The role of limb alignment on natural tibiofemoral kinematics and kinetics

a pilot study using dynamic videofluoroscopy

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Aims
This study aimed to analyze kinematics and kinetics of the tibiofemoral joint in healthy subjects with valgus, neutral, and varus limb alignment throughout multiple gait activities using dynamic videofluoroscopy.

Methods
Five subjects with valgus, 12 with neutral, and ten with varus limb alignment were assessed during multiple complete cycles of level walking, downhill walking, and stair descent using a combination of dynamic videofluoroscopy, ground reaction force plates, and optical motion capture. Following 2D/3D registration, tibiofemoral kinematics and kinetics were compared between the three limb alignment groups.

Results
No significant differences for the rotational or translational patterns between the different limb alignment groups were found for level walking, downhill walking, or stair descent. Neutral and varus aligned subjects showed a mean centre of rotation located on the medial condyle for the loaded stance phase of all three gait activities. Valgus alignment, however, resulted in a centrally located centre of rotation for level and downhill walking, but a more medial centre of rotation during stair descent. Knee adduction/abduction moments were significantly influenced by limb alignment, with an increasing knee adduction moment from valgus through neutral to varus.

Conclusion
Limb alignment was not reflected in the condylar kinematics, but did significantly affect the knee adduction moment. Variations in frontal plane limb alignment seem not to be a main modulator of condylar kinematics. The presented data provide insights into the influence of anatomical parameters on tibiofemoral kinematics and kinetics towards enhancing clinical decision-making and surgical restoration of natural knee joint motion and loading.

Article focus
- A detailed understanding of the effect of altered limb alignment on tibiofemoral kinematics and kinetics is crucial for establishing the role of anatomical variation, and even arthroplasty implantation parameters, on the joint contact and loading conditions.

Key messages
- Limb alignment was not strongly reflected in the condylar kinematics, but did significantly affect the knee adduction moment.

Strengths and limitations
- Our analysis presents the current state of knowledge of joint kinematics and kinetics

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in healthy subjects with valgus, neutral, and varus limb alignment.
- Although the study population covered a wide range of individual limb alignment (range: 8° valgus to 9° varus), none of the subjects showed extreme varus or valgus limb alignment.

Introduction

Tibiofemoral motion of the healthy knee joint is guided by an interconnected system of bones and soft-tissue structures, enabling a complex interaction of joint rotations and translations.[1] In-depth knowledge of in vivo kinematics and loading is the underlying foundation for a detailed understanding of joint functionality, musculoskeletal pathologies, and injuries of the knee. Despite methodological developments to assess bone motion without the influence of soft-tissue artefact (e.g. videofluoroscopy), healthy tibiofemoral kinematics are still controversially discussed in the literature.[2-5] Variability in study findings is especially notable for tibiofemoral internal/external rotation and condylar anteroposterior (A-P) translation, thus resulting in conflicting conclusions about the predominant location of the centre of rotation (CoR) in the transverse plane.[2,5-8] Beside differences in technical motion capture set-ups and variations in data interpretation, the role of anatomical variability between study cohorts remains unclear, especially if study populations are small.

Among the healthy adult population, deviations in the longitudinal alignment of the knee joint are a common anatomical variation. Over 25% of the population are known to present a hip-knee-ankle (HKA) angle of more than 3° varus or valgus.[9] For most adults, this is a constitutional varus or valgus limb alignment, which they have since reaching skeletal maturity.[9,10] Clinically, extreme lower limb alignment is known to influence the risk, development, and progression of osteoarthritis in the knee.[11] This is likely due to the altered line of action of the ground reaction force vector and resulting changes to the knee joint adduction moments.[12] As a result, limb alignment is also thought to critically affect tibiofemoral joint loading.[1,13-15] It is therefore entirely plausible that such anatomical variations also result in alterations in the skeletal motion patterns of the tibiofemoral joint.

Using cadaveric specimens, a significant correlation between subject-specific limb alignment and tibial internal/external rotation and abduction/adduction has been observed during passive flexion.[16] In addition, varus and valgus limb alignment significantly affected intraoperative tibial internal/external rotation in patients undergoing total knee arthroplasty (TKA).[17] Only one study has analyzed the effect of limb alignment on dynamic knee kinematics in vivo,[18] albeit using optical motion capture technologies. Here, osteoarthritic subjects with varus and valgus limb alignment showed significantly different abduction/adduction angles and a reduced range of flexion/extension during the stance phase of walking compared to healthy controls. However, no study has yet investigated the relationship between subject-specific limb alignment and tibiofemoral kinematics during multiple, in vivo gait activities in healthy subjects. While kinematics and kinetics have each been analyzed individually, studies combining both measures in the same varus/valgus cohort without the influence of soft-tissue artefact are currently missing.

Therefore, a detailed understanding of the effect of altered limb alignment on tibiofemoral kinematics and kinetics is critical in order to establish its potential role in varying interpretations of knee joint movement patterns across different study cohorts. Thus, the goal of the present study was to determine whether differences exist in the kinematics and kinetics of the tibiofemoral joint between healthy subjects with valgus, neutral, and varus limb alignments throughout multiple gait activities using dynamic videofluoroscopy.

Methods

Subjects

A total of 27 asymptomatic subjects with no history of orthopaedic injuries or trauma of the lower limbs were included in this pilot study (Table I). Subject-specific alignment of one limb each was evaluated using the EOS biplanar radiograph system (EOS imaging, France) in a standing position.[19] Within the 3D SterEOS (EOS imaging) software, an experienced radiologist manually selected pre-defined osseous landmarks on the femur and tibia, which were then used by the software to semi-automatically match 3D models of the femur and tibia to the respective contours on the frontal and lateral radiographs. Based on the configuration of the individual 3D models (Figure 1), the HKA as a measure of limb alignment was automatically calculated between the mechanical axis of the femur (centre of the femoral head to centre of the femoral notch) and tibia (centre of tibial plateau to centre of the tibial plafond).[19] Subjects with a limb alignment of HKA < -3° were classified as valgus, subjects with a HKA between -3° and 3° as neutral, and subjects with a HKA > 3° as varus.[9] This classification resulted in five subjects with valgus limb alignment (mean HKA -5.6° (SD 1.4°)), 12 subjects with neutral limb alignment (mean HKA 0.5° (SD 1.5°)), and ten subjects with varus limb alignment (mean HKA 5.7° (SD 1.7°)) (Table I). Individual limb alignment between subjects ranged from 8° valgus to 9° varus.

The study was approved by the local ethics committee of the Canton of Zürich (Switzerland) and carried out in accordance with the Declaration of Helsinki.[20] All subjects provided written informed consent prior to participation in the study.

Experimental procedure

All subjects underwent a clinical knee examination to confirm a healthy knee status, followed by an EOS and CT scan (~ 20 cm proximal/distal of the knee joint line, resolution 0.5 × 0.5 mm, slice thickness 1 mm).

Each subject was then assessed during standing (two trials oriented 45° to image intensifier, two trials oriented frontally to image intensifier), as well as throughout multiple complete cycles of level walking (five to six trials), downhill walking (five trials, 10° declined slope), and stair descent (five trials, three 18 cm steps) using a combination of dynamic videofluoroscopy, ground reaction force plates, and optical motion capture (Figure 2a). Fluoroscopic images were acquired at 25 to 30 Hz (1 ms shutter time) with an image resolution of 1,000 × 1,000 pixels.[21] Synchronized ground reaction forces were obtained using five force plates

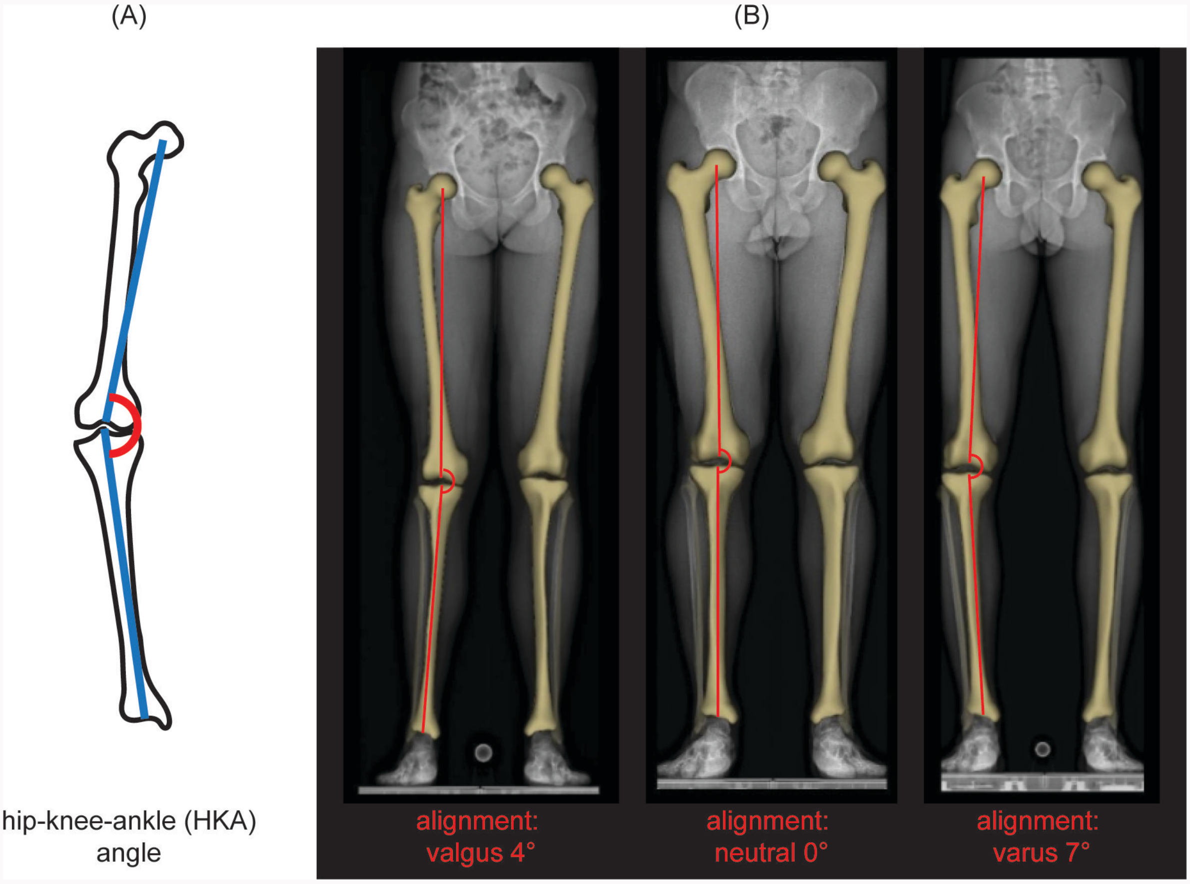

Fig. 1
a) Schematic illustration of the hip-knee-ankle (HKA) angle definition used by the SterEOS software (EOS imaging, France). b) Exemplary visualization of the reconstructed 3D bone models of the femur and tibia by the SterEOS software and the resulting limb alignment for a valgus (left), neutral (middle), and varus (right) subject.

Table I. Group characteristics.

Characteristic	Valgus (n = 5)	Neutral (n = 12)	Varus (n = 10)
Sex (F/M), n	4/1	6/6	4/6
Side (R/L), n	2/3	6/6	7/3
Mean age, yrs (SD)	37.2 (17.9)	24.0 (3.7)	25.8 (7.0)
Mean BMI, kg/m^2 (SD)	22.9 (2.1)	21.3 (2.1)	20.6 (2.0)
Mean HKA, ° (SD)	-5.6 (1.4)	0.5 (1.5)	5.7 (1.7)

HKA: valgus = negative angle, varus = positive angle.
HKA, hip-knee-ankle angle.

embedded in the floor and two additional mobile force plates mounted into the ramp and stairs (Kistler, Switzerland), operating at a sampling frequency of 2,000 Hz. To assess full body kinematics, 55 skin markers mainly attached to the lower limbs were captured using 22 infrared cameras operating at 100 Hz (Vicon MX system, UK).[22] In addition, the moving fluoroscope was also equipped with 11 optical markers to allow transformation of the fluoroscopically determined knee joint centre into the lab coordinate system.[21] A full description of the measurement set-up has been published previously.[2,23] For one subject, data for downhill walking and stair descent were missing due to technical issues.

Data analysis

The open-source software MITK-GEM[24] was used to generate subject-specific volumetric femoral and tibial bone models, based on each subject's knee CT scan.

Distortion correction was applied to all fluoroscopic images and the optical projection parameters were calculated.[21] Fitting of the volumetric femoral and tibial bone models to the fluoroscopic images was performed using a semi-automatic 2D/3D registration software (Figure 2b), with reported mean absolute registration errors of < 1° for all three rotations, < 0.6 mm for in-plane, and < 7.1 mm for out-of-plane translations for a single bone specimen.[25] To mitigate the larger out-of-plane errors, relative tibiofemoral alignment in the frontal plane was confirmed for each radiological image registration.

For both the femur and tibia, anatomical coordinate systems were established. While a detailed description of the coordinate systems can be found in previous publications,[2,23] a brief overview is presented here: the femoral coordinate system was defined using a primary mediolateral axis based on the mean femoral functional flexion axis calculated from two deep knee-bending trials covering 15° to 90° of flexion.[26] For the tibial coordinate system, the CT shaft axis defined using a cylinder fit was used as the primary axis.

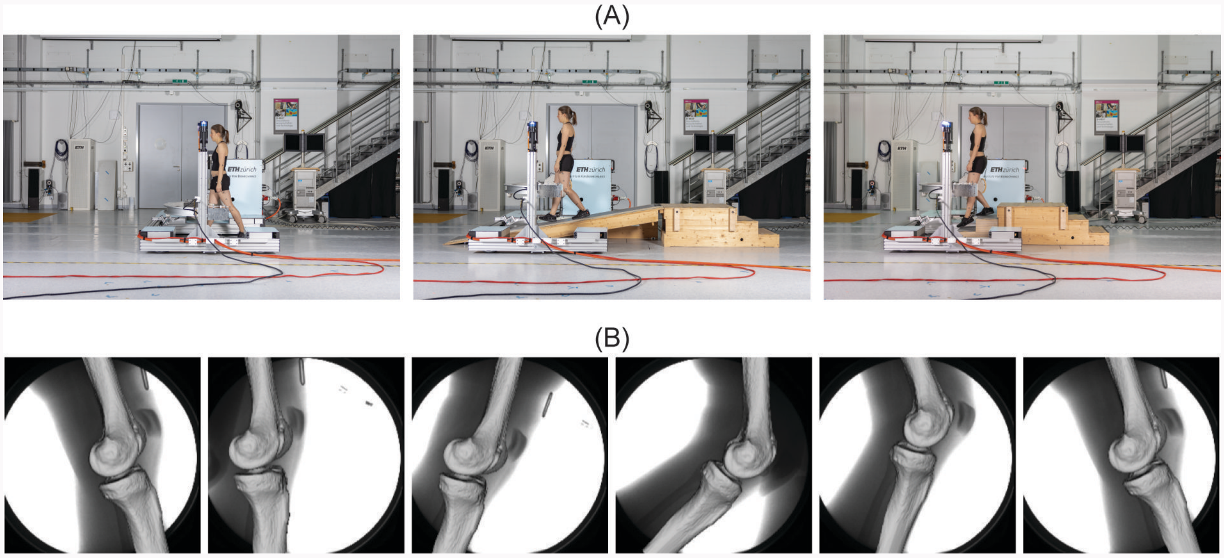

Fig. 2
a) Subject tracked by the moving fluoroscope during level walking (left), downhill walking (middle), and stair descent (right). b) Series of fluoroscopic images with registered femur and tibia bone models during level walking.

Relative tibiofemoral rotations were calculated using the joint coordinate system approach.[27] A-P translations of the medial and lateral condyle were assessed using a medial and lateral point on the functional flexion axis (FFA_P_{med} & FFA_P_{lat}), as well as the nearest point of each femoral condyle relative to a plane parallel to the tibial articular surface (N_P_{med} & N_P_{lat}).[2,23] A-P translations were calculated with regard to the mid-coronal plane of the tibia and scaled to the mean condylar width of all subjects (82.4 mm). Based on the location of the FFA_P_{med} and FFA_P_{lat}, a mean CoR in the transverse plane was calculated over the loaded stance phase of the gait cycle, using the symmetrical centre of rotation estimation.[28]

To calculate knee joint moments, the origin of the femoral anatomical coordinate system was transformed into the global laboratory coordinate system.[21] The knee joint moments were then calculated using a quasi-static inverse dynamics approach for all timepoints where the vertical ground reaction force was > 100 N. Here, calculation of the moments was based on the knee joint centre location,[2,29] ground reaction forces, as well as shank and foot segments, where the centre of mass of these segments was determined based on the skin marker data, and their masses were defined proportional to the subjects' body weights.[30]

Heel-strike and toe-off events were determined based on the ground reaction forces, using a threshold of 25 N. Due to the absence of ground reaction force data, the second heel-strike of downhill walking was defined based on the trajectories of the heel marker. Gait velocity was calculated for each gait cycle based on the trajectories of the sacrum marker. All rotations, translations, and knee joint moments were normalized to a complete gait cycle and linearly interpolated to 101 data points.

Statistical analysis

In order to analyze the effect of limb alignment on kinematics (flexion/extension, tibial internal/external rotation, abduction/adduction, condylar translation of the FFA_P_{med} and FFA_P_{lat}) and kinetics (flexion/extension moment, adduction/abduction moment, tibia internal/external rotation moment) throughout the gait cycle, one-dimensional statistical parametric mapping (SPM) was used.[31] A total of 24 one-way mixed-model analyses of variance (ANOVA) were performed, where the rotation, translation, or knee moment were set as the dependent variable, while the limb alignment group (neutral, varus, valgus) was used as the independent variable. Levels of significance were corrected for multiple comparisons for kinematics and kinetics individually, starting at $\alpha = 0.05$. If the ANOVA revealed significant differences between the groups, a post-hoc paired *t*-test was performed with significance levels adjusted for multiple comparisons.

One ANOVA was then performed to compare the ranges of A-P translation between the medial and lateral condyles of the three limb alignment groups during the loaded stance phase. The range of A-P translation (FFA_P_{med}, FFA_P_{lat}) was set as the dependent variable. The limb alignment group, activity (level walking, downhill walking, stair descent), and condylar side (medial, lateral) were set as fixed effects and the individual subjects as random effect. A further ANOVA was performed to test the effect of limb alignment on the peak knee adduction moment, which was set as the dependent variable, while limb alignment group and activity were set as fixed effects and the individual subjects as random effect. Post-hoc comparisons were conducted using a least significant difference approach, with significance levels adjusted for multiple comparisons using Bonferroni correction. All ANOVAs were conducted using the SPSS software suite (SPSS v.28, IBM, USA).

Correlations between individual HKA and the mean abduction/adduction angle during standing as well as the mean knee adduction moment during level walking, downhill walking, and stair descent were assessed in MATLAB using the Pearson correlation test.

Based on previously described jumps in the location of the nearest points due to a relatively flat femoral surface in certain subjects,[2] no statistical analysis of the translational patterns of the nearest point approach was performed.

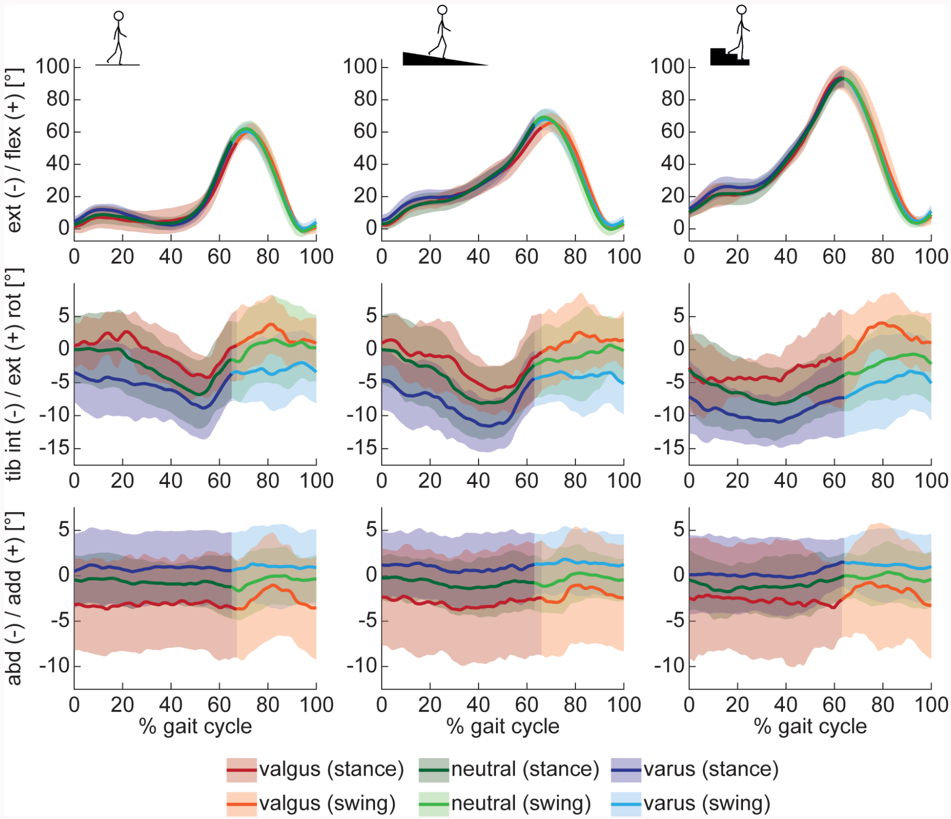

Fig. 3
Tibiofemoral flexion/extension (flex/ext), tibial internal/external rotation (tib int/ext rot), and abduction/adduction (abd/add) throughout complete gait cycles of level walking (left column), downhill walking (middle column), and stair descent (right column). The means (thick lines) and SDs (shaded areas) across each limb alignment group are presented, with lighter shades representing the unloaded swing phases of the activity.

Table II. Tibiofemoral rotations and condylar anteroposterior locations of the medial and lateral functional flexion axis points (FFA_P_{med} and FFA_P_{lat}) as well as the nearest points (N_P_{med} and N_P_{lat}) during standing. Locations posterior of the tibial mid-sagittal plane were defined as negative, and locations anterior as positive. Means and SDs are presented for each subject group.

Variable	Valgus	Neutral	Varus
Standing			
Extension (-)/flexion (+), °	-1.7 (1.7)	-2.7 (5.1)	-0.6 (6.0)
Tibial internal (-) / external (+) rotation, °	3.8 (4.4)	1.8 (7.0)	-0.7 (4.5)
Abduction (-)/adduction (+), °	-3.0 (5.1)	-0.4 (2.3)	1.1 (3.8)
Posterior (-)/anterior (+) location FFA_P_{med}, mm	-9.1 (3.3)	-9.1 (4.2)	-6.3 (3.3)
Posterior (-)/anterior (+) location FFA_P_{lat}, mm	-6.5 (3.2)	-8.0 (3.4)	-7.0 (3.3)
Posterior (-)/anterior (+) location N_P_{med}, mm	0.6 (2.6)	2.2 (2.8)	4.5 (3.6)
Posterior (-)/anterior (+) location N_P_{lat}, mm	9.4 (5.9)	10.1 (7.7)	9.7 (7.2)

FFA_P, functional flexion axis point; N_P, nearest point.

Results

Gait velocity

The mean gait velocities across all subjects were 0.82 m/s (SD 0.08), 0.78 m/s (SD 0.08), and 0.57 m/s (SD 0.05) for level walking, downhill walking, and stair descent, respectively. Similar gait velocities were achieved for all limb alignment groups (Supplementary Table i).

Kinematics

During standing, all subjects showed a fully extended knee. While the neutral and varus subjects showed an almost neutral tibial rotation, the valgus subjects showed a slight externally rotated tibia (Table II). Moderate agreement (r = 0.44) was found between the mean individual abduction/adduction angle during standing and the measured HKA angle using EOS with individual differences ranging from 0° to 13.5°

Table III. Ranges of tibiofemoral rotations and condylar anteroposterior translations of the medial and lateral functional flexion axis points (FFA_P_{med} and FFA_P_{lat}) as well as the nearest points (N_P_{med} and N_P_{lat}) during level walking, downhill walking, and stair descent, each for the loaded stance phase and the unloaded swing phase for the valgus, neutral, and varus groups. Means and SDs are presented for each subject group.

Variable	Phase	Valgus	Neutral	Varus
Level walking				
Flexion/extension, °	Stance	51.3 (6.2)	52.4 (4.7)	51.1 (4.6)
	Swing	63.5 (6.2)	65.8 (3.7)	62.6 (3.9)
Tibial internal/external rotation, °	Stance	11.7 (1.2)	12.7 (1.8)	11.2 (2.0)
	Swing	9.5 (1.1)	11.1 (3.3)	8.8 (1.4)
Abduction/adduction, °	Stance	5.0 (0.7)	5.1 (1.1)	4.2 (0.9)
	Swing	5.2 (0.9)	5.3 (1.0)	4.1 (1.1)
A-P translation FFA_P_{med}, mm	Stance	7.7 (7.3)	7.3 (1.4)	6.8 (0.7)
	Swing	5.7 (5.8)	5.8 (0.8)	5.3 (1.8)
A-P translation FFA_P_{lat}, mm	Stance	6.9 (2.1)	7.8 (1.6)	7.0 (1.8)
	Swing	6.6 (1.9)	8.0 (2.6)	6.8 (1.1)
A-P translation N_P_{med}, mm	Stance	11.2 (2.6)	11.5 (2.8)	11.4 (2.3)
	Swing	12.8 (4.1)	13.3 (3.7)	12.6 (2.3)
A-P translation N_P_{lat}, mm	Stance	15.9 (4.7)	16.5 (7.1)	16.2 (5.6)
	Swing	18.0 (6.0)	23.4 (6.9)	19.3 (8.1)
Downhill walking				
Flexion/extension, °	Stance	61.1 (7.0)	61.9 (3.6)	58.5 (4.5)
	Swing	68.5 (5.7)	71.9 (3.1)	69.1 (4.3)
Tibial internal/external rotation, °	Stance	12.1 (2.3)	12.9 (2.5)	10.6 (1.3)
	Swing	8.7 (2.0)	10.2 (3.0)	8.1 (1.6)
Abduction/adduction, °	Stance	5.2 (0.5)	4.8 (1.3)	4.3 (0.7)
	Swing	4.9 (0.6)	4.8 (1.7)	3.9 (0.8)
A-P translation FFA_P_{med}, mm	Stance	7.5 (2.1)	6.7 (1.5)*	5.6 (1.0)*
	Swing	5.7 (0.8)	6.0 (0.9)	5.1 (1.1)
A-P translation FFA_P_{lat}, mm	Stance	6.9 (1.6)	7.9 (1.4)*	7.3 (1.4)*
	Swing	6.8 (0.8)	7.6 (1.8)	6.2 (1.1)
A-P translation N_P_{med}, mm	Stance	9.1 (1.0)	9.4 (1.7)	9.5 (2.4)
	Swing	12.1 (3.1)	12.1 (3.5)	11.7 (2.7)
A-P translation N_P_{lat}, mm	Stance	14.9 (1.3)	17.2 (8.4)	14.3 (7.0)
	Swing	17.2 (5.6)	21.4 (6.7)	17.9 (8.6)
Stair descent				
Flexion/extension, °	Stance	84.8 (6.7)	84.4 (5.4)	81.8 (4.8)
	Swing	91.9 (6.9)	92.7 (5.2)	90.5 (3.7)
Tibial internal/external rotation, °	Stance	12.3 (5.0)	11.4 (2.0)	9.9 (1.7)
	Swing	12.5 (2.1)	10.0 (3.0)	8.7 (2.7)
Abduction/adduction, °	Stance	6.1 (1.7)	6.0 (1.3)	5.2 (1.6)
	Swing	6.4 (0.6)	4.5 (0.7)	3.7 (1.1)
A-P translation FFA_P_{med}, mm	Stance	6.5 (2.0)*	7.0 (1.5)*	6.0 (1.0)*
	Swing	6.5 (2.2)	6.8 (1.6)	5.4 (1.2)
A-P translation FFA_P_{lat}, mm	Stance	8.3 (2.1)*	8.3 (1.4)*	7.3 (1.2)*

(*Continued*)

(*Continued*)

Variable	Phase	Valgus	Neutral	Varus
	Swing	9.7 (3.4)	9.5 (3.3)	8.4 (2.2)
A-P translation N_P_{med}, mm	Stance	9.9 (3.7)	9.2 (1.7)	8.4 (2.2)
	Swing	10.3 (2.7)	10.4 (2.8)	9.9 (2.3)
A-P translation N_P_{lat}, mm	Stance	11.3 (3.9)	14.6 (6.7)	11.3 (2.8)
	Swing	15.8 (4.3)	20.00 (6.6)	18.7 (6.3)

*Significant differences between the medial and lateral condylar translation during the loaded stance phase based on an adjusted level of significance of $\alpha = 0.0056$.
A-P, anteroposterior.

(Supplementary Figure a). For all subjects, the contact points were located anteriorly of the respective medial and lateral points on the functional flexion axis (Supplementary Figure a, Table II).

No significant differences for the rotational patterns between the different limb alignment groups were found for level walking, downhill walking, or stair descent (Figure 3, Supplementary Figure b, Table III). Similar to standing, the valgus subjects had a more externally rotated tibia and more knee abduction than the neutral and varus subjects throughout the complete gait cycle of all three activities (Figure 3).

Over the complete gait cycle, the patterns of condylar translation were comparable among the three limb alignment groups (Figure 4, Supplementary Figure b). Similar findings were seen for the A-P translation of the medial and lateral nearest points (Figure 4). However, large standard deviations, especially during phases of low knee flexion, were evident for the N_P_{lat}, indicating inter-subject variability in the resultant translational patterns. For all three limb alignment groups, comparable ranges of condylar translation were found during the stance phase of level walking for the FFA_P_{med} and FFA_P_{lat}, whereas significantly more condylar translation was found for the FFA_P_{lat} compared to the FFA_P_{med} during the stance phase of stair descent. During downhill walking, however, significantly more FFA_P_{lat} than FFA_P_{med} A-P translation was found for the neutral and varus subjects, but valgus subjects exhibited a trend towards more FFA_P_{med} than FFA_P_{lat} translation (Table III). As a result, the neutral and varus subjects showed a mean medial CoR for the loaded stance phase of all three gait activities. The valgus subjects, however, showed a centrally located CoR for level walking and downhill walking, but a more medial CoR during stair descent (Figure 4). Overall, inter-subject variability was high, resulting in large differences for the individual CoR locations between subjects (range: 24.6 mm (SD 3.7) to -16.6 mm (SD 10.4) across all activities).

Kinetics

While significant differences were found for the frontal plane adduction/abduction moments (Figure 5), sagittal and transverse plane knee joint moments did not statistically differ between limb alignment groups (Supplementary Figures c and d). The varus group exhibited an increased knee adduction moment compared to the neutral and valgus subjects over the majority of the stance phase (Figure 5). As a result, a significant increase in the peak knee adduction moment was found from valgus through neutral to varus (Table IV). Furthermore, a strong correlation between the subject-specific mean adduction/abduction moment across the loaded stance phase and the HKA was found for all three walking activities (Figure 5).

Discussion

A comprehensive knowledge of subject-specific knee motion and loading is crucial for a clear understanding of knee joint functionality and clinical decision-making. Detailed knowledge of the relationship between limb alignment and subject-specific tibiofemoral kinematics and kinetics is crucial for restoring natural knee joint motion towards improving patient outcomes. To our knowledge, this is the first in vivo study analyzing tibiofemoral kinematics and kinetics in healthy subjects with valgus, neutral, and varus limb alignment throughout complete cycles of different gait activities using dynamic videofluoroscopy. During gait activities, the present data revealed only a minor role of limb alignment on tibiofemoral rotations and condylar translations, but a significant influence on knee adduction/abduction moments, with the adduction moment increasing from valgus through neutral to varus.

A comparison of our data to the few studies available presenting kinematics in knees with varus or valgus limb alignment showed only low agreement.[16-18] While a significant decrease in the range of flexion and altered mean adduction angles over the loaded stance phase were found in osteoarthritic varus and valgus subjects,[18] the results of our study suggest no differences in the rotational range of motion between the groups. However, this low agreement is inherently plausible due to different subject characteristics. While our study has analyzed healthy subjects without symptoms of osteoarthritis, the existing literature is focused on osteoarthritic subjects or subjects undergoing TKA surgery. However, since our results indicating only a weak relationship between limb alignment and the CoR in the transverse plane are somewhat surprising, further studies that include subjects with more extreme limb alignment are clearly needed. Nevertheless, the variability in the location of the CoR in the transverse plane also emphasizes the importance of taking condylar A-P translation into account when aiming to restore healthy knee kinematics.

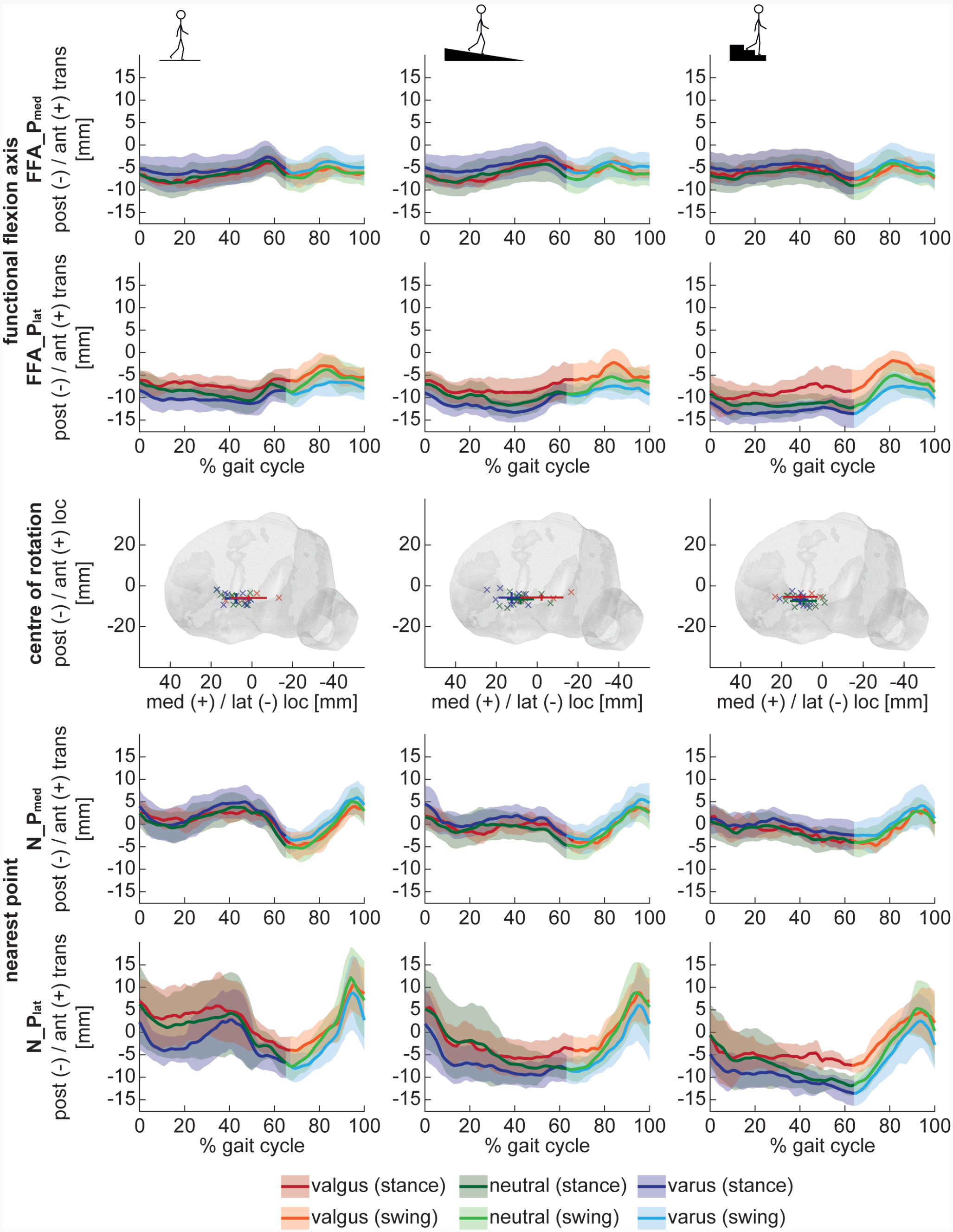

Fig. 4

Anterior (ant)-posterior (post) translation of the medial and lateral functional flexion axis points (FFA_P$_{med}$ and FFA_P$_{lat}$) (top two rows) as well as the nearest points (N_P$_{med}$ and N_P$_{lat}$) (bottom two rows) throughout complete gait cycles of level walking (left column), downhill walking (middle column), and stair descent (right column). The means (thick lines) and SDs (shaded areas) across each limb alignment group are presented, with lighter shades representing the unloaded swing phases of the activity. In addition, the mean location and SD of the centre of rotation during the loaded stance phase for each subject group (thick lines), as well as the individual subject locations (shown as x), are presented (middle row).

The knee adduction moment increased from valgus through neutral to varus alignments for all three gait activities in our study, which is in line with previous findings.[32] While limb alignment was not reflected in the condylar kinematics, it significantly affected the knee adduction moment. Consequently, muscle activation strategies, ligament properties, or bone morphology could be more important in governing individual knee motion than limb alignment or knee joint loading. Together with further musculoskeletal modelling, these data can help to inform decision-making regarding limb alignment when aiming to restore physiological knee joint function.

Within the current study, the subjects were grouped according to their HKA angle. However, only a moderate correlation between the HKA angle measured using the EOS system and the abduction/adduction angle during standing measured using the fluoroscope was found. While the subject position was comparable in both situations, the angle was calculated differently. The EOS system uses anatomical axes,[19] whereas the abduction/adduction angle is calculated based on the functionally defined mediolateral femoral axis and

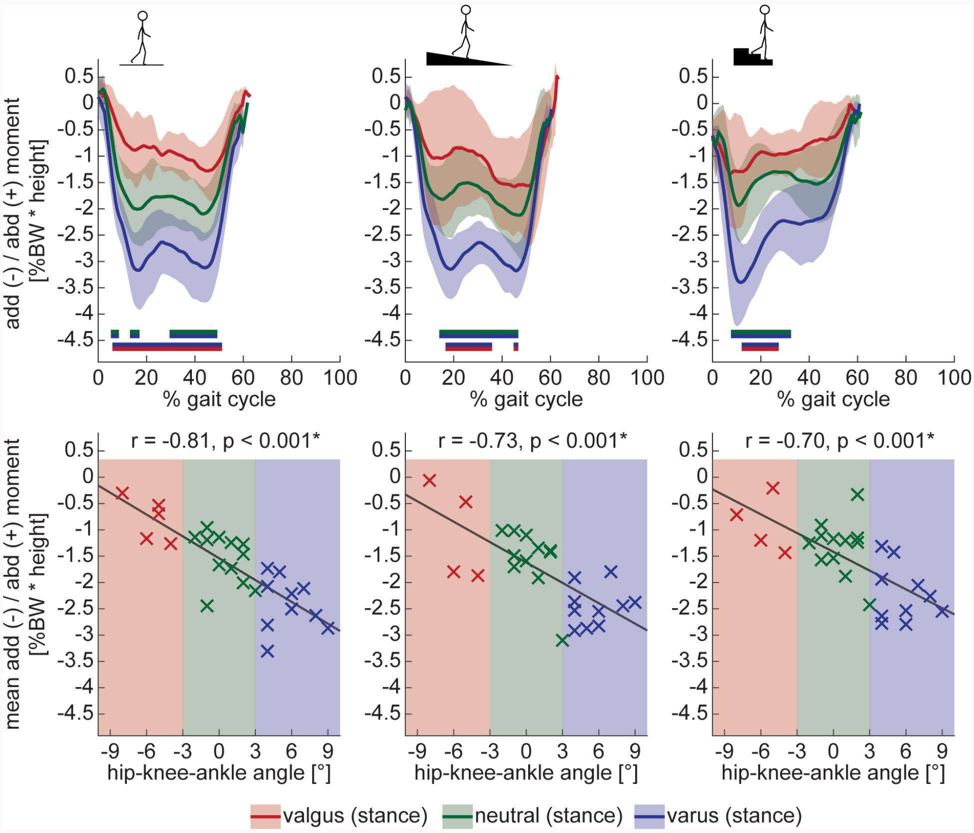

Fig. 5

Frontal plane knee moment (adduction/abduction) throughout complete gait cycles of level walking (left), downhill walking (middle), and stair descent (right). The means (thick lines) and SDs (shaded areas) across each limb alignment group are presented. Significant differences between the neutral, varus, and valgus groups are indicated with bars in the colours of the respective groups with an adjusted level of significance of $\alpha = 0.0167$. In addition, the Pearson correlations of the mean adduction/abduction moment across the loaded stance phase, and the individual hip-knee-ankle angle measured with the EOS (EOS imaging, France), are shown. BW, body weight.

Table IV. Peak knee adduction moment during the stance phase of level walking, downhill walking, and stair descent for the valgus, neutral, and varus groups. Means and SDs are presented for each subject group.

Variable	Valgus	Neutral	Varus
Level walking			
Peak knee adduction moment, %BW*height	-1.7 (0.6)*[1,2]	-2.6 (0.6)*[2,3]	-3.6 (0.6)*[1,3]
Downhill walking			
Peak knee adduction moment, %BW*height	-1.9 (1.2)*[4]	-2.6 (0.7)*[5]	-3.6 (0.4)*[4,5]
Stair descent			
Peak knee adduction moment, %BW*height	-1.8 (0.8)*[6]	-2.3 (0.7)*[7]	-3.7 (0.8)*[6,7]

*Significant differences between limb alignment groups (superscripted numbered pairs) based on an adjusted level of significance of $\alpha = 0.0167$
BW, body weight.

the longitudinal tibial shaft axis.[27] As a result, measurement technique-induced differences in limb alignment are likely to be observed. In this study, we specifically chose to use the EOS evaluation of limb alignment to ensure compatibility with clinical practice and use of clinical classification methods, but also because it allowed the anatomy of the femur and tibia to be considered. However, it is likely that stronger correlations between limb alignment, kinematic, and kinetic parameters could have been achieved if the subjects had been grouped according to the abduction/adduction angle. Furthermore, the HKA angle is a static measure based on the location of the hip, knee, and ankle joint centre. As a result, identical HKA angles can be caused by different combinations of femoral and tibial mechanical axis (Supplementary Figure e). However, the HKA angle provides no information about the orientation of the joint line and the relative angles of the femur and tibia.[10] Therefore, variations in individual tibiofemoral kinematics could be more affected by the orientation of the joint line than the general HKA. In addition, natural femoral and tibial torsion influence the relative positions of the femur and tibia relative to one another, but also with regard to the hip and ankle joint. Future studies aiming to elucidate the role of limb alignment on knee joint kinematics should consider HKA parameters and individual anatomical factors as potential perturbations.

The presented study is clearly limited by an under-representation of subjects with valgus limb alignment. Recruitment of these subjects was challenging, likely since constitutional valgus is only present in a low number of men and women.[9] Moreover, subjects with extreme and even pathological limb alignment were excluded from this study to allow a clear understanding of the relationships between limb alignment and natural physiological gait patterns. However, in hindsight, it became clear that the inclusion of more extreme limb alignments could have added further understanding to these relationships, and even have helped in establishing thresholds between physiological and pathological movement patterns. As a result, it is important to note that the final number of subjects recruited into the study, particularly in the valgus cohort, meant that the study was insufficiently powered for certain statistical analyses. A further limitation of this study was the single-plane videofluoroscopy setup, where accuracy of the 2D/3D registration of the fluoroscopic images was limited by out-of-plane error.[25] While these registration errors could affect the estimation of the CoR in the transverse plane, relative rotations and in-plane translations are known to be less influenced. Across all 15,823 registered frames, the mean frame-to-frame mediolateral translation was 1.3 mm (SD 0.3) while the overall range of translation during the loaded stance phase across all 404 trials was only 5.3 mm (SD 1.5). These extremely low mediolateral translations provide confidence that we were able to exclude any large out-of-plane registration errors and consequent effects on the CoR calculation. Finally, walking with the single-plane moving fluoroscope required a reduced walking speed (with accelerations remaining below 9 m/s^2), in order to allow the knee joint to remain within the field of view throughout the full gait cycles.[21] A previous study showed that despite the reduced walking speed, the reported walking patterns remain comparable to free slow walking.[33] Moreover, the low SD of gait speeds between subjects (< 0.1 m/s), albeit driven by the requirements of the fluoroscope, have ensured high levels of standardization in the test conditions, and therefore a consistent comparison between subjects and groups. Future studies should aim to utilize state-of-the-art mobile assessment systems, such as tracking dual-plane videofluoroscopy, to better understand the specific joint kinematics and kinetics that occur due to anatomical or pathological variations not only during activities of daily living, but also more challenging activities such as running or stop-and-go movements, to ensure that differences found in this study still prevail at higher speeds. In addition, the results presented in this study can provide a basis for sample size estimations and as such help to increase statistical power of future studies.

In our study, the minor influences of individual limb alignment on tibiofemoral kinematics but large differences between subjects suggest that factors other than limb alignment alone (e.g. soft-tissue sufficiency) may also play a role in guiding individual kinematic differences. While the sufficiency and laxity of joint ligaments are known to vary substantially between subjects with varus or valgus limb alignment,[17] musculoskeletal modelling can provide additional insights into the elongation patterns of joint ligaments and therefore enhance our understanding of soft-tissue constraints and laxity on tibiofemoral kinematics.[34] With the recent tendency towards kinematic alignment during TKA surgeries in subjects with a constitutional varus or valgus limb alignment, an in-depth knowledge of the role of subject-specific lower limb alignment in tibiofemoral kinematics and kinetics is crucial for supporting clinical decision-making. Here, a detailed understanding of the relationship between lower limb alignment and tibiofemoral kinematics and kinetics, but also individual soft-tissue loading in both healthy and pathological subjects, could help to develop intraoperative TKA alignment strategies aiming to restore natural mediolateral loading conditions as well as avoiding overloading of the surrounding soft-tissue structures.

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Supplementary material

Additional tables and figures regarding 3D gait velocity, 3D orientation of the knee during standing, knee sagittal and transversal moment, as well as the statistical analysis using statistical parametric mapping.

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Data sharing

The data that support the findings for this study are available to other researchers from the corresponding author upon reasonable request.

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