The effect of simulated marker misplacement on the interpretation of inter-limb differences during a change of direction task

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Abstract

The objective assessment of biomechanical asymmetries during movement tasks is used to monitor rehabilitation following anterior cruciate ligament reconstruction (ACLR). Marker placement is an important source of methodological variability within human motion analysis. It is currently unclear how marker placement error effects the interpretation of biomechanical asymmetries throughout post ACLR rehabilitation. The aim of this investigation was to determine the effect of random marker placement variation on the interpretation of inter-limb differences during a change of direction (CoD) task. Forty-seven participants 9 months post-ACLR and fifty uninjured controls completed a 90° CoD task on both limbs. Inter-limb differences in kinematic and kinetic metrics during the CoD stance phase were calculated for both groups using the Vicon Plug-in Gait model, and ACLR subjects were classified as having 'normal' or 'abnormal' inter-limb differences relative to the control group. Simulated random marker displacements based on published marker placement error ranges were then repeatedly applied to the lateral thigh, femoral epicondyle and tibia markers. ACLR inter-limb differences were recalculated each time, allowing the estimation of 95% confidence intervals and minimal identifiable between-session changes. ACLR subjects were also reclassified relative to the control group after each simulation and the percentage of participants to change classification was calculated. Marker displacements caused large deviations in inter-limb difference measures in several variables including hip rotation angle, knee abduction angle and knee abduction moment, thus limiting the ability to identify participants with large inter-limb differences relative to a control group. These findings highlight the challenges in using marker-based biomechanical models to conduct objective assessments of inter-limb differences during CoD tasks.

Introduction

Following anterior cruciate ligament reconstruction (ACLR), inter-limb differences in kinematic and kinetic measures have been observed across various tasks including walking (Wellsandt et al. 2016; White, Logerstedt, and Snyder-Mackler 2013), running (Kline et al. 2016), jumping (Jordan, Aagaard, and Herzog 2015; Orishimo et al. 2010), landing (Gokeler et al. 2010; Orishimo et al. 2010) and change of direction (CoD) (King et al. 2019; King, Richter, Franklyn-Miller, Daniels, Wadey, Jackson, et al. 2018). Individuals exhibiting large inter-limb differences are believed to be at increased risk of negative long-term outcomes, including the development of osteoarthritis and re-injury (Paterno et al. 2010; Wellsandt et al. 2016). Objective assessment of inter-limb differences is proposed as a means of monitoring rehabilitation post ACLR (Jordan, Aagaard, and Herzog 2015; Myer, Ford, and Hewett 2011; Oberländer et al. 2013; Paterno et al. 2007). Implementing such assessments in a clinical environment necessitates that the metrics of interest be reliable and robust to methodological sources of variability.

Data from human motion analysis are prone to error from multiple sources, including instrumental errors, soft tissue artefact and inaccurate placement of anatomical markers (Schwartz and Dixon 2018). Error in marker placement is recognized as a key source of methodological variability, with low between-session reliability measures attributed to variation in marker positions between sessions (Alenezi et al. 2016; Baker, Finney, and Orr 1999a; Fonseca et al. 2020; Ford, Myer, and Hewett 2007; Gorton, Hebert, and Gannotti 2009; Groen et al. 2012; Kadaba et al. 1989; McGinley et al. 2009; Szczerbik and Kalinowska 2011). Experimental studies conducted in walking attribute large errors in calculated joint angles and moments to erroneous marker placement (Groen et al. 2012; Szcserbik and Kalinowska 2014).

Extrapolating findings from studies conducted in walking directly to different tasks is challenging. The effect of marker placement error is likely task specific, with features such as sagittal plane range of motion and walking speed shown to influence the observed effect of marker placement (Baker, Finney, and Orr 1999a; Cockcroft, Louw, and Baker 2016; Groen et al. 2012; Szczerbik and Kalinowska 2011). Despite the use of marker-based biomechanical models to study various lower-limb movement tasks, previous research examining marker placement has focused primarily on walking (Baker, Finney, and Orr 1999a; Cockcroft, Louw, and Baker 2016; Groen et al. 2012; Szczerbik and Kalinowska 2011).

CoD tasks are commonly examined in studies related to ACL injury and rehabilitation (King et al. 2019; McLean, Huang, and Van Den Bogert 2005; Pollard, Sigward, and Powers 2007; Dos Santos et al. 2018; Sigward and Powers 2007; Stearns and Pollard 2013). CoD manoeuvres are ubiquitous in field based sports, mechanically demanding and reported as the most common mechanism of non-contact ACL injury (Geli-Alentorn et al. 2009; Olsen et al. 2004). Recent research identified multiple inter-limb differences during CoD tasks at 9 months post ACLR despite no statistical difference in performance times between limbs (King, Richter, Franklyn-Miller, Daniels, Wadey, Jackson, et al. 2018). Inter-limb differences were observed in variables associated ACL injury, suggesting their assessment may be relevant to rehabilitation. It is unclear how error in marker placement influences the ability to identify and monitor such inter-limb differences. Were marker placement error to cause substantial changes to inter-limb differences and their interpretation, it could result in an individual returning to play despite the continued presence of deficits that place them at increased risk of injury.

The conventional gait model (CGM) is a widely used marker-based biomechanical model originally developed for use in clinical gait analyses (Kadaba, Ramakrishnan, and Wooten 1989). While alternative modelling techniques are more commonly used for dynamic tasks, the CGM has nevertheless been used in the analysis of a broad range of CoD tasks (Franklyn-Miller et al. 2016; Marshall et al. 2014; Pollard, Sigward, and Powers 2007; Stearns and Pollard 2013). In the CGM, the anterior/posterior positions of markers on the lateral thigh (THI), lateral femoral epicondyle (KNE) and lateral tibia (TIB) directly influence calculated kinematics and kinetics at the hip, knee and ankle (Baker, Finney, and Orr 1999; Groen et al. 2012; Kadaba, Ramakrishnan, and Wooten 1989; Stagni et al. 2000). Previous studies examining these marker positions have tended to implement fixed, systematic marker displacements, whereby a marker’s position is moved by a set amount from its original position and the subsequent effect on model outputs is examined. (Baker, Finney, and Orr 1999b; Cockcroft, Louw, and Baker 2016; Groen et al. 2012; Ciarán McFadden, Daniels, and Strike 2020). For example, Groen et al., (2012) demonstrated that systematic 14 mm anterior displacements to the THI, KNE and TIB markers caused errors greater than 10° in lower extremity joint angles between repeated walk trials.

While systematic differences in marker placement such as those outlined may exist, these study designs fail to account for the inherent randomness to be expected in real world marker placement error (Myers et al. 2015; Osis et al. 2016). Challenges also exist in separating the effect of marker displacements from that of movement variability, as any observed changes in kinematics and/or kinetics will be attributable to both the marker displacement and natural trial-to-trial movement variability. Utilising a simulated approach offers the opportunity to control for movement variability and examine the effect of marker placement in isolation. This approach has been used previously to study marker displacements during walking (Myers et al. 2015) and running (Osis et al. 2016). Simulated marker displacements sampled from the Gaussian distribution have been used to mimic expected real-world variation in marker placement (Myers et al. 2015). Establishing how such marker displacements impact the ability to identify and monitor changes in inter-limb differences will inform the contexts in which their use as objective rehabilitative measures is appropriate, and those in which they are not. Thus, the aim of this investigation was to determine the effect of random THI, KNE and TIB marker displacements on the interpretation of inter-limb differences during a CoD task.

Methods

Participants

Forty-seven male participants aged 18-35 (mean ± SD age 24.8 ± 4.8 years, height 180 ± 6 cm and mass 84 ± 6.4 kg) approximately 9 months (8.7 ± 0.7) post primary ACLR were recruited from the caseload of two orthopaedic surgeons, based in the Sports Surgery Clinic, Dublin, Ireland. Inclusion criteria for ACLR participation in the study were male, aged 18-35, participation in multi-directional field-based sports prior to injury and the intention to return to the same level of participation post rehabilitation. Participants who had multiple ligament reconstructions, meniscal repair or did not intend to return to multidirectional field-based sport were excluded from the study. A matched healthy cohort (NORM) of 52 participants (23.4 ± 3.7 years, 182.8 ± 6.38 cm, 81.9 ± 7.4 kg) with no history of lower limb injury were recruited locally from multi-directional field-based sports teams. Ethical approval was received from the University of Roehampton, London (LSC 15/122) and the Sports

Surgery Clinic Hospital Ethics Committee (25AFM010). Participants gave informed, written consent prior to participation in the study.

Data collection took place in a biomechanics laboratory using a ten-camera motion analysis system (200 Hz; Bonita-B10, Vicon, UK), synchronized (Vicon Nexus 2.3) with two force platforms (1000 Hz BP400600, AMTI, USA) recording the positions of 28 reflective markers (14 mm diameter). Markers were secured using tape at bony landmarks on the lower limbs, pelvis and trunk according to a modified Plug-in-Gait marker set (Marshall et al. 2014). Participants completed a pre-planned 90° CoD task, which followed a wider testing battery that formed part of a larger, on-going study. The full testing battery comprised of a standardised warm-up, consisting of a 2-minute jog, 5 bodyweight squats, 2 submaximal and 3 maximal countermovement jumps, followed by a series of double and single leg jump exercises. The CoD task involved the participants running maximally towards the force platforms before planting their outside foot on the force platform to cut left or right, i.e. planting their right foot to cut to the left. The start line was 5 m from the force plates, while the finish line was 2 m from the force plates. Three trials were collected on both the ACLR and contralateral limbs. A full description of the testing protocol is given in King et al. (2018).

<u>Data Processing</u>

A fourth order zero-lag Butterworth filter (cut-off frequency 15 Hz) was used to filter marker trajectory and force data (Kristianslund, Krosshaug, and Bogert 2012). Kinematic variables at the hip, knee and ankle have been associated with increased knee loading, quantified in the form of knee joint moments (Dempsey et al. 2007; McLean, Huang, and Van Den Bogert 2005). Tri-planar hip, knee and ankle angles, as well as tri-planar knee joint moments, were therefore extracted during stance phase for each trial. Initial contact and toe-off were identified from vertical ground reaction force using a 20 N threshold. Kinematic and kinetic signals were time normalised to 101 data points and the mean of each participant's three trials was used for further analysis. Inter-limb differences were calculated for each variable at 20% of stance. Video analyses of ACL injuries suggest injury occurs within this period (Koga et al. 2010; Krosshaug et al. 2007; Olsen et al. 2004) and thus it is extensively studied in ACL and CoD research (Dempsey et al. 2007; Olsen et al. 2004; Robinson et al. 2014; Stearns and Pollard 2013). Inter-limb differences were calculated in the ACLR and NORM groups respectively as

$$\text{ACLR} - \text{Contralateral}$$

$$\text{NonDominant} - \text{Dominant}$$

The 'dominant limb' was defined in the NORM group as the self-selected preferred kicking leg. The time point of 20% of stance corresponded to 0.065 ± 0.02 ms and 0.068 ± 0.01 ms for the ACLR and contralateral limbs respectively, and 0.065 ± 0.01 ms and 0.064 ± 0.02 ms for the dominant and non-dominant limbs respectively.

Following initial data processing, we simulated a scenario in which our ACLR cohort underwent repeated testing sessions, with random marker displacements introduced in each session. One hundred copies of each ACLR participant's six original trials (3 x cutting off ACLR limb and 3 x cutting off contralateral limb) were generated, with each set of six trials corresponding to a "simulated" testing session. In each of the one-hundred simulated sessions, random displacements were sampled and applied to each marker (THI, KNE and TIB) on the CoD stance leg in all trials completed on the ACLR and contralateral limbs, mimicking a real-world scenario in which individual marker positions were invariant across trials within a session but the displacement applied to each marker was independent. Unique displacements were generated for each participant and were sampled from the Gaussian distributions created from variance based on previously reported intra-tester variability in anatomical landmark location (Della Croce, Cappozzo, and Kerrigan 1999; Myers et al. 2015). For markers that did not have directly reported intra-tester variability ranges (THI and TIB), the mean variance of anatomical landmarks located on the associated segment was used (Della Croce, Cappozzo, and Kerrigan 1999). Thus, displacements were drawn from distributions with standard deviations of 5.8 mm (THI), 3.9 mm (KNE) and 3.4 mm (TIB). To simulate anterior/posterior positioning error, displacements were applied about the anterior-posterior axis of the corresponding segment coordinate system using

$$X_{K'} = R.X_k$$

where $X_{k'}$ are the new, displaced marker coordinates within the segment coordinate system, *R* is the translational matrix containing the randomly generated marker displacement and X_k are the original marker coordinates within the segment coordinate system. Within each simulated testing session, mean kinematic and kinetics were extracted as described previously. Using these newly formed mean kinematic and kinetic measures inter-limb differences were recalculated in each of the one-hundred simulated testing sessions. This process produced a total of 4700 inter-limb differences for each variable (47 ACLR participants x 100 inter-limb differences). The displacement process described was completed using a custom written MATLAB script (version2019, The Mathworks Inc, Natick, Massachusetts, USA).

Each ACLR participant's original inter-limb difference was subtracted from their original 100 simulated inter-limb differences for each variable. This produced a distribution of changes in inter-limb differences attributable to marker displacements, from which 95% confidence intervals were estimated. These intervals constituted a range in which the true value of an inter-limb difference was expected to fall on 95% of occasions when accounting for variability introduced from marker placement. Using the identified confidence intervals, the minimal change in inter-limb differences that could be identified with 95% certainty between two assessments was estimated for each variable. This was identified as the point in which 95% of possible values for an initial observation fell outside a range which contained 95% of possible values for a second observation and corresponded to change of 3.6 SD between two assessments (Fig 1).

Following this, descriptive statistics were calculated for NORM inter-limb differences. Each ACLR participant was classified relative to the NORM group as having either a "normal" or "abnormal" inter-limb difference for each variable. ACLR participants with original inter-limb differences between ± 2 SD of the NORM group's original inter-limb difference were classified as "normal", while those > ± 2 SD were classified as "abnormal" (Fig 2). ACLR participants were reclassified using each of their 100 simulated inter-limb differences. The percentage of participants whose classification changed from their original in at least one simulation was calculated for each variable.

Results

The distribution of changes in inter-limb differences and change in classifications for hip angles, knee angles, ankle angles and knee moments are presented in Figures

3, 4, 5 and 6 respectively. The largest minimal identifiable changes and highest percentage of participants to change inter-limb difference classification were in transverse plane hip as well as frontal and transverse plane knee kinematics (Table 1).

Hip Kinematics

Marker displacements caused a change in hip flexion inter-limb differences with a standard deviation of 1.3°, from which a 95% confidence interval of -2.5°–2.5° was estimated (Fig 3A). Changes in hip abduction angle inter-limb differences had a standard deviation of 0.2° and a confidence interval of -0.47°–0.47° (Fig 3B), while for hip rotation angle the standard deviation was 6.2° and confidence interval -12.2°–12.2° (Fig 3C). Minimal identifiable changes of 4.6° in hip flexion, 0.9° in hip abduction and 22.2° in hip rotation inter-limb differences were estimated (Table 1).

For hip flexion angle inter-limb differences, 40 (85.1%) ACLR participants maintained their original inter-limb difference classification in all one hundred simulations, while 7 (14.9%) participants' classification changed on at least one occasion (Fig 3D). The number of simulations in which each participant changed classification ranged from 1 – 10, with a median of 8 (Table 1). 46 (97.9%) maintained their original classification for hip abduction angle inter-limb differences in all one hundred simulations, with 1 (2.1%) participant changing classification in 15 simulations (Table 1). Lastly, for inter-limb differences, 8 (13%) participants maintained their original classification while 39 (87%) changed classification in at least one simulation (range 1 – 53, median 13) (Table 1).

Knee Kinematics

Marker displacements caused a change in knee flexion inter-limb differences with a standard deviation of 2.3°, from which a 95% confidence interval of -3.2°–3.2° was estimated (Fig 4A). The standard deviation for changes in knee abduction inter-limb differences was 5.1° with an estimated confidence interval of -10°–10° (Fig 4B), while in knee rotation angle the standard deviation was 6.8° and confidence interval -13.4°–13.4° (Fig 4C). Minimal identifiable changes of 5.4° in knee flexion, 18.3° in knee abduction and 24.5° in knee rotation inter-limb differences were estimated (Table 1).

For knee flexion inter-limb differences, 42 (89.4%) participants maintained their original inter-limb difference classification in all simulations, while 5 (10.6%) changed classification in at least one simulation (range 5 – 17, median 9) (Table 1). 6 (12.8%) participants maintained their original classification for knee abduction angle inter-limb differences in all simulations, with 41 (87.2%) changing classification on at least one occasion (range 1 – 53, median 8). Lastly, for knee rotation angle inter-limb differences, 4 (8.5%) ACLR participants maintained their original classification and 43 (91.5%) changed classification on at least one occasion (range 1 – 52, median 7).

<u>Ankle Kinematics</u>

Marker displacements caused a change in ankle plantar-flexion inter-limb differences with a standard deviation of 1.3°, from which a 95% confidence interval of -2.5°–2.5° was estimated (Fig 5A). For ankle abduction angle the standard deviation of changes in inter-limb differences was 1.8° with an estimated 95% confidence interval of -3.5°–3.5° (Fig 5B), while in ankle rotation angle (defined as the angle between the long axis of the foot segment and the long axis of the shank segment in the transverse plane) the standard deviation was 6.4° and confidence interval -12.5°–12.5° (Fig

5C). Minimal identifiable changes of 4.6° in ankle plantarflexion, 6.3° ankle abduction and 23° ankle rotation inter-limb differences were estimated from these distributions (Table 1).

For ankle plantar-flexion angle inter-limb differences, 40 (85.1%) participants maintained their original inter-limb difference classification throughout all simulations, 7 (14.9%) changing classification in at least one simulation (range 1 – 36, median 4). 14 (29.8%) participants maintained their original classification for ankle abduction angle, while 33 (70.28%) changed classification in at least one simulation (range 1 – 50, median 4). Lastly, in ankle rotation angle inter-limb differences, 12 (25.5%) participants maintained their original classification, while 35 (74.5%) changed classification in at least one simulation (range 1 – 48, median 9) (Table 1).

<u>Knee Moments</u>

Marker displacements caused changes in knee flexor moment inter-limb differences with a standard deviation of 0.21 Nm/kg, from which a 95% confidence interval of -0.41–0.41 Nm/kg was estimated (Fig 6A). For knee abduction moment inter-limb differences, the standard deviation was 0.2 Nm/kg and estimated confidence interval -0.39–0.39 Nm/kg, while in knee rotation moment, the standard deviation was 0.01 Nm/kg and confidence interval -0.02–0.02 Nm/kg (Table 1). The minimal identifiable changes in inter-limb differences were estimated as 0.75 Nm/kg in knee flexor moment, 0.72 Nm/kg in knee abduction moment and 0.05 Nm/kg in knee rotation moment (Table 1).

For knee flexor moment inter-limb differences, 35 (74.5%) participants maintained their original classification throughout all simulations, while 12 (25.5%) changed classification in at least one simulation (1 – 51, median 18). 15 (32%) participants maintained their original inter-limb difference classification for knee abduction moment inter-limb differences, while 32 (68%) changed classification in at least one simulation (2 – 44, median 6) (Table 1). Lastly, in knee rotation inter-limb differences, all 47 participants maintained their original classification throughout all simulations (Table 1).

Discussion

Our findings highlight challenges in using marker-based biomechanical models such as the CGM to conduct objective assessments of inter-limb differences during CoD. These assessments have been proposed as a means of monitoring rehabilitation progress post ACLR (Jordan, Aagaard, and Herzog 2015; Myer, Ford, and Hewett 2011; Oberländer et al. 2013; Paterno et al. 2007; Di Stasi et al. 2013). Marker displacements caused large changes in inter-limb differences in several variables, which in turn limited the ability to reliably identify participants with large inter-limb differences relative to a NORM cohort (Table 1).

Frontal plane knee and ankle, as well as transverse plane hip, knee and ankle angles were most effected by marker placement error. Previous work examining marker placement reports similar findings (Baker, Finney, and Orr 1999b; Groen et al. 2012; C. McFadden, Daniels, and Strike 2020; Myers et al. 2015; Osis et al. 2016; Szczerbik and Kalinowska 2011), with frontal and transverse plane angles consistently identified as most sensitive to marker placement. Change in the anterior/posterior positions of the THI, KNEE and TIB markers alters the orientation of the femur and shank segments, which manifests as large errors in frontal and transverse plane angles. The ability to identify, monitor and classify inter-limb difference measures in these variables using the CGM appears minimal.

Several of these variables are considered important in the context of CoD and ACL injury, including transverse plane hip and ankle angles as well as frontal plane knee angles and moments. For example, increased knee abduction angle (KAA) during CoD is associated with higher frontal plane knee loading, considered an important risk factor for ACL injury (McLean, Huang, and Van Den Bogert 2005; Sigward and Powers 2007; Stearns and Pollard 2013). Our data indicate that KAA inter-limb differences are highly sensitive to marker displacements, with an estimated 95% confidence interval of -10°-10° (Fig 4B). A confidence interval of this magnitude presents significant challenges in any assessment of KAA inter-limb differences. Unless the observed difference is outside this range i.e. > 10° or < -10°, the direction, i.e. which limb has the greater value, is unclear. A hypothetical inter-limb difference of 5° may range from -5° to 15°, a range which, as well as encapsulating two alternative interpretations of inter-limb difference direction, also contains the possibility that the true difference is close to zero. This variety of possible values and subsequent interpretations means it is challenging to identify which limb, if any, requires training interventions that may be designed to restore deficits, improve frontal plane alignment and reduce frontal plane loading during CoD (Fox 2018).

Considerable challenges also exist in the assessment of between session changes in KAA inter-limb differences. A minimal change of 18.3° is necessary to be 95% certain that the observed change is a manifestation of genuine differences in movement as opposed to variability from marker placement (Table 1). Depending on the specifics of the population, task and phase being analysed, KAA’s of between 1 - 11° have been reported during CoD (Alenezi et al. 2016; Jones, Herrington, and Graham-Smith 2015; Kristianslund et al. 2014; Sigward and Powers 2007). In a similar 90° CoD task to the one examined in this study, Clark et al., (2019) examined inter-limb differences in ACLR participants who had completed rehabilitation and returned to sport. They reported peak KAA's of 10.2° and 8.9° for the ACLR and contralateral limbs respectively with a mean inter-limb difference of 1.3° (Clark et al. 2019). While inter-limb differences may be more pronounced at earlier stages of rehabilitation, it is unlikely that they will be of the magnitude necessary to be reliably identified and monitored due to the variability introduced by marker placement upon repeated testing.

41 (87.2%) of ACLR participants changed their KAA inter-limb difference classification throughout the simulated testing sessions (Fig 4E). Thresholds based on group variability have been used previously as a means of determining ACL injury risk, with individuals with extreme values thought to be at increased risk of injury (Kristianslund et al. 2014; Robinson et al. 2014; Sigward and Powers 2007). There appears to be a high probability of mistakenly classifying an individual as having what may be considered normal or abnormal inter-limb differences in KAA due to variability from marker placement (Table 1). For example, all 5 participants who were initially classified as having "abnormal" inter-limb differences in KAA subsequently changed classification to "normal" in the simulated testing sessions, suggesting that incorrect classifications may arise solely from marker placement error as opposed to changes in movement (Fig 4B).

We have chosen to focus on KAA inter-limb differences to convey the implications of this study's findings. This is because frontal plane knee motion is considered important with respect to ACL injury and CoD (Kristianslund et al. 2014; McLean, Huang, and Van Den Bogert 2005; Sigward and Powers 2007). However, the most sensitive variables to marker placement identified were transverse plane kinematics, with knee rotation angle the variable with the largest confidence intervals, minimal identifiable change, and highest percentage of participants to change classification (Table 1). The CGM appears limited in its ability to assess inter-limb differences in these variables as they are sensitive to relatively small variations in marker placement. Alternative techniques for modelling human movement exist and aim to overcome certain limitations ascribed to the CGM. These include models that allow for six degrees of freedom (6DOF) at each joint, those that implement the calibrated anatomical systems technique (CAST) (Cappozzo et al. 1995) or utilise optimisation based joint centre positions (Charlton et al. 2004). However, in any model utilising anatomical landmarks locations to define joint centres and/or segment orientations, there is a continued assumption that marker placement is consistent and repeatable between and within practitioners. Indeed, Groen et al., (2012) observed that although implementing the optimized lower limb gait analysis model reduced errors due to marker placement during walking in certain variables, it also exacerbated those in others. Further research investigating the sensitivity of alternative modelling techniques across various movement tasks is warranted to inform their utility in assessing inter-limb differences.

Within the current study design, several limitations necessitate discussion. Marker displacements were sampled from distributions based on previously reported intra-tester variability ranges in anatomical landmark location (Della Croce, Cappozzo, and Kerrigan 1999; Myers et al. 2015). Our results are therefore directly limited to the distributions chosen *a priori.* It is possible that in some scenarios i.e. differing laboratories and practitioners, that these distributions underestimated the true variation in marker placement, while in others, overestimated it. Additionally, while similar trends and observations are likely in other tasks and at different time points, the specific results observed in this study i.e. confidence intervals and minimal identifiable changes, are limited to the 90° CoD task studied and the distinct time point of 20% of stance. The change in inter-limb differences across the entire stance phase for each variable is included as supplementary material (see Appendix A). Lastly, the implemented marker displacements do not directly mimic real world marker placement error. We implemented anterior/posterior displacements as model definitions indicate that these are the displacements that will have the most substantial effect on model outputs (Kadaba, Ramakrishnan, and Wooten 1989). Real world marker placement will also vary proximally/distally as well as medio-laterally. We also did not account for the variation in soft tissue artefact that would be expected by varying marker positions anteriorly/posteriorly. However, given the relatively small magnitude of displacements it is unlikely these artefacts would substantially affect our findings (Nazareth, Mueske, and Wren 2016).

In conclusion, we present an approach to quantify the minimal changes in inter-limb differences that can be reliably identified given realistic marker placement error and demonstrate how the variability resulting from these errors affects inter-limb difference classifications in a post-ACLR population. Our findings highlight challenges in using the CGM in the assessment of inter-limb differences and the critical importance of accurate and repeatable marker placement. Where possible extensive and regular training, as well as standardisation processes should be implemented to try and reduce intra-tester variability in marker placement. However, for several variables this may not be sufficient given the relatively small distributions from which displacements were sampled and the subsequent large effect observed. These include hip rotation angle, knee rotation angle, knee abduction angle, ankle abduction angle and ankle rotation angle (Table 1). Definitively alluding to the efficacy of the CGM’s continued use in this setting is difficult as it will be dependent on the magnitude of inter-limb difference and subsequent change considered clinically relevant. What constitutes clinically relevant is often difficult to define and may vary for the same variable depending on the task, population and injury being assessed (King, Richter, Franklyn-Miller, Daniels, Wadey, Jackson, et al. 2018; Wellsandt et al. 2016). With respect to the specific CoD task examined in this study, the CGM appears limited in the assessment of inter-limb differences for multiple kinematic and kinetic variables.

Conflict of interest statement

The authors confirm that there is no financial or personal relationship with other individuals or organisations that could inappropriately influence this work.

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Table and Figure Captions

Table 1. Summary results for effect of marker displacements on inter-limb differences. Columns ‘SD’, 95% CI’ and ‘Min identifiable change’ present the standard deviation, 95% confidence interval and minimal identifiable change in each variable. The number and percentage of participants who changed their inter-limb difference classification on at least one occasion in the one-hundred simulated testing sessions is presented in column ‘Classification change’. For these participants, the median percentage of simulations in which their individual classification changed from its original status is presented in column ‘Median classification change’ alongside the range of percentages for individual participants.

Figure 1. Example of confidence interval and minimal identifiable change estimation process. Fig 1A depicts the distribution of all observed changes in knee flexion inter-limb differences from marker displacements (standard deviation of 1.6°). Fig 1B shows the resultant 95% confidence interval for knee flexion angle inter-limb differences was -3.2° < 0 < 3.2° (1.96 x SD). Lastly, Fig 1C depicts the calculation of the minimal identifiable change, which was identified as 5.8°.

Figure 2. Example of inter-limb difference classifications. Image depicts each ACLR participants’ original mean inter-limb difference in knee flexion angle at 20% of stance. Participants with mean inter-limb difference between ±2SD of NORM group mean difference were classified as having “normal” inter-limb differences (green). Participants with mean inter-limb difference above or below 2SD were classified as having an “abnormal” inter-limb difference (red).

Figure 3. Effect of marker displacements on the interpretation of inter-limb differences in hip kinematics at 20% of stance. Top panel depicts the distribution of changes in inter-limb differences and 95% confidence intervals for hip flexion (A), hip abduction (B) and hip rotation (C) inter-limb differences. Bottom panel depicts each ACLR participants inter-limb difference (black = original inter-limb difference, blue = simulated inter-limb differences) relative to the NORM group variability (red lines) for hip flexion (D), hip abduction (E) and hip rotation (F) inter-limb differences.

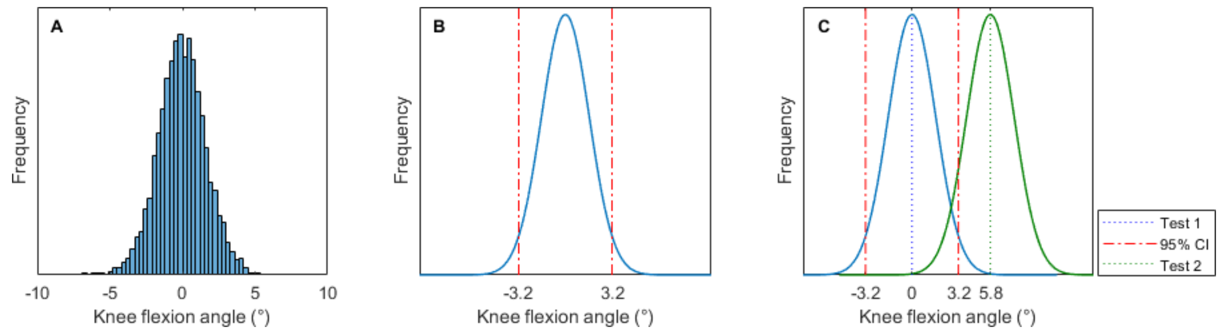
Figure 4. Effect of marker displacements on the interpretation of inter-limb differences in knee kinematics at 20% of stance. Top panel depicts the distribution of changes in inter-limb differences and 95% confidence intervals for knee flexion (A), knee abduction (B) and knee rotation (C) inter-limb differences. Bottom panel depicts each ACLR participants inter-limb difference (black = original inter-limb difference, blue = simulated inter-limb difference) relative to the NORM group variability (red lines) for knee flexion (D), knee abduction (E) and knee rotation (F) inter-limb differences.

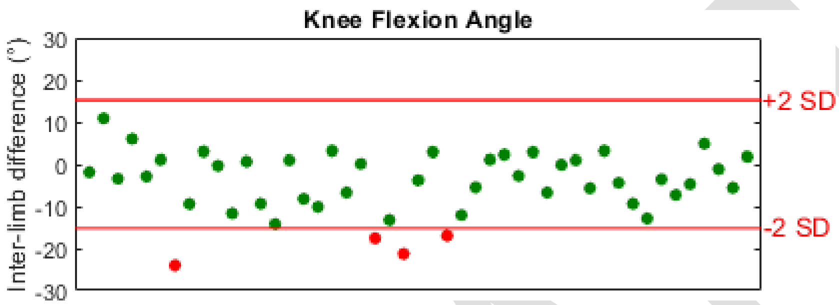
Figure 5. Effect of marker displacements on the interpretation of inter-limb differences in knee kinematics at 20% of stance. Top panel depicts the distribution of changes in inter-limb differences and 95% confidence intervals for ankle plantar-flexion (A), ankle abduction (B) and ankle rotation (C) inter-limb differences. Bottom panel depicts each ACLR participants inter-limb difference (black = original inter-limb difference, blue = simulated inter-limb difference) relative to the NORM group variability (red lines) for ankle plantar-flexion (D), ankle abduction (E) and ankle rotation (F) inter-limb differences.

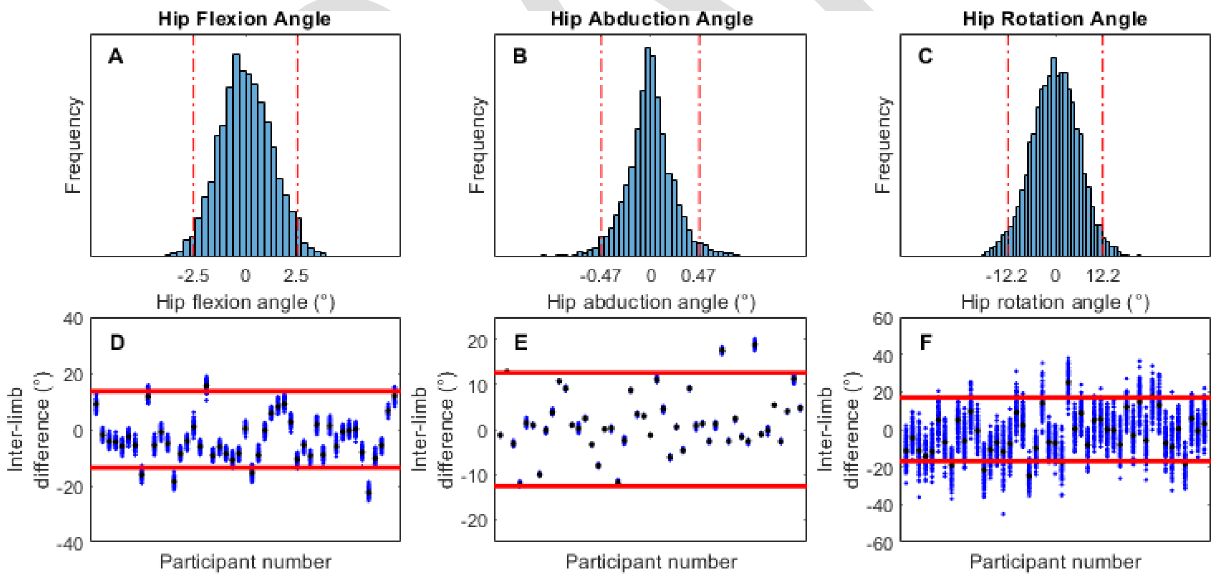
Figure 6. Effect of marker displacements on the interpretation of inter-limb differences in knee moments at 20% of stance. Top panel depicts the distribution of changes in inter-limb differences and 95% confidence intervals for knee flexor moment (A), knee abduction

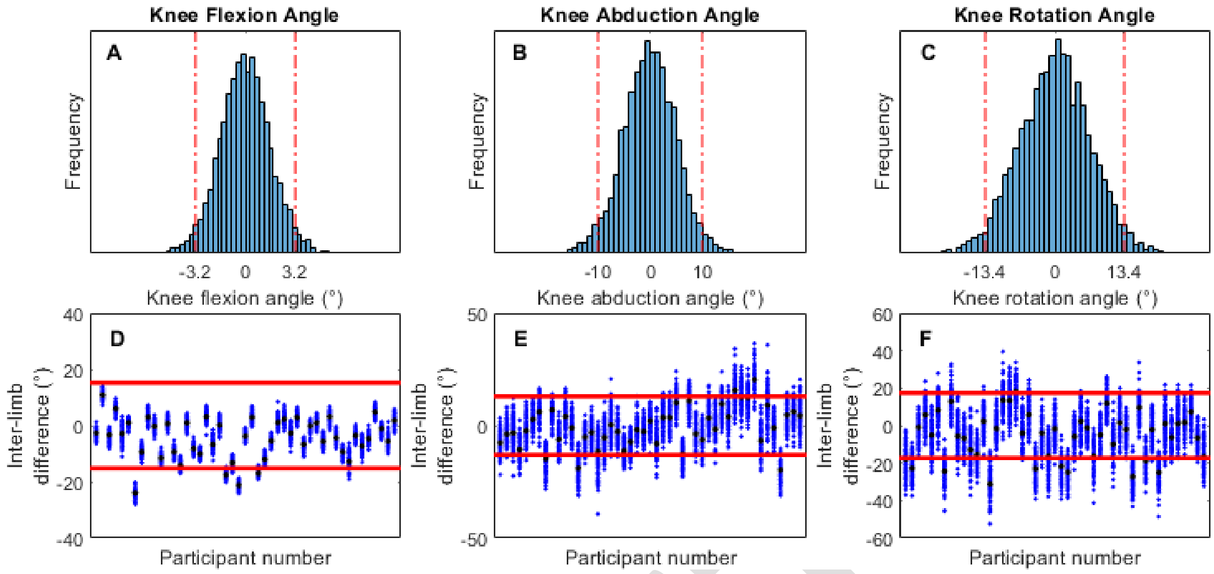
moment (B) and knee rotation moment (C) inter-limb differences. Bottom panel depicts each ACLR participants inter-limb difference (black = original inter-limb difference, blue = simulated inter-limb difference) relative to the NORM group variability (red lines) for knee flexor (D), knee abduction moment (E) and knee rotation moment (F) inter-limb differences.

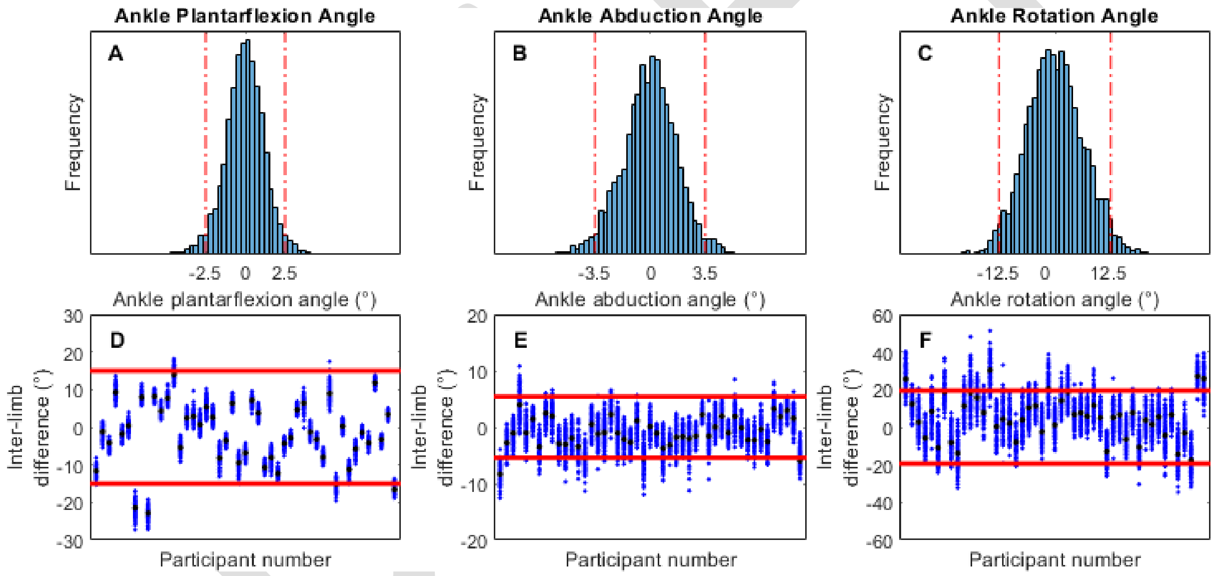
			NA		
Variable	**SD**	**95% CI**	**Min Identifiable Change**	**Classification Change**	**Median Classification Change (Min – Max)**
Hip flexion angle	1.3°	2.5°- 2.5°	4.6°	7 (14.9%)	8% (1 – 10%)
Hip abduction angle	0.2°	-0.47° – 0.47°	0.9°	1 (2.1%)	15% (-)
Hip rotation angle	6.2°	-12.2° – 12.2°	22.2°	39 (83%)	13% (1 – 53%)
Knee flexion angle	1.6°	-3.2° – 3.2°	5.8°	5 (10.6%)	9% (5 – 17%)
Knee abduction angle	5.1°	-10° – 10°	18.3°	41 (87.2%)	8% (1-53%)
Knee rotation angle	6.8°	-13.4° – 13.4°	24.6°	43 (91.5%)	7% (1-52%)
Ankle plantarflexion angle	1.3°	-2.5° – 2.5°	4.6°	7 (14.9%)	2% (1-36%)
Ankle abduction angle	1.8°	-3.5°– 3.5°	6.3°	33 (70.2%)	4% (1-50%)
Ankle rotation angle	6.4°	-12.5° – 12.5°	23°	35 (74.5%)	9% (1-48%)
Knee flexor moment	0.2 Nm/kg	-0.41 – 0.41 Nm/kg	0.8 Nm/kg	12 (25.5%)	18% (1-51%)
Knee abduction moment	0.2 Nm/kg	-0.38 – 0.39 Nm/kg	0.7 Nm/kg	15 (32.0%)	6% (2-44%)
Knee rotation moment	0.01 Nm/kg	-0.02 – 0.02 Nm/kg	0.05 Nm/kg	0 (-)	-

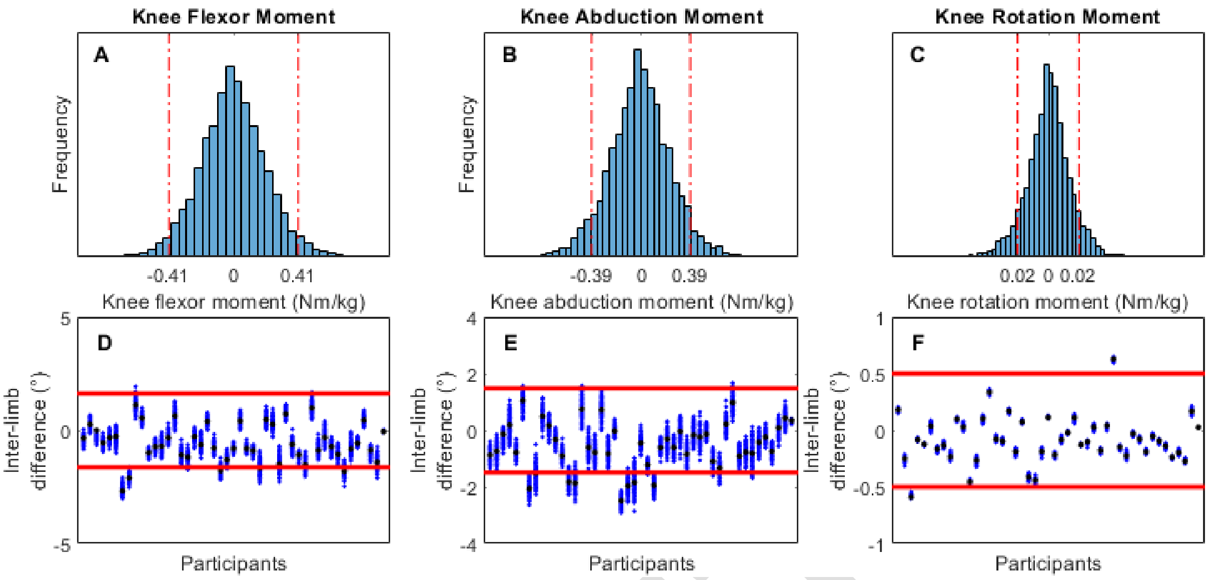

A
B
C
Frequency
Knee flexion angle (°)
Test 1
95% CI
Test 2
-10
-5
0
5
10
-3.2
3.2
5.8


Knee Flexion Angle
Inter-limb difference (°)
+2 SD
-2 SD
30
20
10
0
-10
-20
-30


Hip Flexion Angle
Hip Abduction Angle
Hip Rotation Angle
A
B
C
D
E
F
Frequency
Hip flexion angle (°)
Hip abduction angle (°)
Hip rotation angle (°)
-2.5
0
2.5
-0.47
0.47
-12.2
12.2
Inter-limb difference (°)
Participant number


Knee Flexion Angle
Knee Abduction Angle
Knee Rotation Angle
A
B
C
Frequency
-3.2 0 3.2
Knee flexion angle (°)
-10 0 10
Knee abduction angle (°)
-13.4 0 13.4
Knee rotation angle (°)
D
E
F
Inter-limb difference (°)
40 20 0 -20 -40
50 0 -50
60 40 20 0 -20 -40 -60
Participant number


Ankle Plantarflexion Angle
Ankle Abduction Angle
Ankle Rotation Angle
A
B
C
Frequency
-2.5 0 2.5
Ankle plantarflexion angle (°)
-3.5 0 3.5
Ankle abduction angle (°)
-12.5 0 12.5
Ankle rotation angle (°)
D
E
F
Inter-limb difference (°)
30 20 10 0 -10 -20 -30
20 10 0 -10 -20
60 40 20 0 -20 -40 -60
Participant number



Knee Flexor Moment
Knee Abduction Moment
Knee Rotation Moment
A
B
C
Frequency
-0.41 0 0.41
-0.39 0 0.39
0.02 0 0.02
Knee flexor moment (Nm/kg)
Knee abduction moment (Nm/kg)
Knee rotation moment (Nm/kg)
D
E
F
Inter-limb difference (°)
Participants