Robust features of knee osteoarthritis in joint moments are independent of reference frame selection

Scott C.E. Brandon *, Kevin J. Deluzio

Department of Mechanical and Materials Engineering, Queen's University, Kingston, ON, Canada

ARTICLE INFO

ABSTRACT

Background: Changes in lower-limb joint moments are important outcome measures for treatment and prevention of knee osteoarthritis. However, it is known that both the magnitude and amplitude of joint moments are affected by the choice of anatomical reference frame. The purpose of this study was to identify features of joint moment waveforms that, regardless of the choice of reference frame, are different for subjects with knee osteoarthritis as compared to asymptomatic control subjects.
Methods: External joint moments during the stance phase of gait were calculated for 44 subjects with moderate knee osteoarthritis and 44 asymptomatic subjects. Moments were then expressed using four anatomical reference frames: Joint Coordinate System, Plane of Progression, Proximal, and Distal. Principal component analysis was used to extract features of the moment waveforms that differed between control and osteoarthritis groups across all reference frames.
Findings: Principal component analysis revealed that, regardless of the choice of reference frame, subjects with knee osteoarthritis exhibited significantly decreased overall hip adduction moment magnitudes, increased overall knee adduction moment magnitudes, decreased knee internal rotation moment amplitudes, and increased early-stance ankle adduction magnitudes.
Interpretation: The four robust features identified in this study are sensitive to the effect of knee osteoarthritis, but independent of changes in the anatomical reference frame. These features can be solely attributed to the pathogenesis of the disease, and not to the artifact of reference frame selection.

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1. Introduction

Subjects with medial compartment knee osteoarthritis have been shown to exhibit changes in joint moments at the ankle, knee, and hip (Astephen et al., 2008a; Baliunas et al., 2002; Gok et al., 2002; Mundermann et al., 2005). These changes are considered to be risk factors for disease progression (Chang et al., 2005; Miyazaki et al., 2002) and have been implicated as predictors of surgical outcome (Prodromos et al., 1985). The external knee adduction moment has received particular attention due to its correlation with medial compartment loading (Zhao et al., 2007) and osteoarthritis severity (Maly et al., 2008; Miyazaki et al., 2002).

It has been shown that lower-limb joint moments, particularly in the transverse plane, are sensitive to the choice of anatomical reference frame (Schache and Baker, 2007; Schache et al., 2007). Both the magnitude and temporal location of local maxima and minima throughout the gait cycle are significantly altered when expressed in differing anatomical reference frames (Schache and Baker, 2007). This makes it difficult to compare joint moments between studies. Furthermore, Newell et al. (2008) found that the ability to detect changes in knee adduction moments due to knee osteoarthritis depends on the choice of anatomical reference frame. Using different anatomical reference frames can even influence whether or not a gait modification is found to successfully reduce the knee adduction moment (Schache et al., 2008).

While the Joint Coordinate System developed by Grood and Suntay (1983) is widely accepted as the standard for expression of lower-limb joint kinematics (Wu and Cavanagh, 1995), there is no standard anatomical reference frame for the expression of joint moments (Schache et al., 2008). Moments can be expressed using the Distal segment coordinate system (Gok et al., 2002; Kaufman et al., 2001), the Proximal segment coordinate system (Schache and Baker, 2007), or the Joint Coordinate System (Astephen et al., 2008a; Landry et al., 2007), which is a combination of both systems. Another option, referred to in this paper as the Plane of Progression (PoP) frame, projects anterior–posterior and inferior–superior moments from the Distal frame onto the plane of progression (Baliunas et al., 2002; Mundermann et al., 2005; Sharma et al., 1998). These four reference frames are shown in Fig. 1.

All of these reference systems are mathematically correct, and may be appropriate for specific analyses, depending on the parameters of interest (Schache and Baker, 2007; Schache et al., 2008). Without

* Corresponding author. 130 Stuart St, McLaughlin Hall, Queen's University, Department of Mechanical and Materials Engineering, Kingston, ON, Canada K7L 3N6.
E-mail address: brandon@me.queensu.ca (S.C.E. Brandon).

Distal   Proximal   Joint Coordinate   Plane of Progression
System (JCS)   (PoP)
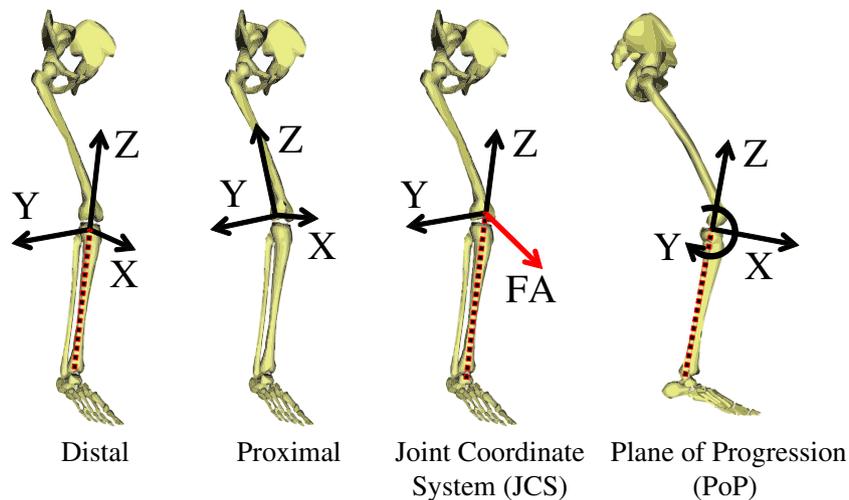
Fig. 1. Four alternative anatomical reference frames, shown using the knee for example. The Distal frame follows the distal segment in three dimensions, while the Proximal frame follows the proximal segment. The Joint Coordinate System (JCS) frame uses the flexion axis from the Proximal frame, the internal rotation axis from the Distal frame, and a floating adduction axis, FA, that is perpendicular to both of these axes. The Plane of Progression (PoP) frame fixes the flexion axis perpendicular to the plane of progression, while the adduction and internal rotation axes are taken from the Distal frame and projected onto the plane of progression.

evidence demonstrating the superior reliability, anatomical relevance, or diagnostic capability of one anatomical reference system over the others, it is difficult to dictate a standard. However, Newell et al. (2008) found that it is possible to select robust parameters for the knee adduction moment that are not affected by the choice of anatomical reference system. Other moments at the hip, knee, and ankle may also be important for characterizing knee osteoarthritis and developing future gait interventions (Huang et al., 2008; Munder-mann et al., 2005); it is therefore important to investigate additional robust features of knee osteoarthritis in lower-limb joint moments.

Principal component analysis (PCA) was shown to be a particularly useful tool for detecting features of the knee adduction moment that are sensitive to the effects of knee osteoarthritis but are independent of the choice of reference frame (Newell et al., 2008). Principal component features are measureable biomechanical changes. Additionally, the biomechanical features extracted using PCA are objective (Chau, 2001; Deluzio et al., 1995) and encompass variation through-out the entire gait cycle (Astephen and Deluzio, 2004; Landry et al., 2007). For these reasons, PCA is well suited for detecting robust features of lower-limb joint moments across all reference frames.

The purpose of this study was to identify features of joint moment waveforms using PCA that, regardless of the choice of anatomical reference frame, are different for subjects with knee osteoarthritis as compared to asymptomatic control subjects.

2. Methods

2.1. Subjects

Forty-four subjects with radiographically confirmed medial knee osteoarthritis were recruited from the Orthopaedic and Sports Medicine Clinic of Nova Scotia. Forty-four asymptomatic subjects were recruited for the control group through postings on the Dalhousie University campus. All subjects gave informed consent and the study was approved by the Institutional Review Board. Subjects were excluded if they had any other forms of arthritis, neuromuscular disorders, trauma or major surgery to the lower limb, or a history of stroke or cardiovascular disease. Osteoarthritis subjects were included based on radiographic Kellgren–Lawrence (KL) scores between 1 and 3, and were also assessed using the Western Ontario and McMaster Universities (WOMAC) scale. Additionally, osteo-thritis subjects were screened for bilateral osteoarthritis through a clinical examination, and were excluded if the contralateral limb was

in the same or worse condition as the affected limb. The limb of interest was randomized for control subjects.

2.2. Gait

Gait analysis methods have been described previously (Landry et al., 2007). Subjects performed at least 4 walking trials at self-selected speed in their own low-top walking shoes. Kinematic data were collected from the affected limb at 100 Hz using an Optotrak 3D motion analysis system (Northern Digital Inc., Waterloo, ON, Canada). Segment orientation was obtained using least-squares optimization of rigid tracking clusters (Challis, 1995). Marker triads were placed on the pelvis, thigh, shank, and foot in addition to single markers placed over the greater trochanter, lateral epicondyle, and lateral malleolus. The right and left anterior superior iliac spine (ASIS), medial epicondyle, fibular head, tibial tuberosity, medial malleolus, second metatarsal head, and calcaneus were digitized as virtual points to allow the creation of anatomical reference frames (Cappozzo et al., 1995). Unilateral ground reaction forces and moments were collected at 1000 Hz using an AMTI force platform (Advanced Mechanical Technology Inc., Watertown, MA, USA).

Marker coordinate data were smoothed using a Butterworth filter with a 10 Hz cutoff frequency. Joint kinematics were calculated using the Joint Coordinate System (JCS) (Grood and Suntay, 1983). Net lower-limb external joint moments were calculated using a standard inverse dynamics approach implemented in MATLAB (The MathWorks, Natick, MA, USA) (Landry et al., 2007). Segment inertial parameters were estimated from regression equations based on anthropometric mea-sures (Clauser et al., 1969). Joint moments were time normalized, using cubic spline interpolation, to 101 points representing each percent of the stance phase of gait. The intra-subject mean moment was obtained for each subject across all walking trials. Moments were also normalized to body mass, then resolved into components along anatomical axes in each of the four alternative reference frames: JCS, PoP, Distal, and Proximal. Anatomical axes are defined by the landmarks used to construct segment coordinate systems, while each anatomical reference frame represents a unique combination of axes taken from the proximal and distal segment coordinate systems.

2.3. Segment coordinate systems

Ankle and knee joint centers were defined as the midpoint of the inter-malleolar and inter-epicondylar axes, respectively. Hip joint

centers were defined using regression equations (Bell et al., 1989). The pelvis segment coordinate system was defined based on left and right ASIS markers and a sacral marker (Kadaba et al., 1990). The thigh segment coordinate system was defined using the inter-epicondylar flexion axis as in Pennock and Clark (1990), with the exception that the adduction plane contains the greater trochanter instead of the hip joint center. The shank segment coordinate system was defined in the same way as the thigh segment, substituting the medial and lateral malleoli and fibular head for the medial and lateral epicondyles and greater trochanter, respectively. For the foot segment coordinate system, the anterior–posterior axis was defined from the calcaneus to the second metatarsal head. The inferior–superior axis was mutually perpendicular to the anterior–posterior axis and a vector from the lateral malleolus to the medial malleolus. The lateral–medial axis was mutually perpendicular to the other two axes.

While the shank reference frame can be constructed based on either proximal or distal landmarks to account for tibial torsion, it has been shown that moments calculated during stance using the proximal definition of the shank frame are similar to those calculated using the Joint Coordinate System (Schache et al., 2008). As the purpose of this study is to investigate features of osteoarthritis that are independent of reference frame selection, we will consider only the distal definition of the shank frame to provide the largest possible difference between reference frames.

2.4. Anatomical reference frames

To obtain a physiological interpretation, moments can be expressed about anatomical axes taken from the segment distal to the joint, proximal to the joint, or a combination of both. These four alternative anatomical reference frames, the Distal, Proximal, Joint Coordinate System (JCS), and Plane of Progression (PoP) frames, are shown in Fig. 1. The Distal frame uses all three axes of the distal segment coordinate system as the flexion, adduction, and internal rotation axes (Gok et al., 2002; Kaufman et al., 2001). Conversely, the Proximal frame uses the axes from the proximal segment (Schache and Baker, 2007). The Joint Coordinate System uses the proximal segment medial–lateral axis as the flexion axis, the distal segment inferior–superior axis as the internal rotation axis, and then creates a mutually perpendicular floating axis for the adduction axis (Grood and Suntay, 1983). Because the proximal flexion and distal internal rotation axes are not perpendicular, this is a non-orthogonal coordinate system. Finally, the PoP frame fixes the flexion axis perpendicular to the plane of progression (Baliunas et al., 2002; Mundermann et al., 2005; Sharma et al., 1998). The internal rotation axis becomes a projection of the inferior–superior axis of the distal segment onto the plane of progression. The adduction axis is the mutual perpendicular of the flexion and internal rotation axes.

2.5. Data analysis

For each joint moment, principal component analysis (PCA) was applied to a set of waveforms from all 88 subjects expressed in all four anatomical reference frames. Thus, PCA was applied separately to nine joint moment matrices consisting of 101 columns representing each percent of the stance phase of gait, and 352 rows representing four

alternative reference frames for each of the 88 subjects. Principal component analysis yields a set of orthogonal loading vectors which represent biomechanical differences in magnitude, amplitude, and temporal synchronization between subjects (Deluzio and Astephen, 2007). Using PCA, these biomechanical features are ranked according to the percentage of the total variation that they explain within the dataset. It is thus possible to objectively identify features of variation between subjects. Furthermore, for a given biomechanical feature, each waveform observation (i.e. a single joint moment for a single subject, expressed in a single anatomical reference frame) receives a weight factor, called a PC-score. These normally distributed PC-scores indicate the degree to which each observation differs from the group mean in terms of a single biomechanical feature. The product of a loading vector and a PC-score is a waveform showing the difference from the mean in original data units. It is therefore possible to relate a PCA feature directly to a biomechanical waveform change by a) examining the shape of the loading vector, b) plotting the waveforms of subjects with extremely high and low PC-scores, and c) considering the effect of a loading vector for high and low PC-scores in original data units. In this study, only the first three or four principal components were retained for analysis in accordance with the 90% trace criterion; that is, once the cumulative percentage of the total variation that is explained by the retained principal components exceeds 90%, all further principal components are discarded (McKean et al., 2007).

2.6. Statistics

Joint moments for control and osteoarthritis subject groups, expressed in four alternative anatomical reference frames, were compared using their PC-scores (Newell et al., 2008). A two-way repeated measures ANOVA was implemented in MATLAB (The MathWorks, Natick, MA, USA) to test PC-scores for significant reference frame, group, and reference frame–group interaction effects using a significance level of $\alpha = 0.05$ (Glantz and Slinker, 2001). Reference frame was the repeated measure. A significant reference frame effect indicates that, for a given feature, the amplitude and/or magnitude of the joint moments differs between reference frames. In contrast, a significant group effect indicates that regardless of the reference frame, the joint moments of osteoarthritis subjects are different from controls. Finally, a significant group–reference frame interaction effect indicates that there may be a difference between the joint moments of control and osteoarthritis groups, but this difference is not evident in all reference frames. Post-hoc Tukey tests were used to investigate pair-wise comparisons between osteoarthritis and control groups for each of the four reference frames. When a significant interaction effect was found, the pair-wise comparisons identified which reference frames can be used to detect a difference between osteoarthritis and control subjects.

3. Results

Subjects with osteoarthritis were taller, heavier, older, and had a greater BMI than control subjects, as shown in Table 1. There was no difference in walking speed between the two groups. Osteoarthritis

Table 1
Control and osteoarthritis group demographics and walking speeds: mean (standard deviation).

	n	Kellgren–Lawrence			Height [m][a]	Weight [kg][a]	Age [year][a]	BMI [kg/m^2][a]	Speed [m/s]
		1	2	3					
Control	44	–	–	–	1.70 (0.09)	74.5 (12.5)	50.7 (10.3)	25.9 (3.7)	1.32 (0.14)
OA	44	4	24	16	1.74 (0.10)	92.5 (16.5)	59.4 (8.50)	30.4 (4.6)	1.28 (0.17)

[a] Statistical difference ($P < 0.05$) between control and osteoarthritis groups.

Table 2
Five biomechanical changes in joint moments due to moderate knee osteoarthritis. *P*-values (italic) are shown for group, reference frame, and interaction effects from a 2-factor ANOVA with reference frame as the repeated measure. Bold denotes statistical significance ($P<0.05$). Significant group effects indicate robust features associated with knee osteoathritis. The significant interaction effect for hip flexion moment amplitude indicates a group difference in the Proximal frame ($P=0.03$) but not in the Distal ($P=0.83$) or PoP frames ($P=0.07$). *Note: The JCS frame uses the same flexion axis as the Proximal frame, and the same internal rotation axis as the Distal frame. The JCS frame was therefore omitted from the ANOVA for these moments.

Gait measure	PC	Group	Frame	Interaction	Interpretation: OA subject trends
Hip					
Adduction moment	1	**<0.01**	**<0.01**	0.12	Decreased magnitude throughout stance
Flexion moment*	1	0.17	**<0.01**	**<0.01**	Increased magnitude throughout stance (only Proximal frame)
Knee					
Adduction moment	1	**0.03**	**<0.01**	0.98	Increased magnitude throughout stance
Internal rotation moment*	2	**<0.01**	**<0.01**	0.30	Decreased amplitude
Ankle					
Adduction moment	3	**<0.01**	**<0.01**	0.36	Increased magnitude 0–50% stance

subjects had mean WOMAC pain scores of 7 (SD = 4) and function scores of 23 (SD = 13).

Robust features that discriminated between control and osteoarthritis groups regardless of the choice of reference frame were detected using PCA in four joint moments: hip adduction, knee adduction, ankle adduction, and knee internal rotation moments (Table 2, Fig. 2). Subjects with osteoarthritis exhibited hip adduction moments with significantly lower magnitudes and flatter waveforms throughout stance. Together, these features describe an overall decrease in hip adduction magnitude during stance. Conversely, knee adduction magnitudes were increased throughout stance for subjects with osteoarthritis. The magnitude of ankle adduction moments was greater in the first half of stance for the osteoarthritis group, while the amplitude of the biphasic knee internal rotation moments was reduced for subjects with osteoarthritis, regardless of the choice of reference frame.

Only one feature that discriminated between control and osteoarthritis groups showed a significant group–frame interaction effect: hip flexion moment magnitude (Table 2). A group–frame interaction exists when the detection of group differences is confounded by the
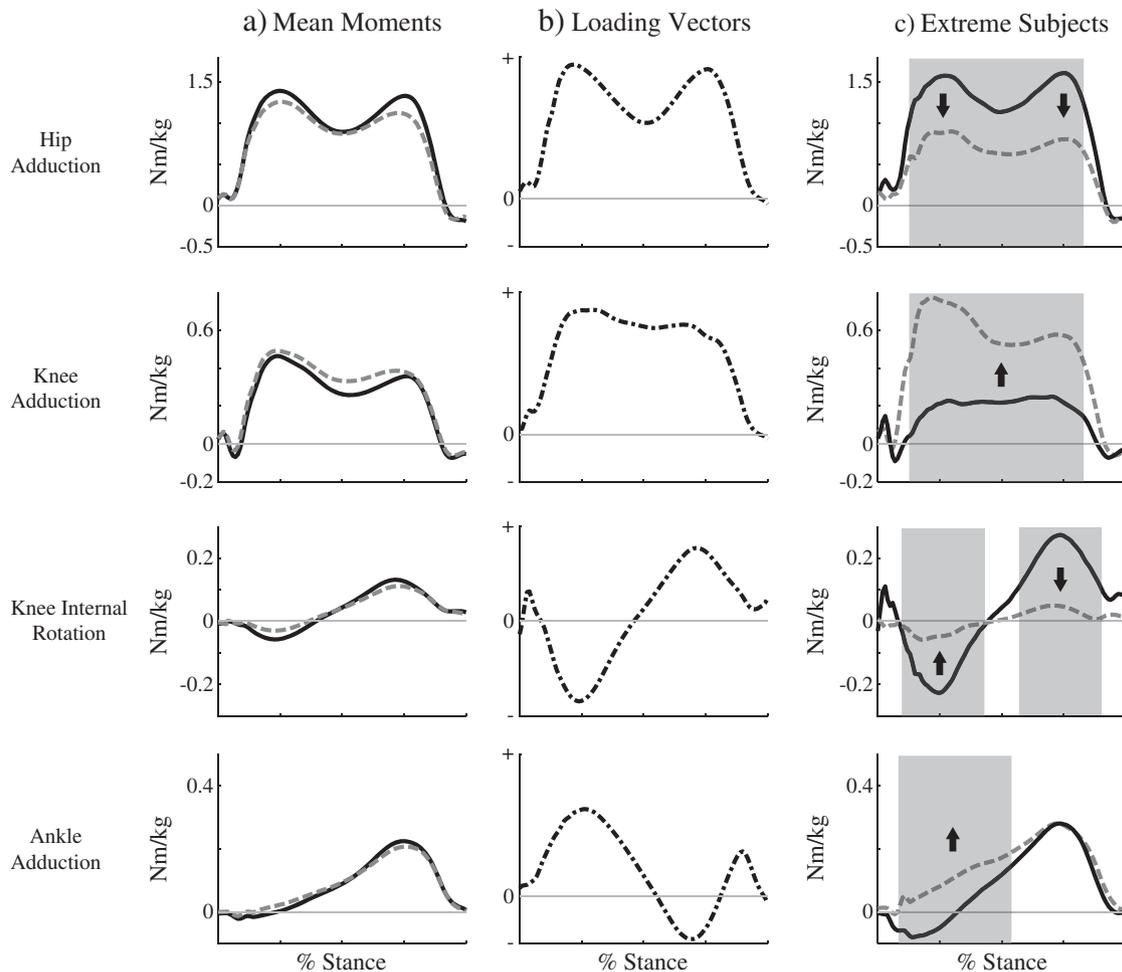
Fig. 2. Four robust changes due to osteoarthritis that are independent of the choice of reference frame, identified using principal component analysis. a) Mean waveforms, averaged across all anatomical reference frames for control (solid black line) and osteoarthritis (dashed grey line). b) Loading vectors that indicate biomechanical changes in overall magnitude (hip and knee adduction), amplitude (knee internal rotation), and early-stance magnitude (ankle adduction). c) Extreme subjects are shown for control (solid black line) and osteoarthritis (dashed grey line) groups to characterize robust group differences. Arrows give the direction of the osteoarthritis group relative to the control group throughout the shaded regions.
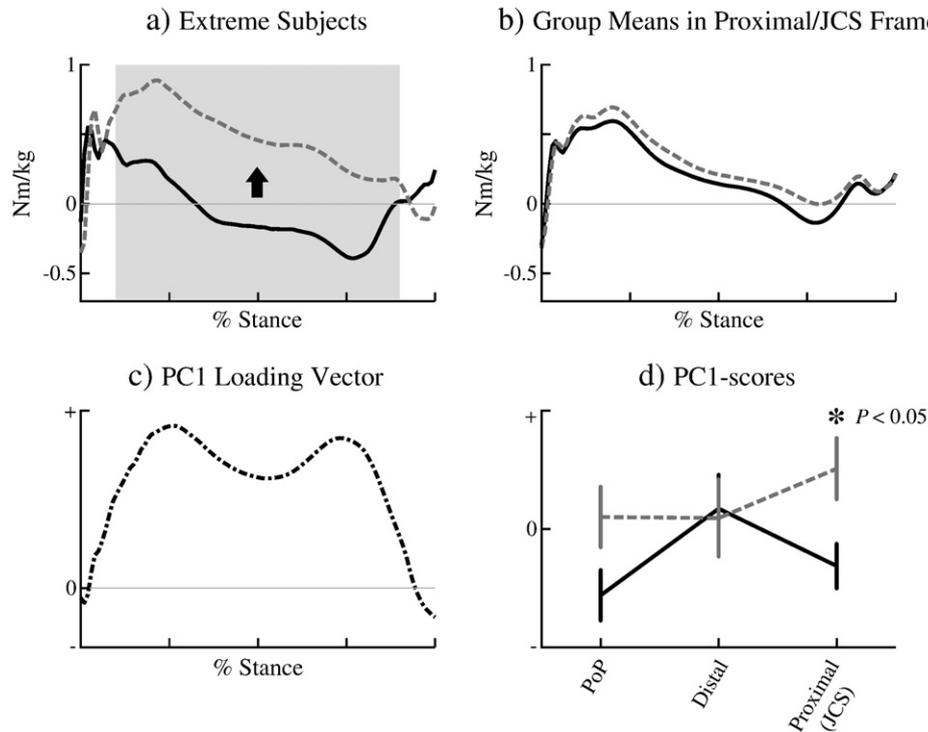
Fig. 3. The hip flexion moment magnitude difference identified by the first principal component (PC1) depends on the choice reference frame. a) Extreme subjects demonstrate increased hip flexion moment magnitude for osteoarthritis (dashed grey line) subjects compared with control (solid black line) subjects. b) Mean waveforms for osteoarthritis (dashed grey line) and control (solid black line) groups, expressed in the Proximal/JCS reference frame. c) The loading vector, or biomechanical feature, identified as the first principal component for hip flexion moments. The positive value throughout stance indicates a magnitude feature. d) Mean PC-scores, bounded by standard error, for the magnitude difference detected by the first principal component (PC1) between osteoarthritis (dashed grey) and control (solid black) groups. The group difference is significant only in Proximal/JCS reference frame ($P = 0.03$).

choice of reference frame. Subjects with osteoarthritis showed an overall increase in hip flexion moment magnitude throughout stance (Fig. 3b) when moments are expressed using the Proximal/JCS reference frame ($P = 0.03$), but not in the PoP ($P = 0.07$) or Distal frames ($P = 0.83$), as shown in Fig. 3d. The choice of reference frame thus significantly affects the ability to detect changes due to knee osteoarthritis in hip flexion moments.

The magnitudes and shapes of moment waveforms were always different when expressed using different reference frames, regardless of whether the subjects were in the osteoarthritis or control groups. This frame effect was statistically significant for every waveform feature extracted using PCA, including the four robust measures shown in Table 2.

4. Discussion

The choice of anatomical reference frame used to express lower-limb joint moments significantly affects the magnitudes and shapes of the waveforms, as explained in a previous study (Schache and Baker, 2007). However, the goal of this study was not to contrast the frames themselves, but rather to examine how the difference between frames affects the analysis of joint moments in subjects with knee osteoarthritis.

This study identified four robust waveform features using principal component analysis that, regardless of the choice of reference frame, were significantly different between subjects with and without knee osteoarthritis. These are features that can be attributed solely to the pathogenesis of the disease, and not to the artifact of reference frame selection. It is interesting to note that these four features were divided between the frontal plane (hip and knee adduction moments) and transverse plane (knee internal rotation and ankle adduction moments). While the relationship between frontal plane joint moments and knee osteoarthritis has been well documented

(Hurwitz et al., 1999; Miyazaki et al., 2002; Mundermann et al., 2005; Newell et al., 2008; Sharma et al., 1998) the transverse plane moments have received considerably less attention (Landry et al., 2007; McKean et al., 2007). The use of principal component analysis in this study facilitated the detection of robust biomechanical changes, at the ankle, knee, and hip joints, due moderate knee osteoarthritis.

For some joint moments, the choice of reference frame does matter; we have shown that for hip flexion moments, the use of a Distal or PoP frame can inhibit the detection of altered loading patterns associated with knee osteoarthritis. Mundermann et al. (2005) reported a significant peak difference in terminal stance hip flexion moments when expressed in the PoP frame, which assumes a common, globally-fixed flexion axis. In this study, the terminal stance peak difference was incorporated into the overall stance-phase magnitude effect shown in Fig. 3, which was significant only in the Proximal/JCS frame. While this feature verged on significance in the PoP frame ($P = 0.07$), the use of a subject-specific mediolateral axis in the Proximal frame enhanced the separation between control and osteoarthritis groups. The Distal frame cannot be used to detect stance-phase changes in joint moments due to moderate knee osteoarthritis.

Increased knee adduction moment magnitude throughout stance, captured by the first principal component (PC1), was a robust characteristic of the osteoarthritis group across all reference frames in accordance with previous studies that used principal component analysis (Astephen et al., 2008b; Deluzio and Astephen, 2007; Newell et al., 2008). As noted by Newell et al. (2008), comparing groups using an overall magnitude parameter is preferable to using discrete peak measures which are sensitive to the changes in shape and magnitude associated with different reference frames. A significant magnitude effect was also detected as the first principal component (PC1) for hip adduction moments. In this case, an overall reduction in hip adduction moment magnitude during stance corresponds with the finding of a

peak difference by Mundermann et al. (2005) using a PoP reference frame for subjects with severe (KL grade ≥3) osteoarthritis.

Previous studies have reported a reduction in the early-stance knee external rotation (negative internal rotation) moment using both principal component analysis and discrete peak parameters (Landry et al., 2007; McKean et al., 2007). In this study, the presence of reduced magnitudes in both early and late stance led to a principal component that captured an overall amplitude reduction across all reference frames as a characteristic of subjects with osteoarthritis (Fig. 2). It is important to note that the shape of the internal rotation moment waveforms was not consistent across the four reference frames. In the PoP frame, the osteoarthritis group had an increased positive internal rotation moment in early stance, as opposed to the decreased external rotation moment found in all other frames. Thus, while the knee internal rotation moment amplitude changes due to osteoarthritis regardless of the choice of reference frame, the physiological meaning of this change is frame-dependent.

It is possible that the same robust features of knee osteoarthritis could have been detected using traditional peak and impulse parameters instead of principal component analysis. Other multivariate techniques, such as Factor Analysis and Independent Component Analysis, may also be useful for extracting biomechanical features of variation (Stone, 2002), but to our knowledge have not been extensively applied to gait data. In this study, principal component analysis allowed objective determination of the joint moment features that differentiate between osteoarthritis and control subjects. Furthermore, comparing overall waveform changes rather than discrete locations of the waveform reduced sensitivity to the choice of reference frame selection (Newell et al., 2008).

We have shown that joint moments are not merely affected by the choice of reference frame; joint moments are affected differently for subjects with medial knee osteoarthritis as compared with asymptomatic controls. Using principal component analysis, we found robust changes in the magnitudes of hip, knee, and ankle adduction moments, and in the amplitude of knee internal rotation moments, regardless of the choice of reference frame. The four robust characteristics of osteoarthritis identified in this paper may be useful for the future evaluation of gait interventions and for the continued investigation of disease pathomechanics.

Acknowledgement

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