Real-Time Three-Dimensional Knee Moment Estimation in Knee Osteoarthritis: Toward Biodynamic Knee Osteoarthritis Evaluation and Training

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***Abstract*—We investigated differences in knee kinetic variables (external knee adduction, flexion, internal rotation moments, and impulses) between patients with knee osteoarthritis (KOA) and healthy controls during stepping on a custom elliptical trainer; and searched knee kinetic variable candidates for real-time biofeedback and for complementing diagnosis/evaluation on the elliptical trainer based on the knee kinetic variables' associations with the knee injury and osteoarthritis outcome score (KOOS). Furthermore, we explored potential gait re-training strategies on the elliptical trainer by investigating the knee kinetic variables' associations with 3-D ankle angles. The knee kinetic variables and ankle angles were determined in real-time in a patient group of 10 patients with KOA and an age-and sex-matched control group of 10 healthy subjects. The mean peak external knee adduction moment of the patient group was 47% higher than that of the control group. The KOOS-Sports and Recreational Activities and KOOS-Pain scores were found to be significantly associated with the knee kinetic variables. All the ankle angles were associated with the knee kinetic variables. The findings support the use of the knee kinetic variables on the elliptical trainer to complement KOA diagnosis quantitatively and provide potential real-time KOA gait re-training strategies/guides.**

***Index Terms*—Knee osteoarthritis, biomechanics, elliptical trainer, kinetics.**

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Nomenclature

EKAM	External knee adduction moment
EKFM	External knee flexion moment
EKIRM	External knee internal rotation moment
EKM	External knee moment
EKTRM	External knee total reaction moment
KOA	Knee osteoarthritis
KOOS	Knee injury and osteoarthritis outcome score

I. Introduction

MEDIAL knee osteoarthritis–a disease of mechanics [1], [2]–is prevalent [3]–[5]; and causes disabling pain, functional impairments, and reduced independence and may eventually lead to chronic disability in older adults [3], [4], [6], [7]. Recently, to achieve the long-term goal of providing repetitive and consistent medial KOA gait re-training on a custom elliptical trainer with real-time biofeedback of relevant knee kinetic variables in clinics and gymnasiums, the authors have developed a reliable and accurate real-time three-dimensional (3-D) EKM vector estimation method based on a modified 3-D inverse dynamics during closed-chain stepping on a custom elliptical trainer (Fig. 1) [8], [9]; verified the method thoroughly with healthy subjects [8]; and reported a single case preliminary study of a patient with KOA [9]. For patients with KOA, stepping on an elliptical trainer is recommended [10], [11]. Without much assistance, elliptical trainers allow repetitive, consistent, and closed-chain functional weight-bearing stepping that has kinematic similarity to ground walking with much-reduced

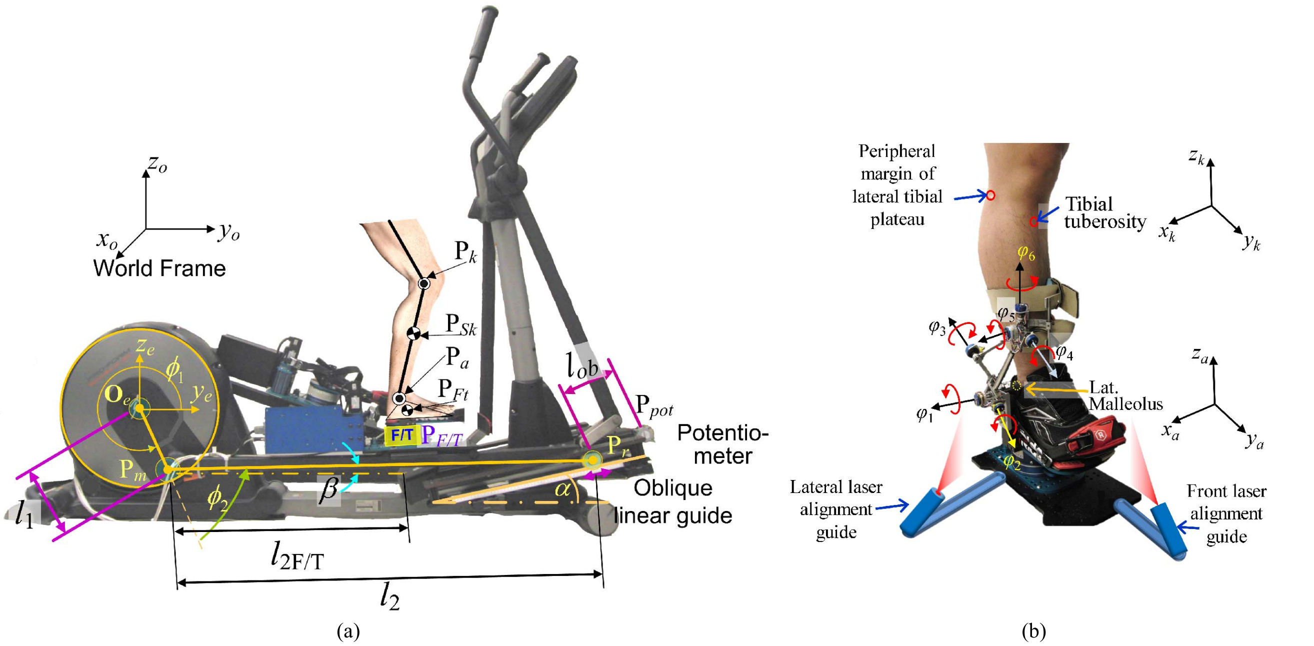


Fig. 1. A modified elliptical trainer: (a) sagittal plane view of the elliptical trainer with the right leg and (b) a subject on the elliptical trainer wore a compact and inexpensive 6-degrees-of-freedom goniometer on her/his right leg. The elliptical trainer was instrumented with a 6-axis force/torque (F/T) sensor ($\mathbf{P}_{Ft}$) underneath each footplate and a precision potentiometer ($\mathbf{P}_{pot}$) measuring the distance (l_{ob}) along the oblique linear guide. $\mathbf{P}_{Sk}$ and $\mathbf{P}_{Ft}$ denote the center of mass (COM) of the shank and foot, respectively. One end of the goniometer was securely strapped to the tibia's flat anteromedial surface to mitigate the slip of the goniometer and the other end was connected to the lateral side of footplate while lining up the lateral malleolus and one potentiometer of the goniometer. The easily detachable front/lateral laser lights helped the initial alignment of the ankle and knee.

ground reaction force [8], [9], [12]–[15], indicating a beneficial KOA gait re-trainer suitable for clinics and gymnasiums. Moreover, multi-axis elliptical trainers, having pivoting and/or frontal sliding DOFs at each footplate, improved the functional activities of patients with KOA and with other knee injuries [8], [16]–[18]. Real-time biofeedback of peak EKAM–estimated using kinematic data from a 10-camera motion capture system and a force-plate embedded split-belt treadmill–for one-session KOA gait re-training with three different specific kinematic modifications succeeded in reducing the peak EKAM [19], as was predicted from studies with healthy individuals [20]–[22]. However, in clinics and gymnasiums (outside motion analysis laboratories), estimation of the 3-D EKM vector is impractical, especially in *real-time*, as a routine evaluation [8], [9].

The purpose of this study is, thus, to take the next steps to achieve the long-term goal. For walking, many knee kinetic variables of patients with KOA have been studied. The peak EKAM is a commonly used surrogate measure of knee medial compartment compressive load [4], [23], [24], the aberrance of which is strongly related to the KOA pathomechanics [4], [9], and is strongly associated with the presence, progress, severity, and symptoms of medial KOA [25]–[27]. Peak EKFM is also positively correlated with knee medial compartment compressive load [28] and is reduced in patients with KOA [29]. The EKIRM of patients with KOA may be changed [29] considering a potential relationship between changes in knee rotation in the transverse plane and pathomechanics [1], [30], [31]. Peak EKTRM (the magnitude of a 3-D EKM vector) was proposed as a composite measure reflecting alterations in all of the EKM components, was more sensitive than peak EKAM, and was associated with walking speed [32]. The time integral of EKAM, EKFM, and EKIRM (EKAM impulse, EKFM impulse, and EKIRM impulse, respectively) were proposed to provide cumulative measures of the corresponding moments that incorporate both the magnitude and duration of each component [33], [34]. EKAM impulse was associated with pain like EKAM [26] and is more sensitive than peak EKAM [33], [34]. During stepping on an elliptical trainer, for patients with KOA, studies on knee kinetic variables and clinical relevance of those variables are, however, scarce, although kinematics [12], [14], [35]–[37] and knee moments [14] of other populations on an elliptical trainer have been reported.

Moreover, for the patients with KOA, real-time EKAM biofeedback during gait re-training is promising only when combined with instructions on specific kinematic modifications [19]. Thus, it is necessary to provide kinematic modifications during the training on the elliptical trainer.

Thus, this study has three aims. The first *aim* is to investigate the differences in the knee kinetic variables during stepping on the elliptical trainer between the patients with KOA and healthy individuals. We *hypothesized* that mean-peak EKAM, EKAM impulse, and mean-peak EKTRM of patients with KOA are larger than those of age- and sex-matched healthy individuals, mean-peak EKFM and EKFM impulse of the patients are smaller than those of the healthy individuals, and mean-peak EKIRM and EKIRM impulse of the patients are different from those of the healthy individuals.

The second *aim* is to find the candidates for the real-time biofeedback and for complementing the evaluation/diagnosis

TABLE I
SUBJECTS' CHARACTERISTICS, MEAN (SD)

		Patients with KOA (n=10)	Control Group (n=10)	p-value
Age (years)		67.9 (11.1)	60 (6.0)	0.071
Sex		7F/3M	4F/6M	0.370
Height (m)		1.70 (0.08)	1.71 (0.09)	0.767
Body mass (kg)		78.4 (16.0)	77.3 (16.7)	0.883
Body Mass Index (kg/m^2)		26.89 (4.19)	26.17 (4.35)	0.712
Duration of KOA (years)		11.6 (5.7)		
Side of KOA		9 bilateral/1 right		
Normalized KOOS	Pain (%)	58.3 (14.3)		
	Symptoms (%)	57.9 (12.5)		
	Activities of daily living (%)	68.7 (18.0)		
	Sports and recreation activities (%)	36.5 (11.3)		
	Knee-related quality of life (%)	47.5 (22.1)		

with the investigation of the associations between the KOOS score [38], [39] and the knee kinetic variables. Considering these previous studies, we *hypothesized* that peak EKAM, peak EKTRM, and EKAM impulse at the loading phase are associated with the KOOS-Sports and Recreational Activities score (related to the functional activities similar to exercise on an elliptical trainer), and that peak EKAM, EKAM impulse, and EKIRM impulse are associated with the KOOS-Pain score.

The last *aim*is to explore potential kinematic instructions in company with the real-time biofeedback of knee kinetic variables with an investigation of the associations between 3-D ankle angles and the knee kinetic variables during the closed-chain stepping on the elliptical trainer. Since computing knee kinetic variables need ankle angles in the process physically and biomechanically [8], [9], we *hypothesized* that the 3-D ankle angles are associated with the knee kinetic variables.

II. METHOD

A. Subjects

Based on a previous study, twenty subjects were recruited from the local community (Table I) to detect a difference in mean-peak-normalized EKAM between a patient group and a control group at a significance level of 0.05 and a statistical power of 0.95. The patient group consisted of ten patients with clinically diagnosed medial KOA, and the control group consisted of ten age- and sex-matched subjects who had no previous history of musculoskeletal injury, neurological impairment, and prolonged joint pain. All subjects signed an informed consent form approved by the Institutional Review Board of Northwestern University. For patients with bilateral KOA, the right side was more severely affected (painful) and was the limb analyzed.

B. Experimental Procedure

The patients completed KOOS (lower represents worse status). The subjects' kinematic and inertial properties were determined [8], [9], [40], [41] and given to the real-time 3-D EKM estimation program as explained in [8], [9]. Subjects wore their comfortable gym shoes. One end of a compact and

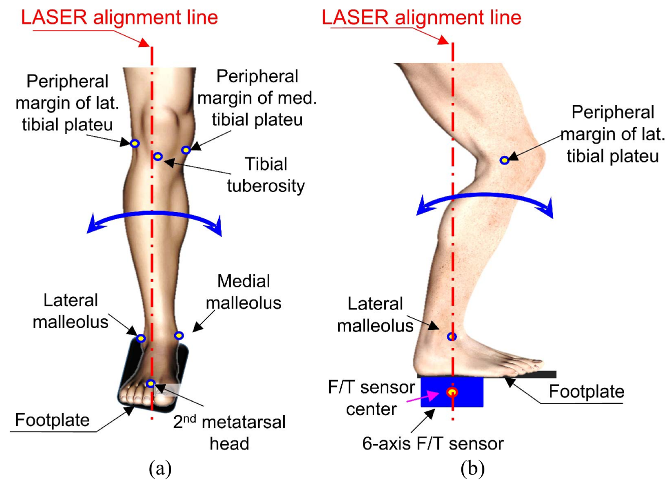


Fig. 2. Alignment of the 6 degrees-of-freedom goniometer. (a) Frontal plane alignment of the leg with laser light (red dash-dot line). A subject could adjust her/his leg in the frontal plane (blue curved arrow) by following the clinicians' guide. (b) Sagittal plane alignment with laser light. The frontal and sagittal alignments were performed simultaneously. Palpable anatomical landmarks are used.

inexpensive 6-degrees-of-freedom goniometer measuring 3-D ankle angles [8], [9] was strapped to the right tibia/shank's flat anteromedial surface using neoprene bands to mitigate the slip of the goniometer while lining up the lateral malleolus and one potentiometer of the goniometer (Fig. 1(b)). The other end of the goniometer was attached to the lateral side of the footplate, which did not move relative to the foot strapped to it (Fig. 1(b)). For familiarization, the subjects stepped on the elliptical trainer for 3 minutes with the adjustment of foot straps to mitigate relative motion between the foot and footplate. After adequate rest, the subjects stepped for 1.5 minutes on the elliptical trainer under the lowest level flywheel resistance at a self-selected pace without firmly grasping the handles during data collection.

For each foot, the 3-D force and moment exerted to the foot on the footplate was measured by using a 6-axis force/torque sensor (JR3, Woodland, CA) underneath the footplate of the elliptical trainer (Reebok®Spacesaver RL; Fig. 1(a)) with subtraction of the footplate's gravitational and inertial contributions [8], [9]. For all kinematic and kinetic measurements, the sampling frequency was 100 Hz. With l_{ob} (measured by a precision potentiometer ($\mathbf{P}_{pot}$)), l_1, l_2, $l_{2F/T}$, and the inclination of the oblique linear guide (α), footplate orientation (β) was computed by adding ϕ_1 and ϕ_2 and the coordinate of the force/torque sensor's center ($\mathbf{P}_{F/T}$) was determined. The 6-degrees-of-freedom goniometer measured 3-D ankle angles (x (dorsiflexion/planar flexion)–y (inversion/ eversion)–z (internal/external rotation) Euler angel set) accurately [8] with an online calibration of anatomical ankle zero angles on the elliptical trainer using front and lateral laser alignment guides (Fig. 1 (b); Fig. 2) before the subjects stepped on the elliptical trainer. For the control group, the calibration was performed at the footplate's lowest position where the subjects bore $\sim$ 100% body weight (BW) on that leg, and, for the patient group, at a position s/he could adjust her/his lower leg without pain. In the frontal plane (Fig. 2 (a)), the force/torque sensor's center, the second metatarsal head, the midpoint between the medial and lateral malleoli, and the tibial tuberosity were aligned. The midpoint between the peripheral margins of the medial and lateral tibial plateaus could be additionally considered. In the sagittal plane (Fig. 2 (b)), the force/torque sensor's center, the lateral malleolus, and the peripheral margin of lateral tibial plateau were aligned. These points were marked with dome-shaped rubber pads (diameter: 0.01 m) for calibration [8].

The elliptical trainer frame, ankle anatomical frame, and tibial anatomical frame were defined using palpable anatomic landmarks (Fig. 1) and utilized in computing the knee kinetic variables using the modified 3-D inverse dynamics [8], [9]. The elliptical trainer frame [origin ($\mathbf{O}_e$): the center of the driving wheel; and the positive directions of the x_e, y_e, and z_e axes: lateral, anterior, and upward direction, respectively] was a fixed frame. The ankle anatomical frame [origin ($\mathbf{P}_a$): the midpoint between the lateral and medial malleoli; and the directions of the x_a, y_a, and z_a axes: the cross-product of the y_a and z_a axes, the projection of a vector from $\mathbf{P}_a$ to the 2$^{\text{nd}}$ metatarsal head on to the footplate, and the upward vector normal to the footplate top surface], and the tibial anatomical frame [origin ($\mathbf{P}_k$): the midpoint between the peripheral margins of the medial and lateral tibial plateaus; the directions of the x_k, y_k, and z_k axes: the cross-product of the y_k and z_k axes, the cross-product of the z_k axis and a vector from the medial to the lateral tibial plateaus, and the vector from $\mathbf{P}_a$ to $\mathbf{P}_k$ (long axis)] were the moving coordinate frames [8], [9].

With the kinematic measurements and forces and moments measured at the footplate, the EKM vector was computed in real-time using the EKM vector estimation program based on the modified 3-D inverse dynamics, the reliability and accuracy of which have been extensively verified [8], [9].

C. Data Processing

The patients' Kellgren-Lawrence grade was estimated based on the KOOS and Kellgren-Lawrence grade relationship given in Table 3 of [42]. An elliptical cycle (EC) was defined as follows: an elliptical cycle started at the time when the measured (right)-side foot reached the most anterior position and ended at the very next time the foot reached the same position [8], [9], [14]. A loading phase was determined as follows: it started at 0% elliptical cycle and ended at the time when the measured-side foot reached the most posterior position the very first time within the same elliptical cycle [14]. Ten elliptical cycles of data of stepping on the elliptical trainer were selected for each subject. EKTRM was obtained by computing the magnitude of the EKM vector at each time point. All three components of EKM and EKTRM were normalized to the product of BW and height (HT) and expressed as a percentage (%(BW × HT)). The impulse of each component of the EKM vector was obtained by integrating the corresponding normalized EKM component over the loading phase. The EKM vector and EKTRM were time-normalized using the elliptical cycle (0–100%) with the unit of %EC. For each subject, the 10 elliptical cycles' mean of the EKM vector, EKTRM, and all three impulses were obtained. Similarly, the 3-D ankle angles were time-normalized and ensemble-averaged.

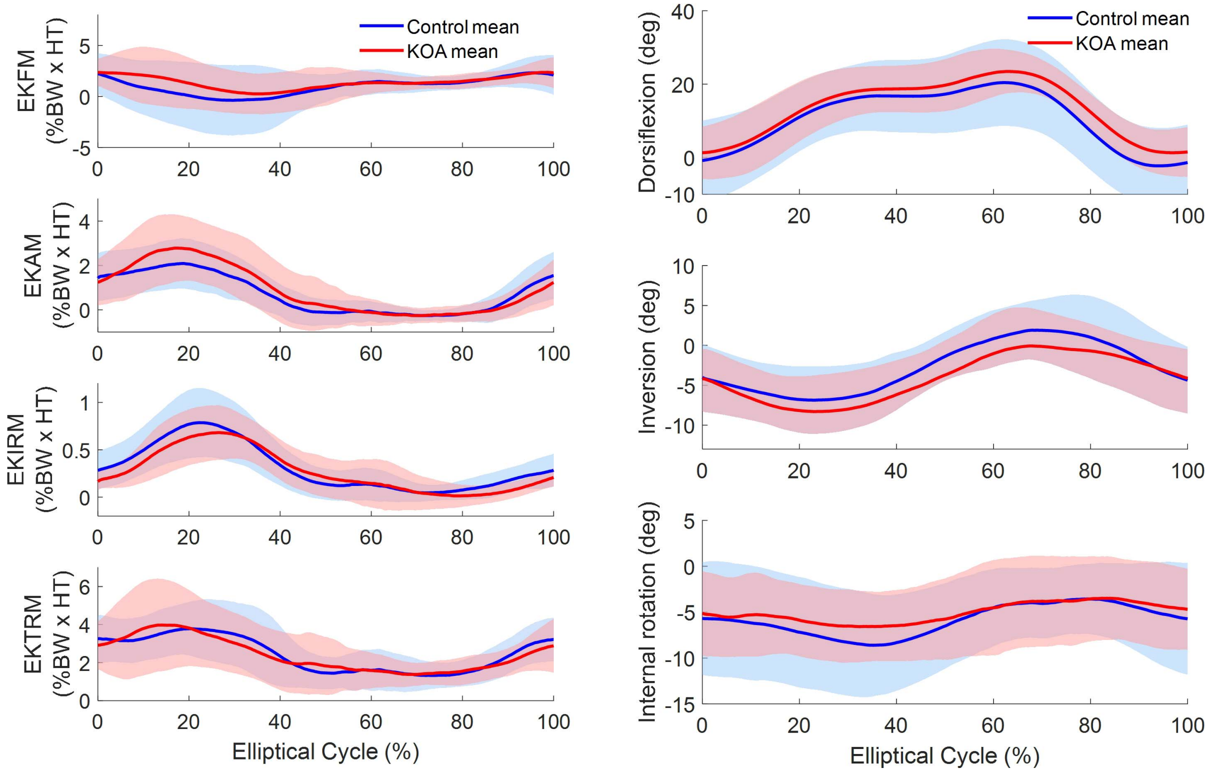
TABLE II
KINETIC AND TEMPORAL VARIABLES DURING THE STEPPING ON THE ELLIPTICAL TRAINER, MEAN (SD)

		Patients with KOA (n=10)	Control Group (n=10)	p-value
Stepping speed (rev/min)		34.1 (10.2)	29.7 (6.5)	0.228
End of loading phase (%EC)		51.5 (1.3)	51.1 (0.7)	0.303
Peak EKAM at the loading phase	Magnitude (%(BW × HT))	**3.37 (1.19)**	**2.29 (1.15)**	**0.030**
	Location (%EC)	18.8 (8.1)	16.2 (2.8)	0.328
Peak EKFM at the loading phase	Magnitude (%(BW × HT))	3.06 (2.31)	2.61 (2.27)	0.641
	Location (%EC)	6.4 (4.5)	5.5 (6.1)	0.665
Peak EKIRM at the loading phase	Magnitude (%(BW × HT))	0.77 (0.28)	0.85 (0.37)	0.516
	Location (%EC)	27.2 (6.8)	22.5 (4.7)	0.059
Peak EKTRM at the loading phase	Magnitude (%(BW × HT))	4.76 (2.18)	4.54 (1.51)	0.778
	Location (%EC)	17.9 (8.5)	14.1 (8.9)	0.308
EKAM impulse at the loading phase (%(BW × HT) × s)		1.82 (1.42)	1.49 (1.20)	0.552
EKFM impulse at the loading phase (%(BW × HT) × s)		0.90 (1.72)	0.53 (2.56)	0.689
EKIRM impulse at the loading phase (%(BW × HT) × s)		0.46 (0.23)	0.55 (0.30)	0.403

Significant values are in bold font. EC: elliptical cycle

D. Statistical Analysis

The number of male and female subjects in each group was compared using Fisher's exact test. Student's t-test was used to compare age, height, body mass, and body mass index (BMI). Seemingly unrelated regression, which takes into account the potential correlation between dependent variables, was used to simultaneously test the effect of the presence of KOA (yes or no) on a large number of dependent variables means [43]: mean kinetic variables (peak EKAM, peak EKFM, peak EKIRM, peak EKTRM, EKAM impulse, EKFM impulse, and EKIRM impulse) and mean temporal parameters (stepping speed, duration of loading phase, peak EKAM location, peak EKFM location, peak EKIRM location, and peak EKTRM location) across the elliptical cycles. The Spearman correlation coefficient, ρ, was used to test for multiple associations of the KOOS-Sports and Recreational Activities score with mean-peak EKAM, mean-peak EKTRM, and mean EKAM impulse and associations of the KOOS-Pain score with mean-peak EKAM, mean EKAM impulse, and mean EKIRM impulse with adjusting p-values based on Holm-Bonferroni method. Outliers were removed before determining Spearman correlation coefficients between the KOOS-Sports and Recreational Activities score with the knee kinetic variables using Cook's distance obtained with data transformed to rank (see IV.B.1)). Hierarchical multiple linear regression was used to test for the influence of 3-D ankle angles and the presence of KOA



(a) (b)

Fig. 3. Knee external moments (a) and 3-D ankle angles (b) during stepping on the elliptical trainer. The blue solid line represents the grand mean across the subjects in the control group (10 cycles) and the light blue shade stands for ±1 standard deviation across the subjects in the control group. The red solid line represents the grand mean across the patients with KOA (10 cycles), and the light red shade stands for ±1 standard deviation across the patients. (a) 3-D external knee moments normalized to body weight × height (%(BW×HT)). From the top to the bottom plot: the external knee flexion moment (EKFM), the external knee adduction moment (EKAM), the external knee internal rotation moment (EKIRM), and the external knee total reaction moment (EKTRM). (b) 3-D ankle angles. From the top to the bottom plot: dorsiflexion angle, inversion angle, and internal rotation angle.

on knee kinetic variables at the loading phase after controlling for age, sex, and BMI. 3-D ankle angles for peak EKAM are the angles at which the EKAM is maximum at the loading phase. The same goes for the peak EKFM and peak EKTRM. 3-D ankle angles for EKAM impulse, EKFM impulse, and EKIRM impulse were the maximum angles during the loading phase. The forward stepwise method was used in constructing the regression models. Collinearity was tested for with the variance inflation factor. No violation of homoscedasticity was assessed with the Breusch-Pagan test and the Koenker test [44]. The significance level was taken as 0.05.

III. Results

There were no significant differences in age, sex, height, body mass, and BMI between the patient group and the control group (Table I). Nine patients' estimated Kellgren-Lawrence grade was 4 (severe), and the other patient's was 3 (moderate). The knee kinetic variables (the EKM vector, EKTRM, and impulses), 3-D ankle angles, and associated temporal parameters were determined (Fig. 3; Table II). The stepping speed of the patient group was not significantly different from that of the control group (Table II). For the two groups, the loading phase ended at ∼ 51%. The grand mean of the peak EKAM at the loading phase across the patients was significantly higher (47%) than that across the control group at the loading phase (Table II; Fig. 4).

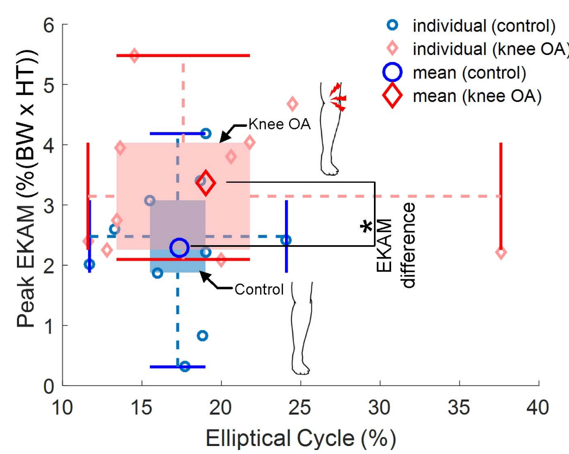


Fig. 4. Comparison of peak external knee adduction moment (EKAM) at the loading phase of the control group and that of patients with KOA. Individual mean data (small circle: control group; small diamond: patients with KOA) are given with double boxplots providing distribution (quartiles) of the data sets in peak EKAM and EC dimension. For each box, the lower end and upper end indicate 1^{st} quartile and 3^{rd} quartile in terms of peak EKAM, respectively; the left end and right end represent 1^{st} quartile and 3^{rd} quartile in terms of elliptical cycle, respectively. The peak EKAM of patients with KOA (large diamond) was significantly higher (47%) than that of the control group (large circle).

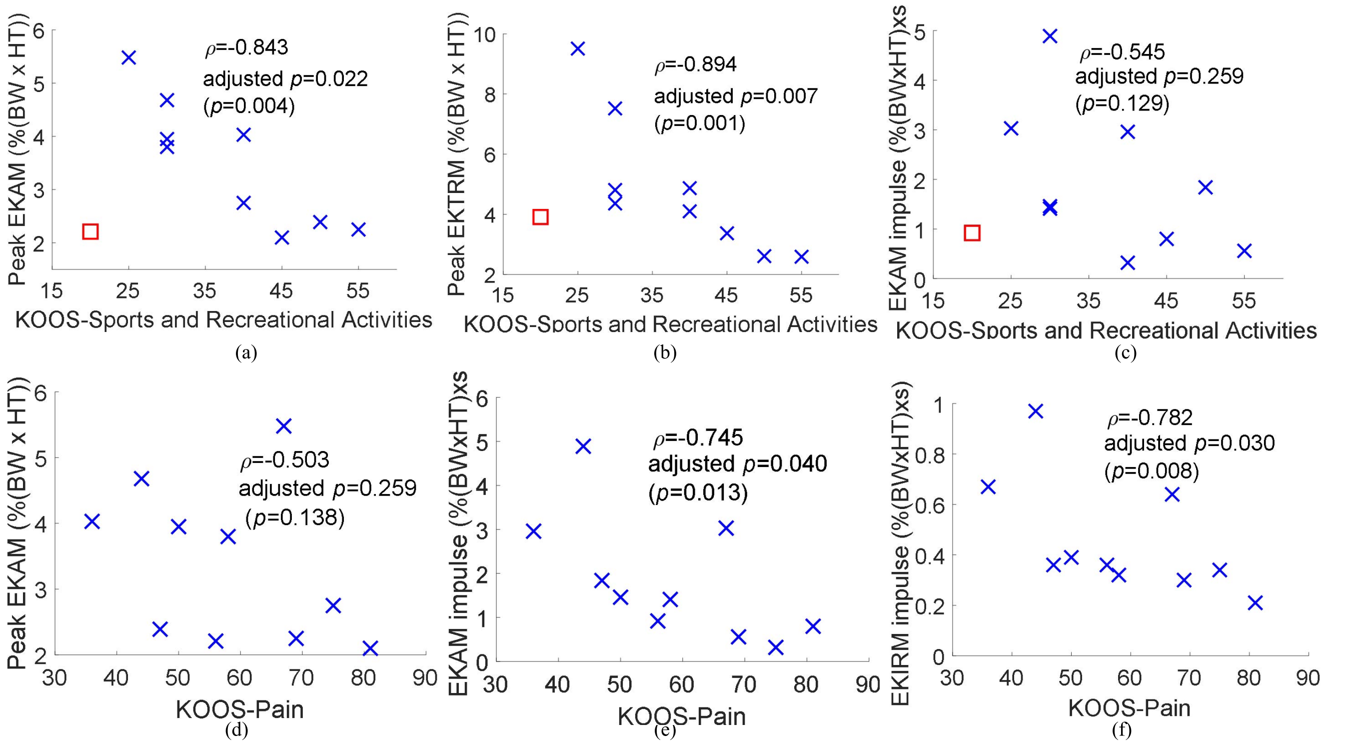


Fig. 5. Association (Spearman correlation coefficient $\rho\lhd$ between the knee kinetic variables and KOOS of patients with KOA ($n = 10$). (a) Association between the KOOS-Sports and Recreational Activities section and mean-peak EKAM (ρ =-0.843; adjusted p = 0.022). (b) Association between the KOOS-Sports and Recreational Activities section and mean-peak EKTRM ($\rho = -0.894$; adjusted $p = 0.007$). (c) Association between the KOOS-Sports and Recreational Activities section and the mean EKAM impulse ($\rho = -0.545$; adjusted $p = 0.259$). (d) Association between the KOOS-Pain section and mean-peak EKAM ($\rho = -0.503$; adjusted $p = 0.259$). (e) The KOOS-Pain section and the mean EKAM impulse ($\rho = -0.745$; adjusted $p = 0.040$). (f) Association between the KOOS-Pain section and the EKIRM impulse ($\rho = -0.782$; adjusted $p = 0.030$). For (a) to (c), the red rectangles denote outliers.

A. The Relationship Between the Knee Kinetic Variables and the Clinical Scores of the Patient Group

The KOOS-Sports and Recreational Activities score was strongly and negatively associated with mean-peak EKAM (Fig. 5(a)) and with mean-peak EKTRM (Fig. 5(b)) at the loading phase of the patient group after the removal of an outlier (see IV.B.1) for the discussion on the outlier). The association between the KOOS-Sports and Recreational Activities score and mean EKAM impulse at the loading phase was not significant (Fig. 5(c)). The KOOS-Pain score was not significantly associated with the mean-peak EKAM at the loading phase (Fig. 5(d)). The KOOS-Pain score was significantly, strongly, and negatively associated with mean EKAM impulse (Fig. 5(e)) and EKIRM impulse (Fig. 5(f)) at the loading phase.

B. The Relationship Between the 3-D Ankle Angles and the Knee Kinetic Variables

The relationships between the 3-D ankle angles and the knee kinetic variables during closed-chain stepping are summarized in Table III. It was found that i) ankle dorsiflexion and eversion was positively associated with the mean-peak EKAM at the loading phase and ii) mean-peak EKAM at the loading phase of the patient group was significantly higher than that of the control group (the coefficient of the presence of KOA). Similar to the mean-peak EKAM at the loading phase, mean EKAM impulse was positively associated with maximum ankle dorsiflexion and maximum ankle eversion at the loading phase and was negatively associated with the maximum ankle internal rotation at the loading phase. The mean-peak EKFM at the loading phase was positively associated with ankle dorsiflexion.

Similarly, mean EKFM impulse was positively associated with maximum ankle dorsiflexion at the loading phase. Mean EKIRM impulse at the loading phase was positively associated with maximum ankle eversion at the loading phase. The mean EKIRM impulse at the loading phase of the patient group was significantly smaller than that of the control group. Mean-peak EKTRM at the loading phase was positively associated with ankle dorsiflexion and negatively associated with ankle internal rotation.

IV. Discussion

A. Differences in the Knee Kinetic Variables

Differences in the knee kinetic variables of patients with KOA during stepping on the elliptical trainer–a recommended exercise for patients with KOA–were estimated by using an accurate real-time 3-D EKM estimation method [8], [9] without typical long-time preparation and post-processing of the motion capture data. Indeed, during the stepping, a small monitor displayed the EKM in real-time to check the system, which can potentially be used in real-time feedback rehabilitation training in the future. Furthermore, right after the stepping trial, the patients were able to see the summarized results. Similar to ground walking, the peak EKAM at the loading phase of the patient group on the elliptical trainer was significantly higher than that of the control group at

TABLE III
ASSOCIATION BETWEEN THE KNEE KINETIC VARIABLES AND THE 3-D ANKLE ANGLES. REGRESSION COEFFICIENTS (95% CI) ($n = 20$ SUBJECTS)

Knee Kinetic Variable		Presence of KOA (yes: 1/no: 0)	3-D Ankle Angles (°)			Overall Model	
			Dorsiflexion	Eversion	Internal Rotation	Adjusted R^2	p-value
Peak EKAM (%(BW×HT))	Coefficient	**0.84 (0.00, 1.68)**	**0.09 (0.04, 0.14)**	**0.13 (0.03, 0.23)**	-	0.691	0.0009
	p-value	0.049	0.002	0.016	-		
EKAM impulse (%(BW×HT)×s)	Coefficient	-	**0.07 (0.02, 0.12)**	**0.24 (0.14, 0.33)**	**−0.08 (−0.16, −0.01)**	0.718	0.0005
	p-value	-	0.010	0.0002	0.036		
Peak EKFM (%(BW×HT))	Coefficient	-	**0.21 (0.17, 0.24)**	-	-	0.896	<0.0001
	p-value	-	<0.0001	-	-		
EKFM impulse (%(BW×HT)×s)	Coefficient	-	**0.25 (0.20, 0.29)**	-	-	0.881	<0.0001
	p-value	-	<0.0001	-	-		
EKIRM impulse (%(BW×HT)×s)	Coefficient	**-0.21 (-0.41,-0.01)**	-	**0.04 (0.01, 0.06)**	-	0.583	0.003
	p-value	0.040	-	0.004	-		
Peak EKTRM (%(BW×HT))	Coefficient	-	**0.13 (0.02, 0.24)**	-	**−0.20 (−0.32, −0.08)**	0.541	0.005
	p-value	-	0.022	-	0.003		

The table shows the association between the knee kinetic variables, the 3-D ankle angles, and the presence of KOA based on a hierarchical regression model, adjusted for age, sex, and BMI. Significant values are in bold font. All of the knee kinetic variables were obtained during the loading phase.

a self-selected and comparable stepping speed without any adjustment (Fig. 4, Table II) and with adjustment for age, sex, and BMI (Table III). The peak EKAM of patients with KOA during stepping on the elliptical trainer was within the range of the peak EKAM of patients with KOA during over-ground walking (2.8–5.1 % (BW × HT)) [23], [25]. The difference between the peak EKAM of the healthy controls during stepping on the elliptical trainer (2.29 %(BW × HT); Table II) and that during over-ground walking (3.3 % (BW × HT)) [23] was 1.01%(BW × HT), 1.5 standard deviations given in [23]. Moreover, the EKIRM impulse at the loading phase of the patient group was significantly smaller than that of the control group (Table III), indicating the potential association of the transverse plane knee rotational mechanics on the pathomechanics of KOA [1], [29]–[31].

B. The Knee Kinetic Variables and Clinical Scores

Many of the knee kinetic variables at the loading phase during the stepping on the elliptical trainer were associated with the clinical scores.

1) The Koos-Sports and Recreational Activities Score and Peak Ekam: The KOOS-Sports and Recreational Activities score was negatively associated with mean-peak EKAM (i.e., a higher mean-peak EKAM indicates a worse status) after the removal of an outlier, the left end data point from a 75 years old female who has suffered from bilateral KOA for 20 years (Fig. 5(a)). Based on her KOOS-Sports and Recreational Activities score, it can be said that she was the worst case among the patients who participated in this study. However, it might be possible that her low KOOS-Sports and Recreational Activities score was an exaggerated response [38]. She might have a low-activity lifestyle because of 20 years of suffering, and the Sports and Recreational Activities section might thus be less relevant for her [39].

2) The Koos-Sports and Recreational Activities Score and Peak Ektrm: EKTRM, the magnitude of the 3-D EKM vector, is a composite measure to account for the effect of not only EKAM but also all of the other directional external knee moments (i.e., EKFM and EKIRM) on medial compartment loading [32], [33], and can reflect the changes in magnitude (EKFM) and distribution (EKAM) of the loading at the knee [32]. Mean-peak EKTRM was negatively associated with the KOOS-Sports and Recreational Activities score (i.e., a higher peak EKTRM indicates a worse status) after the removal of the same outlier (the 75 years old female data). Thus EKTRM might be a measure that can be used with peak EKAM [32].

Since EKFM contributed to EKTRM, a smaller EKFM may be desirable for the patients with KOA [28]. EKFM has been reported to be significantly associated with the knee medial compartment compressive load and tibial cartilage thickness change [45], and the peak knee medial compartment compressive load has been found to be associated with EKFM as well as EKAM [28].

3) The Koos-Pain Score and The Ekam Impulse: EKAM impulse incorporates both the duration and magnitude of EKAM throughout the loading phase of an elliptical cycle whereas peak EKAM only provides the magnitude at the peak [34], [46]. It has been reported that 1) the EKAM impulse of patients with moderate KOA is significantly higher than that of patients with mild KOA; 2) EKAM impulse of patients with symptomatic KOA is significantly higher than that of patients with asymptomatic KOA; and 3) EKAM impulse at the baseline is associated with loss of medial tibial cartilage volume over a year [46]. On the elliptical trainer, a negative association between the EKAM impulse and the KOOS-Pain score (larger EKAM impulse indicates severer pain) was found, similar to the previous reports, indicating the potential of EKAM impulse to assess the pain.

4) The Koos-Pain Score and The Ekirm Impulse: It has been hypothesized that alterations in transverse plane knee rotation are associated with the degenerative process of KOA by shifting the loading to unconditioned areas of the cartilage [1], [30], [31]. The alterations in the transverse plane knee rotational moment (EKIRM) of patients with KOA may reflect alterations in the knee rotational mechanics related to the knee screw home mechanism [1], [9], [29], [30] that could place loads on a region of cartilage that may not be able to adapt to the rapidly increased load and can experience degenerative changes leading to KOA [1], [30], [31]. Though there was no significant difference in EKIRM between the two groups, the EKIRM impulse of the patient group was significantly different from that of the control group. Moreover, EKIRM impulse and the KOOS-Pain score displayed a significant negative association (i.e., a larger EKIRM impulse means a severer pain), indicating the potential of EKIRM impulse as a sensitive measure of assessing pain.

The prevalent medial KOA is a disease of mechanics ("wear and tear") associated with repetitive, cyclic, and dynamic overloading, especially knee medial compartment compressive load, due to risk factors (e.g., obesity, knee injury, occupational overuse), and develops over long-time period with the disruption of healthy knee homeostasis [1], [2]. These associations between the knee kinetic variables and clinical scores may be used as a tool to complement the diagnosis and evaluation, allowing one to have objective interval scales (i.e., knee kinetic variables) that can be used in company with ordinal clinical scores and to consistently use the objective interval scales for diagnosis, training, and evaluation. It could be that, with further studies on the investigation of sensitivity and specificity of the knee kinetic variables compared with those of KOOS (a self-reported questionnaire) and other clinical scales (e.g., Kellgren-Lawrence grade, a radiographic classification system insensitive to change [47]), the knee kinetic variables could potentially provide quantitative and specific characterizations of knee OA severity. Moreover, the associations could be used as a guide for which target knee kinetic variables to reduce/increase throughout the gait re-training on the elliptical trainer.

C. The Knee Kinetic Variables and 3-D Ankle Angles

With the associations between the knee kinetic variables and the clinical scores found, the associations between the 3-D ankle angles and the knee kinetic variables during stepping were investigated, because instructions on specific kinematic modifications are needed in company with direct feedback of targeted knee kinetic variable(s) for effective re-training of patients with KOA [19]. The followings were found. Each 1 °reduction in ankle eversion leads to a 3.9% reduction in EKAM, a 13.2% reduction in EKAM impulse, and an 8.7% reduction in EKIRM impulse. Each 1 °reduction in ankle dorsiflexion leads to a 2.7% reduction in EKAM, a 3.8% reduction in EKAM impulse, a 6.9% reduction in EKFM, 27.8% reduction in EKFM impulse, and a 2.7% reduction in EKTRM. Each 1 °increase in ankle internal rotation leads to a 4.4% reduction in EKAM impulse and a 4.2% reduction in EKTRM. Clinical significance of those changes needs to be verified most probably with KOA gait re-training studies.

Ankle eversion (lateral shift of knee joint) could increase EKAM similar to a previous study [8] on the elliptical trainer because ankle eversion accompanies the lateral shift of the knee joint (i.e., tibia rotated away from the median plane with rotation center at ankle origin) that can lengthen the moment arm from the knee joint to the ground reaction force. The lateral shift of the knee joint could mean knee adduction (varus) angle–one of the best predictors of high EKAM [4]–increase (with the potential lateral leaning of the body), and EKAM could increase with the ankle eversion. Ankle dorsiflexion (forward inclination of the shank) could increase EKAM considering that dorsiflexion is coupled with eversion [48]. Moreover, ankle dorsiflexion on the elliptical trainer may mean knee flexion that would increase the quadriceps force and thus the compressive forces across the knee [23]. Because EKAM is a surrogate measure of the compressive force [23], [24], the increase in compressive forces can increase EKAM. An increase in EKAM impulse with the increase of ankle dorsiflexion and eversion can be explained similarly. Ankle internal rotation (outward rotation of the shank with respect to the foot) might accompany the ankle inversion [48] that could reduce EKAM impulse (and EKAM). Note that ankle internal rotation on the elliptical trainer is similar to toe-in walking, which could reduce EKAM [49], [50] in the sense of the relative motion between the foot and the tibia. It is rather obvious that the increase in ankle dorsiflexion could increase EKFM and EKFM impulse because ankle dorsiflexion may accompany knee flexion on the elliptical trainer. EKIRM impulse increased with the increase in the maximum ankle eversion that was coupled with ankle external rotation (which may accompany tibial axial rotation on the elliptical trainer) and could increase the knee adduction angle, the best predictor of EKAM [4]. Thus, it may be that the EKIRM impulse changed with the changes in knee transverse rotation mechanics and could have a role in the pathomechanics of KOA in addition to EKAM, as hypothesized in [1], [30], [31], [51].

Nevertheless, this relationship may need further investigation. Peak EKTRM increased with ankle dorsiflexion and decreased with ankle internal rotation. Ankle dorsiflexion could increase EKTRM considering that many of the knee kinetic variables (peak EKAM, peak EKFM, EKAM impulse, EKFM impulse, and EKIRM impulse) increased with ankle dorsiflexion. Ankle internal rotation is coupled with ankle inversion and planar flexion [48], which reduce many of the knee kinetic variables (peak EKAM, EKIRM impulse, peak EKFM, and EKAM impulse). Thus, ankle internal rotation may decrease EKTRM. Of note is that ankle internal rotation on the elliptical trainer could induce tibial axial rotation that may change the loaded part of the cartilage [1], [30], [31]. This transverse plane knee rotation mechanics is believed to be related to the initiation of KOA [1], [9], [29]–[31], [51]. For the first time, for patients with KOA, these findings provided significant associations between ankle angles and knee medial compartment compressive load (and surrogate measures) that is a chain reaction of the ground reaction force that is transferred to the knee via the ankle in a closed-chain. Moreover, these associations are useful in developing

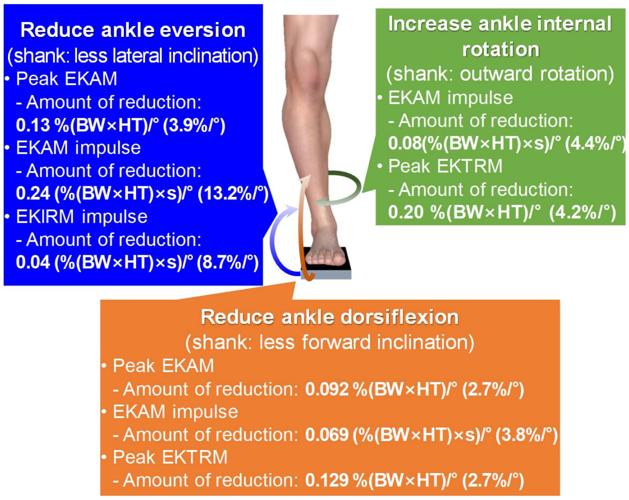


Fig. 6. Potential real-time biofeedback training strategies based on 1) the associations between the clinical scores and the knee kinetic variables and 2) the associations between the knee kinetic variables and the 3-D ankle angles. Reducing EKAM (and other knee kinetic variables) fed back to patients in real-time with adjusting of the 3-D ankle angles (reducing dorsiflexion and eversion, and increasing internal rotation) or equivalently adjusting the shank movement (reducing the lateral inclination and forward inclination, and increasing the outward rotation). For instance, the EKAM impulse can be reduced with an increase in ankle internal rotation (0.081(%(BW×HT)×s)/°), which may be accompanied by the shank/tibia external rotation with respect to the femur, thereby potentially improving the KOOS-Pain score (i.e., reducing knee pain) by considering the significant association between the EKAM impulse and the KOOS-Pain score ($\rho = -0.745$).

patient-specific KOA gait re-training instructions, as discussed in the following subsection.

D. Potential Real-Time Biofeedback Training Strategies on the Elliptical Trainer

Ankle inversion could reduce peak EKAM (the KOOS-Sports and Recreational Activities score), EKAM impulse (the KOOS-Pain score), and EKIRM impulse (the KOOS-Pain score). Ankle internal rotation could reduce EKAM impulse (the KOOS-Pain score), and peak EKTRM (the KOOS-Sports and Recreational Activities score). Ankle planar flexion could reduce peak EKAM (the KOOS-Sports and Recreational Activities score), EKAM impulse (the KOOS-Pain score), peak EKFM, peak EKTRM (the KOOS-Sports and Recreational Activities score). Thus, reducing EKAM (and other knee kinetic variables) fed back to the patients in real-time with adjusting ankle angles (reducing eversion, increasing internal rotation, and reducing dorsiflexion; Fig. 6) could comprise instructions for closed-chain gait re-training for patients with KOA on the elliptical trainer. To make the kinematic instructions intuitive for patients with KOA, the aforementioned instructions on ankle angle modification can be translated into shank movements relative to the foot fixed to the footplate (Fig. 6).

E. The Potential of the Elliptical Trainer as a Routine Evaluation and Real-Time Biofeedback Gait Re-Training Platform

To date, it has been challenging to provide the 3-D knee kinetic variables in real-time for KOA gait re-training outside motion analysis laboratories without cumbersome preparation and long-time post-processing. The elliptical trainer with the real-time biofeedback of EKAM (and other 3-D knee kinetic variables) can be used in clinics and gymnasiums with a few minutes' preparations and no post-processing of the motion analysis data. The results of this study warrant follow-up studies testing the efficacy of the KOA gait re-training on the elliptical trainer and the validity of the routine evaluation using the elliptical trainer. Further, the translation of the training effect on the elliptical trainer to the ground walking deserves to be studied in the future to achieve the long-term goal. The 6-degrees-of-freedom goniometer is inexpensive, occupies a small space in the vicinity of the footplate, and can provide 3-D ankle angles at any sampling rate [8], [9], allowing us to use the elliptical trainer outside motion analysis laboratories. The real-time feedback of knee kinetic variables with the potential strategies of modifying ankle angles is expected to allow us to immediately check the effectiveness of gait modification within a training session and what could be an effective strategy for each subject [8], [9], thereby allowing us to achieve the long-term goal. It is an advantage compared with other laboratory-based non-motion analysis gait re-training systems tested with healthy subjects [52]–[55] requiring separate motion analysis to obtain knee kinetic variables for checking the effectiveness of the training.

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