Contents lists available at ScienceDirect

Journal of Clinical Orthopaedics and Trauma

journal homepage: www.elsevier.com/locate/jcot

Association between stages of medial compartment osteoarthritis and three-dimensional knee alignment in the supine position: A cross-sectional study

Futoshi Ikuta^{a, b, *}, Kei Yoneta^c, Takeshi Miyaji^d, Kenichi Kidera^e, Akihiko Yonekura^e, Makoto Osaki^e, Kazuyoshi Gamada^a

^a Department of Medical Engineering and Technology, Graduate School of Medical Technology and Health Welfare Sciences, Hiroshima International University, 555-36 Kurosegakuendai, Higashihiroshima City, Hiroshima, 739-2695, Japan

^b Inanami Spine and Joint Hospital, 3-17-5 Higashishinagawa Shinagawa-ku, Tokyo, 140-0002, Japan

^c Department of Rehabilitation, Kobayashi Hospital, Kita 3 Jo Nishi 4, Kitami City, Hokkaido, 090-0043, Japan

^d Department of Orthopaedic Surgery, Aino Memorial Hospital, 3838-1 Ainocho, Unzen City, Nagasaki, 854-0301, Japan

^e Department of Orthopaedic Surgery, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki City, Nagasaki, 852-8501, Japan

ARTICLE INFO

Article history:

Received 18 May 2019

Received in revised form

24 August 2019

Accepted 28 October 2019

Available online 2 November 2019

Keywords:

Medial compartment osteoarthritis

Knee alignment

Osteoarthritis

Progression

ABSTRACT

Background: Osteoarthritis (OA) of the knee causes changes in knee alignment. A detailed knowledge of knee alignment is needed for correct assessment of the extent of disease progression, determination of treatment strategy, and confirmation of treatment effectiveness. However, deterioration of knee alignment during progression of OA has not been adequately characterized. The aims of this study were to clarify the changes in three-dimensional static knee alignment as knee OA stage progressed and to lay a foundation for an optimal treatment strategy to prevent knee malalignment.

Methods: A total of 106 knees of 81 patients ((men/women) 45/36; mean age 48.4 ± 19.9 years; body mass index (BMI) 25.7 ± 4.4 kg/m²) were enrolled in this cross-sectional study, comprising 34 (33/1) in Kellgren-Lawrence (KL) grade 0, 17 (8/9) in KL grade 1, 26 (5/21) in KL grade 2, 19 (4/15) in KL grade 3, and 10 (1/9) in KL grade 4. In all cases, computed tomography images were obtained with the subject in a reclined and relaxed position with the knee straight. Three-dimensional bone models were created from the images and knee alignment was calculated with six degrees-of-freedom. Then, 40 knees were selected consisting of 10 sex- and BMI-matched knees from each KL grade group: KL grade 1 (mean age 54.6 ± 8.4 years; BMI 23.3 ± 3.5 kg/m²), grade 2 (64.7 ± 10.9 years; 27.3 ± 3.2 kg/m²), grade 3 (69.2 ± 11.4 years; 27.1 ± 4.3 kg/m²), and grade 4 (71.9 ± 9.2 years; 27.2 ± 3.6 kg/m²). The Mann–Whitney *U* test with Bonferroni correction for multiple comparisons was used to analyze static alignment ($\alpha < 0.05/6$).

Results: Alignment of the knee in flexion was -4.0 [95% confidence interval (CI): -6.4 , -1.5] degrees, -3.4 [-8.0 , 1.3] degrees, -0.1 [-3.7 , 3.5] degrees, and 0.4 [-0.9 , 1.6] degrees in the order of KL grade 1 to 4. There were significant differences between KL grade 1 and 4 ($p = 0.0081$). Anterior tibial translation was 6.6 [4.6 , 8.6] mm, 5.8 [1.9 , 9.7] mm, 1.0 [-2.5 , 4.5] mm, and 1.3 [-2.4 , 5.1] mm in the order of grade 1 to 4. There were significant differences between KL grade 1 and 4 ($p = 0.0081$). There were no significant differences in lateral tibial translation nor tibial rotation.

Conclusions: The severely osteoarthritic knee joint was flexed and the tibia was displaced posteriorly with respect to the femur. Preventing these changes in alignment would assist in the prevention and treatment of knee OA.

© 2019

Abbreviations: BMI, body mass index; CT, computed tomography; KL grade, Kellgren-Lawrence grade; OA, osteoarthritis; 3D, three-dimensional; 95% CI, 95% confidence interval.

* Corresponding author. Department Medical Engineering and Technology, Graduate School of Medical Technology and Health Welfare Sciences, Hiroshima International University, 555-36 Kurosegakuendai, Higashihiroshima City, Hiroshima, 739-2695, Japan.

E-mail address: futoshi.ikuta@gmail.com (F. Ikuta).

<https://doi.org/10.1016/j.jcot.2019.10.011>

0976-5662/© 2019

1. Introduction

Osteoarthritis (OA) is a joint disease that causes pain and dysfunction and is associated with both social and economic problems.¹ Among US adults 60 years of age or older, the prevalence of radiographic knee OA was 37.4%.² In Japanese adults 40 years of age or older, the prevalence of radiographic knee OA was 42.6% in men and 62.4% in women.³ The average cost per patient for outpatient management of knee OA was \$506 per year.⁴ Therefore, prevention of knee OA is a critical issue.

The alignment of the knee gradually changes with progression of OA. Knee malalignment is a significant risk factor; varus knee alignment, in particular, has been reported to be a risk factor for incidence and progression of knee OA.⁵ Several studies have evaluated alignment of the knee in OA.^{6–8} In medial compartment OA, the alignment changes to varus and flexion; however, the details of changes other than those in the coronal plane remain unknown. An ultrasonographic study reported that the tibia in the OA knee demonstrated internal rotation by measuring a line connecting the posterior surface of the femoral condyles.⁹ However, computed tomography (CT) studies found either external rotation of the tibia¹⁰ or no difference in alignment from that in a healthy knee.¹¹ The former used the clinical epicondylar axis and the latter used the posterior tangential line of the distal femoral condyle. We hypothesized that these conflicting results reflected a difference in the reference axes used in the two-dimensional plane. OA of the knee may occur simultaneously and/or continuously with changes in six degrees-of-freedom, but there have not been any three-dimensional (3D) studies of static alignment of the knee according to disease stage. Therefore, changes in knee alignment with the stage of knee OA need to be evaluated in three dimensions.

The aims of this study were to clarify the changes in 3D static knee alignment as knee OA stage progressed and to lay a foundation for an optimal treatment strategy to prevent knee malalignment.

2. Methods

2.1. Ethics

The study protocol was approved by the ethics committees of our institutions and was conducted in accordance with the Declaration of Helsinki. The patients were informed that data from the study would be submitted for publication, and all gave their consent.

2.2. Participants

All patients enrolled in the study had attended our hospital and been found to have radiographic evidence of medial compartment OA. The severity of OA was classified according to Kellgren-Lawrence (KL) grade.¹² The contralateral healthy knee in patients diagnosed with unilateral anterior cruciate ligament or/and meniscus injury was included as KL grade 0. The following exclusion criteria were applied: history of lower limb surgery; central nervous system disease; childbearing potential; communication difficulties; and inability or refusal to provide informed consent.

2.3. Methods of analysis

2.3.1. CT imaging and creation of 3D bone models

The patient was supine with the knees maximally extended such that the patella was pointed straight up. Then, only the thighs were bound with a belt by the examiner in order to avoid alteration of the natural knee alignment and to help the patient relax. The

patient was then instructed to relax. CT data were obtained using a SOMATOM Definition system (Siemens AG, Erlangen, Germany) with a slice pitch of 0.5 mm spanning approximately 150 mm above and below the joint line of the knee. The exterior cortical bone edges were segmented using 3D-Doctor software (Able Software Corp., Lexington, MA), and 3D models of the femur and tibia were created. The knee model included both the femur and tibia.

2.3.2. Embedding the coordinate system in the 3D models (Fig. 1)

Local coordinate systems were embedded in each bone using a 3D-Aligner (GLAB Corp., Hiroshima, Japan) to allow all the procedures detailed below to be performed in a virtual space and the reproducibility of these procedures was confirmed.

2.3.2.1. Femoral coordinate system. The femoral coordinate system was defined around a virtual cylinder as proposed by Eckhoff et al.^{13,14} The virtual cylinder is composed of medial and lateral cylinders that share a co-axis with independently adjustable radii. First, the virtual cylinder was embedded in the distal femur by manipulating the cylinders in the virtual space and adjusting their radii to align with the medial and lateral posterior condyles. Areas of the medial and lateral posterior condyles that fit the circumference of the virtual cylinders were tibiofemoral contact areas at 15–115° of flexion (Fig. 2a). The co-axis of the cylinder was defined as the Z-axis. After the position of the virtual cylinder relative to the femur was set, the length of the cylinder was adjusted to fit the top and bottom of the cylinder to the most prominent points of the medial and lateral condyles of the femur, and the midpoint of the co-axis was defined as the origin of the femoral coordinate system (Fig. 2b). The Y-axis was defined visually as the line parallel to the projection line of the femoral shaft onto the XY plane, which is perpendicular to the Z-axis through the origin. The X-axis was the cross product of the Y- and Z-axes (Fig. 1a).

2.3.2.2. Tibial coordinate system. The tibial coordinate system was defined around a virtual rectangle fitted onto the contour of the tibial plateau at a right angle to the tibial long axis. To avoid highly variable morphology and a high prevalence of osteophyte formations at the posterior contour of the OA tibial plateau, the rectangle was fitted at the level of the fibular apex parallel to the tibial plateau plane. The four lines of the rectangle were fitted visually onto the posterior co-tangent of the medial and lateral tibial condyles, the medial and lateral tangents of the medial and lateral tibial condyles, respectively, and the anterior tangent of the medial tibial condyle (Fig. 3a). Then, the rectangle was translated superiorly so that it fit the bottoms of both tibial plateaus (Fig. 3b). The center of the rectangle was defined as the tibial origin, through which the medial/lateral (Z) and anteroposterior (X) axes were defined as two axes of the tibial coordinate system. The vertical (Y) axis of the tibia was, by definition, a cross product of these two axes proximally (Fig. 1b).

2.3.2.3. Reproducibility of the femoral and tibial coordinate systems. In total, 10 OA knees (70.7 ± 7.8 years; 9 women and 1 man; 5 right and 5 left knees in 10 subjects) and 10 healthy knees (29.0 ± 7.5 years; 10 men; 5 right and 5 left knees in 10 subjects) were included in this assessment. Classifying the grade of knee OA according to the KL system resulted in four patients in grade II, three grade III, and three grade IV. The first author, who was experienced with the above technique, embedded bony coordinate systems twice at an interval of 3 days. The intra-researcher reproducibility was analyzed using Geomagic Studio's best-fit alignment algorithm (Geomagic Inc., Morrisville, NC).

Fig. 1. (a): The virtual cylinder was composed of medial and lateral cylinders sharing a co-axis with independently adjustable radii (left). The co-axis of the cylinder was defined as the flexion-extension axis of the femur (right). (b): The virtual rectangle (left) was fitted at the tibial plateau (right).

Fig. 2. (a): The distal femur was manipulated in virtual space by positioning and enlarging cylinders to fit both posterior condyles until a good fit was obtained leaving only a small rim of condylar bone outside the cylinder (arrow). (b): After the position of the virtual cylinder relative to the femur was set, the length of the cylinder was adjusted until the top and bottom of the cylinder fit the most prominent points of the medial and lateral condyles of the femur (arrow).

2.3.3. Measuring the alignment of 3D models

The models of the femur and tibia were fitted to form a knee model using the Geomagic Studio best-fit alignment algorithm (Geomagic, Inc.) (Fig. 4). Knee alignment was calculated with six degrees-of-freedom on CT images acquired while the patient was in a comfortable position. The outcomes were (1) knee alignment comprising the anterior/superior/lateral position of the tibia in relation to the femur and (2) the angles of flexion, adduction, and external tibial rotation.

2.4. Statistical analysis

The Mann–Whitney *U* test with Bonferroni correction for multiple comparisons was used to analyze age, height, weight,

body mass index (BMI), and alignment. All the statistical analyses were performed using Statistical Package for the Social Sciences version 23 (SPSS Inc., Chicago, IL). Statistical significance was determined at $\alpha = 0.05$. Since all *p*-values for fixed effects were adjusted for multiple comparisons of four groups (KL grades 1–4) using Bonferroni correction, we used $\alpha = 0.05/6$.

3. Results

3.1. Reproducibility of femoral and tibial coordinate systems (Supplementary Table 1)

The largest errors in the healthy femur/tibia were translation on the Z-axis (means: 0.36 [95% confidence interval (CI): 0.15, 0.57]

Fig. 3. (a): The virtual rectangle was matched in the tibial cross section at the top of the fibular apex level. (b): The virtual rectangle was translated to the tibial plateau (arrow).

Fig. 4. Calculation of alignment of the tibia relative to the femur. (a): Based on the positional relationship between the femur and the global coordinate system. (b): Based on the positional relationship between the tibia and the global coordinate system. G: global coordinate system

mm)/X-axis (0.30 [0.16, 0.43] mm) and rotation on the Z-axis (0.40 [0.00, 0.81] degrees)/Z-axis (0.44 [0.21, 0.67] degrees), respectively. The largest errors in the OA femur/tibia were translation on the Z-axis (0.49 [0.16, 0.82] mm)/X-axis (0.56 [0.22, 0.91] mm) and rotation on the Y-axis (0.54 [0.24, 0.84] degrees)/X-axis (0.86 [0.32, 1.40] degrees), respectively (Table 1).

3.2. Static alignment

The study included 106 knees of 81 patients ((men/women) 45/36; mean age 48.4 ± 19.9 years; BMI 25.7 ± 4.4 kg/m²), comprising 34 knees (33/1) classified as KL grade 0, 17 (8/9) classified as KL grade 1, 26 (5/21) classified as KL grade 2, 19 (4/15) classified as KL

grade 3, and 10 (1/9) classified as KL grade 4. Demographic data of all subjects and the alignment results are shown in Table 2 and Fig. 5.

Among the bone models from KL grades 1–4, 10 BMI- and sex-matched knees (1 man, 9 women) were selected in each of the 4 groups: grade 1 (mean age 54.6 ± 8.4 years; BMI 23.3 ± 3.5 kg/m²), grade 2 (64.7 ± 10.9 years; 27.3 ± 3.2 kg/m²), grade 3 (69.2 ± 11.4 years; 27.1 ± 4.3 kg/m²), and grade 4 (71.9 ± 9.2 years; 27.2 ± 3.6 kg/m²). There were significant differences in age between grades 1 and 3 ($p = 0.0080$) and between grades 1 and 4 ($p = 0.0011$) (Table 3). Tibial external rotation was 3.6 [95% CI: 0.0, 7.2]°, 2.4 [0.0, 4.7]°, 0.3 [−3.1, 3.8]°, and 1.4 [−0.1, 3.0]° in the order of KL grade 1 to 4 (Table 4). There were no significant differences between the groups.

Table 1
Reproducibility of femoral and tibial coordinate systems.

		Translation [mm]		Rotation [degrees]	
		Healthy	OA	Healthy	OA
X-axis	Femur	0.09 [0.02, 0.17]	0.20 [0.01, 0.40]	0.15 [0.08, 0.22]	0.10 [0.05, 0.15]
	Tibia	0.30 [0.16, 0.43]	0.56 [0.22, 0.91]	0.24 [0.06, 0.42]	0.86 [0.32, 1.40]
Y-axis	Femur	0.12 [0.04, 0.20]	0.09 [0.03, 0.15]	0.28 [0.19, 0.36]	0.54 [0.24, 0.84]
	Tibia	0.14 [0.07, 0.21]	0.15 [0.08, 0.23]	0.43 [0.23, 0.62]	0.39 [0.28, 0.50]
Z-axis	Femur	0.36 [0.15, 0.57]	0.49 [0.16, 0.82]	0.40 [0.00, 0.81]	0.43 [0.25, 0.61]
	Tibia	0.14 [0.07, 0.21]	0.21 [0.03, 0.40]	0.44 [0.21, 0.67]	0.78 [0.28, 1.28]

Data are shown as the mean [95% CI]. OA, osteoarthritis.

Table 2
Demographic and anthropometric characteristics of the study population.

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Subjects (men/women)	34 (33/1)	13 (6/7)	21 (4/17)	15 (4/11)	10 (1/9)
Knees (men/women)	34 (33/1)	17 (8/9)	26 (5/21)	19 (4/15)	10 (1/9)
Age* [years]	28.2 (7.4)	55.4 (8.6)	61.3 (10.9)	69.3 (9.8)	71.9 (9.2)
Height* [m]	1.71 (0.06)	1.60 (0.10)	1.58 (0.09)	1.52 (0.06)	1.51 (0.05)
Weight* [kg]	73.6 (17.7)	62.9 (14.2)	65.8 (10.6)	63.1 (8.6)	61.6 (7.9)
BMI*	25.2 (5.3)	24.2 (3.2)	26.2 (3.6)	27.2 (4.1)	27.2 (3.6)

Data are shown as the mean and standard deviation (*). BMI, body mass index.

Fig. 5. Rotation and translation of the tibia in relation to the femur. (a): External tibial rotation, (b): Knee adduction, (c): Knee flexion, (d): Anterior tibial translation, (e): Lateral tibial translation, (f): Superior tibial translation CI: confidence interval.

Table 3
Demographic and anthropometric characteristics of the bone models of KL grade 1–4 knees matched for sex and BMI.

	Grade 1	Grade 2	Grade 3	Grade 4
Knees (men/women)	10 (1/9)	10 (1/9)	10 (1/9)	10 (1/9)
Age* [years]	54.6 (8.4)	64.7 (10.9)	69.2 (11.4)†	71.9 (9.2)††
Height* [m]	1.55 (0.06)	1.55 (0.08)	1.51 (0.05)	1.51 (0.05)
Weight* [kg]	56.2 (9.7)	65.9 (9.5)	61.4 (8.4)	61.6 (7.9)
BMI*	23.3 (3.5)	27.3 (3.2)	27.1 (4.3)	27.2 (3.6)

Data are shown as the mean and standard deviation (*). There were significant differences between KL grade 1 and 3 (†; $p = 0.0080$) and between 1 and 4 (††; $p = 0.0011$) for age. BMI, body mass index.

The alignment of the knee in adduction was -0.5 [95% CI: $-2.1, 1.2$] $^{\circ}$, 0.4 [$-0.7, 1.5$] $^{\circ}$, 1.5 [$0.6, 2.5$] $^{\circ}$, and 3.0 [$1.0, 5.1$] $^{\circ}$ (Table 4). There were no significant differences between the groups. Alignment of the knee in flexion was -4.0 [95% CI: $-6.4, -1.5$] $^{\circ}$, -3.4 [$-8.0, 1.3$] $^{\circ}$, -0.1 [$-3.7, 3.5$] $^{\circ}$, and 0.4 [$-0.9, 1.6$] $^{\circ}$ (Table 4). There were significant differences between KL grade 1 and 4 ($p = 0.0081$).

Anterior tibial translation was 6.6 [95% CI: $4.6, 8.6$] mm, 5.8 [$1.9, 9.7$] mm, 1.0 [$-2.5, 4.5$] mm, and 1.3 [$-2.4, 5.1$] mm in the order of grade 1 to 4 (Table 4). There were significant differences between KL grade 1 and 4 ($p = 0.0081$). Lateral tibial translation was 3.9 [95% CI: $2.9, 4.8$], 3.8 [$2.7, 4.9$] mm, 3.3 [$1.8, 4.7$], and 6.6 [$4.9, 8.4$] mm (Table 4). There were no significant differences between the groups. Superior tibial translation was 25.4 [95% CI: $-26.7, -24.1$] mm, -26.0

Table 4
Static alignment of KL grades 1–4.

	Grade 1	Grade 2	Grade 3	Grade 4
External rotation [degree]	3.6 [0.0, 7.2]	2.4 [0.0, 4.7]	0.3 [-3.1, 3.8]	1.4 [-0.1, 3.0]
Adduction [degree]	-0.5 [-2.1, 1.2]	0.4 [-0.7, 1.5]	1.5 [0.6, 2.5]	3.0 [1.0, 5.1]
Flexion [degree]	-4.0 [-6.4, -1.5]	-3.4 [-8.0, 1.3]	-0.1 [-3.7, 3.5]	0.4* [-0.9, 1.6]
Anterior translation [degree]	6.6 [4.6, 8.6]	5.8 [1.9, 9.7]	1.0 [-2.5, 4.5]	1.3* [-2.4, 5.1]
Lateral translation [degree]	3.9 [2.9, 4.8]	3.8 [2.7, 4.9]	3.3 [1.8, 4.7]	6.6 [4.9, 8.4]
Superior translation [degree]	-25.4 [-26.7, -24.1]	-26.0 [-27.9, -24.0]	-24.8 [-26.3, -23.3]	-26.7 [-28.1, -25.4]

Data are shown as the mean [95% CI]. There were significant differences between KL grade 1 and 4 (*: $p = 0.0081$).

[-27.9, -24.0] mm, -24.8 [-26.3, -23.3] mm, and -26.7 [-28.1, -25.4] mm (Table 4). There were no significant differences between the groups.

4. Discussion

The results of this study show that knee extension and anterior translation of the tibia are reduced in end-stage knee OA. There was no association between stage of knee OA and external tibial rotation.

Knee extension/flexion consists of a rolling and sliding motion that causes the tibia to translate anteriorly during extension.¹⁵ The findings of the present study demonstrated limitation of extension and translation in knees with severe OA. OA knees with flexion contracture have histological changes in the posterior joint capsule.^{16,17} Therefore, it is considered that knee OA simultaneously occurs with limitation of tibial anterior translation and extension. Individuals with early knee OA maintained the knee in more flexion and more posterior tibial translation during stance phase of the gait cycle.^{18,19} This chronic gait habit may have caused changes in the posterior joint capsule and altered static alignment. Prevention of posterior tibial translation and flexion contracture is important for prevention and treatment of knee OA.

There were no significant between-group differences in tibial external rotation in this study. Various results for tibial rotation have been reported previously. During squat, knees with OA reportedly showed external rotation^{20,21}; however, internal rotation was demonstrated at initial contact during gait, which is a more dynamic activity than squat.²² The measurement conditions in this study differed from those of previous studies. A systematic review and meta-analysis²³ reported that individuals with OA of the knee showed increased co-contraction of the lateral knee muscles. Under dynamic and weight-bearing conditions, external rotation of the tibia would increase. Accordingly, tibial external rotation is unlikely to be affected by the severity of OA in a static and non-weight bearing position.

This study has a major limitation. Grade 0 was taken as the contralateral knee in patients with unilateral anterior cruciate ligament and/or meniscus injury and included a high percentage of young men. There were sex differences in the anatomic features.²⁴ The grade 0 knee alignment and statistical results of this study should be kept in mind as only a reference with regard to progression of knee OA. However, these limitations were considered necessary to avoid radiation exposure for potentially pregnant women, and thus were inevitable. Therefore, grade 0 knees were excluded from the statistical analysis, and grade 1–4 knees matched for sex and BMI were analyzed, resulting in significant differences in age. Although knee OA progresses with age, age matching is left as a task for future research. On the other hand, this study has several strengths. The cylinder axis was used in this study because the transepicondylar axis, which is frequently used for femoral flexion-extension axis, is different from the functional flexion axis.²⁵ Tibial coordinate systems were embedded to

minimize the influence of osteophytes. The virtual rectangle was fitted at the level of the fibular apex parallel to the tibial plateau plane in order to avoid the highly variable morphology and high prevalence of formation of osteophytes at the posterior contour of the tibial plateau in the presence of OA. This method can analyze alignment with high reproducibility.

This study evaluated changes in knee alignment with the progression of knee OA using 3D models obtained from patients while they were in the supine position. The severely osteoarthritic knee was flexed and the tibia was displaced posteriorly with respect to the femur. Preventing these changes in alignment would assist in the prevention and treatment of knee OA.

Author statement

Futoshi Ikuta: Conceptualization, Methodology, Software, Validation, Formal Analysis, Data Curation, Writing – Original Draft, Visualization. **Kei Yoneta:** Conceptualization, Methodology, Software, Validation, Data Curation, Writing – Review & Editing. **Takeshi Miyaji:** Investigation, Resources, Writing – Review & Editing. **Kenichi Kidera:** Investigation, Resources, Writing – Review & Editing. **Akihiko Yonekura:** Investigation, Resources, Writing – Review & Editing. **Makoto Osaki:** Investigation, Resources, Writing – Review & Editing. **Kazuyoshi Gamada:** Conceptualization, Methodology, Software, Writing – Review & Editing, Supervision, Project Administration.

Declaration of competing interest

The custom-made 3D-Aligner program used in this study was developed by GLAB Corp., of which a co-author is the president. The first author purchased this software at the standard retail price, and the company provided no financial support for this study. The authors declare that there are no other potential conflicts of interest regarding the contents of this paper.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcort.2019.10.011>.

References

- March L, Smith EU, Hoy DG, et al. Burden of disability due to musculoskeletal (MSK) disorders. *Best Pract Res Clin Rheumatol*. 2014;28:353–366.
- Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the third national health and nutrition examination survey 1991–94. *J Rheumatol*. 2006;33:2271–2279.
- Yoshimura N, Muraki S, Oka H, et al. Prevalence of knee osteoarthritis, lumbar spondylosis, and osteoporosis in Japanese men and women: the research on

- osteoarthritis/osteoporosis against disability study. *J Bone Miner Metab.* 2009;27:620–628.
4. Bedard NA, Dowdle SB, Anthony CA, et al. The AAHKS Clinical Research Award: what are the costs of knee osteoarthritis in the year prior to total knee arthroplasty? *J Arthroplast.* 2017;32:S8–S10.e1.
 5. Sharma L, Song J, Dunlop D, et al. Varus and valgus alignment and incident and progressive knee osteoarthritis. *Ann Rheum Dis.* 2010;69:1940–1945.
 6. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *J Am Med Assoc.* 2001;286:188–195.
 7. Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ. The effect of body weight on progression of knee osteoarthritis is dependent on alignment. *Arthritis Rheum.* 2004;50:3904–3909.
 8. Brouwer GM, van Tol AW, Bergink AP, et al. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis Rheum.* 2007;56:1204–1211.
 9. Nagao N, Tachibana T, Mizuno K. The rotational angle in osteoarthritic knees. *Int Orthop.* 1998;22:282–287.
 10. Matsui Y, Kadoya Y, Uehara K, Kobayashi A, Takaoka K. Rotational deformity in varus osteoarthritis of the knee: analysis with computed tomography. *Clin Orthop Relat Res.* 2005;433:147–151.
 11. Yagi T. Tibial torsion in patients with medial-type osteoarthrotic knees. *Clin Orthop Relat Res.* 1994;(302):52–56.
 12. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis.* 1957;16:494–502.
 13. Eckhoff DG, Bach JM, Spitzer VM, et al. Three-dimensional mechanics, kinematics, and morphology of the knee viewed in virtual reality. *J Bone Joint Surg Am.* 2005;87(Suppl 2):71–80.
 14. Eckhoff D, Hogan C, DiMatteo L, Robinson M, Bach J. Difference between the epicondylar and cylindrical axis of the knee. *Clin Orthop Relat Res.* 2007;461:238–244.
 15. Goodfellow J, O'Connor J. The mechanics of the knee and prosthesis design. *J Bone Joint Surg Br.* 1978;60-B(3):358–369.
 16. Malinowski K, Góralczyk A, Hermanowicz K, LaPrade RF, Więcek R, Domżański ME. Arthroscopic complete posterior capsulotomy for knee flexion contracture. *Arthrosc Technol.* 2018;7:e1135–e1139.
 17. Campbell TM, Trudel G, Laneuville O. Knee flexion contractures in patients with osteoarthritis: clinical features and histologic characterization of the posterior capsule. *Pharm Manag PM R.* 2015;7:466–473.
 18. Li JS, Tsai TY, Felson DT, Li G, Lewis CL. Six degree-of-freedom knee joint kinematics in obese individuals with knee pain during gait. *PLoS One.* 2017;12, e0174663.
 19. Li JS, Tsai TY, Felson DT, Li G, Lewis CL. Correction: six degree-of-freedom knee joint kinematics in obese individuals with knee pain during gait. *PLoS One.* 2019;14, e0213084.
 20. Saari T, Carlsson L, Karlsson J, Kärrholm J. Knee kinematics in medial arthrosis. Dynamic radiostereometry during active extension and weight-bearing. *J Biomech.* 2005;38:285–292.
 21. Hamai S, Moro-oka TA, Miura H, et al. Knee kinematics in medial osteoarthritis during in vivo weight-bearing activities. *J Orthop Res.* 2009;27:1555–1561.
 22. Farrokhi S, Tashman S, Gil AB, Klatt BA, Fitzgerald GK. Are the kinematics of the knee joint altered during the loading response phase of gait in individuals with concurrent knee osteoarthritis and complaints of joint instability? A dynamic stereo X-ray study. *Clin Biomech (Bristol, Avon).* 2012;27:384–389.
 23. Mills K, Hunt MA, Leigh R, Ferber R. A systematic review and meta-analysis of lower limb neuromuscular alterations associated with knee osteoarthritis during level walking. *Clin Biomech (Bristol, Avon).* 2013;28:713–724.
 24. Nguyen AD1, Shultz SJ. Sex differences in clinical measures of lower extremity alignment. *J Orthop Sport Phys Ther.* 2007;37:389–398.
 25. Mochizuki T, Sato T, Blaha JD, et al. The clinical epicondylar axis is not the functional flexion axis of the human knee. *J Orthop Sci.* 2014;19:451–456.