Sex-specific hip osteoarthritis-associated gait abnormalities: alterations in dynamic hip abductor function differ in men and women

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1 Abstract

2 Background: Hip osteoarthritis results in abnormal gait mechanics, but it is not known whether 3 abnormalities are the same in men and women. The hypothesis tested was that gait abnormalities 4 are different in men and women with hip osteoarthritis vs. sex-specific asymptomatic groups. 5 *Methods*: 150 subjects with mild through severe radiographic hip osteoarthritis and 159 6 asymptomatic subjects were identified from an Institutional Review Board-approved motion 7 analysis data repository. Sagittal plane hip range of motion and peak external moments about the 8 hip, in all three planes, averaged from normal speed walking trials, were compared for men and 9 women, with and without hip osteoarthritis using analysis of variance. 10 *Findings*: There were significant sex by group interactions for the external peak hip adduction 11 and external rotation moments (P=0.009-0.045). Although asymptomatic women had peak 12 adduction and external rotation moments that were respectively 12% higher and 23% lower than 13 asymptomatic men (P=0.026-0.037), these variables did not differ between men and women with 14 hip osteoarthritis ($P \ge 0.684$). The osteoarthritis vs. asymptomatic group difference in the peak hip adduction moment was 45% larger in women than in men. The osteoarthritis vs. asymptomatic 15 group difference in the peak hip external rotation moment was 55% larger for men than for 16 17 women (P < 0.001). Sex did not influence the association between radiographic severity and gait 18 variables.

19 Interpretation: Normal sex differences in gait were not seen in hip osteoarthritis. Sex-specific 20 adaptations may reflect different aspects of hip abductor function. Men and women with hip 21 osteoarthritis may require different interventions to improve function.

22 Keywords: hip osteoarthritis, gait, sex differences, biomechanics

1 Introduction

2 Hip osteoarthritis (OA) is associated with abnormal gait mechanics (Ardestani and Wimmer, 2016, Chabra, Shakoor, & Foucher, 2012, Chabra and Foucher, 2013, Constantinou et 3 4 al., 2014, Eitzen et al., 2012, Eitzen et al., 2015, Foucher et al., 2012, Hurwitz et al., 1997, 5 Kumar et al., 2015b, Leigh, Osis, & Ferber, 2016, Rutherford, Moreside, & Wong, 2015, Watelain et al., 2001). There is overlap between the gait variables that have been found to differ 6 7 between people with and without hip OA and those that differ between healthy men and women. 8 For example, reduced dynamic sagittal plane hip range of motion, (Eitzen et al., 2012, Foucher et 9 al., 2012, Hurwitz et al., 1997, Hurwitz et al., 1998, Watelain et al., 2001) and reductions in the 10 peak external hip adduction moment (Ardestani and Wimmer, 2016, Foucher, Hurwitz, & Wimmer, 2007, Foucher et al., 2011, Hurwitz et al., 1997, Hurwitz et al., 1998) are commonly 11 12 seen in hip OA. These same variables reportedly differ between healthy men and women. (Boyer, Beaupre, & Andriacchi, 2008, Kerrigan, Todd, & Della Croce, 1998, Ko et al., 2011b, Moisio et 13 al., 2003) Moreover, it has been shown that knee OA affects gait in sex-specific ways (Ko et al., 14 15 2011a, Kumar et al., 2015a, McKean et al., 2007, Phinyomark et al., 2016). There may be sex-16 specificity in hip OA gait abnormalities as well. If so, there may be a need for sex-specific biomechanically-based interventions to improve function in men and women with hip OA. 17

Because of a dearth of sex-specific analyses in the hip OA biomechanics literature, the aim of this study was to identify sex-specific hip OA-related gait abnormalities in a previously described cohort of subjects with and without hip OA (Foucher et al., 2012). The hypothesis tested was that men with hip OA, when compared to asymptomatic men, would have different gait abnormalities than women with hip OA compared to asymptomatic women. Although there was no a priori expectations regarding the specific variables, or the direction or magnitude of the

differences, the sagittal plane hip range of motion and peak external hip adduction moment were
of particular interest. These variables are known to be different in healthy men and women, and
are both linked to hip OA. Other gait variables discussed in the parent publication (Foucher et
al., 2012), were included as well. Within the OA group, interactions between sex and
radiographic OA severity were also investigated.

6 2. Methods

7 2.1. Subjects

8 An Institutional Review Board-approved data repository was used to identify 150 subjects with 9 symptomatic, radiographically-verified hip OA. 159 asymptomatic subjects were identified from 10 the same repository by selecting subjects whose ages were within two standard deviations of the 11 mean age of the hip OA group. All subjects provided written informed consent for the original 12 studies in which they were enrolled, and for the inclusion of their data in the repository, for 13 secondary analyses. Asymptomatic subjects were slightly younger and had lower Body Mass 14 Indices (BMIs) ($P \le 0.006$) than the subjects with hip OA, but these differences did not influence 15 the results of the previous study (Foucher et al., 2012). This difference persisted when the groups were separated by sex (Table 1), so these factors were considered in the statistical 16 17 analysis. For the hip OA subjects, radiographic severity information was included in the database. A modified Kellgren-Lawerence (KL) grading system (0 – no OA to 4 – most severe) 18 had been used to rate the severity of the osteoarthritic changes from Anterior-Posterior pelvic 19 20 radiographs that were originally obtained for clinical purposes. The rater was a rheumatologist who was aware of a subject's status as an OA patient, but not necessarily aware of their 21 22 participation in a research study.

	Hip O	steoarthritis		Asy	ymptomatic			
	Women (N = 86)	Men (N = 64)	<i>P</i> value	Women (N = 104)	Men (N = 55)	P value	OA vs. Asympto- matic Women	OA vs. Asympto- matic Men
Age (yrs)	63.5 (SD 9.1) (44 – 85)	60.6 (SD 10.8) (29 – 79)	0.082	55.6 (SD 8.6) (41 – 78)	55.8 (SD 8.0) (42 - 80)	0.869	< 0.001	0.008
BMI (kg/m ²)	27.8 (SD 5.5) (16.1 – 46.3)	28.9 (SD 4.6) (21.8 - 41.9)	0.190	26.6 (SD 5.9) (16.5 - 46.9)	26.8 (SD 3.7) (21.4 – 36.3)	0.818	0.141	0.006
Walking Speed (m/s)	1.0 (SD 0.2) (0.3 – 1.5)	1.1 (SD 0.2) (0.4 – 1.4)	0.009	1.3 (SD 0.2) (0.8 – 1.9)	1.4 (SD 0.2) (0.8 – 1.9)	0.195	<0.001	< 0.001
KL Grade (N)	KL 1: 6 KL 2: 9 KL 3: 24 KL 4: 47	KL 1: 0 KL 2: 3 KL 3: 7 KL 4: 54	0.001					

Table 1. Subject Characteristics

1 2.2 Gait Analysis

2 Previously published (Foucher et al., 2012) gait analysis data were used. Methods have been 3 described in detail elsewhere (Andriacchi, Natarajan, & Hurwitz, 2005, Andriacchi, 1990, 4 Hurwitz et al., 1998). Briefly, an optoelectronic camera system (Qualisys North America, Deerfield IL) tracked the motion of reflective markers placed at bony landmarks, while a 5 6 multicomponent forceplate (Bertec, Columbus OH) measured ground reaction forces as subjects walked across a 10 m walkway at self-selected speeds of slow, 'normal', and fast. Between 2 and 7 8 8 trials for each limb were collected at the self-selected normal walking speed, depending on the 9 protocol of the original study. These trials were selected for the present analysis. To identify the 10 ankle and knee joint centers, calipers were used to measure the width of the respective joint 11 (distance from medial to lateral malleoli and the width of the knee at the joint line). The anterior-12 posterior position of the hip center was assumed to be at the location of the superiormost aspect of the greater trochanter, which was located by palpation and indicated with a marker. The 13 superior-inferior position was determined by location a point 2.5 cm inferior to the midpoint of 14 15 the distance between the anterior superior iliac spine and the pubic tubercle, which were 16 identified by palpation. Custom software (CFTC — Computerized Functional Testing 17 Corporation, Chicago, IL) was used to determine spatiotemporal gait variables and sagittal plane joint kinematics, from marker positions, and to calculate external moments in the sagittal, 18 frontal, and transverse planes, using inverse dynamics. For the OA subjects, we selected data 19 20 from the affected hip side. For the asymptomatic subjects, a random study limb was selected. 21 There were no differences between the distribution of right and left limbs between the hip OA 22 group and the asymptomatic group (Chi-square P = 0.452).

1 The variables of interest here were the dynamic sagittal plane range of motion (RoM) and 2 the peak external moments about the hip joint in the sagittal, frontal, and transverse planes, as in 3 the parent study (Foucher et al., 2012). These variables were averaged from normal speed 4 walking trials. External moments were normalized to subjects' body weight and height (%BWH) 5 (Moisio et al., 2003).

6 2.3 Statistical Analysis

7 Statistical analysis was performed using IBM SPSS Statistics V.24 (IBM Corporation, Armonk, 8 NY). Two way ANOVAs were used to compare gait variables for men and women, with and 9 without hip OA. Sex, group (OA vs. Control), and a sex by group interaction term were included 10 in the models. Age, BMI, and walking speed were included as covariates. For each gait variable, a statistically significant (P < 0.05) sex by group interaction term indicated that the difference 11 between OA and control subjects varied between men and women. Effect sizes (Cohen's d) were 12 calculated and post-hoc *t*-tests were used to assess the magnitude of the difference. This analysis 13 14 was repeated within the OA group, using KL grade as the grouping variable and a KL by sex interaction term. 15

16

17 **3. Results**

In the sagittal plane (dynamic hip range of motion and peak external hip flexion and extension moments), there were no statistically significant sex by group interaction terms (respectively, P = 0.895, 0.052, 0.409; Table 2). All three variables were significant lower in the OA group than in the asymptomatic group (main effect of group P < 0.001). There was a significant main effect of sex for the dynamic sagittal plane hip RoM (P < 0.001) and peak

- 1 external hip extension moment (P = 0.030). In both the OA and the asymptomatic groups, values
- 2 of these variables were higher for women than men (Fig. 1). There were no sex differences for
- 3 the peak external hip flexion moment (P = 0.389).



Fig. 1. Sagittal plane dynamic hip range of motion and peak sagittal plane hip external moments for asymptomatic women and men and for women and men with hip OA. Lines represent the median, 25th and 75th percentile; whiskers represent the 5th and 95th percentile. Horizontal lines above data represent pairwise comparisons with $P \le 0.05$. There were no sex-specific group differences in the sagittal plane.

6

Table 2. Mean, standard deviations, P values and effect sizes(Cohen's d) for gait variables in women and men with and without hip OA. All moments refer to peak external moments about the hip. P values shown in table refer to main effect comparisons. Footnotes indicate significant sex by group interactions (i.e. presence of sex-specific deficits in the hip OA groups compared to the sex-matched asymptomatic groups).

Variable	Asympto- matic Group Women	Hip OA Group Women	Asympto- matic vs. Hip OA Women	Asympto- matic Group Men	Hip OA Group Men	Asympto- matic vs. Hip OA Men	Asympto- matic Groups Women vs. Men	Hip OA Groups Women vs. Men
Dynamic Sagittal Plane Hip Range of motion (Deg)	33.39 (SD 5.25)	20.18 (SD 7.52)	<i>P</i> < 0.001 d = 2.07	28.32 (SD 4.98)	15.02 (SD 6.39)	<i>P</i> < 0.001 d = 2.34	<i>P</i> < 0.001 d = 0.99	P < 0.001 d = 0.74
Flexion Moment	6.59	4.39	<i>P</i> < 0.001	7.05	4.48	P < 0.001	P = 0.175	P = 0.734
(%BWH)	(SD 1.96)	(SD 1.63)	d = 1.23	(SD 2.05)	(SD 1.55)	d = 1.43	d = 0.23	d = 0.06
Extension Moment	3.58	2.03	<i>P</i> < 0.001	3.50	1.80	<i>P</i> < 0.001	P = 0.783	P = 0.110
(%BWH)	(SD 1.63)	(SD 0.92)	d = 1.21	(SD 1.40)	(SD 0.85)	d = 1.52	d = 0.05	d = 0.27
Abduction Moment	5.13	3.35	P = 0.052	4.53	3.29	P = 0.021	P = 0.006	P = 0.051
(%BWH)	(SD 1.16)	(SD 1.01)	d = 1.64	(SD 1.04)	(SD 1.06)	d = 1.19	d = 0.54	d = 0.07
Adduction Moment	1.74	1.50	<i>P</i> < 0.001	2.16	1.77	P < 0.001	P = 0.002	P = 0.684
(%BWH) [†]	(SD 0.87)	(SD 0.81)	d = 0.29	(SD 0.94)	(SD 0.87)	d = 0.43	d = 0.46	d = 0.32
External Rotation Moment (%BWH) [‡]	0.62 (SD 0.32)	0.35 (SD 0.23)	<i>P</i> < 0.001 d = 1.00	0.76 (SD 0.32)	0.34 (SD 0.21)	<i>P</i> < 0.001 d = 1.57	P = 0.009 d = 0.44	P = 0.908 d = 0.02
Internal Rotation Moment (%BWH)	0.85 (SD 0.28)	0.40 (SD 0.24)	<i>P</i> < 0.001 d = 1.74	0.87 (SD 0.27)	0.37 (SD 0.19)	<i>P</i> < 0.001 d = 2.13	P = 0.694 d = 0.07	P = 0.439 d = 0.13

[†]Sex by group interaction P = 0.045

[‡]Sex by group interaction P = 0.009

1 In the frontal plane (peak external hip adduction and abduction moments), there was a significant sex by group interaction term for the peak external hip adduction moment only (P =2 0.045). Asymptomatic women had a peak external hip adduction moment that was 13% higher 3 4 than asymptomatic men (d = 0.54, P = 0.002). By contrast (Fig. 2), women with OA had a peak 5 external hip adduction moment that was not different than that of the men with OA (P = 0.684). Accordingly, the difference between the peak external hip adduction moment for asymptomatic 6 7 men compared to men with hip OA was 1.25 % BWH, while the difference between the peak 8 external hip adduction moment for asymptomatic women compared to women with hip OA was 9 1.77% BWH. In other words, the magnitude of the OA vs. asymptomatic group difference in the peak external hip adduction moment was 43% larger for women than men, as reflected by the 10 statistically significant interaction term. By contrast, the peak external hip abduction moment did 11 12 not differ between the asymptomatic and OA groups (P = 0.073), however the value of this 13 variable was higher for men compared to women in both the hip OA and the asymptomatic groups (P = 0.012). 14



15

Fig. 2. Peak frontal plane hip external moments for asymptomatic women and men and for women and men with hip OA. Lines represent the median, 25th and 75th percentile; whiskers represent the 5th and 95th percentile. Horizontal lines above data represent pairwise comparisons with $P \le 0.05$. As a group, asymptomatic women had higher peak adduction moments than asymptomatic men, but this difference was not seen in the hip OA group. There were no other sex-specific group differences.

7

In the transverse plane (peak external hip external rotation and internal rotation moments) 8 9 there was a statistically significant sex by group interaction for the peak external hip external 10 rotation moment (P = 0.009). The peak external hip external rotation moment (Fig. 3) was lower in asymptomatic women than asymptomatic men (d = 0.43, P = 0.009). As with the peak 11 external hip adduction moment, there was no sex difference in the hip OA group (P = 0.908). 12 Accordingly, the difference between the peak external hip external rotation moment for 13 14 asymptomatic men compared to men with hip OA was 0.27% BWH, while the difference 15 between the peak external hip external rotation moment for asymptomatic women compared to 16 women with hip OA was 0.41 %BWH. In other words, the magnitude of the OA vs. 17 asymptomatic group difference in the peak external hip external rotation moment was 34% smaller for women than men, as reflected by the statistically significant interaction term. The 18 peak external hip internal rotation moment was smaller in the OA group vs. the asymptomatic 19 20 group (P < 0.001) and there was no significant sex difference (P = 0.130).



Fig. 3. Peak transverse plane hip external moments for asymptomatic women and men and for women and men with hip OA. Lines represent the median, 25th and 75th percentile; whiskers represent the 5th and 95th percentile. Horizontal lines above data represent pairwise comparisons with $P \le 0.05$. As a group, asymptomatic men had higher peak external rotation moments than asymptomatic men, but this difference was not seen in the hip OA group. There were no other sex-specific group differences.

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9 Within the OA group, radiographic disease severity affected gait variables in men and 10 women in the same way, as indicated by a lack of statistically significant sex by KL grade 11 interactions (P = -0.232 to 0.984). There was a significant main effect of KL grade for all three 12 sagittal plane variables (P < 0.001 to P = 0.022). In all cases, the value of the gait variable 13 decreased with increased radiographic disease severity ($R|_{age, BMI, Speed} = -0.223$ to -0.573, P <14 0.007). In the frontal plane, there were no statistically significant associations between KL grade 15 and gait variables (P = 0.632 and P = 0.809). In the transverse plane, the peak external hip 1 internal rotation moment decreased with increased KL grade ($R|_{age, BMI, Speed} = -0.392, P < 0.001$) 2 but there was no association with the peak external rotation moment (P = 0.190). Sex differences 3 in these models were the same as those described above.

4

5 **4. Discussion**

6 The purpose of this study was to investigate potential sex differences in gait associated 7 with hip OA. The key finding was that gait differences between asymptomatic men and women 8 were not present in the hip OA group. Specifically, sex-specific gait adaptations were seen in the 9 peak external hip adduction and external rotation moments. Across both the hip OA and control 10 groups, women had higher sagittal plane dynamic hip range of motion and peak external hip 11 extension moments. Men and women did not have different associations between radiographic 12 disease severity and any of the gait variables examined. As in previous reports (Foucher et al., 2012), this analysis confirmed a general apparent unloading (as reflected by reduced peak hip 13 14 external moments) due to hip OA severity.

15 In the sagittal plane, sex differences in the OA group mirrored those seen in the 16 asymptomatic group. In both, women had a larger sagittal plane dynamic hip range of motion 17 than men. This finding was in contrast to a publication by Ko and colleagues, who found that men had a larger sagittal plane dynamic hip range of motion than women (Ko et al., 2011b). Ko, 18 19 however, also found a significant association between age and hip range of motion. This is important because our group was younger than that in the Ko study. Some age-related gait 20 changes are different in men and women (Kobayashi et al., 2016), so this age difference could 21 22 explain the discrepancy in our findings.

1 Several studies have identified differences in peak external hip adduction moment 2 between healthy men and women (Boyer, Beaupre, & Andriacchi, 2008, Ko et al., 2011b, Moisio et al., 2003). Here, this expected difference was not present in people with hip OA. Moreover, 3 4 the OA vs. asymptomatic group difference in the hip adduction moment in women was larger 5 than the group difference in men. To maintain mechanical equilibrium, internal structures must 6 produce an equal and opposite moment to the external moments measured during gait analysis 7 (Andriacchi, Natarajan, & Hurwitz, 2005). Thus, because the hip abductors are able to produce large internal abduction moments about the hip joint, when we measure an external hip 8 9 adduction moment, we know that there must be an equal and opposite internal abduction 10 moment, and we typically infer that this moment is produced largely by the hip abductors. Therefore the peak external hip adduction moment can be interpreted as a reflection of net 11 12 dynamic hip abductor demand (Andriacchi, Natarajan, & Hurwitz, 2005). There are several factors that could contribute to modifying the peak external hip adduction moment, and these 13 could potentially differ between men and women. Any factor that alters the magnitude of the 14 15 ground reaction force or its position relative to the hip center may influence the external moment that is measured. These could include the body weight moment arm, which is typically larger in 16 17 women due to differences in pelvic geometry or alterations in the base of support during walking (Wesseling et al., 2015). In addition, the external hip adduction moment has been linked to hip 18 contact force in modeling studies of young healthy adults (Giarmatzis et al., 2015), older heathy 19 20 adults (Wesseling et al., 2015) and people with total hip replacements (Foucher, Hurwitz, & Wimmer, 2009). Thus it may further be speculated that the reductions in the external hip 21 adduction moment may reflect an improved ability of women with hip OA to reduce joint 22 23 loading compared to men. By this interpretation, the larger difference in women would reflect a

beneficial compensation. More work is needed to determine whether or not men and women
 utilize different mechanisms to alter these frontal plane moments, and to explore the
 consequences for joint loading.

4 We further speculate that transverse plane abductor function may be more highly affected by hip OA in men. Based on their anatomical orientation, the hip abductors may also participate 5 6 in balancing the peak moments in the transverse plane (Flack, Nicholson, & Woodley, 2012, 7 Flack, Nicholson, & Woodley, 2014). Specifically, we know that the peak external hip external 8 rotation moment must be primarily balanced by muscles that are able to internally rotate the hip 9 joint. Based on anatomy and muscle activation patterns, this moment balance is most likely 10 accomplished by the internal rotation function of the anterior portion of the gluteus medius, 11 although other muscles and structures may participate as well. The sex difference seen in the 12 asymptomatic group was not seen in the hip OA group. Moreover the difference in the peak external hip external rotation moment between men with and without hip OA was larger than in 13 14 women. Again, previous modeling studies have found that the peak external rotation moment is 15 associated with hip contact forces (Foucher, Hurwitz, & Wimmer, 2009). Thus, these findings 16 may also indicate a different strategy in men that seeks to reduce hip loading. Together these 17 findings suggest that the effect of hip OA on hip abductor mechanics during gait may be 18 different in men and women, with more frontal plane influence in women and more transverse 19 plane influence in men. However, it should be noted that the effect on the abductor musculature 20 cannot be distinguished from the other potential biomechanical differences that could affect these 21 gait variables, and that it is not possible to distinguish a harmful effect of OA from a beneficial 22 compensation. It is interesting to note that pre-to-post surgical changes in both of these gait 23 variables are associated with improvements in self-reported function after total hip arthroplasty

(Behery and Foucher, 2014). Future work should assess whether associations with clinical
 outcomes are also sex-specific.

3 Because the study relied on an existing dataset, there were several unavoidable 4 limitations. First, some gait abnormalities in the OA group are potentially attributable to pain. 5 Unfortunately pain scores were not available for all subjects in the database. There is some 6 evidence in subjects undergoing total hip arthroplasty, that women typically report more severe 7 pain relative to the radiographic disease stage, than men do.(Holtzman, Saleh, & Kane, 2002, 8 Katz et al., 1994, Lavernia et al., 2011, Novicoff and Saleh, 2011) but this may or may not be the 9 case for subjects with less severe disease and we do not know whether the influence on gait 10 would be the same or different in men and women. Second, subjects with severe radiographic 11 disease were overrepresented in the OA group, particularly in men. The subanalysis suggests that 12 the findings are robust across KL Grades, however, future studies are needed to confirm that sex-13 differences are not present in earlier disease stages. Finally, because the prevalence of 14 radiographic hip OA exceeds the prevalence of symptomatic hip OA,(Kim et al., 2014, Kim et 15 al., 2015, Lawrence et al., 2008) it is possible that some subjects in the asymptomatic group had 16 radiographic hip OA. Despite these limitations this study is an important first step toward a better 17 understanding of the sex-differences in gait biomechanics seen in men and women with clinical hip OA. Future prospective studies are needed to address the issues raised above. 18

This work has several implications for future research. It has already been shown that sex-specific gait abnormalities are present in knee OA (Ko et al., 2011a, Phinyomark et al., 2016). These differences has been linked to structural differences (Kumar et al., 2015a). The present study shows that hip OA may also have different biomechanical effects on men and women. Future work should investigate structural links, as at the knee, and links to pain and

symptoms. These results suggest that non-surgical, non-pharmacological interventions may
 require different strategies for men and women. Finally, this study highlights the critical
 importance of accounting for sex when designing and conducting biomechanical studies
 involving hip OA.

5 **5. Conclusions**

6 The aim of this secondary analysis was to determine whether or not there are sex-specific gait alterations in people with hip OA. The rationale was that differences in gait between healthy 7 8 men and women have previously been observed, but we do not know whether these differences 9 are also seen in hip OA. The data showed that normal sex differences in hip mechanics during 10 walking were not present in hip OA. There were no sex-specific differences in sagittal plane range of motion, sagittal plane moments, the peak abduction moment, or the peak internal 11 12 rotation moments. However, gait kinetics differed in frontal plane gait kinetics in men and women with hip OA. Specifically, when comparing women with hip OA to asymptomatic 13 14 women, there was a larger difference seen in the peak hip adduction moment, than there was 15 when comparing that variable for men with and without hip OA. The opposite trend was seen 16 with the peak external rotation moment. The OA vs. asymptomatic group difference in this gait 17 variable was larger in men than it was in women. These findings demonstrate that gait kinetics in 18 the transverse and frontal plane associated with hip OA are different in men and women, 19 compared to sex-specific control groups.

20

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- 3

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Figure Captions