



# Lower-limb joint reaction forces and moments during modified cycling in healthy controls and individuals with knee osteoarthritis<sup>☆</sup>



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## ABSTRACT

**Background:** Osteoarthritis (OA) is a clinical problem affecting an estimated 27 million adults in the United States, with the only clear treatment options being pain management. Cycling is an integral component of exercise for individuals with knee osteoarthritis, while the joint reaction forces during cycling remain unknown. **Methods:** Thirteen subjects with medial compartment knee osteoarthritis and eleven healthy subjects performed a cycling protocol with a neutral pedal and four pedal modifications. Six hundred muscle-actuated inverse-dynamic simulations (24 subjects, 5 trials in each of 5 conditions) were performed to estimate joint reaction force differences between conditions.

**Findings:** Subjects with knee osteoarthritis had many significant changes among them was a reduction in knee adduction-abduction moment by 45% (5° lateral wedge), 77% (10° lateral wedge), 54% (5° toe-in) and 58% (10° toe-in). Conversely the healthy subjects had no significant changes in the knee adduction-abduction moment for the lateral wedge conditions and the 5° toe-in but did decrease by 18% for the 10° toe-in condition. When comparing the cohorts across the different pedal conditions, the data showed many significant differences among the groups.

**Interpretation:** This study showed that while cycling in different pedal modifications, the knee osteoarthritis subjects had more beneficial changes in their knee adduction-abduction moment compared to the healthy subjects with the lateral-wedge modification resulting in the greatest impact on the subjects with knee osteoarthritis. Both groups had greater contact forces at the hip and ankle across pedal modifications compared to neutral. For the knee, subjects with osteoarthritis mostly decreased their knee contact forces but the healthy subjects mostly increased these forces with all pedal modifications.

## 1. Introduction

Osteoarthritis (OA) is a joint disease significantly altering the quality of life (Mundermann et al., 2005) for an estimated 27 million people in the United States (Lawrence et al., 2008). OA causes a breakdown and wear on joint cartilage triggering disabling pain and disability (Peat et al., 2001). Knee OA usually affects the aging population, 60 years of age and older with 37.4% being affected by OA (Dillon et al., 2006; Lawrence et al., 2008). Of those, one-fourth reported problems with activities of daily living (ADL) (Cheng et al., 2010; Semanik et al., 2012). Treatment of OA is a \$128 billion industry

(Cheng et al., 2010; Hootman and Helmick, 2006), creating a disturbing clinical burden with 36 million ambulatory care visits and 750,000 hospitalizations per year (Hootman and Helmick, 2006), resulting in high socioeconomic expense (Gerbrands et al., 2014). OA is a clinical problem with few solutions beyond pain management until the disease progresses far enough to need invasive and expensive surgery (Shull et al., 2015).

One common treatment used in current rehabilitation for knee OA is the prescription of exercise (i.e., walking and cycling) (Kutzner et al., 2012; Roddy et al., 2007), though effects of exercise modifications on joint reaction forces and moments (JRF&M) are not well understood.

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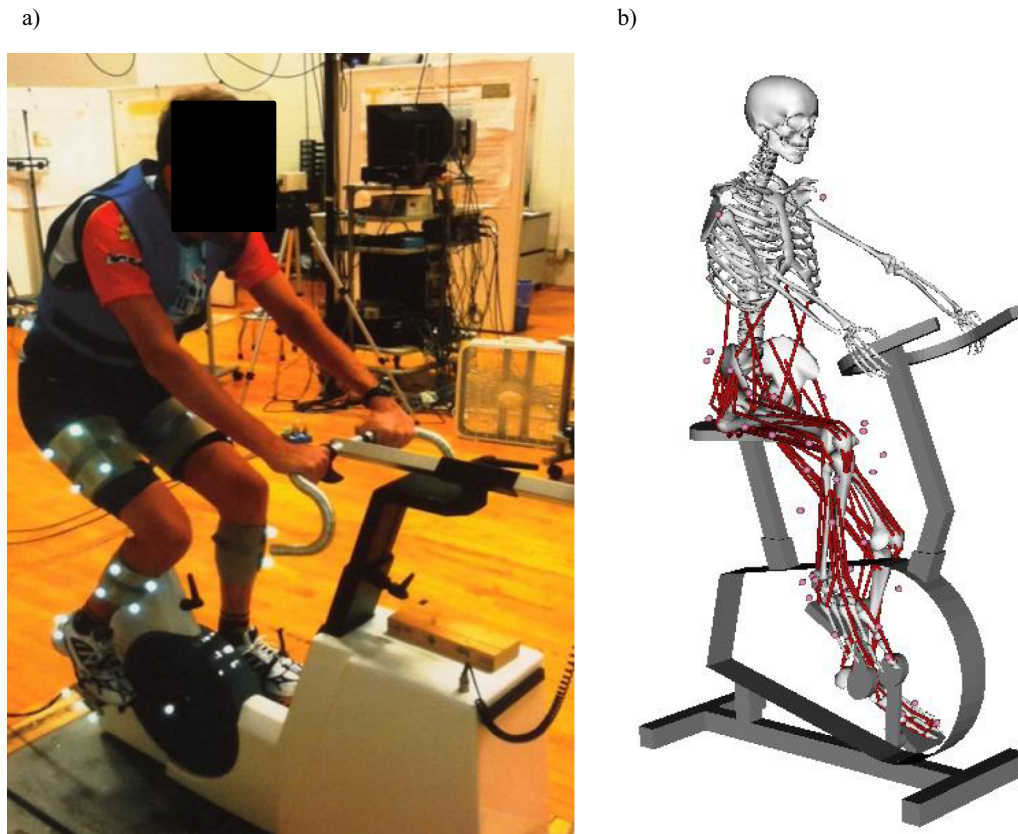
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**Fig. 1.** Example subject during a) data collection and example b) subject-specific musculoskeletal model for muscle force estimation with the added patella.

For subjects with knee OA, low-intensity cycling is as effective as high-intensity cycling for improving joint function, decreasing pain, and increasing aerobic capacity (Mangione et al., 1999). Health benefits of cycling include potentially reduced OA-related JRF&M but there is little scientific evidence of magnitude and location of these contact loads during cycling. Loading plays a crucial role in progression of joint degeneration and severity of pain during exercise and ADL (Akbarshahi et al., 2014; Mundermann et al., 2005); thus, a better understanding of how different cycling modifications affect JRF&M is necessary for improving knee OA related treatments. The external knee adduction moment and the internal knee abduction moment is used as an indirect measurement for the medial loading in the knee and has been linked to progression and severity of OA (Schipplein and Andriacchi, 1991). However, these moments, estimated from inverse dynamics, do not account for muscle force contributions to the JRF&M, and is not always a proper representation of the medial load at the knee (Walter et al., 2010). Cycling modifications have not been studied as often as walking (Hinman et al., 2008; Shull et al., 2013a; Shull et al., 2013b). One study (Gardner et al., 2016) found a 22% decrease in peak internal knee abduction moment with a 10° lateral-wedge intervention. Another study (Gardner et al., 2015) using a toe-in intervention found a decrease in the peak knee adduction angle for subjects with (61% for 5°, 73% for 10°) and without knee OA (77% for 5°, 109% for 10°). No studies have shed light on OA-related JRF&M during cycling with pedal modifications.

The current study used muscle-actuated inverse-dynamic simulations, in combination with experimental data, to identify differences that pedal modifications have on knee JRF&M for subjects with and

without knee OA during cycling. First, we hypothesized pedal modifications would cause a change (increase or decrease) in peak JRF&M compared to neutral pedal condition for each cohort. Secondly, we hypothesized that peak JRF&M for subjects with knee OA would be different (higher or lower) compared to healthy subjects during cycling in each pedal condition. Identifying effects of modified cycling exercise on JRF&M, and differences between the cohorts, will contribute to a better understanding for improving the treatment of knee OA with cycling exercise; ultimately allowing for patient-specific rehabilitation.

## 2. Methods

### 2.1. Subject demographics

Previously collected data (Gardner et al., 2015) from twenty-four subjects were included in this study. Thirteen subjects had medial compartment tibiofemoral (knee) OA (7 females, 6 males | weight: mean 83.2 kg (SD 22.3) | BMI: mean 25.6  $\frac{\text{kg}}{\text{m}^2}$  (SD 3.6) | height: mean 1.75 m (SD 0.14) | age: mean 56.8 yrs (SD 5.2)) and 11 subjects without knee OA (5 females, 6 males | weight: mean 80.2 kg (SD 23.1) | BMI: mean 25.9  $\frac{\text{kg}}{\text{m}^2}$  (SD 5.4) | height: mean 1.75 m (SD 0.12) | age: mean 50.0 yrs (SD 9.7)) (Gardner et al., 2015). To be included in this study, all subjects were between 50 and 66 years of age and had a BMI of no > 35  $\frac{\text{kg}}{\text{m}^2}$ . The OA cohort had been radiographically diagnosed with medial compartment knee OA by a rheumatologist in one or both knees, with or without patella-femoral knee OA, with a grade 1 to 4 on the Kellgren-Lawrence scale (Gardner et al., 2015; Gardner et al., 2016).

They were excluded, if they had a previous lower extremity joint replacement, had OA in the hips or ankles, had a previous arthroscopic surgery or intra-articular injections prior to testing, and/or had a type of systemic arthritis. Two days prior to testing all subjects were asked to stop pain medication. For more criteria on the inclusion, exclusion, and OA severity please refer to [Gardner et al. \(2015, 2016\)](#).

## 2.2. Experimental motion capture data collection

Prior to data collection participants performed 3 min of treadmill walking at a self-selected pace, which served as an initial warm-up. Participants were then asked to sit on a cycle ergometer and researchers fit it to each subject accordingly by adjusting seat height, seat depth and trunk angle. Next, participants performed a 3-minute warm-up on the cycle ergometer to assess proper positioning and observation of pain levels. For the data collection, each trial of cycling was performed for 2 min at a pedal cadence of 60 RPM and an 80 W work-rate (5 conditions with 5 trials for each condition); creating 600 trials. The five conditions were Neutral, 5° Lateral wedge, 10° Lateral Wedge, 5° Toe-in and 10° Toe-in. For more information on the data collection process and the pedal modifications, please refer to [Gardner et al. \(2015, 2016\)](#).

## 2.3. Development and analysis of muscle-actuated inverse-dynamic simulations

We created subject-specific models using the generic, full-body musculoskeletal model ([Rajagopal et al., 2016](#)) in OpenSim that contains 10 body segments, 23 degrees of freedom and 92 muscle-tendon actuators ([Fig. 1](#)). The pelvis is defined as 6 degrees of freedom relative to the ground. Another segment was the head, arms, and torso which were represented as one segment that connected to the pelvis through a ball-and-socket joint ([Anderson and Pandy, 1999](#)). Another ball-and-socket joint was used to model the hip joint ([Delp et al., 1990](#)). The knee was modeled as a planar joint with tibiofemoral and patellofemoral translational constraints as a function of knee flexion ([Delp et al., 1990](#)). The ankle and subtalar joints were designed as separate revolute joints ([Hoy et al., 1990](#)). We enhanced our musculoskeletal model further by adding a patellar ligament constraint to the model so that it articulated with the femur and allowed the muscles to constrain and wrap around the patella ([DeMers et al., 2014](#)). This allowed the patella to function as a pulley that mandates the quadriceps forces to act in the corresponding direction of the patellar ligament. This refined the muscle force estimates for generating the measured knee kinematics, and it allowed for a more accurate estimation of the JRF&M.

The procedure for creating and analyzing muscle-actuated inverse-dynamic simulation of each individual's movement consisted of a four-step procedure. This procedure was done while utilizing the OpenSim standard coordinate system ([Arnold et al., 2010](#)), in which the anatomical positions and positive is oriented so that the x-axis points anteriorly, the y-axis points superiorly, and the z-axis points to the right. In step one, we modified an existing, generic model of the musculoskeletal system and scaled it to account for differences in the subject's height, mass properties, and muscle moment-generating capacity due to the muscles moment arms ([Delp et al., 2007](#)). The model was scaled ([Fig. 1](#)) by using the musculoskeletal geometry of the generic model and the marker data collected from experimental motion analysis. In step two, we used inverse kinematics to solve for the model's joint angles to minimize errors between experimental and model markers. In step three, we used inverse-dynamics along with kinematics from the previous step and experimental pedal reaction forces to determine the net joint moments. In step four, we used static optimization ([Anderson and](#)

[Pandy, 2001](#)) to determine the muscle activations and corresponding muscle forces that generate the net joint moments. We chose to use the inverse-dynamics approach for our large number of simulations (600) created because this approach is well-established and computationally efficient ([Anderson and Pandy, 2001](#)).

## 2.4. Estimation of joint reaction forces and moments

To determine the effects of the pedal modifications on the JRF&M, the contact forces and moments were estimated using the joint reaction analysis in OpenSim ([Seth et al., 2011](#)). This analysis is used to estimate joint contact forces and moments that are transferred between two adjacent bodies accounting for the model including the muscle-tendon actuators ([Millard et al., 2013](#); [Thelen, 2003](#); [Winters, 1995](#); [Zajac, 1989](#)). This tool takes into account the muscle forces that were calculated in step four, the kinematic movement in step two, and the pedal reaction forces from the experimental data collection. The joint reaction analysis results in six different outputs, including three contact forces in the anterior-posterior shear, compression, and medial-lateral shear, as well as three contact moments in the adduction-abduction, internal-external rotation, and flexion-extension, all of which are expressed in the child reference frame (tibia). This analysis is used to extract information from the subject-specific model and cycling simulations to better understand the experimentally measured motion capture data ([Seth et al., 2011](#)). All joint contact forces were normalized to body weight and joint reaction moments to body weight × height.

## 2.5. Tests of the hypothesis

We evaluated our first hypothesis regarding the differences in peak JRF&M within each cohort by conducting a repeated measure one-way analysis of variance (ANOVA) in Matlab 2015 at a significance level set to 0.05. An ANOVA tells us if there is a difference across the pedal conditions. The ANOVA allows for comparisons to be made across the five different pedal conditions within each group. We then set the alpha level ( $p \leq 0.05$ ) in order to determine where the significances may be located. All of the peak percent changes were compared to the neutral pedal condition for four pedal modifications. Peak JRF&M were chosen for the first peak in the JRF&M during the power phase of the cycle (0°–180°). We evaluated our second hypothesis regarding the differences in peak JRF&M between cohorts (knee OA and healthy) by conducting a *t*-test between the two groups with a level of significance at 0.05. Again, the alpha level was adjusted to find the significant differences. Lastly, we created two identity grids to visually analyze and summarize the significant differences in the associated JRF&M between 1) pedal modifications compared to the neutral pedal condition ([Table 1](#)), and 2) the two cohorts in the same corresponding pedal condition ([Table 2](#)). [Table 3](#), portrays the results for the peak JRF&M for both cohorts in all pedal conditions.

## 2.6. Validation of the model and simulation results

Experimental data was used to validate the 24 inverse-dynamics subject-specific models and 600 simulations. Every subject's model markers were placed in precise locations to match experimentally collected data. For scaling, the models marker locations were inspected and the positions were adjusted in order to match experimental positions and reduce error from static markers. Marker positions were then compared to verify they were underneath the acceptable threshold ( $\leq 2$  cm). After inverse kinematics, the root mean square (RMS) and peak marker errors were examined, and the marker weightings were

**Table 1**

The JRF&M change identity grid showing the significant differences within each cohort in all contact loads compared to neutral, for the peak contact loads. Red indicates an increase compared to neutral, while blue indicates a decrease compared to neutral; the darker the color the greater the increase or decrease.



adjusted to reduce these errors under a suitable threshold (RMS error  $\leq 2$  cm and maximum error  $\leq 3$  cm). Results were then compared to the experimental kinematics from the data collection process. Specifically the resulting joint angles (hip, knee, and ankle) were examined visually and compared to those from Visual 3D motion capture analysis software (Gardner et al., 2015; Gardner et al., 2016). After inverse-dynamics was carried out, the resulting net joint moments were compared with the experimental data (Gardner et al., 2015; Gardner et al., 2016) for the hip, knee, and ankle. After static optimization, the muscle activations for the healthy subjects in neutral cycling were compared to published EMG data (Neptune et al., 1997) with the understanding that there were similarities in the pedal cadence (60 RPM) and a difference in the

work-rate (80 W; Fig. 2). Additionally, the compressive force was compared between the healthy subjects and a subject from the Orthoload database for with a prosthetic knee implant (Supplemental Document). These steps were done in accordance with previous literature (Neptune et al., 1997).

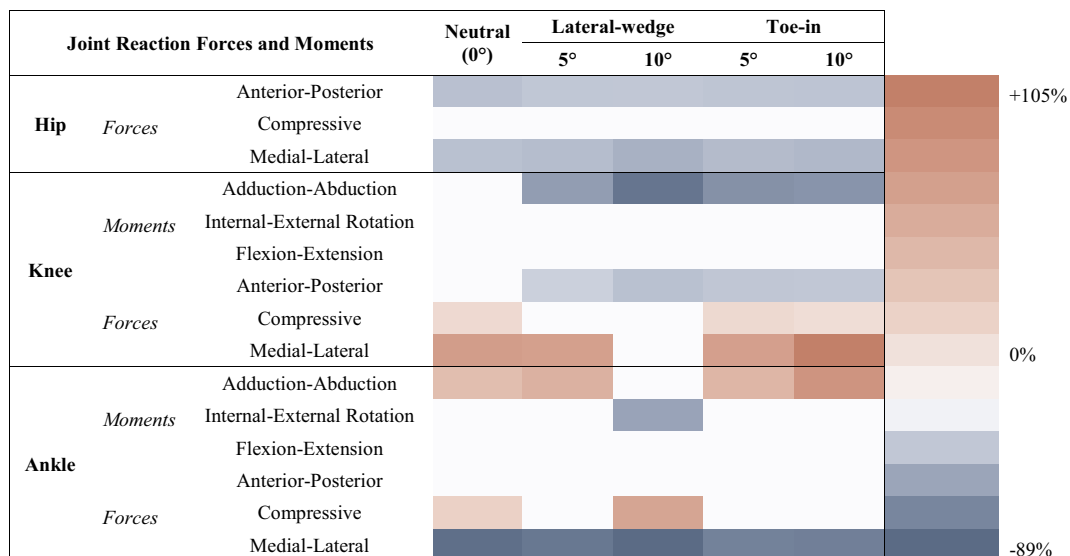
### 3. Results

#### 3.1. Lateral-wedge peak joint reaction force differences across conditions

Subjects with knee OA had 11 significant ( $p < 0.05$ ) changes (6 for 5°, 5 for 10°), for the lateral-wedge conditions (Table 3). For the 5°

**Table 2**

The peak JRF&M significant differences between OA (+) and healthy (−) across all conditions. Red indicates knee OA cohort was greater within that conditions, while blue indicates healthy cohort was higher within that conditions; the darker the color the greater the difference.



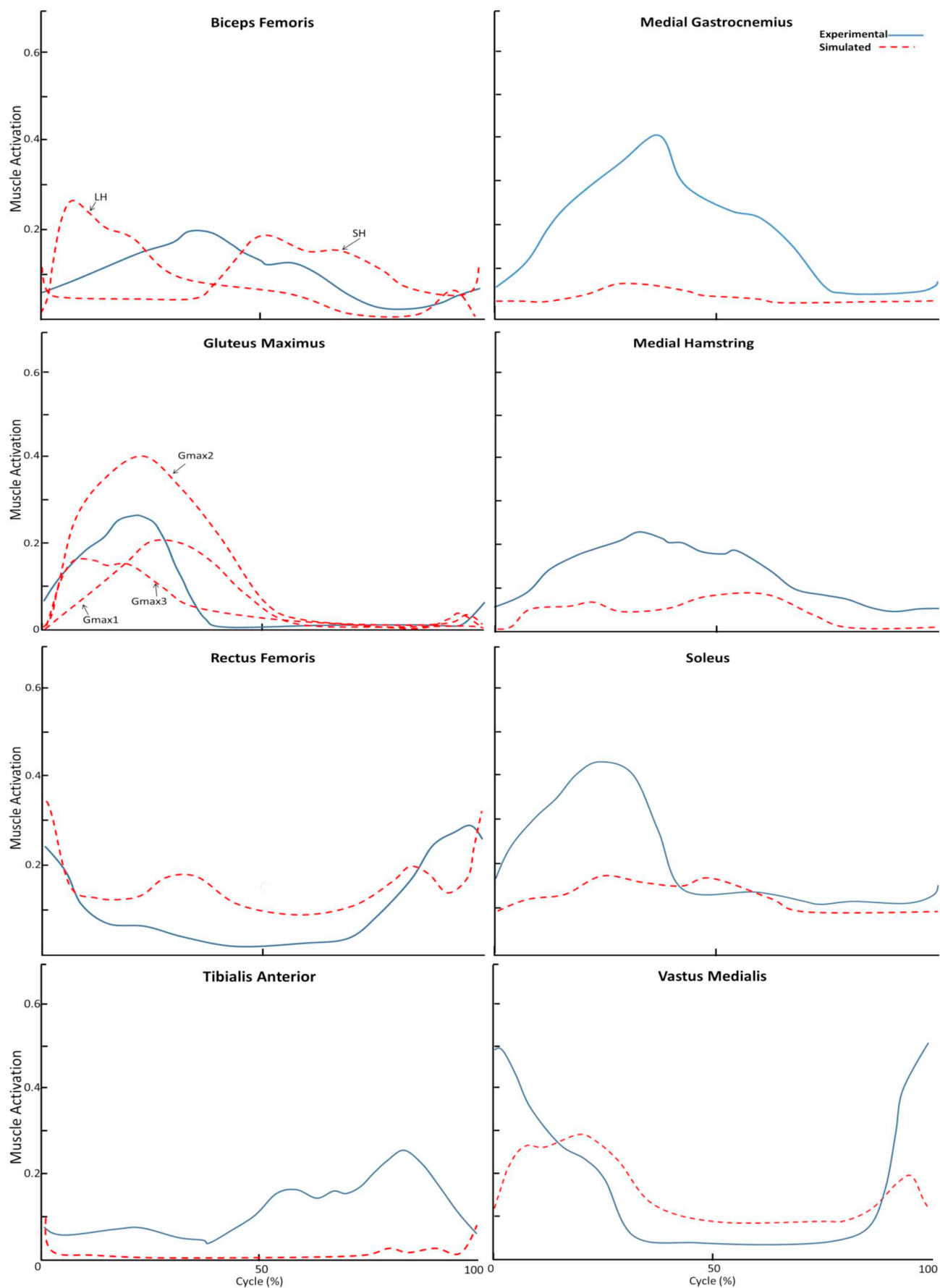


Fig. 2. EMG validation: The neutral pedal condition (at 80 W and 60 RPM) with Neptune et al. (1997), EMG data of elite male cyclists (at 127 W and 60 RPM).



**Table 3**

The peak JRF&M mean peak and standard deviations (SD) for both cohorts and all five pedal conditions. The forces are expressed in %BW and the moment are expressed in %BW\*HT. A negative for the adduction-abduction moment, shows the direction on the coordinate system to the lateral side. However, it is important to note that these are also associated with a large standard deviation.

Joint reaction forces and moments				Neutral		Lateral wedge				Toe-in			
				0°		5°		10°		5°		10°	
				Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Healthy subjects	Hip	Forces	Anterior-posterior	38.36	20.33	43.81	30.28	42.38	20.97	37.08	19.83	34.73	20.63
			Compressive	102.95	55.09	120.23	52.99	135.81	62.98	116.06	68.13	122.99	72.48
			Medial-lateral	25.98	14.95	31.77	16.36	30.04	15.48	28.12	15.11	27.44	14.67
	Knee	Moments	Adduction-abduction	0.50	0.58	0.38	0.57	0.42	0.48	0.52	0.52	0.44	0.48
			Internal-external rotation	0.46	0.29	0.58	0.35	0.62	0.47	0.54	0.36	0.57	0.42
			Flexion-extension	0.52	0.39	0.65	0.43	0.76	0.47	0.51	0.38	0.49	0.42
		Forces	Anterior-posterior	58.78	29.87	70.01	29.12	81.73	39.11	62.96	32.40	66.29	37.06
			Compressive	118.31	42.75	137.77	71.32	136.00	56.90	123.95	47.30	127.92	47.13
			Medial-lateral	2.09	2.93	1.98	2.68	2.27	2.34	2.27	2.07	2.09	2.12
	Ankle	Moments	Adduction-abduction	0.09	0.13	0.12	0.14	0.06	0.24	0.15	0.14	0.12	0.11
			Internal-external rotation	0.19	0.25	0.17	0.15	0.28	0.48	0.25	0.12	0.24	0.11
			Flexion-extension	0.02	0.05	0.02	0.02	0.04	0.09	0.03	0.05	0.03	0.02
		Forces	Anterior-posterior	20.18	36.43	19.81	38.75	32.68	37.86	19.72	27.15	20.80	30.34
			Compressive	71.83	72.97	82.19	67.70	65.00	63.09	78.00	43.05	73.49	47.17
			Medial-lateral	10.37	19.17	11.27	23.22	12.80	19.74	14.22	21.95	12.31	17.05
Subject with knee OA	Hip	Forces	Anterior-posterior	21.79	19.88	22.54	24.51	24.12	24.47	22.02	21.72	18.50	21.91
			Compressive	102.75	99.98	117.81	98.08	127.46	142.10	117.83	100.42	125.93	109.13
			Medial-lateral	10.86	40.15	8.35	41.06	10.66	45.31	12.85	37.58	13.47	37.55
	Knee	Moments	Adduction-abduction	-0.33	1.38	-0.34	1.20	-0.60	1.35	-0.52	1.19	-0.58	1.13
			Internal-external rotation	0.37	0.57	0.46	0.52	0.52	0.72	0.45	0.47	0.50	0.56
			Flexion-extension	0.36	0.83	0.26	0.68	0.26	0.77	0.30	0.76	0.27	0.84
		Forces	Anterior-posterior (X)	47.41	39.79	50.67	30.30	52.60	41.25	45.21	25.17	49.54	40.05
			Compressive	141.00	91.67	160.82	122.72	157.65	121.62	155.85	120.86	152.67	123.40
			Medial-lateral	1.68	6.32	1.70	6.09	1.58	6.38	2.09	6.68	2.59	6.80
	Ankle	Moments	Adduction-abduction	0.11	0.31	0.16	0.26	0.10	0.29	0.18	0.27	0.17	0.27
			Internal-external rotation	0.09	0.45	0.19	0.38	0.11	0.30	0.17	0.28	0.18	0.39
			Flexion-extension	-0.02	0.06	-0.02	0.07	-0.02	0.04	-0.01	0.05	-0.01	0.05
		Forces	Anterior-posterior	5.11	21.73	11.58	64.37	29.87	37.03	19.19	34.15	22.70	27.35
			Compressive	108.93	79.46	122.61	122.90	140.71	167.05	133.20	175.74	114.85	132.41
			Medial-lateral	6.47	17.29	5.74	15.70	13.63	27.81	4.33	14.83	4.99	15.31

lateral-wedge condition, the knee showed the largest increase in the compressive force by 10%, however the largest decrease was in the adduction-abduction moment by 45%. For the 10° lateral-wedge condition, the knee showed no noticeable increases, but the largest decrease was in the adduction-abduction moment by 77%.

Healthy subjects had 22 significant ( $p < 0.05$ ) changes (12 for 5°, 10 for 10°), for the lateral-wedge conditions (Table 1, Fig. 3). For the 5° lateral-wedge condition, the knee showed the largest increase in the flexion-extension moment by 19%, while there was no significant decrease. For the 10° lateral-wedge condition, the largest increase at the knee was the flexion-extension moment by 33%; similarly, there was no noticeable significant decrease. Subjects without knee OA showed many overall significant increases for the lateral-wedge condition compared to neutral. These differences were also accompanied by mostly increases in the hip and ankle JRF&M.

### 3.2. Toe-in peak joint reaction force differences across conditions

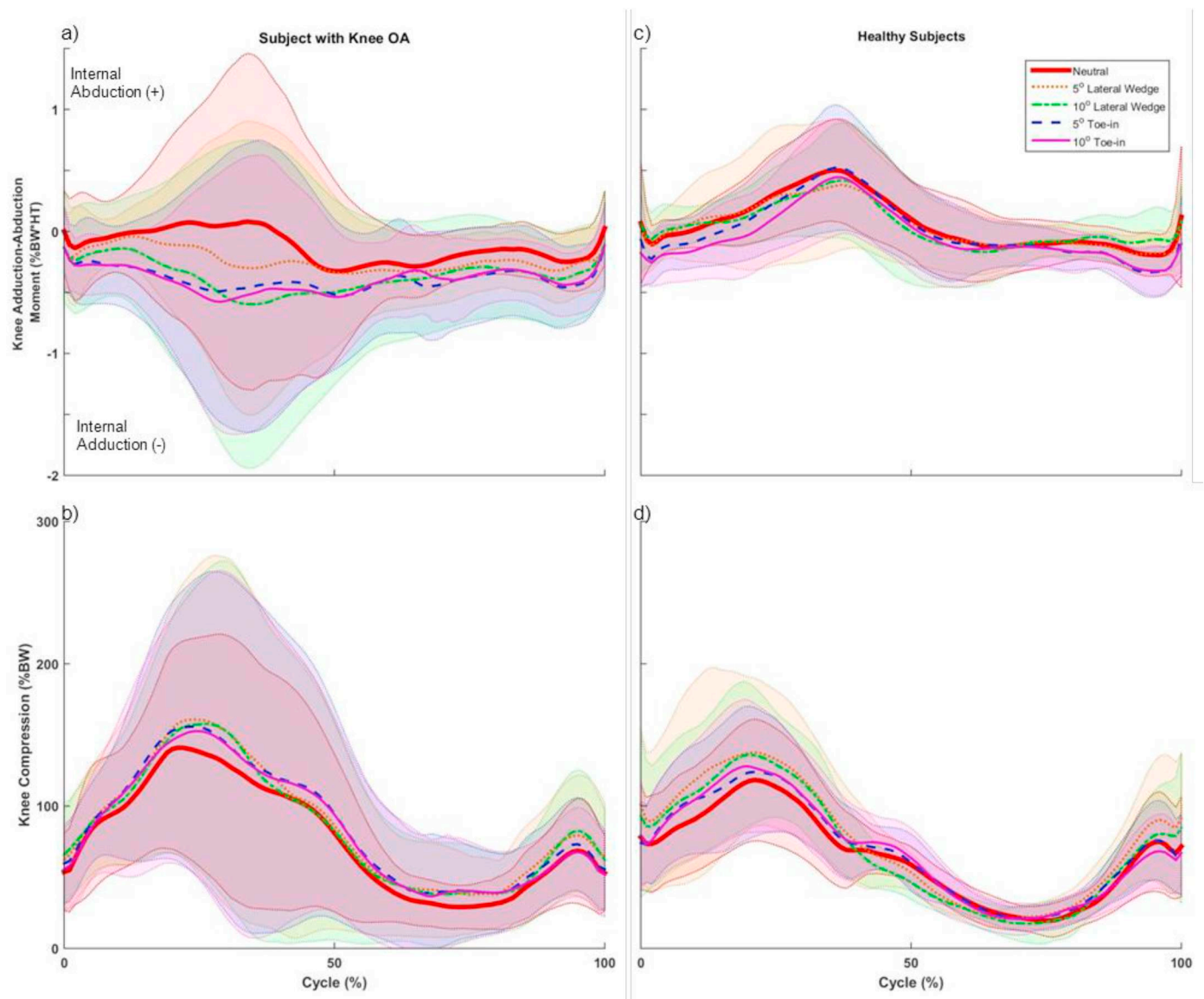
There were many changes in the peak JRF&M for the subjects with and without knee OA in the toe-in modification compared to the neutral pedal condition, which confirmed our hypothesis that pedal modifications would lead to changes in peak JRF&M (Table 1, Fig. 3). Subjects with knee OA had 12 significant ( $p < 0.05$ ) changes (6 for 5°, 6 for 10°), for the toe-in conditions. For the 5° toe-in condition, the knee showed no noticeable increase, and the largest decrease was in the adduction-abduction moment by 54%. For the 10° toe-in condition, the knee showed an increase in the medial-lateral force by 15%, and the largest decrease was in the adduction-abduction moment by 58%.

Healthy subjects had 14 significant ( $p < 0.05$ ) changes (6 for 5°, 8 for 10°), for the toe-in conditions (Table 1, Fig. 3). For the 5° toe-in

condition the knee showed the largest increase in the internal-external rotation moment by 15%, and there was no obvious decrease at the knee. For the 10° toe-in condition, the knee showed the largest increase in the internal-external rotation moment by 26%. The largest decrease was in the adduction-abduction moment by 18%.

### 3.3. Peak JRF&M differences between cohorts

There were many differences in the peak JRF&M for the subjects with knee OA in each pedal condition compared to healthy subjects and this confirmed our hypothesis that cohort differences would lead to differences in peak JRF&M (Table 2). The neutral pedal condition revealed 7 significant ( $p < 0.05$ ) differences. For the neutral condition the knee's medial-lateral shear force showed the largest positive (OA > healthy) difference by 76%; while there was no obvious negative (OA < healthy) difference. The lateral-wedge conditions revealed 14 significant differences (7 for 5°, 7 for 10°). For the 5° lateral-wedge condition, the knee showed the largest positive (OA > healthy) difference in the medial-lateral force by 73%, while the adduction-abduction moment showed the largest negative (OA < healthy) by 52%. For the 10° lateral-wedge condition, there was no significant positive (OA > healthy) difference at the knee joint, while the adduction-abduction moment showed the largest negative (OA < healthy) difference by 80%. The toe-in conditions, revealed 16 significant ( $p < 0.05$ ) differences (8 for 5°, 8 for 10°). For the 5° toe-in condition, the knee showed the largest positive (OA > healthy) difference was in the medial-lateral force by 74%, while the knee adduction-abduction moment showed the largest negative (OA < healthy) difference of 60%. For the 10° toe-in condition, the knee showed the largest positive (OA > healthy) difference was in the medial-lateral force by 104%,



**Fig. 3.** Plotting the knee's important joint contact loads for cohorts. The adduction-abduction moment (top), which is used as a surrogate measurement for the medial compartment knee loading and the compressive weight bearing load (bottom). (a.) Subjects with knee OA showed an overall decrease in the adduction-abduction moment, on average, compared to the neutral pedal condition (red solid line), (b.) while the compressive load did not show many statistically significant differences ( $p < 0.05$ ), on average; though some subjects were affected more than others in the contact moment and compressive load as seen by the wide range in the standard deviation, while subjects without OA (c.) did not change their knee adduction-abduction contact moment as much and was only seen to be statistically significant ( $p < 0.05$ ) in the 10° toe-in pedal condition, on average, compared to the neutral condition, (d.) while the compressive load did not show any statistically significant differences ( $p < 0.05$ ), on average; though some subjects were affected more than other in the contact moment and compressive load as seen by the standard deviation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

while the adduction-abduction moment showed the largest negative (OA < healthy) difference by 57%. Subjects without knee OA had overall greater knee adduction-abduction moments in all conditions except neutral while they also showed to have mostly greater contact loads in almost all pedal conditions and JRF&M.

#### 4. Discussion

We examined the effects of five different pedal modifications on the joint reaction forces and moments during cycling. We confirmed our hypothesis that pedal modifications caused changes in the peak JRF&M compared to the neutral pedal condition for each cohort. Moreover, the second hypothesis is confirmed that the peak JRF&M for subjects with knee OA are different compared to healthy subjects while cycling in each pedal condition. Our findings suggest that subjects with knee OA

have a greater potential than subjects without knee OA to significantly improve their important JRF&M (knee adduction-abduction moment) overall by using pedal modifications. Conversely, the healthy subjects were affected overall more harshly (by increasing JRF&M) using the pedal modifications compared to the neutral condition, more than the OA cohort did. Furthermore, these changes for the subjects with knee OA were mostly increases in the hip and ankle contact loads, but mostly decreases at the knee when compared to the neutral pedal condition. The changes for healthy subjects without knee OA were mostly increases in the hip, knee and ankle contact loads compared to the neutral condition.

There were many changes in the peak JRF&M for the subjects with and without knee OA in the lateral-wedge condition compared to the neutral pedal condition which confirmed our first hypothesis (Table 1, Fig. 3). Subjects with knee OA showed many overall significant

differences for the lateral-wedge condition the toe-in condition. Even though there were many decreases seen in the knee adduction-abduction moment (Fig. 3) and mostly decreases at the knee in general, it is important to note that this did cause some notable increases at the hip and ankle JRF&M for both lateral wedge and toe-in conditions. Subjects without knee OA showed many overall significant differences for the toe-in condition these differences at the knee were mostly increases. Even though there was a decrease seen in the knee adduction-abduction moment for the 10° toe-in condition, while the rest were also mostly noticeable increases in the hip and ankle JRF&M. It is also important to note that unlike the healthy subjects, the knee OA subjects had a large standard deviation between subjects for the knee adduction-abduction moment as can be seen in Fig. 3. Three OA subjects were in the negative (or lateral direction), while the other subjects were in the positive direction.

The current study has a few research challenges and results should be interpreted in the context of these limitations. First, the use of static optimization to estimate muscle forces instead of dynamic optimization. Static optimization was chosen due to the large amount of simulations created and the low computational expense associated with this approach. Additionally, it has been previously determined by Anderson and Pandey (2001) that static and dynamic optimization is essentially equivalent for estimating in vivo quantities such as muscle forces and joint contact forces for gait (Anderson and Pandey, 2001). Therefore, the results from static optimization should not affect our conclusions drawn from this study. Second, electromyography (EMG) data was not obtained from the data collection process for our subjects. Even with not having EMG, our results of healthy subjects matched well with experimentally collected data from elite male athletes in a neutral pedal condition (Neptune et al., 1997). Third, the load values reported in the current study represent the whole knee JRF&M, rather than narrowing in on the medial compartment where subjects exhibit radiographic evidence of knee OA. The adduction-abduction moment relates to the unbalanced forces compressing the medial and lateral compartments and contribution to the bone-on-bone contact characteristics leading to knee OA, thus finding a reduction in this contact load shows an improvement for subjects with medial knee OA. Fourth, the data was obtained with only one instrumented pedal; this restriction allowed us to only analyze one side of the participants, though this will not alter the results of the analyzed leg. Although the magnitude of JRF&M may change if we made different modeling assumptions, our conclusions regarding the relative changes in these loads during modified cycling compared to neutral cycling would unlikely change significantly since the same assumptions would be used across all 600 simulations.

Despite these research challenges, our results are consistent with findings of others. The muscles activations from the subjects without knee OA were similar to EMG data from another study by Neptune et al. (1997), with the same pedal cadence (60 RPM) and a higher work-rate of 120 W versus our 80 W. We also visually compared the joint angles of the hip, knee and ankle (Sanderson and Black, 2003) as well as the moments (Ericson et al., 1986; Mornieux et al., 2007; Neptune and Hull, 1998; Sanderson and Black, 2003; Smak et al., 1999) and both compared well to previous studies for the subjects without knee OA at a different work-rate. The pedal reaction forces compared well noting differences in pedal cadences and work-rates (Neptune and Hull, 1998; Neptune and Hull, 1999). In addition, our results agreed with the experimental study carried out by Gardner et al. (2015, 2016), where they found a decrease in the peak internal knee abduction moment for lateral pedal wedge conditions rather than toe-in pedal conditions.

What has not been discovered in previous research until now is the question of whether subjects with and without knee OA have different JRF&M during cycling that may change with different cycling modifications. Previous literature focused on calculating the magnitude of the inverse-dynamic moments, which does not take into account the muscle forces contributing to JRF&M while cycling at different pedal modifications, cadences and work-rates (Ericson, 1988; Ericson and

Nissell, 1986; Mornieux et al., 2007; Neptune and Kautz, 2000). For example, Mornieux et al. (2007), examined male cyclists while testing the utility and robustness of the estimated joint moments during cycle. Our study investigated and compared both subjects with and without knee OA and all subjects were not competitive cyclists. Previous literature has not examined the effects of cycling modifications (lateral-wedge and toe-in) on the JRF&M in subjects with and without knee OA. These pedal modifications alter the kinematics, which in turn changes the joint moments generated by the muscle forces (Too, 2012). This newly found information on the JRF&M will aid in improving rehabilitation prescription.

One previously published paper (Gardner et al., 2016) examined the same lateral pedal wedge condition determining the peak internal knee abduction moment, this is used by scientists as a measurement for the medial compartment loading of the knee. There was an effective decrease in the lateral-wedge (10°) condition by reducing the internal knee abduction moment by over 22% compared to neutral pedal in both cohorts. Our use of the JRF&M, which takes into account the estimated muscle forces and the effects on the overall joint motion, also found a decrease for the subjects with knee OA but not the healthy subjects in the lateral-wedge conditions. The 5° wedge decreased by just about half compared to the neutral condition, and the 10° decreased by over three-fourths. Another previously published toe-in study (Gardner et al., 2015), which also examined the internal knee abduction moment, found that this pedal was not effective in reducing the internal knee abduction moment across all participants. In contradiction to these findings, we found that subjects with knee OA were able to reduce their adduction-abduction moment compared to neutral in both the 5° and 10° toe-in conditions. Where the 5° toe-in was able to reduce the adduction-abduction moment by over half and 10° toe-in was able to decrease the same moment by almost 60% compared to neutral. Conversely, the healthy subjects were only able show a significant reduction in the 10° toe-in by about one-fifth compared to neutral. These differences may be because JRF&M take into account the estimated muscle forces as opposed to the knee abduction moment calculation which does not contain input from the associated muscle forces that span the joint. These values might be significant within individual subjects, but not across the cohort as a whole, which may be skewing the results. This may be due to individual muscles contributing to dynamic movements that affect joints in which they do not span. Hence, in order to examine the knee JRF&M, the critical input from the muscles is necessary in order to examine the influence the cycling movement has on the joint reaction forces.

In conclusion, this study showed different pedal modifications have a greater effect on the knee adduction-abduction moments for subjects with knee OA compared to healthy subjects. More specifically, lateral-wedge pedal modifications had a greater effect than toe-in modifications on subjects with knee OA, which allowed them to decrease their knee adduction-abduction moment and the compressive load when compared to the neutral condition. Regardless of pedal condition, the healthy subjects had more significant differences (mostly increases) when compared to subjects with OA. This study has shown how cycling modifications change JRF&M for improving exercise in subjects with knee OA, but further research is needed to optimize cycling in order to see what kinematics and coordination patterns minimize the unbalanced joint forces in the knee, leading to OA progression. Additionally, future research needs to examine the effects of the pedal modification on the increase JRF&M of the lateral compartment and its possibility for Lateral OA progression. Thus, in return reduce the knee OA progression. Joint loading plays a crucial role in the progression of joint degeneration and severity of pain during exercise and ADL. Therefore, a better understanding of optimizing joint reaction force distribution is necessary for designing and adapting exercise prescription for subjects with knee OA.

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## Declaration of competing interest

None of the authors had any conflict of interest regarding this manuscript.

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