Inter-laboratory comparison of knee biomechanics and muscle activation patterns during gait in patients with knee osteoarthritis

Schrijvers, J. C.; Rutherford, D.; Richards, R.; van den Noort, J. C.; van der Esch, M.; Harlaar, J.

DOI
10.1016/j.knee.2021.03.001

Publication date
2021

Document Version
Final published version

Published in
Knee

The Knee 29 (2021) 500–509

Contents lists available at ScienceDirect

The Knee

journal homepage:

Inter-laboratory comparison of knee biomechanics and muscle activation patterns during gait in patients with knee osteoarthritis

J.C. Schrijvers [a,*], D. Rutherford [b,c], R. Richards [a], J.C. van den Noort [a,d], M. van der Esch [e,f], J. Harlaar [a,g,h]

[a] Department of Rehabilitation Medicine, Amsterdam Movement Sciences, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands
[b] School of Physiotherapy, Dalhousie University, Halifax, Nova Scotia, Canada
[c] School of Biomedical Engineering, Dalhousie University, Halifax, Nova Scotia, Canada
[d] Department of Radiology and Nuclear Medicine, Amsterdam Movement Sciences, Amsterdam UMC, University of Amsterdam, Medical Imaging Quantification Center (MIQC), Amsterdam, the Netherlands
[e] Amsterdam Rehabilitation Research Center, Reade, Amsterdam, the Netherlands
[f] Faculty of Health, Centre of Expertise Urban Vitality, Amsterdam University of Applied Science, Amsterdam, the Netherlands
[g] Department of Biomechanical Engineering, Delft University of Technology, Delft, the Netherlands
[h] Department of Orthopedics, Erasmus Medical Center, Rotterdam, the Netherlands

ARTICLE INFO

Article history:
Received 10 October 2020
Revised 24 January 2021
Accepted 1 March 2021

Keywords:
Gait
Inter-laboratory
Knee biomechanics
Muscle activation
Harmonization
Protocol

ABSTRACT

Background: Gait analysis has been used for decades to quantify knee function in patients with knee osteoarthritis; however, it is unknown whether and to what extent inter-laboratory differences affect the comparison of gait data between studies. Therefore, the aim of this study was to perform an inter-laboratory comparison of knee biomechanics and muscle activation patterns during gait of patients with knee osteoarthritis.
Methods: Knee biomechanics and muscle activation patterns from patients with knee osteoarthritis were analyzed, previously collected at Dalhousie University (DAL: n = 55) and Amsterdam UMC, VU medical center (VUmc: n = 39), using their in-house protocols. Additionally, one healthy male was measured at both locations. Both direct comparisons and after harmonization of components of the protocols were made. Inter-laboratory comparisons were quantified using statistical parametric mapping analysis and discrete gait parameters.
Results: The inter-laboratory comparison showed offsets in the sagittal plane angles, moments and frontal plane angles, and phase shifts in the muscle activation patterns. Filter characteristics, initial contact identification and thigh anatomical frame definitions were harmonized between the laboratories. After this first step in protocol harmonization, the offsets in knee angles and sagittal plane moments remained, but the inter-laboratory comparison of the muscle activation patterns improved.
Conclusions: Inter-laboratory differences obstruct valid comparisons of gait datasets from patients with knee osteoarthritis between gait laboratories. A first step in harmonization of gait analysis protocols improved the inter-laboratory comparison. Further protocol harmonization is recommended to enable valid comparisons between labs, data-sharing and multicenter trials to investigate knee function in patients with knee osteoarthritis.

* Corresponding author at: VU Medical Center, Department of Rehabilitation Medicine, Amsterdam UMC, PO Box 7057, 1007 MB Amsterdam, the Netherlands.
E-mail address: j.schrijvers@amsterdamumc.nl (J.C. Schrijvers).

https://doi.org/10.1016/j.knee.2021.03.001
0968-0160/

1. Introduction

Gait analysis has been used for decades to quantify knee function in patients with knee osteoarthritis (KOA) and to objectively evaluate the efficacy of interventions [1,2]. There is evidence that changes in knee angles [3] and moments [4] during gait are associated with the initiation or progression of KOA [5,6]. Moreover, knee muscle activations are often altered during gait of patients with KOA compared with healthy controls [7,8]. These alterations might be a compensation strategy to control the symptoms of KOA (pain, stiffness, instability). Furthermore, elevated co-contractions could cause increased loading of the knee cartilage [9–11]. Comprehensive gait analyses, including electromyography to measure muscle activation, can help in understanding the implications of changes in knee biomechanics and muscle activation on the joint structure and assist in identifying individuals for appropriate treatment, i.e. to design strategies to delay or prevent KOA progression.

To date, gait laboratories have typically integrated standardized biomechanics [12] and electromyography protocols [13], through the use of customized measurement setups, data collection procedures and data processing methods to obtain the gait parameters of interest. While similarities exist in gait analysis protocols, many decisions made in the protocols may present inter-laboratory differences when comparing gait datasets of patients with KOA. Few studies have been performed on inter-laboratory differences [14–16] and, as far as we know, none of them included patients with KOA. Overall these studies in healthy subjects showed good agreement on the spatiotemporal parameters [14], but lower consistency in knee biomechanics [14–16]. Even with similar anatomical frame definitions [15] or methods to improve marker placement [16], inter-laboratory differences were still present. This suggests that other components in the measurement setups, data collection or data processing may also contribute to the inter-laboratory differences. Further investigation into gait analysis protocols is therefore needed to explore whether and to what extent inter-laboratory differences affect the comparison of gait data of patients with KOA.

The Joint Action Research Laboratory at Dalhousie University, Halifax, Canada (DAL) and the Virtual Reality laboratory at the Amsterdam UMC, location VU medical center, Amsterdam, the Netherlands (VUmc) both performed gait studies in patients with KOA using the same treadmill and a comprehensive knee function assessment including motion, moments and electromyography allowing comparable results (i.e. not statistically different) to be expected [17–19]. Comparable gait data between laboratories enable possibilities such as data-sharing and performing large international multicenter trials on knee function in patients with knee osteoarthritis, which eventually creates more evidence-based research on KOA. Therefore, the aim of this study was to perform an inter-laboratory comparison of knee biomechanics and muscle activation patterns during gait of patients with KOA.

2. Methods

2.1. Study population

2.1.1. Dalhousie University, joint Action Research Laboratory (DAL)

Previously collected gait datasets from 55 patients with KOA were used in this study [19,20]. All patients gave informed consent. Patients had KOA classified as moderate severity based on functional status [20], no previous or planned hip or knee replacement and were able to walk unaided. In addition, anthropometrics, quadriceps and hamstrings strength (isometric) and questionnaires (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC [21]), Numeric Pain Rating Scale (NPRS [22])) were collected [20]. Patient characteristics from DAL are presented in Table 1.

2.1.2. Amsterdam UMC, VUmc

The gait datasets of 39 patients with KOA from a previous study were used [18] (one patient was excluded, because of an outlying low walking velocity (0.5 m/s)). All patients provided informed consent. Patients had radiographic evidence of medial KOA, radiographic disease severity of grade 1 or higher on the Kellgren–Lawrence (KL) classification system [23], no previous or planned hip or knee replacement and were able to walk unaided. Anthropometrics, quadriceps and hamstrings strength (isokinetic) and questionnaires (WOMAC [21], NPRS [22]) were also collected [18]. The patient characteristics from VUmc are presented in Table 1.

2.2. Measurement setup and data collection

2.2.1. Dalhousie University, joint Action Research Laboratory (DAL)

Details on the DAL measurement setup and data collection are presented in Supplementary Table S1. The laboratory of DAL contained an R-Mill dual-belt instrumented treadmill with built-in force plates (Motek Forcelink BV, Amsterdam, the Netherlands), a motion capture system (Qualisys, Gothenburg, Sweden) and wired electromyography (EMG) system (Bortec Inc., Calgary, Canada). Skin surface motion capture markers were placed using a custom-developed marker model [24]. EMG electrode placement was performed following the SENIAM guidelines [13] in order to retrieve the muscle activations of the vastus medialis, vastus lateralis, rectus femoris, medial hamstring, lateral hamstring, medial gastrocnemius and lateral gastrocnemius. Before recording of the gait data, patients were familiarized with barefoot treadmill walking for 6 min at a walk-

Table 1
Characteristics of patients previously measured at Dalhousie University (DAL) and Virtual Reality Laboratory at the VU medical center (Vumc).

Characteristic	DAL (n = 55)	VUmc (n = 39)	*P*
Age	61 (6)	62 (6)	0.61
Body weight (kg)	83 (15)	77 (11)	0.04
Height (m)	1.69 (0.09)	1.74 (0.10)	0.02
Body mass index (BMI) (kg/m^2)	29 (7)	25 (3)	<0.01[nn]
Sex (n)	28 (51%)	24 (62%)	0.31
KL Grade (n)	21 (38%)	19 (49%)	0.03
1	24 (44%)	8 (20%)	
2	8 (14%)	9 (23%)	
3	0 (0%)	3 (8%)	
4	2 (4%)	0 (0%)	
Missing			
NPRS (0–10)	1 (2)	2 (4)	0.09[nn]
WOMAC Pain (0–20)	6 (4)	12 (6)	<0.01
WOMAC Stiffness (0–8)	3 (2)	3 (2)	0.80[nn]
WOMAC Physical Function (0–68)	17 (19)	17 (18)	0.98[nn]
Quadriceps strength (Nm/kg)	1.39 (0.41)	1.54 (0.45)	0.09
Hamstrings strength (Nm/kg)	0.87 (0.30)	0.69 (0.24)	<0.01
Walk velocity (m/s)	1.05 (0.16)	1.12 (0.26)	0.02

Median and interquartile range are provided instead of mean and standard deviation. KL, Kellgren–Lawrence; NPRS, Numeric Pain Rating Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[nn] Non-normal distribution.

ing velocity determined from over-ground walking [19]. After 6 min, a 20-s recording (14–18 strides) was performed of three-dimensional (3D) marker trajectories, 3D ground reaction forces and EMG.

2.2.2. Amsterdam UMC, VUmc

Details on the VUmc measurement setup and data collection are provided in Supplementary Table S1. The gait laboratory of VUmc had the same R-Mill dual-belt instrumented treadmill as DAL (Motek Forcelink BV, Amsterdam, the Netherlands). Furthermore, the laboratory contained a motion capture system (VICON, Oxford, UK) and a wireless EMG system (Cometa, Milan, Italy). Skin surface motion markers were placed using the calibrated anatomical systems technique (CAST) marker model [25]. EMG electrode placement was performed following the SENIAM guidelines [13] in order to retrieve the muscle activations of the vastus medialis, vastus lateralis, rectus femoris, medial hamstring, lateral hamstring, medial gastrocnemius and lateral gastrocnemius. Before recording gait data, patients were familiarized with shod treadmill walking for 3 min at a preferred walking velocity determined by incrementing the velocity until the patient was satisfied. When satisfied, a recording of 1 min (~60 strides) was completed and included 3D marker trajectories, 3D ground reaction forces and EMG.

2.3. Data processing

2.3.1. Dalhousie University, Joint Action Research Laboratory (DAL)

The marker trajectories, ground reaction forces and muscle activation patterns of DAL were processed in a custom-made Matlab program to acquire the ensemble-averaged knee angles, moments and muscle activation patterns. Details on the data processing of DAL can be found in Supplementary Table S1. The marker trajectories were filtered using a two-way 6-Hz fourth-order low-pass Butterworth filter and the ground reaction forces were filtered using a two-way 30-Hz fourth-order low-pass Butterworth filter. Technical and local anatomical coordinate systems were derived from skin surface markers to allow knee angle calculations through Cardan/Euler decomposition [26]. Net external knee moments were calculated using inverse dynamics [27], filtered using a two-way 10-Hz fourth-order low-pass Butterworth filter and expressed using a floating axis. The muscle activation patterns were band-pass filtered (two-way 10–500 Hz fourth order), full-wave rectified and low-pass filtered using a two-way 6-Hz fourth-order low-pass Butterworth filter. The knee angles, moments and muscle activation patterns were time-normalized to gait cycle or to stance (moments) using a cubic spline interpolation function and the ground reaction force data (2000 Hz) to determine initial contact and toe off identification (threshold: 30 N). Furthermore, the moments were amplitude-normalized to body mass (Nm/kg) and the muscle activation patterns were amplitude-normalized for each gait cycle to the peak activation that occurred during that gait cycle.

2.3.2. Amsterdam UMC, VUmc

The marker trajectories, ground reaction forces and EMG of VUmc were processed in a custom-made Matlab program ('BodyMech', VUmc, Amsterdam) to obtain the ensemble-averaged knee angles, moments and muscle activation patterns. Details on the data processing of VUmc are presented in Supplementary Table S1. The marker trajectories were filtered using the cross-validated quintic spline from Woltring [28] and the ground reaction forces were filtered using a two-way 10-Hz second-order low-pass Butterworth filter. Segment and joint kinematics were calculated using the anatomical frame definitions of Cappozzo et al. [25,26] and the joint coordinate systems described by Grood and Suntay [29] to acquire the knee

angles. Net external knee moments were calculated using inverse dynamics and expressed in the distal segment [30]. No post-filtering was applied on the calculated angles or moments. The muscle activation patterns were filtered with a one-way 20-Hz third-order high-pass Butterworth filter, full-wave rectified and filtered with a two-way 6-Hz second-order low-pass Butterworth filter. The knee angles, moments and muscle activation patterns were time-normalized to gait cycles or to stance (moments) using cubic interpolation function and the ground reaction force data (100 Hz, previously down-sampled to match marker data) to determine initial contact and toe off identification (threshold: 25 N). The initial contacts for the muscle activation patterns were up-sampled to 1000 Hz to match the signals. Furthermore, the moments were amplitude-normalized to body mass (Nm/kg) and the muscle activation patterns were amplitude-normalized for each gait cycle to the peak activation that occurred during that gait cycle.

2.4. Protocol harmonization

To identify components of the protocols that required harmonization, a healthy male subject (age: 28 years, body mass index (BMI): 21 kg/m^2) was measured at both locations using the local measurement setups, data collection and data processing. The subject walked barefoot at a selected velocity of 1.48 m/s. Furthermore, a walking trial was recorded with both DAL and VUmc marker models placed on the subject, which enabled data processing with the same data processing program (VUmc). The components of the protocols that required harmonization were, when possible, implemented in the reprocessing of the gait datasets of the patients with KOA to observe the effect on the inter-laboratory comparison after protocol harmonization.

2.5. Inter-laboratory comparisons

The inter-laboratory comparisons were quantified for the knee biomechanics and muscle activation patterns during gait using statistical parametric mapping analysis [31] and by calculation of discrete gait parameters (i.e. peak, initial contact, mean and range). Statistical parametric mapping analysis enables statistical comparison of the gait data at each point of the gait cycle. Offsets were defined as an upward or downward shift on the y-axis between two gait patterns and phase shifts were defined as a horizontal shift on the x-axis between two gait patterns.

2.6. Statistics

Descriptive statistics were calculated for patient characteristics and for discrete gait parameters of the knee biomechanics and muscle activation patterns. The KL grades and sex distributions were compared between the laboratories using the chi-squared test. A one-way analysis of variance (ANOVA) was used to compare the participant characteristics when normally distributed (Shapiro–Wilcoxon test); otherwise a non-parametric Mann–Whitney U-test was performed. In the statistical parametric mapping analysis a one-way ANOVA was used to analyze the differences at each point of the gait cycles between the laboratories (paired-samples *t*-test for data of healthy subject). The discrete gait parameters were tested on normality of the distribution (Shapiro–Wilcoxon test) and a square root transformation was performed if the data were not normally distributed. After this, a multivariate analysis with walking velocity as a covariate was used to compare the discrete gait parameters. Moreover, an additional analysis was performed with covariates (differences in patient characteristics) added to the inter-laboratory comparison after protocol harmonization. The significance level was $P < 0.05$.

3. Results

3.1. Comparison of patient characteristics

The DAL patient group had a higher BMI (mean difference: 3 kg/m^2, $P < 0.01$), a different distribution of the KL grades ($P = 0.03$), lower pain scores (WOMAC Pain, mean difference: 6, $P < 0.01$), higher hamstrings strength (mean difference: 0.15 Nm/kg, $P < 0.01$) and lower walking velocity (mean difference: 0.07 m/s, $P = 0.02$) compared with the group of patients of the VUmc (Table 1).

3.2. Inter-laboratory comparison

The knee angles and moments during gait of patients with KOA of both laboratories are presented in Figure 1. Offsets between the laboratories were observed (upward or downward shift on y-axis) in the sagittal plane and frontal plane angles (statistical parametric mapping analysis: $P < 0.02$). The group of patients measured at VUmc had on average 11.8° higher sagittal angles and 3.8° lower frontal plane angles over the full gait cycle. Furthermore, all discrete gait parameters of the knee angles were different between the laboratories (Table 2), except for the range of motion during full gait cycle of the frontal plane angles ($P = 0.69$). Offsets were also observed in the sagittal plane knee moments with an average difference of 0.16 Nm/kg over stance between the laboratories (statistical parametric mapping analysis: $P < 0.05$). The frontal plane moments were more comparable between the laboratories, only showing offsets during 1–5% and 25–30% of stance (statis-

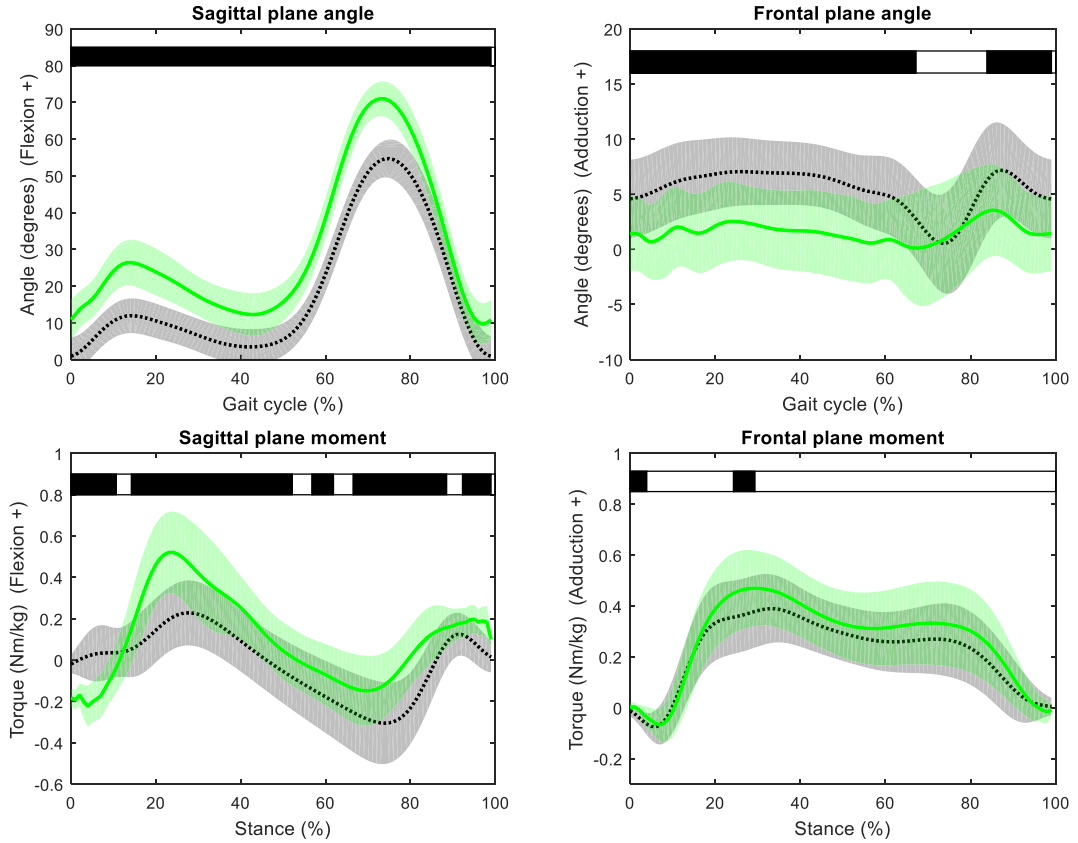

Figure 1. Knee angles and moments of patients with knee osteoarthritis previously measured at the Virtual Reality Laboratory at the VU medical center (Vumc; solid line, green) and Dalhousie University (DAL; dotted line, black). The line represents the mean and the shaded area the standard deviation. The bar on top of each graph indicates a significant difference (black) or no significant difference (white) between the labs determined with SPM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

tical parametric mapping analysis: $P < 0.05$). The comparison of the discrete gait parameters presented the same result with differences in the parameters between the laboratories for the sagittal plane moments ($P < 0.01$) and similarities for the frontal plane moments ($P > 0.09$).

The muscle activation patterns during gait of patients with KOA at both laboratories are shown in Figure 2. Phase shifts were identified between the laboratories in all muscle activation patterns (horizontal shift on x-axis), varying from −3% to 8% of the gait cycle (Table 2, distance between the indices of peak activation). The statistical parametric mapping analysis presented differences in all muscle activation patterns ($P < 0.05$). The discrete gait parameters of the muscle activation patterns were different between the laboratories, except for the mean activation of lateral ($P = 0.18$) and medial hamstring ($P = 0.73$).

3.3. Protocol harmonization

The measurement of the healthy subject in both laboratories (Supplementary Figs. S1 and S2) showed that the components of the gait analysis protocols that needed to be harmonized were: (1) filter characteristics, (2) initial contact identification, (3) anatomical frame definitions, (4) knee moment calculation and (5) marker models (details described in Supplementary Material). Unfortunately, the previously collected patient data from DAL and VUmc did not use a comparable marker model, thus not all of these components of the data processing could be harmonized. The components used for inter-laboratory comparison after protocol harmonization were, therefore: alignment of (1) filter characteristics (characteristics of DAL), (2) initial contact identification (i.e. input force signal of 1000 Hz, 25-N force threshold and the force filter characteristics of VUmc) and (3) thigh anatomical frame definitions (use of estimated hip joint center instead of greater trochanter marker).

3.4. Inter-laboratory comparison after protocol harmonization

The knee angles and moments during gait of patients with KOA of both laboratories after protocol harmonization are presented in Figure 3. The offsets in the sagittal plane angles, frontal plane angles and sagittal plane moments were still present

Table 2
Overview of the differences between the labs in the discrete gait parameters of the knee biomechanics and muscle activation patterns of the gait datasets of the patients with knee osteoarthritis.

Knee angles			
Discrete gait parameter (°)		Before harmonization Difference between labs	After harmonization Difference between labs
Sagittal plane angle	Mean offset	***11.8***	***11.3***
	Initial contact	9.9*	8.9*
	Peak stance	14.6*	13.8*
	Peak terminal stance	8.9*	8.6*
	Peak swing	16.0*	15.3*
	ROM full gait cycle	8.6*	6.5*
	ROM stance	5.0*	4.7*
Frontal plane angle	Mean offset	***3.8***	***4.0***
	Initial contact	3.2*	3.2*
	ROM full gait cycle	0.0	2.0*
	ROM stance	0.8*	0.8
Knee moments			
Discrete gait parameter (Nm/kg)		Difference between labs	Difference between labs
Sagittal plane moment	Mean offset	***0.16***	***0.14***
	Peak flexion	0.29*	0.22*
	Peak extension	0.17*	0.19*
	Range stance	0.21*	0.13*
Frontal plane moment	Mean offset	***0.05***	***0.08***
	First peak adduction	0.08	0.12*
	Second peak adduction	0.07	0.03
	Range stance	0.07	0.12*
Knee muscle activations			
Discrete gait parameter (%)	Difference between labs	Difference between labs	
Vastus medialis	*Phase shift*	*4% of gait cycle*	*2% of gait cycle*
	Mean activation	3*	1
Vastus lateralis	*Phase shift*	*4% of gait cycle*	*2% of gait cycle*
	Mean activation	11*	2
Rectus femoris	*Phase shift*	*3% of gait cycle*	*2% of gait cycle*
	Mean activation	5*	1
Medial hamstring	*Phase shift*	*7% of gait cycle*	*2% of gait cycle*
	Mean activation	0	0
Lateral hamstring	*Phase shift*	*−3% of gait cycle*	*−1% of gait cycle*
	Mean activation	2	0
Medial gastrocnemius	*Phase shift*	*8% of gait cycle*	*5% of gait cycle*
	Mean activation	4*	1
Lateral gastrocnemius	*Phase shift*	*6% of gait cycle*	*5% of gait cycle*
	Mean activation	6*	1

ROM, range of motion.
* Significantly different ($P < 0.05$) between gait laboratories.

between the laboratories. Similar results were observed in the discrete gait parameters, except for the range of motion during full gait cycle ($P = 0.04$) and stance ($P = 0.27$) of the frontal plane angle. The offsets in the frontal plane moments changed due to the harmonization with differences observed during 23–36% of gait cycle (statistical parametric mapping analysis: $P < 0.01$). Besides this, the discrete gait parameters first peak and range of the frontal plane moments became significantly different between the laboratories.

The muscle activation patterns during gait of patients with KOA of both laboratories after protocol harmonization are shown in Figure 4. The phase shifts between the laboratories in the muscle activation patterns were reduced from −3% to 8% of gait cycle to −1% to 5% of gait cycle (Table 2). Furthermore, the statistical parametric mapping analysis presented no differences in the medial and lateral hamstring patterns ($P > 0.05$). Furthermore, all discrete gait parameters of the muscle activation patterns became comparable due to the harmonization ($P > 0.07$). The additional analysis with extra covariates (Supplementary Table S2, e.g., BMI, KL grades, WOMAC pain and hamstrings strength) revealed a similar range of motion of the frontal plane angle ($P = 0.07$) and more alike discrete gait parameters of the frontal plane moments ($P > 0.16$).

4. Discussion

The aim of the study was to perform an inter-laboratory comparison of knee biomechanics and muscle activation patterns during gait of patients with KOA. Offsets and phase shifts were present when comparing gait data of patients with KOA

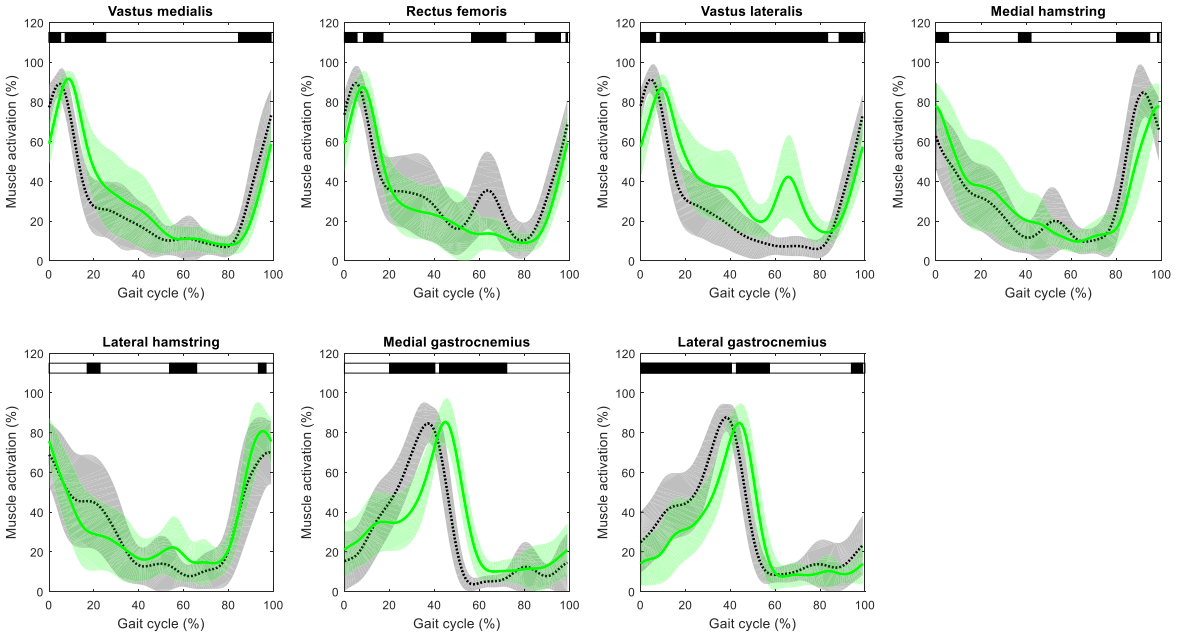

Figure 2. Muscle activation patterns of patients with knee osteoarthritis previously measured at Virtual Reality Laboratory at the VU medical center (Vumc; solid line, green) and Dalhousie University (DAL; dotted line, black). The solid line represents the mean and the shaded area the standard deviation. The bar on top of each graph indicates a significant difference (black) or no significant difference (white) between the labs determined with SPM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

between the laboratories, which can partly be explained by differences in gait analysis protocols. A first step in harmonization of the protocols was made by aligning components of the data processing. This resulted in an improved similarity of the muscle activation patterns and a reduction of the phase shifts. Harmonization of gait analysis protocols is therefore recommended.

The results of this study demonstrate that inter-laboratory differences affect the comparison of gait data from patients with KOA. In agreement with studies investigating healthy subjects, the results of the healthy subject measured in this study showed that different marker placement and anatomical frame definitions contribute to these inter-laboratory differences [15,16]. This could also partly explain the remaining offsets in knee biomechanics in the inter-laboratory comparison of the patients after partial protocol harmonization, because the anatomical frame definitions and marker placement could not be fully harmonized for the previously measured patient data. Other components of the protocols also affected the inter-laboratory comparison, such as filter characteristics, knee moment calculation and initial contact identification. In particular, the inter-laboratory comparison of the muscle activation patterns improved after alignment of the filter characteristics and initial contact identification. Therefore, we recommend that future gait studies using electromyography (EMG) come to a consensus on which filter characteristics and initial contact identification to use. Unfortunately, not all inter-laboratory differences in the knee biomechanics and muscle activation patterns of the patient data could be fully explained by differences in the data-processing. For instance, the offsets in the sagittal plane angles and the phase shifts in the muscle activation patterns were still present (although reduced) after partial protocol harmonization. Statistically correcting for potential covariates between the patient groups (e.g., BMI, KL grades, WOMAC pain) did not have an effect on these inter-laboratory differences. Therefore, components of the data collection or measurement setup could have had an effect, such as barefoot vs. shod walking (e.g., higher range of motion during stance of the sagittal plane angles during shod walking) [32] or wired vs. wireless EMG (e.g., possible delay in data transfer). Further investigation by measuring a large group of patients at both laboratories could assist in determining whether these remaining inter-laboratory differences are caused by components of the data collection or measurement setup or are due to differences in patient characteristics. Thus the quality of comparison of patient data between gait laboratories in future research is warranted.

Further harmonization of gait analysis protocols of laboratories with similar research interests requires international collaboration. This opens the question of where to start with the protocol harmonization. A first step would be to agree on the same gait outcomes, by calculating the same set of discrete gait parameters, by using statistical parametric mapping analyses to compare each point of the gait cycle or both. Furthermore, laboratories/researchers must provide a healthy control group for their protocol as a reference comparison with the patient group. Next, inter-laboratory comparisons are needed to investigate which components in the gait analysis protocols cause large inter-laboratory differences and are relatively easy to harmonize. For example, it is easier to align the anatomical frame definitions in the post-processing than changing an EMG system to be identical between the laboratories. Furthermore, these inter-laboratory comparisons will also provide insight

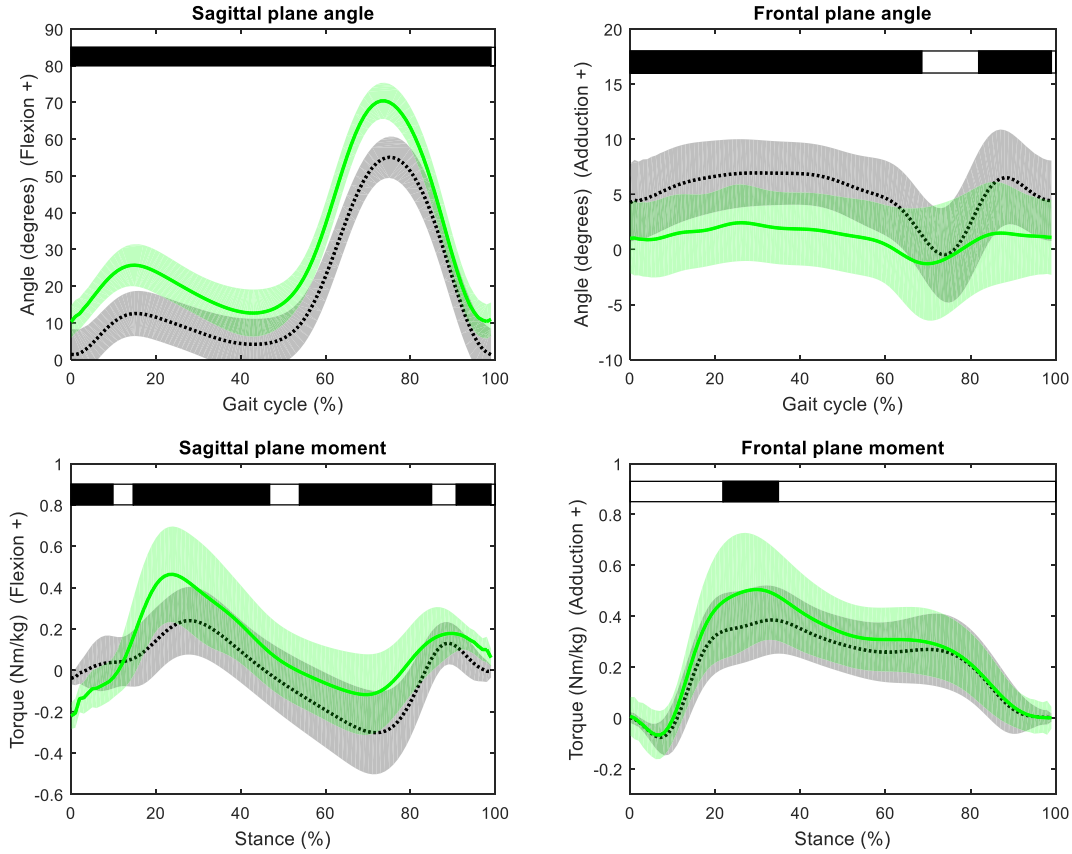

Figure 3. Knee angles and moments of patients with knee osteoarthritis previously measured at Virtual Reality Laboratory at the VU medical center (Vumc; solid line, green) and Dalhousie University (DAL; dotted line, black) after protocol harmonization. The line represents the mean and the shaded area the standard deviation. The bar on top of each graph indicates a significant difference (black) or no significant difference (white) between the labs determined with SPM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

into which gait outcomes are less affected by inter-laboratory differences and are already robust enough to be used to compare outcomes between studies. After investigation of these inter-laboratory differences, a consensus needs to be reached on the harmonization of the components of the gait analysis protocols. For example, consensus needs to be reached on which marker model(s) to use and on how to define the anatomical frames in the segments in order to prevent offsets in the knee biomechanics. Lastly, because offsets or phase shifts caused by differences in measurement setup might not be easy to resolve by consensus, a conversion method could possibly be used as an alternative to translate the gait datasets from one lab to another [33]. This incremental harmonization process of the gait analysis protocols will improve objective assessment of knee function during gait in patients with KOA and provide the opportunity to merge or share gait datasets for large international multicenter trials.

This study has some limitations. Firstly, only one healthy subject was measured at both locations to identify protocol components in need of harmonization. However, because measurements of subjects at both locations are costly and time-consuming, we think this is sufficient as a first step in our protocol harmonization. A future study, testing a large group of healthy subjects and KOA patients at both locations could then validate the harmonization steps taken to improve the inter-laboratory comparison. Secondly, this inter-laboratory comparison is performed with patients with KOA, therefore differences in disease severity (KL grades) and symptoms of the disease (pain, stiffness, instability) could also affect the gait outcomes and explain differences between laboratories. However, studies investigating patients with different KL grades did not present these systematic offsets (offsets and phase shifts) in their gait outcomes [17,34,35]. Thirdly, only two gait laboratories were compared. Therefore, the differences observed between these laboratories could be lab-specific and not generalizable to other gait laboratories. However, awareness has been created that inter-laboratory differences in gait outcomes exist, which could initiate other research groups to also perform inter-laboratory comparisons.

5. Conclusions

This inter-laboratory comparison of knee biomechanics and muscle activation patterns during gait of patients with KOA demonstrated offsets and phase shifts. A first step in protocol harmonization was performed by alignment of components of

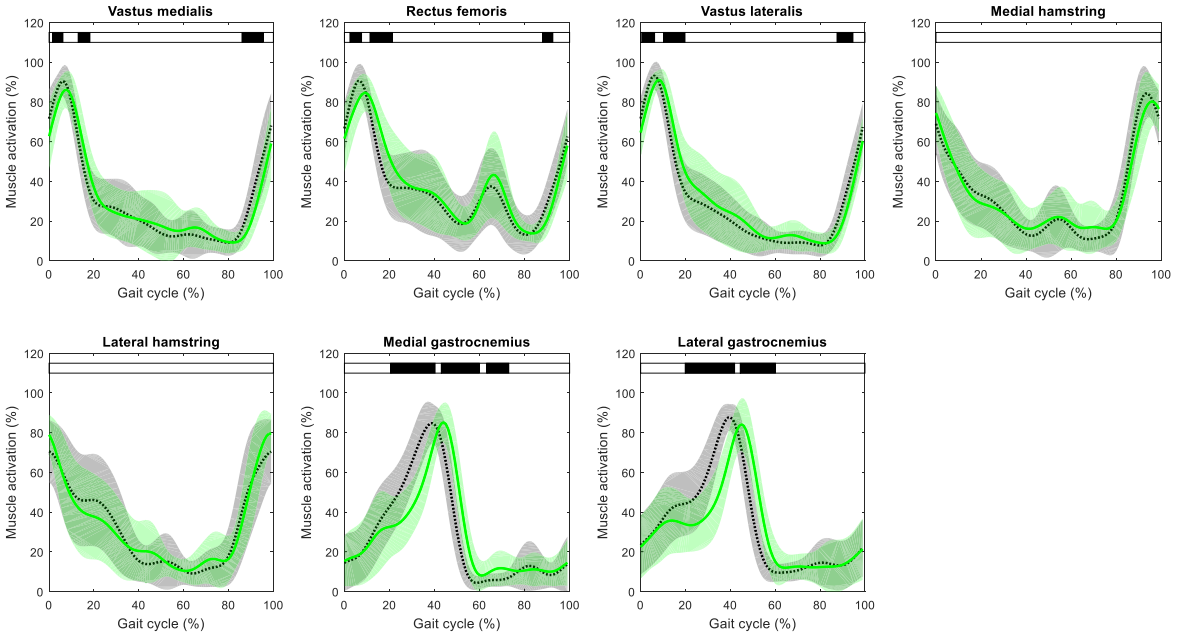

Figure 4. Muscle activation patterns of patients with knee osteoarthritis previously measured at Virtual Reality Laboratory at the VU medical center (Vumc; solid line, green) and Dalhousie University (DAL; dotted line, black) after protocol harmonization. The line represents the mean and the shaded area the standard deviation. The bar on top of each graph indicates a significant difference (black) or no significant difference (white) between the labs determined with SPM. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the data processing, which improved the inter-laboratory comparison, especially for the muscle activation patterns. Harmonization of gait analysis protocols is therefore recommended. Close collaborations from the gait lab community are needed to enable combined gait databases and multicenter trials. This will improve the objective assessment of knee function during gait in patients with KOA thereby enabling evidence-based evaluation of KOA treatments and prevention strategies.

Funding

This work was supported by OsteoArthritis Research Society International (OARSI) with a scholarship awarded to J. Schrijvers in 2017, as well as by the Dutch arthritis foundation (ReumaNederland) (grant number 15–1-402, 2015). The authors confirm that there was no involvement of study sponsors on the study design, in the collection, analysis and interpretation of the data, in the writing of the manuscript and in the decision to submit the manuscript for publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.knee.2021.03.001.

References

[1] Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, DeVita P, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: The IDEA randomized clinical trial. JAMA 2013;310:1263–73. doi: https://doi.org/10.1001/jama.2013.277669.

[2] Hunt MA, Charlton JM, Krowchuk NM, Tse CTF, Hatfield GL. Clinical and biomechanical changes following a 4-month toe-out gait modification program for people with medial knee osteoarthritis: A randomized controlled trial. Osteoarthritis Cartilage 2018;26:903–11. doi: https://doi.org/10.1016/j.joca.2018.04.010.

[3] Favre J, Erhart-Hledik JC, Chehab EF, Andriacchi TP. Baseline ambulatory knee kinematics are associated with changes in cartilage thickness in osteoarthritic patients over 5 years. J Biomech 2016;49:1859–64. doi: https://doi.org/10.1016/j.jbiomech.2016.04.029.

[4] Chehab EF, Favre J, Erhart-Hledik JC, Andriacchi TP. Baseline knee adduction and flexion moments during walking are both associated with 5 year cartilage changes in patients with medial knee osteoarthritis. Osteoarthritis Cartilage 2014;22:1833–9. doi: https://doi.org/10.1016/j.joca.2014.08.009.

[5] Favre J, Jolles BM. Gait analysis of patients with knee osteoarthritis highlights a pathological mechanical pathway and provides a basis for therapeutic interventions. EFORT Open Rev 2016;1:368–74. doi: https://doi.org/10.1302/2058-5241.1.000051.

[6] Butler RJ, Minick KI, Ferber R, Underwood F. Gait mechanics after ACL reconstruction: Implications for the early onset of knee osteoarthritis. Br J Sports Med 2009;43:366–70. doi: https://doi.org/10.1136/bjsm.2008.052522.
[7] Hubley-Kozey CL, Deluzio KJ, Landry SC, McNutt JS, Stanish WD. Neuromuscular alterations during walking in persons with moderate knee osteoarthritis. J Electromyogr Kinesiol 2006;16:365–78. doi: https://doi.org/10.1016/j.jelekin.2005.07.014.
[8] Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. Clin Biomech (Bristol, Avon) 2004;19:44–9.
[9] Smith SL, Allan R, Marreiros SP, Woodburn J, Steultjens MPM. Muscle co-activation across activities of daily living in individuals with knee osteoarthritis. Arthritis Care Res 2019;71:651–60. doi: https://doi.org/10.1002/acr.23688.
[10] Hodges PW, van den Hoorn W, Wrigley TV, Hinman RS, Bowles K-A, Cicuttini F, et al. Increased duration of co-contraction of medial knee muscles is associated with greater progression of knee osteoarthritis. Man Ther 2016;21:151–8.
[11] Schmitt LC, Rudolph KS. Muscle stabilization strategies in people with medial knee osteoarthritis: the effect of instability. J Orthop Res 2008;26:1180–5. doi: https://doi.org/10.1002/jor.20619.
[12] Wu G, Siegler S, Allard P, Kirtley C, Leardini A, Rosenbaum D, et al. ISB recommendation on definitions of joint coordinate system of various joints for the reporting of human joint motion—part I: ankle, hip, and spine. J Biomech 2002;35:543–8. doi: https://doi.org/10.1016/S0021-9290(01)00222-6.
[13] Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. J Electromyogr Kinesiol 2000;10:361–74. doi: https://doi.org/10.1016/S1050-6411(00)00027-4.
[14] Benedetti MG, Merlo A, Leardini A. Inter-laboratory consistency of gait analysis measurements. Gait Posture 2013;38:934–9. doi: https://doi.org/10.1016/j.gaitpost.2013.04.022.
[15] Kaufman K, Miller E, Kingsbury T, Russell Esposito E, Wolf E, Wilken J, et al. Reliability of 3D gait data across multiple laboratories. Gait Posture 2016;49:375–81. doi: https://doi.org/10.1016/j.gaitpost.2016.07.075.
[16] Gorton GE, Hebert DA, Gannotti ME. Assessment of the kinematic variability among 12 motion analysis laboratories. Gait Posture 2009;29:398–402. doi: https://doi.org/10.1016/j.gaitpost.2008.10.060.
[17] Rutherford DJ, Hubley-Kozey CL, Stanish WD. Changes in knee joint muscle activation patterns during walking associated with increased structural severity in knee osteoarthritis. J Electromyogr Kinesiol 2013;23:704–11. doi: https://doi.org/10.1016/j.jelekin.2013.01.003.
[18] Richards RE, van den Noort JC, van der Esch M, Booij MJ, Harlaar J. Effect of real-time biofeedback on peak knee adduction moment in patients with medial knee osteoarthritis: Is direct feedback effective?. Clin Biomech (Bristol, Avon) 2018;57:150–8. doi: https://doi.org/10.1016/j.clinbiomech.2017.07.004.
[19] Rutherford D, Baker M, Wong I, Stanish W. Dual-belt treadmill familiarization: Implications for knee function in moderate knee osteoarthritis compared to asymptomatic controls. Clin Biomech (Bristol, Avon) 2017;45:25–31. doi: https://doi.org/10.1016/j.clinbiomech.2017.04.006.
[20] Rutherford D, Baker M, Wong I, Stanish W. The effect of age and knee osteoarthritis on muscle activation patterns and knee joint biomechanics during dual belt treadmill gait. J Electromyogr Kinesiol 2017;34:58–64. doi: https://doi.org/10.1016/j.jelekin.2017.04.001.
[21] Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833–40.
[22] Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res (Hoboken) 2011;63(Suppl 11):S240–52. doi: https://doi.org/10.1002/acr.20543.
[23] Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16:494–502.
[24] Dunphy C, Casey S, Lomond A, Rutherford D. Contralateral pelvic drop during gait increases knee adduction moments of asymptomatic individuals. Hum Mov Sci 2016;49:27–35. doi: https://doi.org/10.1016/j.humov.2016.05.008.
[25] Cappozzo A, Catani F, Della Croce U, Leardini A. Position and orientation in space of bones during movement: anatomical frame definition and determination. Clin Biomech (Bristol, Avon) 1995;10:171–8. doi: https://doi.org/10.1016/0268-0033(95)91394-T.
[26] Cappozzo A, Della Croce U, Leardini A, Chiari L. Human movement analysis using stereophotogrammetry. Part 1: theoretical background. Gait Posture 2005;21:186–96. doi: https://doi.org/10.1016/j.gaitpost.2004.01.010.
[27] Vaughan CL, Davis BL, O'Connor JC. Dynamics of human gait. Human Kinetics Publishers 1992.
[28] Woltring HJ. A Fortran package for generalized, cross-validatory spline smoothing and differentiation. Adv Eng Softw 1978;1986(8):104–13. doi: https://doi.org/10.1016/0141-1195(86)90098-7.
[29] Grood ES, Suntay WJ. A joint coordinate system for the clinical description of three-dimensional motions: application to the knee. J Biomech Eng 1983;105:136–44. doi: https://doi.org/10.1115/1.3138397.
[30] Zatsiorsky VM, Zaciorskij VM. Kinetics of human motion. Human Kinetics 2002.
[31] Friston KJ, Holmes AP, Worsley KJ, Poline J-P, Frith CD, Frackowiak RSJ. Statistical parametric maps in functional imaging: A general linear approach. Hum Brain Mapp 1994;2:189–210. doi: https://doi.org/10.1002/hbm.460020402.
[32] Franklin S, Grey MJ, Heneghan N, Bowen L, Li F-X. Barefoot vs common footwear: A systematic review of the kinematic, kinetic and muscle activity differences during walking. Gait Posture 2015;42:230–9. doi: https://doi.org/10.1016/j.gaitpost.2015.05.019.
[33] Clouthier AL, Bohm ER, Rudan JF, Shay BL, Rainbow MJ, Deluzio KJ. Correcting waveform bias using principal component analysis: Applications in multicentre motion analysis studies. Gait Posture 2017;51:153–8. doi: https://doi.org/10.1016/j.gaitpost.2016.10.008.
[34] Favre J, Erhart-Hledik JC, Andriacchi TP. Age-related differences in sagittal-plane knee function at heel-strike of walking are increased in osteoarthritic patients. Osteoarthritis Cartilage 2014;22:464–71. doi: https://doi.org/10.1016/j.joca.2013.12.014.
[35] Huang S-C, Wei I-P, Chien H-L, Wang T-M, Liu Y-H, Chen H-L, et al. Effects of severity of degeneration on gait patterns in patients with medial knee osteoarthritis. Med Eng Phys 2008;30:997–1003. doi: https://doi.org/10.1016/j.medengphy.2008.02.006.