone model in order to derive axes and joint orientations for alignment parameters and coordinate systems. However, considering the results of the present study, these principles are not yet universally adopted. Therefore, the authors propose that these principles might be used as the foundation for a higher level of agreement or even consensus on a universal future 3D framework for leg alignment analysis.

Interestingly, although for the purpose of reference, alignment parameters are expressed in the coronal, sagittal or axial anatomical planes [81], only a third of included studies that reported on knee-related leg alignment parameters also reported a complete coordinate system (and their resulting anatomical reference planes). Using a complete coordinate system in the context of alignment analysis and osteotomy planning is important to identify and control the resultant effect of an osteotomy on alignment in all three anatomical reference planes simultaneously [40, 103]. The gold standard to establish 3D joint coordinate systems with anatomical reference planes stems from the International Society of Biomechanics' (ISB) recommendation on definitions of joint coordinate systems' [108]. As per ISB recommendations, indeed, the included papers that reported complete coordinate systems most frequently established a femoral and tibial coordinate system based on their mechanical axis and a central medial-lateral axis (FCA and the PTJ ML, respectively). Still, a relevant minority of 15% of the included papers reported complete tibial coordinate systems based on the longitudinal axis on the normal vector to the best-fit plane of (the articular surface of) the tibial plateau. However, the tibial plateau is tilted (and not orthogonal)

relative to the mTA, and in both the context of osteotomies around the knee and total knee arthroplasties, leg alignment analysis seems most appropriate when it is based on mechanical axes [26, 67]. Therefore, the authors propose that the coordinate systems (in which anatomical planes for alignment parameters of the leg are expressed) be based on mechanical axes and central medial-lateral axes, in addition to the principles described above.

Furthermore, for the central medial-lateral axis of the femoral coordinate system, the ISB recommends using a femoral epicondylar axis. This axis is based on two arbitrary landmark points, instead of an FCA (as per findings of the present study) that is based on the articular surface data of the femoral condyles [108]. The same goes for the central medial-lateral tibial axis of the tibial coordinate system, where the ISB recommends the line connecting two arbitrary landmark points ('most medial point' of the medial tibial plateau and the 'most lateral point' of the lateral tibial plateau) [108]. In these two instances, the principle of using all available relevant surface data of the 3D bone model in order to derive axes and joint orientations is not met. Therefore, the authors propose to define the medial-lateral orientation of a femoral and tibial coordinate system according to the above-described principles, based on all available articular surface data instead of single data points.

To our knowledge, this is the first systematic review investigating the reported methods on how to derive axes and joint orientations of 3D bone models for knee-related leg alignment parameters and coordinate systems for the femur, tibia, and leg. Nevertheless, in addition to the limitations inherent to all systematic reviews, this study has several limitations. First, this review focused on CT-based 3D bone models, thereby excluding studies reporting MRI or the EOS 2D/3D imaging system. However, although interest in MRI- and EOS-based 3D models is increasing, to date, CT is the preferred imaging modality for segmentation purposes. Second, this study focused on native knees, while arthroplasty-related studies show increasing interest in 3D knee-related leg alignment analysis and the optimal positioning of arthroplasty components. Thus, methods to derive axes and joint orientations from 3D bone models for alignment parameters and coordinate systems might have been missed. However, as methods in arthroplasty-related studies might not be applicable for correction osteotomies due to the absence of osseous landmark points, only relevant 3D methods that could be performed on a native knee were included in this systematic review. Third, only papers reporting knee-related leg alignment or coordinate systems that were, ultimately, reported as lines were included. Thus, papers reporting on other methods that define leg alignment parameters might have been missed. However, even studies that used all available

relevant data to define joint orientation ultimately reported this joint orientation as a line (e.g., best-fit plane through all data points of the tibial plateau defines the proximal tibial joint orientation, and the intersecting line of the joint orientation plane with the anatomical coronal and sagittal plane is used to calculate the joint orientation angle). Irrespective of these limitations, the results of this study could spark the community to make progress in this particular area of the field.

The clinical relevance of this work is, first, that it reveals a high variability of reported methods in the field of 3D knee-related leg alignment analysis. This indicates that generalizable 3D reference values for normal alignment parameters are missing, and comparability between alignment parameter values reported in different studies is impossible. Second, this work identifies underlying principles that might lead to agreement on a universal framework for 3D leg alignment analysis. Considering the increasing popularity of 3D use in a clinical setting, one would expect such a universal framework to be a prerequisite, as is the case for the 2D framework.

CONCLUSION

There is high variability in 3D knee-related leg alignment analysis. Therefore, universal 3D reference values for alignment parameters cannot yet be defined, and comparison of alignment parameter values between different studies is impossible. However, several underlying principles to the reported methods were identified, which could serve to reach more agreement on a future universal 3D framework for leg alignment analysis.

AUTHOR CONTRIBUTIONS

Romy M. ten Heggeler, Roy A. G. Hoogeslag and Feike de Graaff all made substantial contributions to the conception and design of the study. Romy M. ten Heggeler, Roy A.G. Hoogeslag and Quinten W. T. Veerman have made substantial contributions to the extraction of data. All authors have made substantial contributions to the analysis and interpretation of data and have been involved in drafting the manuscript and revising it critically for important intellectual content.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

All data are made available in Supporting Information S1.

ETHICS STATEMENT

Ethical approval was not required for this systematic review.

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SUPPORTING INFORMATION

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