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Hip contact load and muscle force in Femoroacetabular Impingement population

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Abstract

With a prevalence of 17% in men and 4% in women, Femoroacetabular Impingement (FAI) of type cam is characterized by a decreased femoral head-neck offset and/or asphericity of the lateral femoral head, associated with groin pain and reduced hip range of motion. Since the aetiology is still unclear, the mechanisms of development, progression and degeneration of FAI are largely investigated. Musculoskeletal modeling can support the development of a biomechanical framework to advance the research on FAI pathomechanisms, expand the knowledge about hip contact load distribution in FAI population, and relate the muscle and hip contact forces to the alterations observed during functional tasks. Therefore, this thesis is composed of two parts: the development of a methodological framework, and its application to the investigation of FAI pathomechanisms.

The variability of the modelling outcomes (*i.e.*, body kinematics, torques, contact and muscle forces) to different marker sets, pelvic marker misplacements, and hip joint center (HJC) location was investigated within an inverse kinematic framework. The findings from such studies supported the modelling choices for the clinical investigation of FAI pathomechanisms. In particular, the performance of three different marker sets (Plug-in-Gait, University of Ottawa Motion Analysis Model and a 3-marker-cluster marker set) was compared, and absolute and relative reliability indices were calculated with the purpose of finding a simple yet reliable marker set to be used within an inverse kinematic framework in a clinical study. Thereafter, the sensitivity of joint angles, moments and hip contact forces to simulated inaccurate pelvic tilt was analyzed. The resulting variability indices were high with variations up to 1.3 times the body weight in hip contact forces. The kinematic variations propagated non-linearly to all planes and joints, showing the importance of adjusting possible pelvic misalignments. A methodology was presented to correct the pelvic alignment when the relative position of surface pelvic markers with respect to bony landmarks is known from medical images.

The HJC location is a crucial modelling parameter in the analysis of hip kinematics and forces. A certain degree of customization could be introduced in the model by using HJC measured from medical images. Therefore, the performance of a generic musculoskeletal model with customized or non-customized HJC was compared during walking. Hip contact forces were highly sensitive to HJC location, especially because of the dependency of muscle moment arms to HJC changes. However, the variation of HJC without consistent muscle anatomy customization introduced artifacts that could potentially produce inaccurate muscle and joint contact forces estimation. When HJC cannot be measured from medical images, regression equations can be used instead. Therefore, the validity of two popular HJC regression equations (Harrington and Davis) was tested on FAI participants using non-parametric statistical and Bland-Altman tests. The results indicated that the equations were valid for FAI population. In addition,

skin thickness measurements were provided for pelvic bony landmarks, and their correlation with body mass index was proposed for systematic error reduction. New adult-specific regression equations were developed from medical images.

The described methodological framework was then applied to investigate the functional alterations observed in FAI population. The differences in muscle and hip contact forces were compared between FAI and healthy control groups during level walking. The FAI group showed reduced muscle and hip contact forces, which were linked to the lower normalized walking speed and shorter step length. These results can be interpreted as a protective mechanism developed by FAI patients to prevent high compression at the site of impingement, given that the compressing hip contact force was directed towards the anterior-superior quadrant of the acetabulum, consistent with the localization of the cam-type deformity and the cartilage and labrum damages. Based on these findings, a possible FAI pathomechanism was proposed, which could be used to support the development of preventive treatment and intervention for symptomatic FAI patients.

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List of Abbreviations

aFAD: asymptomatic Femoroacetabular Deformity
ANOVA: Analysis of Variance
ANCOVA: Analysis of Covariance
AP: Anterior-Posterior
BMI: Body Mass Index
BW: Body Weight
CE: Contractile Element
CMC: Coefficient of Multiple Correlation
CON: Control
CT: Computed Tomography
DK: Direct Kinematics
DOF: Degree of Freedom
EMG: Electromyography
FAI: Femoroacetabular Impingement
HCF: Hip Contact Forces
HJC: Hip Joint Center
ICC: Intra-class Correlation Coefficient
IK: Inverse Kinematics
ISB: International Society of Biomechanics
LASI: Left Anterior Superior Iliac crest
LPSI: Left Posterior Superior Iliac crest
LOA: Limits of Agreement
MAV: Mean Absolute Variation
MDC: Minimum Detectable Change
ML: Medial-Lateral
MRI: Magnetic Resonance Image
MVIC: Maximum Voluntary Isometric Contraction
PD: Pelvis Depth
PE: Passive Element
PiG: Plug-in-Gait
PW: Pelvic Width
RASI: Right Anterior Superior Iliac crest
RPSI: Right Posterior Superior Iliac crest
RMSE: Root Mean Squared Error
ROM: Range of Motion
SEE: Series Elastic Element
UOMAM: University of Ottawa Motion Analysis Model
US: Ultrasound

*“Theories don’t have to be correct,
only facts do”*

Dr. Hans Selye

Vienna, 1907- Montreal, 1982

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Since PhD stands for ‘Doctor of Philosophy’, then I think I deserve it, because I asked myself a lot of philosophical questions during this PhD! Am I in the right path? What is all this for? Am I being useful to this world? Today I am surely a stronger and more knowledgeable person thanks to this path and the people I met along the way. Therefore, I need to give out a lot of ‘Thanks’.

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Outline of the thesis

The present thesis is outlined as follows.

Chapter 1 provides a general introduction, the research objectives and the rationale of this thesis.

Chapter 2 contains a review of the literature of the methodological and clinical topics covered in this thesis. In particular, the first part presents some background knowledge on FAI from the medical and biomechanical perspectives, while the second part provides methodological background to musculoskeletal modelling.

Chapter 3 contains an overview of the methods that are common to all articles. Details specific to every study are not presented in this Chapter 3, but can be found in the method sections of every article.

Chapters 4 to 7 contain the articles that were produced from this research. Every article addresses a specific methodological or clinical objective.

Chapter 8 summarizes the findings, discussions and conclusions of the present thesis; the limitations and general relevance of the findings are also discussed.

Chapter 1. General introduction

Musculoskeletal models of the human body attract great interest in biomechanics, given their potential applications in fields such as surgical planning, wearable robotics, performance improvement and clinical investigations. Consequently, many research groups are focusing their attention towards developing anatomically accurate and physiologically sound musculoskeletal models. Many research groups globally are working towards this goal, and sharing their research with the community. As result, several tools are now available which can perform state of art simulations of body kinematics and dynamics, anatomical parameters, as well as muscle and joint reaction forces.

Muscle forces cannot be easily estimated because of the muscle redundancy problem (larger number of actuators than degrees of freedom). Since *in vivo* measurements are invasive, musculoskeletal models are the most ethically acceptable approach to estimate muscle and joint contact forces (Erdemir et al., 2007). The choice of model depends upon the objective of the research. Optimization models solve the redundancy problem by introducing constraints into the equations (e.g., equality between joint torques obtained from inverse dynamics and the sum of the moments generated by the muscle forces) and cost functions (e.g., minimizing sum of muscle stresses) (Crowninshield et al., 1978; Pandy, 2001; Prilutsky and Zatsiorsky, 2002; Rasmussen et al., 2003). Static optimization algorithms are the simplest example of optimization models because muscle control patterns are not required and, therefore, the muscle dynamics (i.e., relationship between neuronal activation and muscle force production) are not modelled. On the contrary, dynamic optimization problems include muscle dynamics models, and, therefore, are time-dependent, less sensitive to measurement errors and more computationally expensive. Unless the purpose of the study requires muscle control estimation, static optimization problems are usually favoured because static and dynamic optimization models give similar results, with the latter being more computationally expensive (Erdemir et al., 2007).

Musculoskeletal models have contributed to the advancement of knowledge in clinical practice; some examples are studies that investigated the development of osteoarthritis (Crossley et al., 2012; Richards and Higginson, 2010), anterior cruciate ligament injuries (Gardinier et al., 2012; Tsai et al., 2012), and cerebral palsy (Steele et al., 2012). Femoroacetabular Impingement (FAI) is a relatively new concept in orthopedics since it was only introduced 15 years ago, when Myers (1999) reported case studies of periacetabular osteotomy and mentioned an “*impingement [that] is produced by abutment of the femoral head or head to neck junction on the anterior rim of the properly aligned acetabulum*”. Since that first paper, the knowledge about FAI has greatly progressed, and the interest around it has increased, especially because it is now considered a leading factor to hip osteoarthritis (Agricola et al., 2013; Ganz

et al., 2008; Şahin et al., 2011). With a prevalence of 17% in men and 4% in women, FAI of type cam is characterized by a decreased femoral head-neck offset and/or asphericity of the lateral femoral head (Gosvig et al., 2008; Laborie et al., 2011; Leunig et al., 2006; Sink et al., 2008). These conditions can lead to repeated impingement of the head-neck junction and the radius of the acetabulum, associated with groin pain and reduced hip range of motion. Moreover, 14% of the general population is affected by FAI-related anatomical deformities without experiencing any of the associated symptoms (Hack et al., 2010). Since the aetiology is still unclear, the mechanisms of development, progression and degeneration of FAI are largely investigated (Ganz et al., 2008; Hartofilakidis et al., 2011; Imam and Khanduja, 2011; Leunig et al., 2009; Pollard et al., 2010), in order to develop appropriate tests for early diagnosis and treatment, and to prevent the degeneration of the pathology into osteoarthritis.

This thesis focused on the biomechanical understanding of the pathomechanisms¹ leading to FAI. A generic methodological framework was developed and its sensitivity assessed towards the clinical problem investigated. Therefore, the thesis can be divided into a methodological and a clinical part.

1.1. Methodological aspects

One of the most common techniques in motion capture is acquiring body movement through retro-reflective markers. The term “marker set” indicates the organization of the surface markers on the body with respect to palpable bony landmarks. There exists a large body of literature that investigates the performance of different marker sets when the body kinematics are calculated with a direct approach (*i.e.*, direct kinematics). Conversely, inverse kinematics can be used. The main difference between these two methods is in the body reference systems definition; in direct kinematics body reference systems are constructed directly from experimental marker coordinates, as described in Wu (2002) and Cappozzo (1995). In inverse kinematics, instead, the distance (or tracking error) between experimental and virtual markers of the whole body placed in a pre-existing kinematic model is minimized by adjusting the joint angles (Lu and O'Connor, 1999). The model sensitivity to the choice of marker set in inverse kinematics is not well investigated as for direct kinematics, and marker set choices for inverse kinematic analyses are made on the basis of conclusions of direct kinematic studies, which is not appropriate given the intrinsic difference between these two frameworks. Therefore, there is a gap in the literature regarding the level of marker set complexity that can be considered acceptable for clinical investigations, where the simplicity of the experimental protocol is of great importance.

Another challenge is the accurate placement of the markers on the bony landmarks. This constitutes a crucial step for both direct and inverse kinematics, and the literature is rich of studies that show the

¹ ‘Pathomechanism’ is defined as the mechanism by which a pathological condition occurs

sensitivity of the outcomes to the markers variability (Della Croce et al., 1999; El Habachi et al., 2015; Groen et al., 2012; Myers et al., 2015). However, the use of inverse kinematics introduces an extra challenge: errors are given not only by the surface marker placement, but also by an initial inconsistency between positions of the virtual markers in the model and experimental markers. The pelvis segment is the “root” of the lower limb kinematics chain, and a correct estimation of its orientation and position is crucial to obtain accurate kinematics (Winter, 2009), especially when the adjacent hip joint is the focus of the study. A discrepancy between virtual and experimental pelvic markers can cause an offset in the pelvic orientation that will propagate non-linearly to the whole kinematic chain (Della Croce et al., 2005). Medical images of the pelvis, including radiopaque or MRI (Magnetic Resonance Imaging)-visible markers, reveal the relative position of landmarks on the bone and reflective skin markers, allowing a correction of the estimated pelvic angles. While this has been proposed as solution for direct kinematics (Della Croce et al., 2005), it has never been applied to an inverse kinematic framework.

The generic musculoskeletal models can be customized with subject-specific information. Lower limb kinematic and kinetic variables are highly sensitive to the location of the hip joint center (Delp and Maloney, 1993; Stagni et al., 2000), therefore, using subject-specific hip joint center (HJC) measured from medical images could improve the accuracy of the outcomes for inverse kinematic and kinetic analyses. However, the moment generating capacities of the hip muscles are highly influenced by hip joint center position (Delp and Maloney, 1993), and the customization of HJC position without updating the muscle attachments and paths could generate inconsistent moment arms, and unrealistic estimations of muscle and joint contact forces. Testing the sensitivity of the output variables (*i.e.*, kinematics, kinetics, contact forces) to changes in HJC location is of crucial importance to evaluate the feasibility of using subject-specific HJC in an otherwise generic musculoskeletal model.

When medical images are not available, regression equations can be used to estimate HJC (Bell et al., 1989; Bell et al., 1990; Davis III et al., 1991; Harrington et al., 2007; Seidel et al., 1995), but their accuracy may vary according to the population under analysis. Among the available HJC regression models, recent studies showed that Harrington equations provided the highest accuracy (Andersen et al., 2013; Kainz et al., 2015; Sangeux et al., 2011; Sangeux et al., 2014), although this set of equations was developed from a non-homogeneous and relatively small size sample. FAI of type cam is characterized by an elevated alpha angle, femoral retro-torsion and acetabular retro-version, and decreased femoral neck-shaft angle (Ng et al., 2015), thus it cannot be assumed a priori that the same regression equations can properly locate HJCs in individuals with a cam deformity. However, no study has investigated the accuracy of these regression equations applied to subjects with hip deformities such as cam-type FAI. Also, it is not clear from the literature whether the limits of accuracy of such regression equations are due

to the intrinsic variability of HJC, or to the limited and inhomogeneous sample population on which they were developed. Lastly, regression equations are developed based on bony landmarks coordinates, but they are applied to surface markers instead, without taking into consideration the bias introduced by skin thickness, whose value can be measured from medical images.

1.2. Clinical aspects

The mechanisms of development, progression and degeneration of FAI are investigated in the literature with the aim of developing appropriate tests for early diagnosis and treatment, and preventing the degeneration into osteoarthritis. A growing body of literature exist on the biomechanics of FAI population. These studies generally show differences in a variety of functional tasks between symptomatic FAI and healthy control population; FAI subjects show a reduced range of motion at the pelvis and hip during walking and squatting, but also stairs climbing and other functional tasks (Alradwan et al., 2014; Alshameeri and Khanduja, 2014; Ayeni et al., 2013; Brisson et al., 2013; Diamond et al., 2014; Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Lamontagne et al., 2011; Lamontagne et al., 2009b; Rylander et al., 2013; Rylander et al., 2011), as well as reduced muscle activation and strength (Casartelli et al., 2011b; Lamontagne et al., 2013). Some of these functional alterations cannot be solely related to the impingement caused by the bony deformation, but could be linked to other phenomena, such as soft tissue tightness (Brisson et al., 2013; Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2011), pain inhibition mechanisms (Brisson et al., 2013; Hunt et al., 2013), and muscle weakness (Casartelli et al., 2011a; Casartelli et al., 2011b). One of the most accredited hypotheses about FAI development is the presence of high mechanical stresses at the hip joint, especially during developmental age (Agricola et al., 2014; Chegini et al., 2009; Martin and Tashman, 2010; Ng et al., 2012; Philippon et al., 2013). However, there is limited evidence to support such hypotheses, since muscle contribution and neuromuscular activations have never been investigated during functional tasks in FAI population.

Musculoskeletal models can support and expand these investigations by providing estimates of the hip muscle and contact forces that could help explaining the functional differences revealed, by providing grounds to link, support or reject previously proposed hypotheses.

In summary, the purpose of the present thesis was contributing to the understanding of FAI pathomechanisms by use of musculoskeletal models to estimate muscle and hip contact forces through inverse kinematics and static optimization. To ensure the most valid results possible, some technical aspects were also investigated: the choice of marker set, the pelvic orientation correction and the hip joint center estimation, from which guidelines for future studies were also derived.

1.3. Objectives and relevance

The main goal of this thesis was to provide a biomechanical contribution to the understanding of FAI pathomechanisms. Therefore, this thesis is composed by two main objectives: the development of the methodological framework (*i.e.*, methodological objectives), and the investigation of the methods sensitivity to the clinical problem under investigation (*i.e.*, clinical objectives).

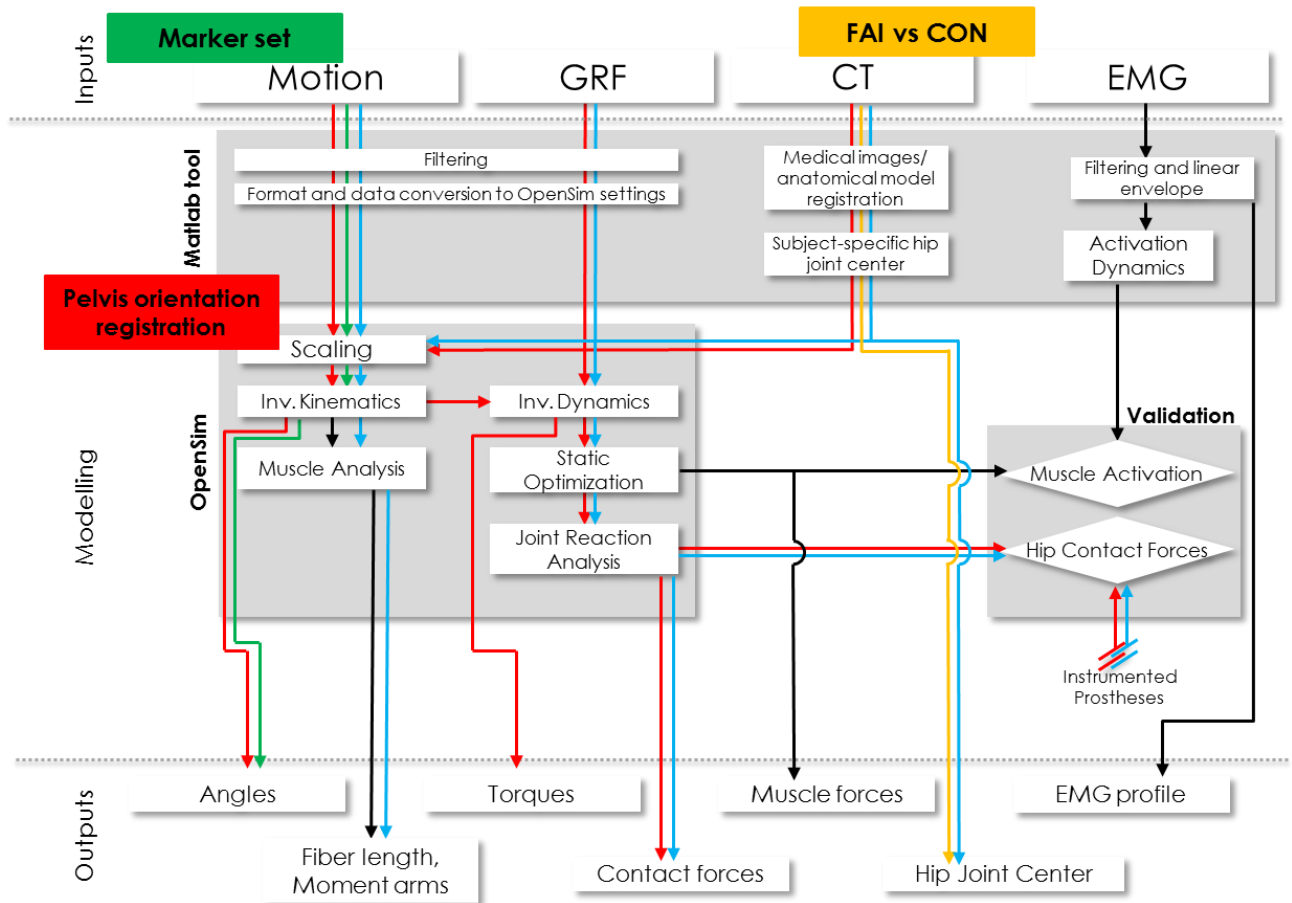


Figure 1-1. Thesis scheme: methodological framework

The inputs of the simulation were: motion data (marker trajectories), ground reaction forces (GRF), hip muscles electromyography (EMG), and pelvic Computed Tomography (CT). Trajectories and GRF were filtered and converted into OpenSim compatible format files. From the CT the coordinates of bony landmarks, radiopaque surface markers and hip joint centers (HJC) were recorded, and appropriate transformations applied to convert the coordinates into the pelvic reference system. EMG were filtered to estimate the muscle activation. The generic musculoskeletal model was scaled, and inverse kinematics, dynamics, muscle analysis, static optimization and joint reaction analysis were run to estimate angles, torques, fiber lengths, moment arms, muscle activation, and muscle and contact forces. The muscle activations estimated from static optimization were compared to those obtained by EMG data for indirect validation. Also the hip contact forces were compared to the data available in the literature from instrumented prostheses. The color boxes and lines highlight the parts of the methodological framework involved in the different objectives

The methodological objectives aimed to investigate the sensitivity of the model and the model workflow to input data and modelling parameters, to estimate hip joint loading and muscle forces in a clinical framework related to hip pathologies. The methodological objectives are stated below and, to better understand them, a brief outline of the simulation background is provided in Figure 1-1.

The **first methodological objective** of the present thesis was to examine the reliability and sensitivity of kinematics outcomes to inter-marker set variability using an inverse kinematic approach. This investigation is relevant to researchers in clinical gait analysis, who are interested in using a simple yet reliable marker set in an inverse kinematic framework. Also, establishing the acceptable thresholds for comparison (the so called, minimum detectable change) can help researchers to understand their results with respect to the available literature, and avoid misinterpreting their data. The first objective corresponded to investigating the kinematic branches highlighted in green on the scheme (Figure 1-1), using different marker sets as variable input.

In clinical FAI investigations, medical images of the pelvis are provided to assess the magnitude of hip deformity and confirm the diagnosis. This information can also be used to improve the accuracy of the model; hence, the **second methodological objective** was to provide an approach to register the position of the surface pelvic markers from medical images to the musculoskeletal model. A sensitivity analysis on hip joint angles, moments and contact forces with simulated incorrect pelvic markers positioning and orientation was also examined using an inverse kinematic framework. The red branches in Figure 1-1 highlight which part of the methodological framework was involved.

Subject-specific hip joint center (HJC) can also be measured from pelvic medical images to increase model accuracy. However, using a subject-specific HJC in an otherwise generic musculoskeletal model could cause some inconsistencies in the model, whose effects on the outcomes cannot be known *a priori*. Therefore, the **third methodological objective** was twofold: 1) evaluate the error in HJC location when using generic scaled model; 2) evaluate the feasibility of using subject-specific HJC in a generic musculoskeletal model by analyzing the sensitivity of the output variables such as muscle moment arms and hip contact forces to changes in HJC location during walking. The branches highlighted in blue in Figure 1-1 help the understanding of this methodological investigation.

Most studies in gait analysis use generic HJC regression equations, however significant anatomical alteration of the femoroacetabular joint could affect the biomechanical outcomes. Consequently, the validity of generic HJC equations cannot be guaranteed *a priori* in FAI patients; hence, the **fourth methodological objective** was threefold: 1) evaluating the validity of HJC regression models for a population characterized with a cam-type deformity, 2) proposing new regression equations to verify if the predictors could provide better estimates in adults when tuned on a larger and adult-specific dataset,

and 3) discussing skin thickness influence on HJC estimations when the equations are applied to surface markers instead of bony landmarks. The first sub-objective is relevant for those clinical studies exploring the biomechanics of cam-type deformity, without direct access to HJC measurements. The second and third are of general interest in clinical gait analysis as they examine the limits of accuracy for HJC regression equations, and a quantification of skin thickness measurements to improve the HJC prediction. Orange branches of Figure 1-1 highlight the methodological outline of this investigation.

The second part of this doctoral thesis focused on the clinical application of the previously discussed methodological framework to detect changes between FAI and healthy control populations. There is limited number of studies in the literature on the muscle contribution and neuromuscular activations of FAI during functional tasks. The **clinical objective** was the investigation of FAI pathomechanisms by looking at the muscle contribution to hip contact loads during walking. This investigation aimed to link FAI deformity and its functional alterations to support future development of preventative treatment and more focused intervention for symptomatic subjects.

For this study, the entire structure of the model was employed, using group differences as independent variable (Figure 1-1).

1.4. Rationale

Solving the FAI paradigm requires a complete analysis of the kinematics, kinetics and neuromuscular conditions of the hip, which is lacking in the literature, due to the relatively recent recognition of this pathology. A solid comprehension of the methodological aspects needed to solve the FAI paradigm is also required. Developing a methodological framework for a complete kinematics, kinetics and neuromuscular analysis of FAI to understand its pathomechanisms is the rational of this thesis.

Chapter 2. Review of the literature

2.1. Femoroacetabular Impingement

Femoroacetabular Impingement (FAI) is a hip deformity that causes hip and groin pain and affects more than 17% of men and 4% of women (Gosvig et al., 2008; Hack et al., 2010; Laborie et al., 2011; Leunig et al., 2006; Sink et al., 2008).

FAI can be classified as either cam or pincer (Figure 2-1). When the anatomical deformity is localized on the femoral head-neck junction, FAI is of type cam; the oversized and aspherical femoral head leads to a reduced head-neck offset, limiting the clearance between the head-neck junction and the labrum (Ganz et al., 2003). If the deformity affects the acetabular rim, FAI is described as pincer. In this case, the ossified labrum over-covers the femoral head limiting the movement (Ganz et al., 2003). However, FAI is more likely to be manifested under both conditions (86% of cases, versus 14% manifesting a unique type of FAI) (Beck et al., 2005; Reid et al., 2010).

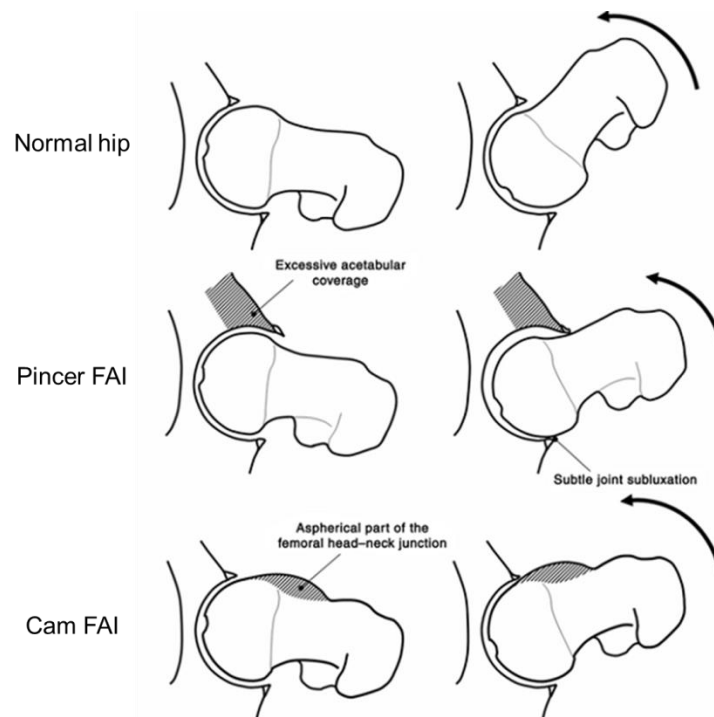


Figure 2-1. FAI classification

Top: normal hip configuration. Center: pincer impingement with excessive acetabular overcoverage that leads to early contact between femoral head-neck junction and acetabular rim. Bottom: cam impingement with aspherical femoral head that jams into the acetabulum. Reproduced with permission from Tannast, M., Siebenrock, K. A., & Anderson, S. E. (2007). Femoroacetabular impingement: Radiographic diagnosis - What the radiologist should know. *American Journal of Roentgenology*, 188(6), 1540-1552

2.1.1. Diagnosis

Early recognition of FAI followed by subsequent behavioural modification (profession, sports, etc), or even surgery, is crucial to prevent joint degeneration and reduce the rate of osteoarthritis due to FAI (Eijer et al., 2001; Leunig et al., 2009; Pollard, 2011). However, the early diagnosis is not always possible because the aetiology is still unclear (Ganz et al., 2008; Hartofilakidis et al., 2011; Imam and Khanduja, 2011; Leunig et al., 2009; Pollard et al., 2010).

Pain is a primary symptom of FAI: the so called “C” sign (named after the typical gesture used by patients to describe the deep interior hip pain, Figure 2-2, A) is a characteristic index of FAI (Byrd, 2014). Positive FABER (hip flexion, abduction, external rotation, Figure 2-2, B), and FADIR (hip flexion, adduction, internal rotation Figure 2-2, C) tests are also indicators of FAI, with a sensitivity greater than 96% and 88%, respectively (Wilson and Furukawa, 2014).

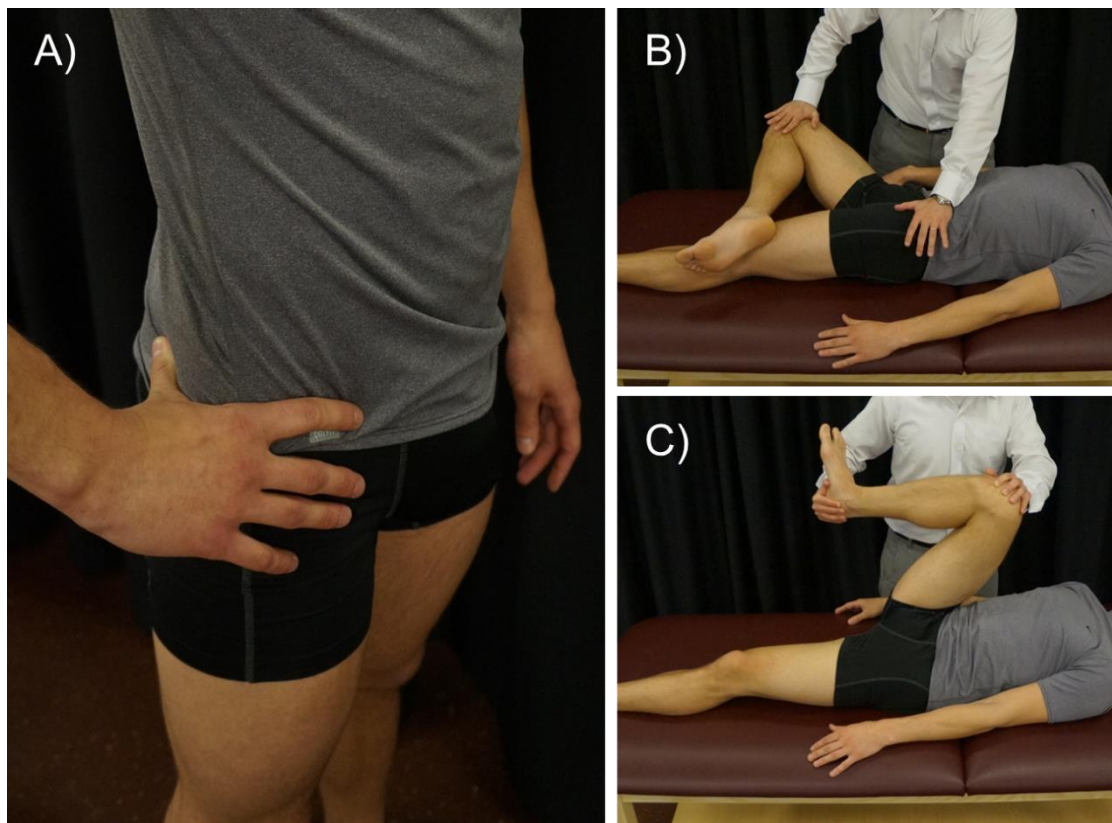


Figure 2-2. FAI diagnostic tests

A) The “C” sign. B) FABER (hip flexion, abduction, external rotation) test, the examiner passively moves the leg into 45° of flexion, then externally rotates and then abducts the leg, placing the ankle to rest proximal to the knee of the contralateral leg. C) FADIR (hip flexion, adduction, internal rotation) test, the examiner moves the leg into full flexion, then into adduction and internal rotation

The pain can aggravate with physical activity, especially if it requires large ranges of motion and levels of impact (Byrd, 2014); in fact, FAI is often correlated to sport practice such as hockey, football, soccer, lacrosse, and baseball for men; and soccer, dance, field hockey, track, baseball, and lacrosse for women (Nawabi et al., 2014).

Besides through pain and physical examinations, FAI is usually evaluated with imaging techniques that distinguish between the anatomical deformity associated with FAI and other types of hip problems (e.g., arthritis). Alpha angle is the angle formed between the axis of the neck and a line connecting the femoral head center to a specific point. This point is located where the distance from the bone to the center of the head first exceeds the radius of the cartilage-covered femoral head (Figure 2-3, A represents a small alpha angle, Figure 2-3, B large alpha angle). Alpha angle is a good descriptor of anterior impingement because is significantly larger in FAI patients than controls (Nötzli et al., 2002). The use of this metric as a FAI diagnosis tool is still debated because of the disagreement on the appropriate threshold to distinguish FAI patients and controls. From Nötzli's paper, an alpha angle of 50.5° in the axial view seems to be the discriminant value between control and FAI population. Under antero-superior view (*i.e.*, radial view), the threshold value for the alpha angle becomes 60° (sensitivity 76%, specificity 75% depending on the reader) (Sutter et al., 2012). From radiographical images, axial or Dunn/Rippstein views provide a good prospective for measuring the alpha angle, and quantify abnormalities of the femoral head-neck junction (Tannast et al., 2007b). An alternative to radiographical images is the Computed Tomography (CT), which provide an even better view for measuring alpha angles (Beaule et al., 2005).

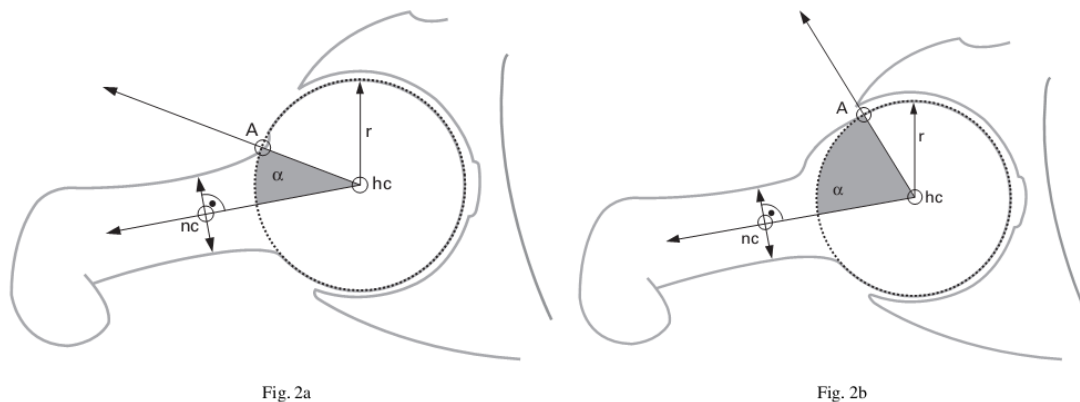


Figure 2-3. Alpha angle

Explanation of how to calculate alpha angle. Point A is located where the distance between the edge and the head center (hc) exceeds the radius (r). nc is the center of the neck at the narrowest point. Alpha angle is calculated between the lines nc-hc and A-hc. Figure 2.a) is an example for small alpha angle, figure 2.b) of large alpha angle. Reproduced with permission and copyright © of the British Editorial Society of Bone and Joint Surgery. Nötzli, H. P., Wyss, T. F., Stoecklin, C. H., Schmid, M. R., Treiber, K., & Hodler, J. (2002). The contour of the femoral head-neck junction as a predictor for the risk of anterior impingement. *Journal of Bone and Joint Surgery - Series B*, 84(4), 556-560

Even if the initial focus for classifying FAI patients was on the alpha angle, from recent studies it emerged that other anatomical features might also have an impact on the development of the symptoms associated to cam-deformity. These are a significantly lower femoral neck-shaft angle (*i.e.*, formed between the femoral neck and shaft axes, in the frontal plane), lower anterior femoral head-neck offset (*i.e.*, the offset distance between the two tangents of the anterior femoral head and neck), and higher femoral torsion (*i.e.*, the difference between the femoral neck and condyle horizontal angles) (Ng et al., 2015; Ranawat et al., 2011).

FAI also causes physiological changes such as early cartilage degeneration associated with a reduced proteoglycan content of the hyaline cartilage (Wagner et al., 2003). The physiological change happens prior to the gross morphological alteration and, consequently, it can be crucial for a timely intervention. Cartilage proteoglycan content can be measured by non-invasive techniques such as T1-rho MRI, which may provide further prognostic information in the management of FAI (Rakhra et al., 2012).

Higher bone mineral density is also associated with FAI (Speirs et al., 2013). This recent study showed how individuals with cam deformity have denser subchondral bones, regardless of symptom status. This important finding may partially explain the degeneration process from FAI into osteoarthritis since high bone mineral density is considered a predictor of early osteoarthritic degeneration of the hip.

Clinical examinations are as important as radiographical evidence for FAI diagnosis. In fact, FAI patients demonstrate a significantly reduced range of motion in hip flexion/extension and internal rotation when subject to a passive dynamic range of motion examination (Tannast et al., 2007b).

2.1.2. Motion analysis

There is a growing body of literature on the joint biomechanics of FAI patients. These studies generally show differences in a variety of functional tasks between symptomatic cam FAI patients and healthy control population. The tasks that most investigated are walking, squatting, stair climbing, and dynamic range of motion (Alradwan et al., 2014; Alshameeri and Khanduja, 2014; Ayeni et al., 2013; Brisson et al., 2013; Diamond et al., 2014; Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Lamontagne et al., 2011; Lamontagne et al., 2009b; Rylander et al., 2013; Rylander et al., 2011).

Walking. The kinematics of level walking is characterized by a general reduction of the range of motion that interests specifically the hip frontal and sagittal planes, and frontal pelvic angles (Hunt et al., 2013; Kennedy et al., 2009; Rylander et al., 2013), and also the hip internal rotation (Hunt et al., 2013; Rylander et al., 2013). The hip extension approaches the angles that FAI population can extend during

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maximum range of motion tasks (Kennedy et al., 2008; Kennedy et al., 2009). Differences in kinetics were only noticed in Hunt et al. (2013), who found reduced hip flexion and external rotation moments.

Squatting. The maximal-depth squat movement has been largely investigated since it is a demanding task approaching the maximum passive hip range of motion registered for FAI populations (Audenaert et al., 2011; Tannast et al., 2007a), and requiring higher muscular forces (Ayeni et al., 2013; Lamontagne et al., 2011; Lamontagne et al., 2009b). During squatting, the FAI group had a reduced sagittal plane pelvic range of motion and maximum squat depth (Lamontagne et al., 2009b), which can be only partially recovered post-surgically (Brisson et al., 2013; Lamontagne et al., 2011). The maximum squat depth task was suggested as diagnostic tool (Lamontagne et al., 2009b; Ng et al., 2015), but its robustness is still debated (Ayeni et al., 2013).

Stair climbing. Rylander (2013) showed that the alterations found in stair climbing (reduced internal hip rotation and sagittal plane range of motion) cannot be restored even after surgical intervention, demonstrating the presence of altered functionality that goes beyond the physical impingement.

Maximum range of motion. In a study investigating maximum dynamic range of motion, Kennedy (2008) reported a reduced sagittal range of motion, mainly caused by reduced hip extension and abduction. Frontal and transverse plane ranges of motion were also significantly reduced, consistent with the literature on passive range of motion (Philippon et al., 2007). The values found during dynamic tasks were considerably lower than the estimates from collision detection algorithms, used to simulate the maximum movement permitted by the deformed hip compared to a healthy one (Kubiak-Langer et al., 2007; Tannast et al., 2007a). Such result indicates the presence of differences other than the bone structure that limit the range of motion.

There is limited evidence that FAI population exhibits altered muscular activation. One study investigating lower limb electromyography (EMG) in FAI found a reduced ability to activate the tensor fasciae latae ($p=0.048$) and rectus femoris ($p=0.056$) during maximal voluntary contractions tasks (Casartelli et al., 2011b). However, the comparison was based upon root mean square parameters, and no normalization techniques were used to account for tissue composition, electrode placements, and more. No differences were found for fatigue indices (Casartelli et al., 2011a). Mantovani et al. (2013) investigated hip muscles activation and flexion/extension co-activation during squatting. They found that FAI participants have the tendency to reduce gluteus maximus and increase rectus femoris activations, which could explain the lower pelvic recline and, consequently, the significantly reduced squat depth.

Because not all the described changes in FAI kinematics and kinetics can be directly related to the impingement, hypotheses regarding the origin of such functional alterations have been proposed. Soft

tissue tightness is one of the hypotheses that is mostly supported (Brisson et al., 2013; Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2011). Great attention was focused on the Iliofemoral ligament and Iliopsoas tendon, suggesting that tightening and motion restriction of these soft tissues could be the cause of reduced hip extension (Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2013), and the presence of herniation pits associated with cam FAI (Daenen et al., 1997; Leunig et al., 2005). Pain inhibition mechanisms have been proposed: increases in range of motion are associated with pain, creating an inhibition response that adapts over time (Brisson et al., 2013; Hunt et al., 2013). However, no hard evidence exists to support either theory. Lastly, muscle weakness was proposed by Casartelli et al. (2011a; 2011b) as cause of functional differences between FAI and control populations. They found reduced muscular strength during maximal isometric voluntary contractions in hip adduction/abduction, flexion and external rotations (Casartelli et al., 2011b), while Lamontagne et al. (2013) only reported a marginal reduction in flexion. This was deemed important especially because FAI is considered an osteoarthritis precursor (Ganz et al., 2003), and is associated with the presence of other pathologies, such as labral tear, for which muscle weakness and altered recruitment patterns have been found (Mendis et al.; Rasch et al., 2007; Sims et al., 2002).

2.1.3. Tissues mechanics

The link between the tissue damages observed during surgical interventions in FAI hips and the altered hip geometry has been investigated with finite element models, by comparing the estimated stress distribution in the cartilages and bones (Chegini et al., 2009; Ng et al., 2012).

A first attempt to represent the cartilage stresses due to FAI alterations was done by Chegini et al. (Chegini et al., 2009). This was a parameterized model where variables like the alpha angle could be adjusted according to the FAI severity. They demonstrated that morphological parameters play a crucial role in minimizing internal stresses, with alpha angles below 50° defining the optimal range, and high von Mises stresses corresponding with the more damaged areas of the acetabular cartilage.

More recently, a validated finite element model applied on subject-specific data (geometry, kinematics and kinetics) of FAI patients confirmed these early findings: during quasi-static loading conditions in standing and maximum squat depth, the peak maximum shear stresses increased in the FAI subjects, and were located at the anterosuperior acetabulum, where acetabular damages were noted during surgery (Lamontagne et al., 2015; Ng et al., 2012). Higher mechanical stimuli might also cause an increased rate of acetabular bone stiffening, also linked to the onset of osteoarthritis (Speirs et al., 2013).

2.2. Musculoskeletal models

Musculoskeletal models constitute a representation of the human body from both the anatomical and physiological points of view. Bone and soft tissue properties are modelled from experimental data, such as cadaveric studies (Friederich and Brand, 1990; Klein Horsman et al., 2007; Ward et al., 2009; Wickiewicz et al., 1983), or medical imaging (Blemker et al., 2007; Scheys et al., 2011; Schmid J. et al., 2009; Valente et al., 2014). If the model has not been built based on the subject-specific imaging, then it must be scaled to match the specific anthropometric characteristics of the participant. The surface marker trajectories are then used to track the motion of the subject, which is typically calculated with an inverse kinematic approach (Lu and O'Connor, 1999). Ground reaction forces are also necessary to estimate the torques acting on the joints (Winter, 2009), which is done through inverse dynamics calculations. Two different types of approaches can lead to muscle force estimation: optimization and EMG-driven (Erdemir et al., 2007). In the following sections, every step of the process will be addressed in more details.

2.2.1. Anatomical model

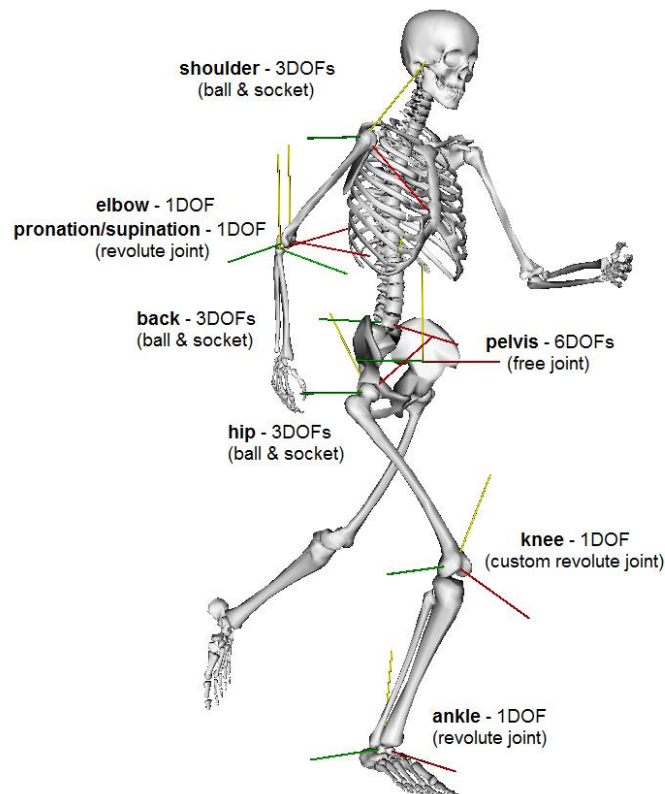


Figure 2-4. Scheme of Hamner's model degrees-of-freedom

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The anatomical model used for a musculoskeletal simulation defines: kinematic properties of the articulations, inertial properties of the body segments, soft tissue attachments and their physiological properties.

The kinematic properties of the articulations outline the type of mechanical joint that can be used to properly represent the kinematics. Information like the joint degrees of freedom and the orientation of the axes are defined. To give an example, the hip is usually modelled as a ball and socket joint, with three degrees of freedom corresponding to flexion/extension, abduction/adduction and internal/external rotation angles, whose axes are oriented according to specific anatomical landmarks (Wu et al., 2002). A detailed review of the joint kinematic models goes beyond the scope of this thesis, but an example of a whole body model is reported in Figure 2-4 (Hamner et al., 2010): 12 segments and 29 degrees of freedom. The hip is modeled as a ball-and-socket joint, the knee is modeled as a complex 1 degree-of-freedom joint as described in Yamaguchi (1989), and the ankle is modeled as a revolute joint. Lumbar and shoulder articulations are modeled as ball-and-socket joints, and the elbow and forearm rotation are each modeled with revolute joints.

The inertial properties of the model characterize the mass and the moment of inertia of the body segments. The inertial properties accuracy is essential for valid kinetic calculation. These are estimated by means of geometrical models (Hanavan Jr, 1964; Hatze, 1980, 2005; Nikolova, 2010; Wicke et al., 2009), cadaveric studies (Dempster, 1955; Dempster and Gaughran, 1967; Drillis et al., 1964), and, more recently, segmented medical images (Bauer et al., 2007; de Leva, 1996; Lee et al., 2009; Mungiole and Martin, 1990; Sheets et al., 2010; Zatsiorsky, 2003).

Similarly, muscle, tendon and ligaments are also modelled from generic anatomical knowledge (Seireg and Arvikar, 1973), cadaveric studies (Brand et al., 1986; Friederich and Brand, 1990; Klein Horsman et al., 2007; Ward et al., 2009; Wickiewicz et al., 1983), or medical images (Blemker et al., 2007; Scheys et al., 2011; Scheys et al., 2009; Valente et al., 2014).

The last aspect described in a musculoskeletal model is the physiological properties of musculotendon actuators. This will be discussed in more details in sections 2.2.5.2 to 2.2.5.4.

SIMM (Motion Analysis), OpenSim (Stanford University) and AnyBody (AnyBody Technology) are three computer applications that enable modelling of musculoskeletal anatomy and dynamic simulation of movement. The main advantage of these tools is the visual representation of bones, muscles, ligaments and other anatomical structures, which allows a quick verification of simulations. The models can be modified and customized for specific analyses to fit the characteristics of real subjects. Following this

trend, add-on tools are being created to automatically transfer patient-specific 3D images into the 3D simulator (e.g., NMSBuilder alpha release from NMSPhysiome).

As Opensim is open-source and free, it offers a repository of freely available models, previously developed and validated by other users, which can be modified according to the specific necessities of the study. A study by Wagner (2013) offers the opportunity to compare the performance of different models available for these platforms, and it shows how substantial variations were observed in the majority of the parameters analyzed, signifying a lack of consistency across models and platforms.

2.2.1.1. *Hip joint center*

Motion analysis and musculoskeletal modelling are highly sensitive to the location of the hip joint center (HJC). Inverse dynamics studies reported differences of up to 22% in hip flexion-extension moments, with discrepancies of 3 cm in HJC location (Stagni et al., 2000). Muscles' capacity to generate moment at the hip joint is most sensitive to vertical displacements of HJC; a 2-cm superior displacement decreases hip abduction moment by about 50% (Delp and Maloney, 1993) and, consequently, leads to inaccurate muscle and hip contact force estimations.

The gold standard to identify HJC is the use of medical images: X-ray, CT, MRI, three-dimensional ultrasound (US), and, more recently, EOS are few examples, with the average accuracy ranging from 0.05 mm of the X-ray method, to the 2.9 mm of the EOS (Kainz et al., 2015).

When medical images are not available, HJC can be estimated with regression equations (Bell et al., 1989; Bell et al., 1990; Davis III et al., 1991; Harrington et al., 2007; Seidel et al., 1995), or functional methods (Camomilla et al., 2006; De Momi et al., 2009; Ehrig et al., 2006; Heller et al., 2011; Leardini et al., 1999; Piazza et al., 2001; Siston and Delp, 2006).

Regression equations are relatively easy to apply since they only require the use of anthropometric measurements (e.g., pelvic width, depth, leg length), but their major limitations are: their dependency on the surface marker placement, the error on the anthropometric measurements, and the intrinsic regression uncertainty. The first two sources of errors are the same for all models, while the latter highly depends upon the population characteristics on which the model has been trained. Therefore, the models' abilities to represent populations with different characteristics (from those on which they have been developed) are often disputed. An early model by Bell (1989) was established from 39 healthy children and 31 healthy adults (Bell et al., 1989; Bell et al., 1990), whereas a conventional model by Davis provided no specific information about the original cohort data as to which the regression equations were developed from (Davis III et al., 1991). Seidel's study later analyzed 65 healthy cadaveric pelves, but the use of pelvic height as predictor prevents the clinical use of this model (Seidel et al., 1995). More recently, a model by

Harrington and associates (2007) examined a mixed population of 14 healthy children, 10 cerebral palsy children, and 8 adults (Harrington et al., 2007). They also investigated the validity of models developed from adult populations when applied to children and young cerebral palsy patients, and found that the prediction errors were similar in all three groups (Harrington et al., 2007). Andersen and colleagues investigated patients who underwent hip resurfacing, where the geometrical features of the pelvis were known to be different from the normal population, and found significant differences in these two groups according to the type of regression equation used (Andersen et al., 2013). Among the available HJC regression models, recent studies showed that Harrington equations provided the highest accuracy, with an average error of 14 to 17 mm (Andersen et al., 2013 ; Sangeux et al., 2011; Sangeux et al., 2014), although this set of equations was developed from a non-homogeneous and relatively small size sample.

When possible, ISB (International Society of Biomechanics) recommends using functional methods (Wu et al., 2002). In fact, functional methods do not rely on the correct placement of markers, and are shown to be more repeatable to inter-trial and inter-operator variability (Besier et al., 2003; Hicks and Richards, 2005; Leardini et al., 1999; Sangeux et al., 2011). Depending on the optimization method, there are two main categories (Ehrig et al., 2006): sphere fitting and transformation techniques. In the sphere fitting approach, a sphere is optimized to fit the trajectories of the markers, and the center constitutes the HJC (Bell et al., 1990; Leardini et al., 1999; Piazza et al., 2001). The transformation techniques are so called because, at every time frame, the local coordinates are transformed into a common reference, and the center of rotation is approximated as the fixed common point between adjacent reference systems (De Momi et al., 2009; Ehrig et al., 2006; Piazza et al., 2004; Siston and Delp, 2006; Speirs et al., 2012). Generic (e.g., walking, squatting) or dedicated (e.g., leg circumduction and swing in different directions) functional tasks are fed to the optimization algorithms to estimate the functional center of rotation, but dedicated functional tasks were shown to perform better (Camomilla et al., 2006; Hicks and Richards, 2005).

In conclusion, when hip calibration movements can be performed by the population under analysis, the functional methods are preferred. In alternative, Harrington regression equations demonstrated excellent accuracy and generalizability, and can be a valid alternative.

2.2.2. Scaling the model

Although there is a growing body of literature about the development and validation of methodologies to automatically construct a musculoskeletal model directly from Magnetic Resonance Images of a subject (Blemker et al., 2007; Scheys et al., 2011; Schmid J. et al., 2009; Valente et al., 2014), it still is challenging from both time and computational perspectives, and not feasible for clinical applications.

Therefore, the generic musculoskeletal models available from repositories are used most of the time. These are usually based on cadaveric data of single average subjects (Delp et al., 1990; Klein Horsman et al., 2007; Modenese et al., 2011). To use the generic models, they have to be adapted to the specific participant's anthropometry: this procedure is usually referred to as scaling, and is crucial for an accurate gait analysis.

The level of complexity in scaling procedures can go from simple linear approaches (Rasmussen et al., 2005) to more complex ones (Lund et al., 2015), and the final results are largely affected by the chosen scaling method (Lund et al., 2015). Software for musculoskeletal analysis usually provides tools that automatically scale the model segments, adjusting inertial properties and muscle properties as well.

The scaling of muscle properties (e.g., like muscle volume, optimal fiber length, tendon slack length) constitutes an even more complex issue since the relationships between such properties and anthropometric measurements are not known. Studies exist that offer a numerical solution to the problem of scaling muscle parameters to subject-specific characteristics (Garner and Pandy, 2003; Hainisch et al., 2012; Lloyd and Besier, 2003; Manal and Buchanan, 2004; Winby et al., 2008), while others try to find significant relationships between muscle volume and body mass and height (Handsfield et al., 2014; Ward et al., 2005), which can be used to scale parameters like the physiological cross sectional area. However, these methods are not fully validated, and the problem of muscle properties scaling is still open.

2.2.3. Inverse Kinematics

Motion capture can be used to derive body kinematics, and a common technique to calculate joint angles consists in decomposing the relative orientation of two adjacent body segments into Cardan angles. In direct kinematics the body orientation is constructed directly from experimental markers coordinates, as described in Wu (2002) and Cappozzo (1995). A minimum of three markers per segment are used to define local reference systems that describe the movement of the body segment in the three-dimensional space. These markers must non co-linear, and are usually joint-defining (e.g., on bony landmarks that identify a joint axis of rotation).

In the inverse kinematic approach introduced by Lu and O'Connor (1999), the experimental markers are tracked by virtual markers placed in a pre-existing kinematic model, by adjusting the joint angles to minimize the tracking error while respecting the joint constraints.

Mathematically, this is obtained by minimizing the tracking error on markers through a weighted least square problem. The equation is reported in equation 2.1, where q is the generalized coordinate vector, x_i^{exp} is the experimental position vector, and $x_i(q)$ is the corresponding marker position vector on the model.

$$\min_q \left[\sum_{i \in \text{markers}} w_i \|x_i^{\text{exp}} - x_i(q)\|^2 \right] \quad 2.1$$

The choice of weights is sensitive for tracking accuracy, and markers that are considered less reliable (e.g., noisy) can have a lower weight and thus less influence on the final result.

The factor $x_i(q)$ in equation 2.1 represents the effect of the joint constraints. Therefore, the kinematic outcomes will depend on the model used to describe the joint kinematics (*i.e.*, the joint constraints). A study by Duprey (2010) compared the outcomes of different sets of joint constraints on the same experimental data, and showed that: 1) the kinematics at one joint are influenced not only by the constraints applied to that same joint, but also to the constraints used in the other joints, and 2) the knee and ankle are more sensitive than the hip to the chosen set of joint constraints.

In inverse kinematics the body reference systems are defined a priori and they might not be aligned with marker-based reference systems, leading to intrinsic kinematic outcomes when comparing results produced with the two approaches. For instance in Delp (1990) and Arnold (2010) the neutral position of the pelvis is set to the anatomical pose, close to the Lewinnek plane (DiGioia et al., 2006), resulting in a forward pelvic tilt of about 14° with respect to the marker based ISB reference system. The introduction of joint constraints aimed to prevent the joint dislocation caused by skin movement artifact in direct kinematics. On simulated lower leg movement from a mechanic linkage with added noise, the use of joint constraints considerably reduced the error on the calculated kinematics (Lu and O'Connor, 1999). However, *in vivo* studies questioned the reliability and accuracy of this method (Andersen et al., 2010a; Stagni et al., 2009). Andersen et al. (2010a) compared the estimated knee angles with bone pin data, and revealed significant differences with both knee joint constraints (spherical or revolute), concluding that the use of those specific knee joint constraints did not reduce the effects of soft tissue artifacts. An even more complete sensitivity analysis was done by Duprey et al. (Duprey et al., 2010), where the influence of all three lower limb joint constraints was analyzed. They demonstrated that knee and ankle non-sagittal angles depend on the chosen set of constraints, while the hip kinematics were less sensitive to the modelling choices.

Despite the discussed limitations, inverse kinematics (in particular, global optimization as defined in Lu and O'Connor (1999)) is becoming a standard in gait analysis, since simulations involving muscle modelling (e.g., muscle force estimation through static optimization, forward dynamics, etc.) requires the a priori definition of joint constraints to maintain anatomical and kinematics consistency in the model.

2.2.4. Inverse Dynamics and Residual Reduction Algorithm

Given the body kinematics and external loads, the net forces and torques at each joint are estimated according to the classical equations of motion (2.2) (Pandy and Andriacchi, 2010), where $M(q)$ is the mass matrix, $C(q, \dot{q})$ is the Coriolis and centrifugal forces, $G(q)$ is the gravitational force, and τ is the vector of generalized forces.

$$M(q)\ddot{q} + C(q, \dot{q}) + G(q) = \tau \quad 2.2$$

Since generalized coordinates and their first and second derivatives are known from the inverse kinematic analysis, as well as the mass properties of the system, the generalized forces can be directly calculated.

However, experimental errors and modelling assumptions cause inconsistency between the measured external loads (i.e., ground reaction forces and moments) and the estimated inverse kinematics. Residual Reduction Algorithm (RRA) has been introduced to reduce these inconsistencies (Delp et al., 2007). The pelvic residual forces are a measure of the model dynamics inconsistency; thus, the ideal result would be null residual forces. RRA refines the kinematics and the mass properties of the model to make it more dynamically consistent. The algorithm is based on the minimization of the cost function reported in equation 2.3, where $\ddot{q}_i^{\text{exp}}$ and $\ddot{q}_i^{\text{sim}}$ are the experimental and simulated accelerations of the i^{th} generalized coordinate; $w_{\ddot{q}_i}$ are the weights assigned to the kinematic component of the object function; R_j are the residual forces/torques of the j^{th} degree of freedom, function of the driving excitations x_j^R and normalized by the maximum residual forces/torques R_j^{max} ; T_k are the joint torques of the k^{th} degree of freedom of the model, function of their driving excitation x_k^T , and normalized by the maximum torques T_k^{max} .

$$J(x) = \min_{x^R, x^T} \left[\sum_{i=1}^{n_q} w_{\ddot{q}_i} (\ddot{q}_i^{\text{exp}} - \ddot{q}_i^{\text{sim}})^2 + \sum_{j=1}^6 \left(\frac{R_j(x_j^R)}{R_j^{\text{max}}} \right)^2 + \sum_{k=1}^{n_T} \left(\frac{T_k(x_k^T)}{T_k^{\text{max}}} \right)^2 \right] \quad 2.3$$

RRA may alter the original kinematics to create a more dynamically consistent simulation. This behaviour may be pursued (Donnelly et al., 2012) if we decide to place the experimental error in the kinematics, or rejected if we accept the presence of experimental error in the dynamics calculations.

2.2.5. Muscle force estimation

Muscle and joint contact forces cannot be easily estimated because of the muscle redundancy problem (larger number of actuators than degrees of freedom). *In vivo* measurements of joint contact forces on

humans are only possible with instrumented prostheses (Brand et al., 1994; Davy et al., 1988; Heller et al., 2001; Kim et al., 2009; Lu et al., 1998; Stansfield et al., 2003), but the obtained joint contact forces are representative of a pathological articulation, and the prosthesis per se adds different material properties and mechanical behavior that is likely to alter the loading condition with respect to a healthy joint. Since *in vivo* measurements of the muscle forces are ethically and technically challenging (Komi et al., 1996; Pourcelot et al., 2005), muscle forces are usually estimated through musculoskeletal models.

Two different types of approaches can be used to estimate muscle forces: optimization and EMG-driven (Erdemir et al., 2007).

2.2.5.1. Optimization models

In the optimization models, the muscle redundancy is solved by optimizing a cost function, assuming that the central nervous system employs optimal activation patterns to develop motion (Prilutsky and Zatsiorsky, 2002; Rasmussen et al., 2003). An inverse or forward dynamic approach can be chosen, depending on the available data and the aim of the study (Pandy, 2001).

Static optimization

In the inverse dynamic approach, static optimization uses joint torques from inverse dynamics to estimate muscle forces frame by frame. This method was introduced for the first time by Seireg and Arvikar, and Penrod in the early '70 (Penrod et al., 1974; Seireg and Arvikar, 1973), initially as a proof of concept, and later as an applied study.

The cost functions (J) vary according to the movement being modelled, and the constraint function imposes the equality between the external torque (from the inverse dynamics solution) and the internal torque (from muscle forces). Sometimes, additional constraints may be used (such as, maximal muscle force, imposing a compressive joint load) to limit the estimated muscle forces within physiologically reasonable limits.

The most common cost functions are: sum of muscle forces, or n th power of muscle forces, sum of muscle stresses or n th power of muscle stresses (Equation 2.4) (Crowninshield and Brand, 1981; Crowninshield et al., 1978; Glitsch and Baumann, 1997).

$$\min J((F^i)^n)$$

or

$$\min J\left(\left(\frac{F^i}{A^i}\right)^n\right)$$

2.4

In general, increasing the power produces the effect of avoiding extreme stress differences among the muscles. For the lower limbs, Crowninshield (1981) found that the sum of cubic muscle stresses gives acceptable results in walking and running simulations, improving convergence with EMG profiles and co-contraction. According to Glitsch (1997), a power of two gives the best correspondence between muscle forces and EMG signals.

Even if joint contact loads are not very sensitive to small changes in the power used in the cost function (Crowninshield and Brand, 1981), a single muscle force can vary up to 50% when the power changes (Glitsch and Baumann, 1997). Using muscle stress instead of muscle force in the cost functions gives lower and more physiologically sound muscle peaks (Glitsch and Baumann, 1997).

As mentioned before, EMG profiles are often used to validate the results from the static optimization, since they do not constitute the input of the model (Crowninshield and Brand, 1981; Crowninshield et al., 1978; Glitsch and Baumann, 1997).

Since static optimization models are relatively inexpensive from a computational point of view, it is common to operate sensitivity analyses on cost functions (Glitsch and Baumann, 1997), or muscle parameters (Brand et al., 1986; Herzog, 1992). From these studies it is shown that physiological cross-sectional area is the most sensitive parameter for static optimization problems, followed by muscle moment arms and the other neuromuscular parameters. However, the level of sensitivity to a parameter also depends on the type of formulation/method being used.

Even by introducing some nonlinearities (squared or cubic cost functions), static optimization is usually not computationally expensive and, consequently, is widely used even in more recent studies (Erdemir et al., 2007; Lin et al., 2010; Modenese and Phillips, 2011).

Dynamic optimization

An alternative to static optimization is the dynamic optimization approach, which employs forward dynamics simulations to solve the optimization problem (Neptune and McGowan, 2011; Piazza, 2006; Steele et al., 2010; Thelen and Anderson, 2006). From an initial set of neural activation patterns, muscle forces are estimated in a forward fashion; muscle forces mobilize the body segments and the resulting

kinematics and kinetics are compared with the experimental measurements of motion and moments of force (Erdemir et al., 2007). The muscle activations are iteratively updated to closely match experimental results. The deviation of the model variables (q) with respect to the experimental data (q_{exp} , which could be joint angles, ground reaction forces, etc.) constitutes the cost function J for the optimization algorithm (McLean et al., 2003; Neptune et al., 2001) (equation 2.5).

$$\min J(q - q_{exp}) \quad 2.5$$

Sometimes, additional criteria similar to those used in static optimization are included to further reduce the dimensionality of the solution space (*e.g.*, minimizing metabolic energy consumption, muscle fatigue, muscle timing) (Anderson and Pandy, 2001a; Davy and Audu, 1987; Neptune and Hull, 1998; Yamaguchi and Zajac, 1990). For example in Equation 2.6 (Yamaguchi and Zajac, 1990), the cost function J is also depending on muscle stresses ($\frac{F^i}{A^i}$, where F^i is the muscle force, and A^i is the physiological cross-sectional area).

$$\min J \left(w_{exp}(q - q_{exp}), w_{muscle\ stress} \left(\frac{F^i}{A^i} \right) \right) \quad 2.6$$

In fact, multiple solutions (a.k.a., muscle activation sets) may exist leading to the same experimental outputs, and additional constraints reduce the solution space. These models have an objective function made of multiple cost functions, and the solution will highly depend on the choice of weights (w_{exp} and $w_{muscle\ stress}$). In Yamaguchi (1990), for example, the model used angular displacements and velocities as variables (q), and muscle fatigue as additional cost function (modelled as cubed muscle stresses). The addition of cubed muscle stresses was introduced to better predict muscle co-activations. Different weights for angular displacement, velocities and muscle stresses were set because the outputs were not equally sensitive to these variables.

Since the output of dynamic models is muscle activation patterns, it is reasonable to use EMG profiles to validate the model (Davy and Audu, 1987; Neptune and Hull, 1998; Yamaguchi and Zajac, 1990). Differently than static optimization where the outputs are muscle forces which can only be qualitatively compared to EMG, in this case the comparison can be quantitative.

Differently than in the static optimization, muscle dynamics equations (section 2.2.5.3) are included in the model. This causes the models to be time-dependent because muscle dynamics involve first and second order derivatives. Consequently, the optimization cannot be completed frame by frame (like in the static optimization), but involves the whole movement, making the algorithm more computationally

demanding than static optimization, even though less sensitive to the measurements errors (kinematics or kinetics).

However, comparative studies revealed how muscle force estimates obtained from static or dynamic optimization algorithms are very close (Anderson and Pandy, 2001b; Lin et al., 2012). Therefore, unless the analysis specifically requires dynamics optimization approaches, using static optimization methods is recommended, because it is computationally less expensive.

Optimal control

A third type of optimization approach is the optimal control. When experimental data for a specific type of movement are not available, the optimal muscle activations can be estimated through forward dynamics approach by imposing a task-related constraint (e.g., max jump height) (Anderson and Pandy, 2001a; Neptune, 1999). This approach is used in predictive simulations but it is not convenient for movements that do not have a clear performance criterion (e.g., walking).

Cost functions aim to optimize quantities such as muscle stress, muscle fatigue, metabolic energy expenditure, movement performance (time, speed, height), or combinations of these factors (Prilutsky and Zatsiorsky, 2002; Rasmussen et al., 2003), and the appropriateness of the objective function depends upon the application and the functional task. When applying different objective functions to the same problem and set of data (*i.e.*, initial conditions and boundaries), it is also shown that different optimum criteria lead to different muscle force patterns, but can result in similar solutions, which equally agree with the experimental data (*i.e.*, movement pattern) (Pandy et al., 1995). This non-uniqueness of the problem (multiple performance criteria for the same optimal control solution) is a limitation for predicting muscle forces. In fact, ‘correct form’ of the optimum criterion is unknown, and different solutions are equally valid in reproducing a movement pattern (Fregly et al., 2012; Pandy and Andriacchi, 2010). Moreover, the basic assumption that the central nervous system selects activation patterns based on optimality criteria is not acceptable when there are external factors altering the musculoskeletal system, such as injuries or pathologies (Buchanan et al., 2004).

An important drawback that is common to all the types of optimization model is the poor ability in predicting muscle co-contractions (Herzog and Binding, 1992). For example, it has been mathematically demonstrated that the static optimization model proposed by Crowninshield (1981) cannot predict co-activation of antagonistic pairs for one-joint muscles, but only for biarticular muscles (Herzog and Binding, 1993). Yamaguchi’s study on dynamic optimization purposely introduced the minimization of muscle fatigue to enable the prediction of co-contraction, but assigned a null weight to this component of

the cost function because the chosen set of muscles was not sufficient to predict co-contraction (Yamaguchi and Zajac, 1990).

The reason of this limitation is quite complex; first, it is not conceptually correct to artificially impose co-contraction constraints to the model because the main objective of optimization models is investigating optimal control criteria, and imposing constraints would interfere with this purpose (Herzog and Binding, 1992), even if the results of the model are closer to the experimental measurements (Brookham et al., 2011). Some degrees of synergic muscle activation can be reached by introducing nonlinearities into the optimization functions, but the level of predicted co-contraction does not seem to comply with the experimental results. Differences in synergistic force production between experimental and theoretical data appear to be mostly related to muscle properties (*i.e.*, fiber composition, physiological cross-sectional area, moment arms) (Herzog and Binding, 1992; Herzog and Leonard, 1991), and degrees of freedom of the analyzed model (Herzog and Binding, 1992; Jinha et al., 2006). For example, for a model using the “minimum fatigue criterion”, large muscles and muscles with higher percentage of slow twitch motor unit fibers are always favored to small muscles and muscles with higher percentage of fast motor unit fibers, respectively (Herzog and Leonard, 1991). Also, force sharing changes with locomotion speed as consequence of a change in the central control of activations. If these speed-control relations were to be known, synergistic activations could be more easily predicted (Herzog and Leonard, 1991).

This is a very important issue because co-contraction mechanisms are fundamental in determining joint stability (Smith et al., 2012), contribute largely to total joint contact forces, and their alteration can be the first sign of the onset of a pathological condition (Herzog and Longino, 2007; Rutherford et al., 2011).

2.2.5.2. *Electromyography-driven musculoskeletal models*

EMG-driven models use the EMG profiles to define the activation patterns. Thus, the control strategy of the neuromuscular system is not estimated but is given as experimental input. This is an appealing approach if the main focus of the study is not on control strategies but on the prediction of muscle and joint contact forces based on experimental muscle activations.

EMG-driven models follow a forward dynamics approach: from EMG to muscle forces, then joint torques, and, potentially, body kinematics. Depending on the researcher's choice, EMG-driven models can have different degrees of complexity according to the desired physiological accuracy. The simplest model is a fitting function between input (*i.e.*, EMG data) and output (*i.e.*, joint torques or angles) variables (Amarantini and Martin, 2004; Winters and Stark, 1987), which are generally referred to as ‘black box’ models because the fitting function does not take into consideration the internal

variables/status of the system. However, such models are not generalizable to a wide range of conditions (*e.g.*, walking or running), and the parameters usually do not have any physical meaning, but are only mathematical entities. To obtain a more robust model with measurable parameters, the underlying physiological structure needs to be represented.

According to Erdemir (2007), Hof's study published in 1981 is one of the first examples that include the three main descriptors of the internal status of the musculoskeletal system: activation dynamics, contraction dynamics and anatomical geometry (Hof and Van den Berg, 1981). This study has inspired a trend of research on musculoskeletal modelling that seems to be very successful in predicting realistic muscle forces and joint torques (Benoit and Dowling, 2006; Bogey et al., 2005; Buchanan et al., 2004; Fregly et al., 2012; Higginson et al., 2012; Koo and Mak, 2005; Lloyd and Besier, 2003; Manal and Buchanan, 2013; Manal et al., 2002; Sartori et al., 2012).

Muscle activation dynamics

The muscle activation dynamics governs the transformation from the EMG signal to a measure of muscle activation, $a(t)$, that varies between 0 and 1. The concept of *active state* was originally proposed by Hill (Hill, 1938), but it was only a qualitative concept, referring to a generic internal state of the muscle when it is capable of producing force. Gradually this term assumed a more concrete meaning linked to the relationship between force and stimulation history, trying to model phenomena like tetanus and twitch. After studies about the rate-limiting role of Calcium dynamics in muscle contraction, the concept of active state was definitely related to the amount of Calcium bound to troponin filaments, even though this assumption is not measurable (Winters, 1990). Different equations have been proposed to reproduce the three fundamental features of muscle activation dynamics: faster time constant in excitation than in relaxation (Hill, 1938; Zajac, 1989), twitch response to short burst (Hof and Van den Berg, 1981), and summation effects in response to a series of impulses.

Hof et al. proposed a model in 1981 that is well described in (Hof and Van den Berg, 1981), where the muscle activation is function of the rectified and filtered EMG. However, this was a non-continuous function, not computationally convenient for function derivatives. Indeed, this equation is not widely used in more recent models, and only Koo and colleagues (Koo and Mak, 2005) employed an equivalent formulation.

The most common filter used to model the muscle activation dynamics $a(t)$ is a first-order linear differential equation (2.7) that well reproduced the excitation and relaxation behavior (He et al., 1991; Zajac, 1989), where $e(t)$ is the rectified and filtered EMG, and τ_{act} is the activation time constant, and $\beta = \tau_{deact}/\tau_{act}$, which is the ratio between deactivation and activation time constants.

$$\frac{da(t)}{dt} + \left[\frac{1}{\tau_{act}} (\beta + (1 - \beta)e(t)) \right] a(t) = \frac{1}{\tau_{act}} e(t) \quad 2.7$$

Other second-order formulations have been used according to Milner's study (1973), where the muscle activation dynamics were described with a critically-damped second order filter. The discretized version of this formulation can be found in (Buchanan et al., 2004), and the time constant d was used, which is the electromechanical delay, defined by Corcos as the 'time between the first discernible electrical activity in a muscle and the first detectable mechanical response', reported to range between 10 and 100 ms (Corcos et al., 1992).

Whether or not the rectified and filtered EMG is a good approximation of the muscle activation is not clear yet. Some researchers think so because, under isometric or quasi-static conditions, the relationship between EMG and force production is considered linear (Lawrence and De Luca, 1983; Lippold, 1952; Woods and Bigland-Ritchie, 1983). However, since the nervous system distinguishes between the twitch and the tetanic response, it is reasonable to introduce nonlinearities in the dynamics. Activation dynamics formulations that introduced nonlinearities can be found in Lloyd et al. (2003), Manal et al. (2003; 2002), and Buchanan et al. (2005).

These models are difficult to validate, therefore, it is not possible to define which relationship produces better results when muscular activation patterns are used to estimate muscular forces.

Muscle contraction dynamics

Muscle contraction dynamics link muscle activation $a(t)$ and force production. These dynamics can be approached from a microscopic or macroscopic perspective, according to the level of physiological detail needed in the study. Huxley's model gives a microscopic insight on the cross-bridge theory, simulating the sliding filament as distributed parameters and requiring partial differential equations. It describes important relations between mechanical, energetics and chemical kinetics in muscles, but it gets extremely complex if the final purpose is describing the macroscopic neuromusculoskeletal behaviour (Zahalak, 1990b). On the other hand, Hill's phenomenological model reproduces the macroscopic behaviour of the muscle contraction through lumped parameters and uses ordinary differential equations (Winters and Stark, 1987; Zahalak, 1990a). Even if some basic assumptions are unrealistic, this model found general acceptance because of its simplicity and the possibility of identifying its parameters through easy experiments. Consequently, Hill model (Hill, 1938) is usually employed and recommended for neuromusculoskeletal modelling problems (Buchanan et al., 2004; Winters and Stark, 1987), and it will be discussed in the following paragraph.

2.2.5.3. Hill model

Hill model consists of a contractile element (CE) in parallel with a passive element (PE) (Figure 2-5). A basic assumption is that the force produced by Hill model (F^M) depends only on the current fiber length (l^M), velocity (v^M) and activation ($a(t)$). Sometimes the model also includes another series elastic element (SEE) that represents the elastic properties of the muscle fibers (located in the cross-bridges) distinguishable from tendon elasticity. However, structural considerations and experimental evidences suggest to discard this SEE and to assign its role to the tendon exclusively. In fact, connective tissues surround the muscle fibers, and the muscle fibers also contain viscoelastic components such as structural proteins, membranes and longitudinal intermediate filaments (Rode et al., 2009). PE is a representation of these structures and, consequently, it depends on contractile components of the muscle (fibers) rather than on the whole musculotendon actuator length. Cross-bridges and Z-lines are also elastic components that could be the structural counterpart of SEE; however, the tendon elasticity dominates over these two elements that, consequently, can be discarded with negligible error. Moreover, if SEE is included in the model, the homogeneity properties between the sarcomere and muscle fiber that allow the extension of the mechanical properties of the single sarcomere to the whole muscle fiber do not hold (Winters, 1990; Zajac, 1989). Lastly, the model arrangement without SEE seems to represent experimental data more accurately (Rode et al., 2009).

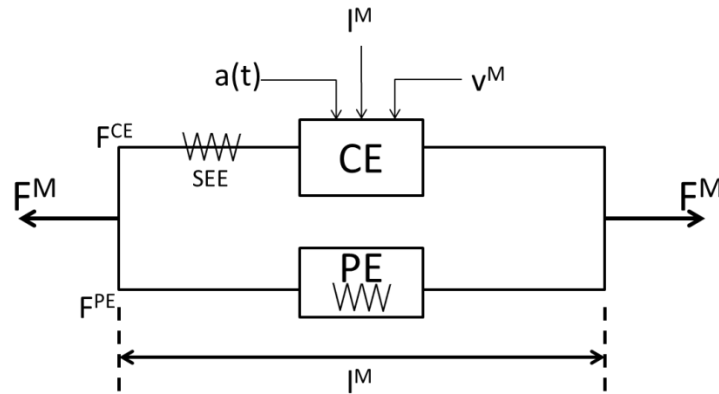


Figure 2-5. Hill model for contraction dynamics

F^M is the total muscle force, F^{CE} and F^{PE} are respectively the active and passive forces produced by the active (CE) and passive (PE) structures. F^{CE} depends on the muscle fiber length l^M , velocity v^M and activation $a(t)$. The series elastic element (SEE) is optional in some models

Force-length (F-L) property

Under isometric conditions muscle fibers develop a steady force. If the fiber is inactive ($a(t) = 0$), the developed force is the passive muscle force, given by the elastic properties of myofibrils (note that the tendon is not considered yet). The passive component is not dependent upon the muscle activation. The difference between the force developed when the fiber is at full activated ($a(t) = 1$) and the passive

component returns the active muscle force. The active muscle force is generated when $0.5l_0^M < l^M < 1.5l_0^M$, where l_0^M is defined as the *optimal muscle fiber length* (Zajac, 1989). At $l^M = l_0^M$, the muscle force is equal to the maximal active force ($F^M = F_0^M$, where F_0^M is the maximal active force). This property is coherent with the sliding filament theory (Gordon et al., 1966). In fact, the amount of force produced is proportional to the number of active cross-bridges and, therefore, to the overlap between the thick and thin filaments. When this overlap is optimal, the number of active cross-bridges is maximal, allowing for the maximal force production. Any deviation from the optimal overlap (i.e., *optimal muscle fiber length*) will decrease the force produced.

The F-L properties of a non-fully activated muscle were modeled by Zajac as a scaled version of the fully activated one (Zajac, 1989). However, more recent studies showed that l_0^m is not constant but depends on the activation level. This property was modeled by Lloyd et al. as reported in Figure 2-6 (Lloyd and Besier, 2003).

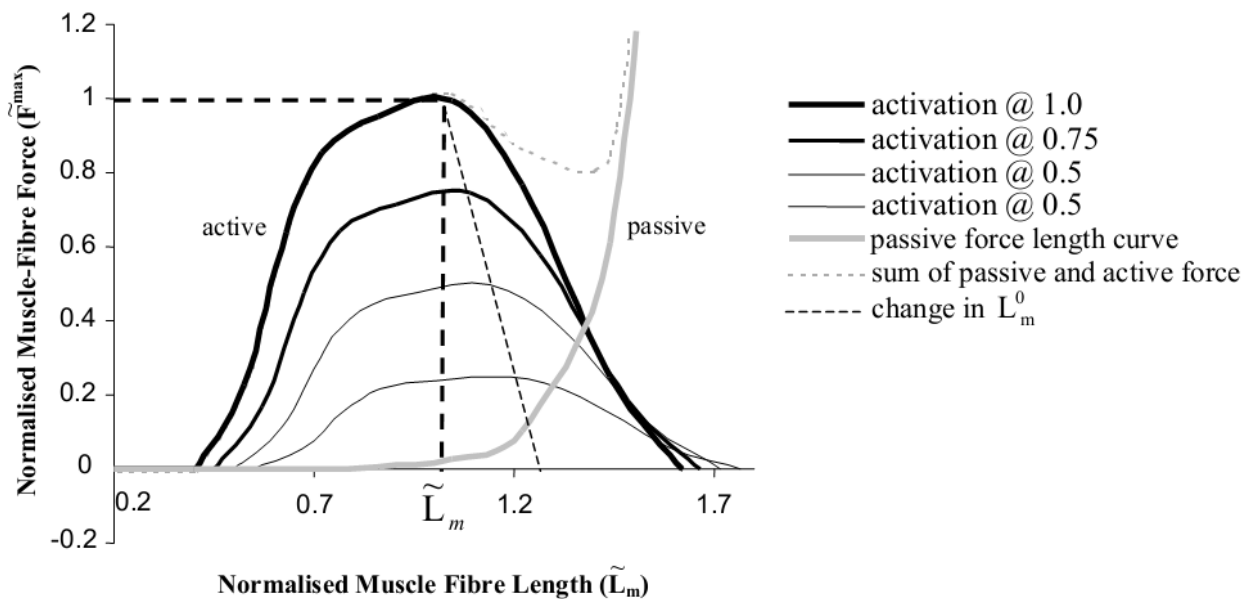


Figure 2-6. Muscle active and passive force length curves

Force and length are normalized by the maximal isometric muscle force and the optimal fiber length respectively. Reprinted from Lloyd, David G., & Besier, Thor F. (2003). An EMG-driven musculoskeletal model to estimate muscle forces and knee joint moments *in vivo*. *Journal of Biomechanics*, 36(6), 765-776 with permission from Elsevier

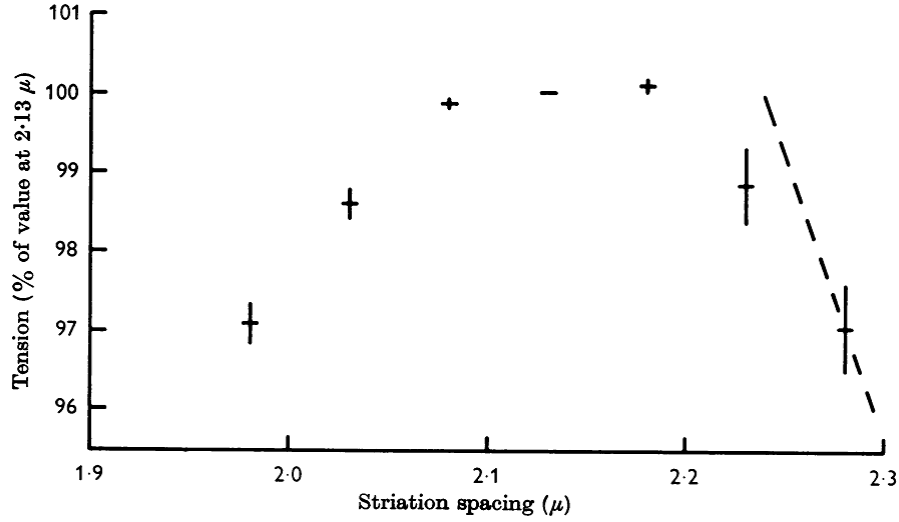


Figure 2-7. Original data points for muscle active tension in frogs

Average and standard deviation of the active tension developed at sarcomere striation spacings near optimum. The dashed line interpolates the data with a zero tension at a striation spacing of 3.65 μ. Reproduced from Gordon, A.M., Huxely, A.F., & Julian, F.J. (1966). The variation in isometric tension with sarcomere length in vertebrate muscle fibers. *Journal of Physiology*, 185, 170-192

Zajac created a dimensionless model of the F-L passive and active properties which is applicable to every muscle and is scalable by using the muscle-specific parameters of maximal isometric muscle force (F_0^M) and the optimal fiber length (l_0^M). Consequently, the isometric muscle force is given by the sum of scaled active and passive components (equation 2.8).

$$F^M = F_A^m + F_P^m = f_A(l)F_0^m a(t) + f_P(l)F_0^m \quad 2.8$$

The active F-L property $f_A(l)$ is usually modeled through a cubic spline that interpolates the experimental data from frog muscles found by Gordon (Gordon et al., 1966) (Figure 2-7).

The passive F-L property $f_P(l)$ is modeled with equation 2.9, where $\tilde{l}^m$ is the muscle length normalized by the optimal muscle fiber length l_0^m (Schutte, 1992).

$$f_P(l) = \frac{e^{10(\tilde{l}^m-1)}}{e^5} \quad 2.9$$

Force-velocity (F-V) property

One of the main finding from Hill model is the hyperbolic force-velocity (F-V) equation governing muscle contractions. Hill developed the equation starting from the study of thermodynamic effects of muscle contraction. However, the relationship properly fitted results from mechanical testing on muscle

tissues and independent studies conducted around 1950 found data compatible to the Hill hyperbola (Winters, 1990).

The original formulation of the F-V equation was $(F^M + a)(v^M + b) = (F_0^M + a)b$ that can be rewritten like in equation 2.10, where v^M is the contraction velocity, a and b are two constants.

$$F^M = \frac{F_0^M b - av^M}{v^M + b} \quad 2.10$$

Other formulations are reported in (Winters, 1990) and more recent works modelled F-V behavior in both concentric and eccentric conditions (Lan, 2002). However, according to Winters, “many curve shapes can be estimated from the same human testing dataset. [...] Results not following a Hill like shape must be contrasted with the dozens of results, ranging from isolated fibers through whole muscle to muscle joint systems, where the Hill hyperbola has been a good fit for shortening muscle” (Winters, 1990).

The intercept between F-V curve and $F = 0$ gives the velocity at which no tension can be sustained (v_m in Figure 2-8). Even though the sliding filament theory predicts that v_m is independent of length and activation, empirical data seem to demonstrate the opposite for working conditions far from optimal fiber length and fully activation, with consequences on the F-V equation (Zajac, 1989). However, according to Zajac, these conditions are not functionally important because muscles never work in that operational range.

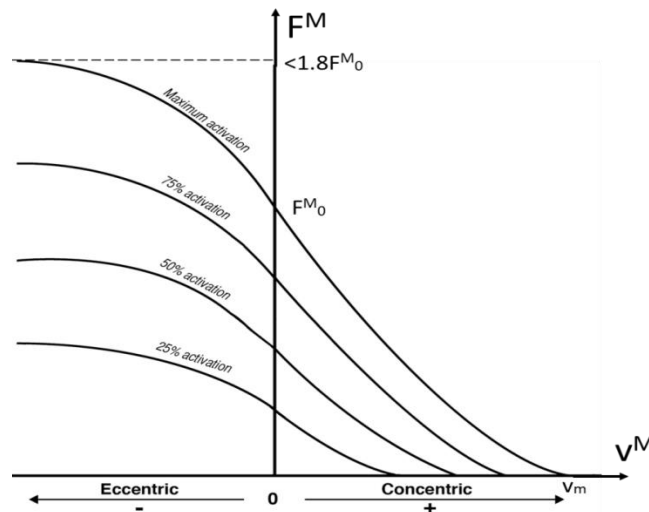


Figure 2-8. Muscle force-velocity curves

Force- velocity relationship of muscle tissues under different activation conditions when fibers are at the optimal fiber length. The maximum force production in eccentric condition is 1.8 times the maximal isometric force, while the force production is null at the maximum shortening velocity v_m

A dimensionless version of F-V curve is also given in (Zajac, 1989). The velocity axis is scaled to the maximum shortening velocity of the muscle ($v_m = l_0^M / \tau_c$), and the force axis to the maximal isometric muscle force (F_0^M). The dimensionless curve is assumed to be valid for every muscle even though this is a rough approximation because fast and slow muscle tissues have different F-V curves (Zajac, 1989). τ_c can be calculated as the ratio between optimal fiber length and maximum shortening velocity, known from experimental data. For fully activated mixed fibers muscles, $v_m = 10l_0^M / s$, therefore, $\tau_c = 0.1s$.

The F-V property described so far is only valid during shortening (concentric contractions), when the muscle works as a power producer. However, some motor tasks may require power absorption of the potential or kinetic energy of the body, such as during descending phases of jumps. Since the energy lost to friction in joints or contact forces is little, muscles cooperate with ligaments and cartilages to absorb this power. This implies that the F-V curve has to include the lengthening condition when the muscle is under tension (eccentric contraction) (Zajac, 1989). Equation 2.11 describes this property, where a' and b' are interpolation parameters, v^M is the fiber lengthening velocity and F_{ECC}^M is a value accounting for the maximum eccentric force, which varies between $1.1F_0^M$ and $1.8F_0^M$ (Buchanan et al., 2004; Winters, 1990; Zajac, 1989).

$$F^M = \left(F_{ECC}^M F_0^M - (F_{ECC}^M - 1) \frac{F_0^M b' - a' v^M}{-v^M + b'} \right) f(l) \quad 2.11$$

Since F-L and F-V curves are obtained under different experimental conditions, F-L and F-V relationships could not theoretically be associated. However, studies demonstrated that there is a direct relationship between F-L and F-V curves: length trajectories can be obtained by integrating the inverted F-V equation (Zajac, 1989), and experimental evidences supported this finding (Winters, 1990). This means that the muscle behavior can now be modeled with a three-dimensional F-L-V relationship that includes both properties. To do so, Epstein and Herzog proposed equation 2.12, which is similar to 2.10 but scaled by the normalized F-L equation (Buchanan et al., 2004). This equation respects the assumption that v_m is independent of length and activation because $v_m = F_0^M \frac{b}{a} = \text{constant}$ when $F^M = 0$.

$$F^M = \frac{F_0^M b - a v^M}{v^M + b} f(l) \quad 2.12$$

Many other equations for modelling force-length and force-velocity relationships can be found in the literature (Brown et al., 1999; Chen and Ren, 2010; Durfee and Palmer, 1994; Siebert et al., 2008), but a detailed review of this subject goes beyond the scope of this literature review. Two different

implementations of Hill muscle models are freely available from the OpenSim repository, and refer to the work of Thelen et al. (2003) and Millard et al. (2013).

2.2.5.4. Tendon properties and pennation angle

The Hill model described so far only defines the muscle fiber properties. However, the musculotendon actuator (MTA) behaviour is highly influenced by the tendon mechanical properties. Tendon and muscle fibers are modeled as two elements in series within the MTA (Figure 2-9). Consequently, the force transmitted by the musculotendon structures (F^{MT}) to the tendon (F^T) is the same ($F^{MT} = F^T$), and the strain is dependent on the mechanical compliance properties of both elements.

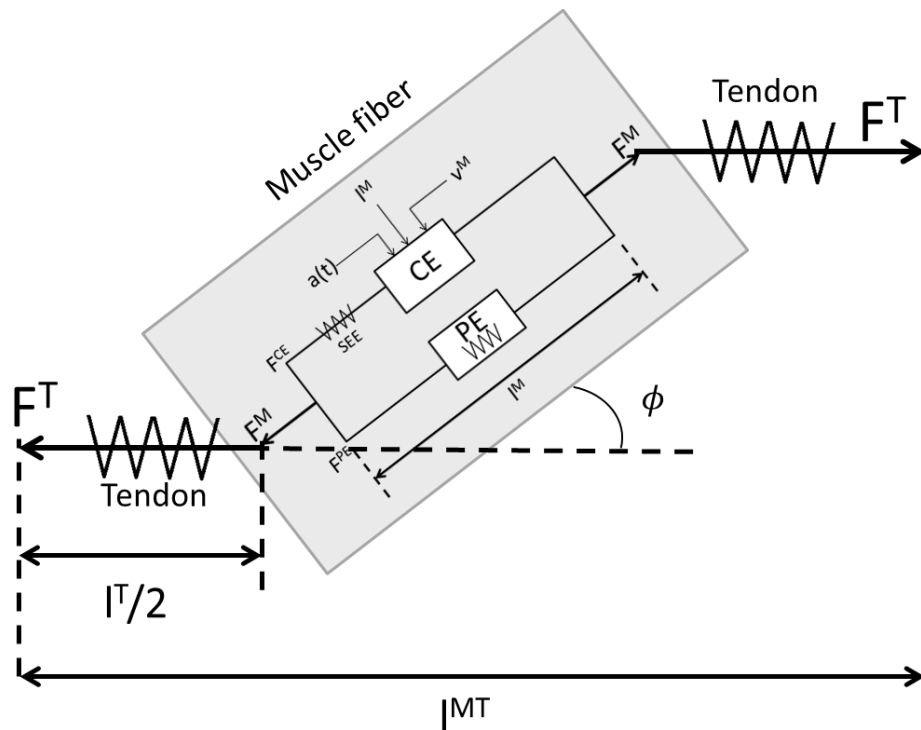


Figure 2-9. Schematic of musculotendon actuator

Muscle fibers are represented in series with the tendon, inclined of an angle ϕ (pennation angle). The total length of the musculotendon actuator is l_{MT} , while the muscle fiber length is l_M and the tendon length is l^T . The gray area reports the schematic of Figure 2-5 for the muscle fiber

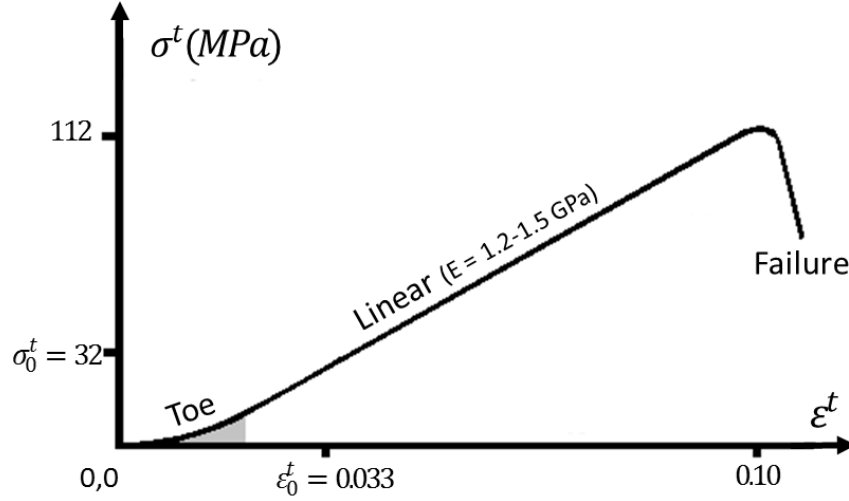


Figure 2-10. Material properties of tendon

The curve represents the nominal stress and strain curve (σ^t vs ϵ^t). In the linear region the elastic modulus is $E = 1.2-1.5$ GPa

In modelling, the viscous material properties of tendons are usually neglected and it is considered as a nonlinear elastic material. The nonlinear tendon stress-strain curve can be described by three different regions: the ‘toe region’ where the elastic modulus increases with strain (0-2%), a linear region with a constant elastic modulus of 1.2-1.5GPa (2-10%), and the failure region (>10%) (Figure 2-10) (Zajac, 1989). The tendon works mainly on its nonlinear region during most daily activities where physiological loading strains the tendon at about 3% (Finni, 2006).

Specific tendons’ force-strain curve can be estimated by scaling a generic curve with two parameters: maximal active force (F_0^M) and tendon slack length (l_s^t , length of the tendon when tendon force is null, $F^T = 0$) (Zajac, 1989). Tendon strain is defined as $\epsilon^t = (l^t - l_s^t) / l_s^t$. Studies suggest that an appropriate value for ϵ_0^t is 3.3%, where ϵ_0^t is the strain corresponding to the tendon stress of 32MPa that occurs at $F^T = F_0^M$ (Zajac, 1989).

Analytical descriptions of tendon stress-strain properties exist based on these data: equation 2.13 is a piecewise curve introduced by Buchanan et al. based on Zajac’s data (Buchanan et al., 2004). Equations 2.13 a-b) define the behavior of the tendon in the toe region, and equation 2.13 c) in the linear region. $\tilde{F}^t$ represents the tendon force normalized by F_0^M , while F^t is the tendon force (equation 2.13 d).

$$\begin{aligned}
 \tilde{F}^t &= 0 & \varepsilon &\leq 0 & 2.13 \text{ a)} \\
 \tilde{F}^t &= 1480.3\varepsilon^2 & 0 < \varepsilon < 0.0127 & & \text{b)} \\
 \tilde{F}^t &= 37.5\varepsilon - 0.2375 & \varepsilon &\geq 0.0127 & \text{c)} \\
 F^t &= \tilde{F}^t F_0^m & & & \text{d)}
 \end{aligned}$$

The tendon model completes the MTA force production model and the total force produced by the MTA can be modelled by equation 2.14.

$$F^{mt} = F^t = [F_A^m + F_P^m] \cos(\phi) = [f_A(l)f(v)a(t)F_0^m + f_P(l)F_0^m] \cos(\phi) \quad 2.14$$

In equation 2.14, $a(t)$ is the muscular activation from the activation dynamics. F_0^m is the maximum isometric muscle fiber force, while F_A^m and F_P^m are the contribution of the contractile (active) element and the elastic (passive) component, respectively. $f_A(l)$ represents the active force-length relationship. ϕ represents the pennation angle, which is the angle between the tendon and the muscle fibers. The pennation angle has the effect of amplifying length change and reducing force change.

Whether the pennation angle model improves the accuracy of the muscle force estimation or not is debated. Some studies suggest that neglecting the pennation angle contribution gives better muscle force estimates (Scott and Winter, 1991), others that the pennation angle can be neglected if less than 20° (Zajac, 1989). However, cadaveric studies demonstrated that several lower limb muscles have an average pennation angle larger than 20° (Ward et al., 2009; Yamaguchi et al., 1990).

2.2.6. Parameters sensitivity

As it has been described in the previous paragraphs, muscle models include several physiological and anatomical parameters. These are usually measured or estimated from cadaveric studies (Klein Horsman et al., 2007; Ward et al., 2009; Wickiewicz et al., 1983; Yamaguchi et al., 1990) or *in vitro* physiological experiments (Gordon et al., 1966; Hill, 1938). Average values are employed for modelling purposes, even if parameters can significantly change among people.

Some anatomical parameters can be measured *in vivo* from ultrasound (Gerus et al., 2012; Li and Tong, 2005; Manal et al., 2010), Magnetic Resonance Imaging (Blemker et al., 2007; Hainisch et al., 2012; Tsaopoulos et al., 2006) or computed tomography scans (McGill et al., 1996). These parameters are: physiological cross sectional areas (Lee et al., 2012), fiber lengths (Li and Tong, 2005), tendon material properties (Gerus et al., 2012), pennation angles (Li and Tong, 2005), moment arms (Manal et

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al., 2010; McGill et al., 1996; Tsaopoulos et al., 2006), and muscle architecture in general (Blemker et al., 2007).

Parameters that cannot directly be measured, such as tendon slack length, optimal muscle fiber length or peak isometric force, can be functionally estimated by using numerical and optimization methods (Garner and Pandy, 2003; Hainisch et al., 2012; Manal and Buchanan, 2004).

Parameters from the muscle activation dynamics have almost no physical counterpart; thus, the boundaries of their values are based on mathematical considerations (*e.g.*, equation stability criteria) (Buchanan et al., 2004).

Sensitivity analyses show that muscle force estimates change considerably with parameters. Some comprehensive studies on how parameters affect muscle force and torque production showed that tendon slack length is the most sensitive parameter, followed by optimal fiber length and maximal isometric force, while the physiological cross-sectional area is the least sensitive (De Groote et al., 2010; Redl et al., 2007; Scovil and Ronsky, 2006).

The parameters' accuracy of muscles that contribute less to the total force production is less critical; in particular, De Groote's study revealed that joint torque sensitivity to Tensor Fasciae Latae, Biceps Femoris Caput Brevis, Gracilis and Sartorius parameters is low and negligible when studying the knee joint contact force. No similar study has been found to verify which muscles are negligible with respect to the hip joint contact force.

Parameters' sensitivity also depend on the type of model (De Groote et al., 2010): static optimization problems are less sensitive to parameter variations than dynamic optimization models, because they do not rely on activation dynamics, and use contraction dynamics only for calculating instantaneous muscle force.

Lastly, sensitivity depends on the type of task. Depending on the muscle, the sensitivity varies between isometric dynamometer tasks and gait (De Groote et al., 2010). Consequently, one must pay attention to the characteristics of the specific muscle under analysis when using a dynamometric task to estimate muscle parameters. Also, the sensitivity varies between different functional tasks, such as walking and running (Scovil and Ronsky, 2006). In fact, while performing different tasks, muscles work under different conditions (*e.g.*, fiber elongation and frequency of movement), indicating that each functional task must be evaluated individually.

Correct muscle geometry is also crucial for valid muscle force estimations. Muscle origins, insertions, and 'via' points of primary movers determine up to 81% of the variation in the force production of the muscle under analysis, and up to 16% of the variation of the force production of the surrounding muscles

(Bosmans et al., 2015; Carbone et al., 2012). However, by comparing muscle estimates from generic scaled models with those obtained from Magnetic Resonance Images, it was found that the prediction of muscle function (*i.e.*, “the direction in which a muscle accelerates a joint or the center of mass and the magnitude of the muscle’s potential acceleration relative to that of other muscles”) is not significantly altered despite the differences in muscle force estimates (Correa et al., 2011).

In conclusion, the choice of whether or not to use subject-specific parameters depends on the purpose of the study: subject-specific models may be not necessary when muscle functional assessment is the main focus of the study, but are likely to be needed in finite-element analysis, where valid estimates of joint contact stresses necessitate accurate descriptions of joint contact geometry (Lenaerts et al., 2008; Pandey and Andriacchi, 2010; Taddei et al., 2006).

2.2.7. Validation of muscle force estimation

In general, a model can be considered validated if: 1) computational and experimental results closely resemble each other, 2) the results can be extrapolated for the condition of interest, and 3) the accuracy is sufficient for the intended use (Hicks and Richards, 2005; Lund et al., 2012).

Without experimental measurements, muscle force estimates from musculoskeletal models cannot be directly validated. Indirect sources of validation are: 1) comparison of muscle forces against EMG profiles, 2) comparison of contact forces against instrumented prosthesis measurements, and 3) sensitivity analyses.

EMG profiles are used for qualitative comparisons: the timing of activation is compared between muscle forces and EMG without focusing on the amplitude (Hamner et al., 2010; Martelli et al., 2011; Modenese et al., 2011). This validation technique is mainly used for optimization models and when motor control strategies are the focus of the study. In fact, if the model is able to produce muscle activation profiles similar to the experimental ones, this means that the model is correctly representing the motor control strategy. However, for EMG-driven models, this validation technique is not very helpful since EMG signals already constitute the input of the model.

Contact forces from instrumented prostheses represent an informative source of data for direct validation; the total contact force obtained from the model is directly compared with the one measured from the instrumented prosthesis (Bergmann et al., 2001; Bergmann et al., 1993; Heller et al., 2001; Modenese et al., 2011; Stansfield et al., 2003). Walking studies reported a difference between estimated and measured hip contact forces of 12% according to Heller (2001), 10.1% according to Modenese (2011), and 15.8% according to Stansfield (2003). For stair climbing studies the figures are 14% (Heller

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et al., 2001) and 7.8% (Modenese et al., 2011), while for sit-to-stand and stand-to-sit it was found 15.6% (Stansfield et al., 2003).

However, two main limitations reduce the usability of this method: these measurements are only available for people who underwent joint replacement, and the dimensionality of the problem is still not sufficient to solve the validity issue unconditionally.

Chapter 3. General methods

3.1. Participants

This thesis was part of a larger research program where a total of 68 participants have been evaluated. A summary of some anthropometric information is reported in Table 3-1, while a complete list of all participants can be found in 0, Subjects.

Table 3-1. Summary of the participants's characteristics

Mean and standard deviations (StDev) for Height, Age and Body Mass Index (BMI) of the 68 patients divided by group (CON = Control, aFAD = asymptomatic femoroacetabular deformity, FAI = femoroacetabular impingement) and gender, plus the grand total

	Number	Height (cm)		Age (y)		BMI (Kg/m ²)	
		Mean	StDev	Mean	StDev	Mean	StDev
Female	9	163.0	5.6	35.5	9.2	22.6	2.4
CON	3	160.1	5.8	39.6	4.8	22.5	0.1
aFAD	3	162.8	6.1	32.0	9.6	23.1	2.2
FAI	3	166.2	2.3	34.9	10.4	22.2	3.5
Male	59	177.8	5.9	33.9	7.3	26.5	3.8
CON	21	176.7	6.1	32.4	6.2	25.9	3.2
aFAD	18	180.4	4.9	31.6	5.6	26.0	2.7
FAI	20	176.1	5.7	37.8	8.1	27.5	4.9
Grand Total	68	175.9	7.7	34.1	7.6	26.0	3.8

The recruitment was done by the Clinical Research staff in the Division of Orthopaedics (The Ottawa Hospital) based on the selection criteria described in the following.

Symptomatic FAI group. Patients diagnosed with cam-FAI, identified by an alpha angle higher than 50.5° in the axial view and higher than 60° in the radial view, and a visible convex ridge at the femoral head-neck junction on radiographs. They had a positive impingement test (*i.e.*, presence of repeatable isolated hip pain by passive motion of the patient's hip into a flexed, then internally rotated and adducted position, while supine). The participants must have had experienced hip pain longer than 6 months near the groin/lateral aspect of the hip, and awaited FAI corrective surgery.

Patients were excluded from the FAI group if they had previous hip surgery, exhibited signs of hip osteoarthritis (Tonnis grade > 1) (Tonnis and Heinecke, 1999), or reported pain patterns inconsistent with FAI (*e.g.*, low back pain).

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Healthy control group (CON). They were recruited from the general population, and matched for gender, age and body mass index (BMI) to the FAI group.

Participants were excluded from the CON group in presence of dysplasia, hip osteoarthritis, cartilage narrowing, previous major lower limb injuries, and pain.

Asymptomatic participants with femoroacetabular deformity. Those participants that had not experienced pain but for whom medical images revealed signs of femoroacetabular deformity consistent with FAI were classified as aFAD (asymptomatic Femoroacetabular Deformity). Signs of femoroacetabular deformity were identified with alpha angles higher than 50.5° in the axial view and 60° in the radial view.

Alpha angles were measured from Computed Tomography (CT) scans (Beaule et al., 2005) by a musculoskeletal radiologist at the Ottawa Hospital; the impingement test was performed by an experienced orthopedic surgeon at the Ottawa Hospital.

All the participants were properly instructed prior to the procedure, and thereafter signed an informed consent form. The study was originally approved by Ottawa Hospital Research Ethics Board and the University of Ottawa Health Sciences and Science Research Ethics Board.

For the study presented in Chapter 4 (How different marker sets affect joint angles in inverse kinematic framework) only 12 of the 68 participants were used. This study required the comparison of different marker sets, and the remaining 56 participants were instrumented with only the UOMAM (University of Ottawa Motion Analysis Model) marker set. The sensitivity study on pelvic orientation presented in Chapter 5 (Sensitivity of kinematic and kinetic parameters to pelvic tilt variation in an inverse kinematic framework) only involved one healthy control subject (FAI 064) since the variability due to pelvic tilt variations (and not to subjects) was under investigation. The study reported in the first part of Chapter 6 (Customization of hip joint center location for contact forces estimation) used ten of the healthy control participants. The second part of Chapter 6 (Regression models to predict hip joint centers in pathological hip population) involved 67 participants (all dataset excluding FAI 068 for which no CT information was available). Lastly, the clinical study reported in Chapter 7 (*In-silico* assessment of muscle and contact forces provide new insights into FAI pathomechanisms) used a total of 37 participants, who represented all available males belonging to FAI and CON groups, who were not excluded for technical problems. Female participants were excluded from the clinical investigation since it was not possible to reach a sample size large enough for statistical evaluations, and using gender as a covariate would have weakened the statistical power of the analysis.

3.2. Equipment

CT scans were acquired with either the Toshiba Aquilion (Toshiba Medical Systems Corporation, Otawara, Japan) or the Discover CT750 (GE Healthcare, Mississauga, ON, Canada).

Motion capture took place at the Human Movement Biomechanical Laboratory (University of Ottawa). The motion capture system included: ten infrared Vicon MX-13 cameras (VICON, Oxford, UK), reflective markers, two fixed Bertec force plates (models FP4060-08, Bertec Corporation, Columbus OH) and two mobile Kistler force plates (models 9286BA, Kistler Instruments Corp, Winterthur, Swtzt). Ground reaction forces and marker trajectories were recorded and synchronized through Vicon Nexus software (version 1.7, VICON, Oxford, UK). The cameras and the force plates were sampled at 200 Hz and 1000 Hz, respectively. Electromyography (EMG) signals were acquired at 1000 Hz with FreeEMG300 (BTS BioEngineering, Milan, Italy) and Bagnoli Desktop EMG System (Delsys, Boston, MA). For data validation purposes, the last 13 participants were instrumented with 24 EMG channels (major muscles of the whole leg), and therefore, two EMG systems were necessary.

Skin tight black shorts and short sleeve outfit was worn by participants to prevent the EMG probes from wobbling, and for participants' comfort.

3.3. Protocol

All participants underwent the same protocol, with slight modifications for the last 13 (addition of cluster marker set, specific functional tasks and whole leg EMG). A short description of the full protocol is reported in this section. Details related to every single study can be directly found in the specific articles (Chapters 4 to 7).

CT scans were acquired at the Ottawa General Hospital. Prior to the scan, participants were instrumented with four radiopaque surface markers (reflective markers with a metallic core) in correspondence of bony anatomical landmarks (left and right anterior and posterior superior iliac spines) in order to register the location of the surface landmarks with respect to the bones.

The participants were transferred to the University of Ottawa facilities (Human Movement Biomechanical Laboratory), where the motion capture session occurred. Participants read and signed the written consent form. Then, they were asked to wear black thigh suit. Anthropometric measurements such as weight, height, knee and ankle widths, and leg length were recorded.

After warm-up (5 minutes) and stretching (5 minutes), the participants were equipped with EMG sensors. The muscles of interest were identified following SENIAM guidelines (Hermens et al., 1999). The muscles monitored bilaterally were the Rectus Femoris, Tensor Fasciae Latae, Gluteus Medius,

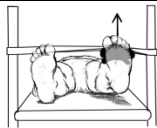
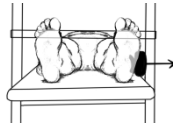
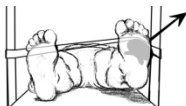
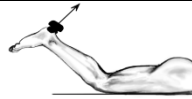
Gluteus Maximus, Biceps Femoris and Semitendinosus. For the last 13 participants other leg muscles were included in the protocol for validation purposes: Sartorius, adductor group, Vastus Lateralis, Vastus Medialis, Tibialis Anterior, Peroneus Longus, Soleus, Gastrocnemii Lateralis and Medialis.

Maximum voluntary isometric contractions (MVIC) were acquired for normalization purposes (Benoit et al., 2003) only for the hip muscles listed in Table 3-2, and according to the described postures and movements. Since the other muscles were acquired for qualitative validation purposes, accurate amplitude normalization was not deemed necessary. A hand-held dynamometer (Manual Muscle Tester, model 01163, Lafayette Instrument, Lafayette, IN) was used to measure the maximum force produced during MVIC.

The first 55 participants were instrumented with 13.5 mm markers according to the UOMAM marker set, while the last 13 included extra cluster markers according to Figure 3-1. More detailed descriptions about the used marker sets can be found in Chapter 4.

Table 3-2. Postures and movement description for Maximal Voluntary Isometric Contraction tasks.

HHD = hand-held dynamometer

Muscle	Posture	Contraction	Illustration
Rectus Femoris	Supine position, feet shoulder-width apart, facing upwards. HHD is placed between the ankle and the strap	With their leg straight, participants are asked to push upwards against the HHD	
Gluteus Medius	Supine position, feet shoulder-width apart, facing upwards. HHD is placed between the ankle and the lateral beam.	With their leg straight, participants are asked to push laterally against the HHD	
Tensor Fasciae Latae	Supine position, feet shoulder-width apart, facing upwards. HHD is placed at 45° between the ankle and the corner between the lateral beam and the strap	With their leg straight, participants are asked to push diagonally against the HHD	
Gluteus Maximus	Prone position, feet shoulder-width apart, facing downwards. HHD is placed between the heel and the strap	With their leg straight, participants are asked to push upwards against the HHD	
Biceps Femoris & Semitendinosus	Prone position, knee bent at 45°. HHD is placed between the heel and the strap	With their knee bent, participants are asked to pull against the HHD	

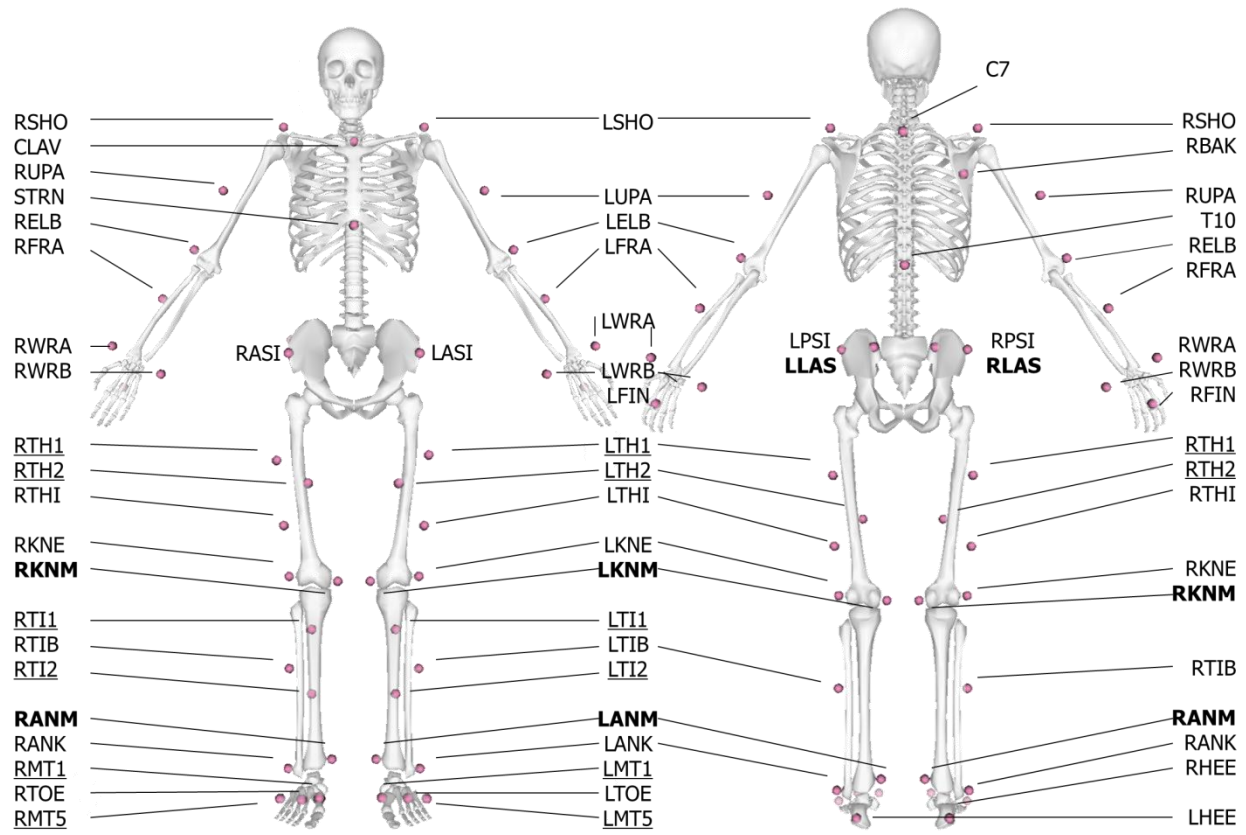


Figure 3-1. Marker set representation

The markers labelled with regular font refer to Plug-in-Gait marker set, the ones in bold are an adjustment made for the UOMAM marker set, and the underlined ones are the extra-markers used for Cluster. To be noticed, Cluster uses RTHI, LTHI, RTIB and LTIB as part of the cluster for right and left thigh, and right and left tibia segments, respectively

A static trial was acquired first for scaling and calibration purposes. This trial was executed with feet shoulder-width apart facing forward, arms extended forward with palms down, and the pelvis maintained in a natural comfortable pose. The walking task was then executed at a self-selected pace. Prior to data acquisition, some practice trials helped the patient finding a comfortable walking speed. Five valid trials were recorded with a full gait cycle per leg

3.4. Data processing

Three readers trained on CT scan images identified the coordinates of bilateral superior anterior and posterior iliac spines (bony landmarks), the geometrical center of the hip joint, and the position of four radiopaque surface markers (RASI, LASI, RPSI and LPSI). The readings were performed in a multi-planar reconstruction view in ITK-SNAP 2.4 (PICSLS, USA) (Taddei et al., 2007). The CT-measured HJC coordinates have been used in Chapter 6, where the method sections of the two articles describe how

these measurements have been used to customize the HJC of the musculoskeletal model, validate commonly used HJC regression equations for FAI populations, and develop new adult-specific regression equations.

The three-dimensional marker trajectories and the ground reaction forces were filtered with a zero-lag fourth order Butterworth filter (cut-off frequency at 6Hz) in Vicon Nexus 1.8.5. All simulations were performed in OpenSim 3.1 (Delp et al., 2007) using the ‘gait2392’ model based on (Delp et al., 1990) or Hamner model based on (Hamner et al., 2010). Both models include the lower body segments plus torso, Hamner model also includes arms. The hip and the lumbar articulations were modelled as a ball and socket joint, the knee as a custom joint (Yamaguchi and Zajac, 1990) and the ankle as a hinge. The reason for using two different models was that it was deemed important to use a full-body model (Hamner) for testing the performance of the different marker sets. However, as emerged from the marker set study, it is difficult to properly track the markers of arms and forearms. This might be due to the inadequate representation of the shoulder joint kinematics. The overall tracking root mean squared error was increased by the presence of the arm segments, therefore worsening the accuracy of the results for the lower-body segments, which were the focus of the other studies. Ultimately, for all studies that concerned exclusively the lower-body ‘gait2392’ was used, which does not include arms.

For every participant included in the study the generic musculoskeletal model was scaled, and the marker trajectories and ground reaction forces used to calculate inverse kinematics, kinetics, static optimization and joint reaction analyses.

Consistent with the tool available in OpenSim, the scaling was divided into two parts: a dimensional linear scaling operated by comparing the positions of the virtual and experimental markers pairs, and a marker adjustment to match the virtual markers position to the experimental one. For the studies presented in Chapters 5 to 7, a more refined scaling was used. Accurate pelvic width, depth and height were measured from CT images and used for the manual scaling of the pelvic segment. Also, the second scaling step (marker adjustment) was not completely left to the OpenSim automated procedure, but it was guided by using a registration method between the virtual pelvis and the bony landmarks coordinates measured from the CT images. A detailed description of this correction method is reported in the method section of Chapter 5.

The muscle properties of the generic musculoskeletal models were based on cadaveric measurements of one specimen, and OpenSim does not provide any automated procedure for adjusting such properties. Therefore, to account for change in height and mass of the different participants, the maximum isometric force of every muscle was scaled by $(M_{exp} \cdot H_{exp}) / (M_{mod} \cdot H_{mod})$, where M is the mass, H the

height, and *exp* and *mod* indicate the experimental and model measurements respectively (Handsfield et al., 2014).

The objective of this thesis required the estimation of hip muscle and contact forces. As explained in the review of the literature, two viable solutions were using EMG-driven or static optimization approaches. After accurate considerations, the latter approach was chosen. In fact the EMG data of only few superficial muscles were available for the hip joint, which would leave out two of the main contributors to hip flexion (*i.e.*, Iliacus and Psoas). Moreover, EMG-driven models require special tasks for the calibration phase of the muscle parameters, which were not available for all subjects, due to the change in protocol previously described. Consequently, the static optimization approach was chosen for muscle force estimation.

After the model had been scaled, inverse kinematics, inverse dynamics, static optimization and joint reaction analyses (Steele et al., 2012) were performed. The inverse kinematic tool in OpenSim uses a global optimization approach for estimating joint angles (Lu and O'Connor, 1999). The static optimization tool for muscle force estimation was set to use a quadratic cost function (Crowninshield and Brand, 1981; Glitsch and Baumann, 1997; Modenese et al., 2011), and without considering muscle contraction dynamics (force-length-velocity – FLV relationship) as they have been shown not to influence muscle predictions for walking (Anderson and Pandy, 2001b), and it did not improve the similarity with the EMG profiles.

An investigation on three subjects compared the correlation between muscle activation curves estimated from the static optimization algorithm with the ones produced by the activation dynamics filter applied directly to the measured EMG data. The average correlation values over the 5 trials demonstrated that there was no improvement in using FLV relationship (Figure 3-2). Indeed, the overall average correlation values were slightly better for the estimations that did not use FLV (Table 3-3).

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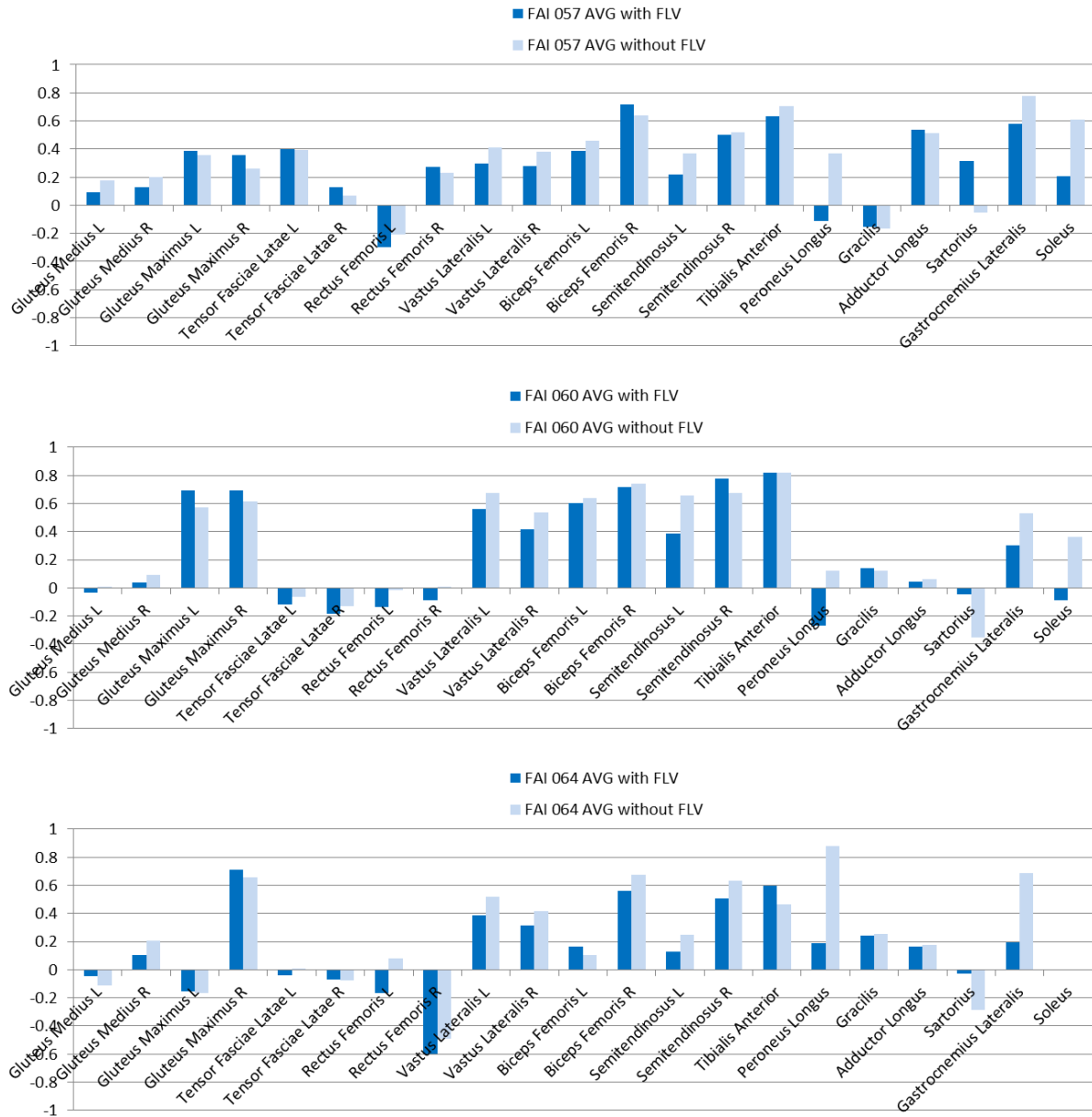


Figure 3-2. Comparison of muscle activations with and without FLV relationship

The figure reports the correlation coefficients between estimated and measured muscle activations with or without the force-length-velocity relationship during static optimization. The correlation coefficients were averaged over the 5 walking trials

Table 3-3. Comparison of muscle activations with and without FLV relationship – average values

The table summarizes the results shown in Figure 3-2. The average across different muscles provides an overall estimation of the difference in performance

	FAI 057	FAI 060	FAI 064
With FLV	0.28	0.25	0.16
Without FLV	0.33	0.32	0.24

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Hip contact force vectors were finally calculated as forces acting on the acetabulum and expressed in the pelvic coordinate system.

The study reported in Chapter 7 also analyzed EMG data. These were processed as the following: high-pass filtered (cut-off frequency 10 Hz, zero-lag fourth-order Butterworth filter) to remove bias and skin motion artifacts, full-wave rectified, and low-pass filtered at 6 Hz (zero-lag fourth-order Butterworth filter). The resulting linear envelopes were amplitude-normalized to the MVIC values, obtained as average activation on a 2-second window around the maximum activation peak during MVIC tasks.

The variables of interest were angles, moments, muscle and contact forces. All variables were time-normalized to either the entire gait cycle, or the stance cycle, depending on the study. Moments and forces were also amplitude normalized to the participant's body weight, to allow inter-subject comparison.

The specific data reduction choices and statistical analysis done for every study are not discussed in this section, as this would constitute a repetition of what will be described in details for every article.

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How Different Marker Sets Affect Joint Angles in Inverse Kinematic Framework

Submitted to Journal of Biomechanical Engineering

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4.1. Abstract

The choice of marker set is a source of variability in motion analysis. Studies exist that assess the performance of marker sets when direct kinematics is used, but these results cannot be extrapolated to the inverse kinematic framework. Therefore, the purpose of this study was to examine the sensitivity of kinematic outcomes to inter-marker set variability in an inverse kinematic framework.

The compared marker sets were Plug-in-Gait, University of Ottawa Motion Analysis Model and a 3-marker-cluster marker set. Walking trials of twelve participants were processed in OpenSim. Curves, peaks and ranges of motion of the resulting angles were compared by means of reliability indices.

Flexion/extension angles showed good agreement (coefficient of multiple correlations > 0.99), although the differences led to knee minimum detectable change of 9.4° . Frontal and transverse planes showed worse results: ranges of motion of hip and knee abduction/adduction angles, and hip and ankle rotations were significantly different among the three marker configurations ($P < 0.001$), with Plug-in-Gait producing the largest ranges of motion.

Although the same model was used for all marker sets, the resulting minimum detectable changes were high, which warns for caution when comparing studies that use different marker configurations, especially if they differ in the joint-defining markers.

4.2. Introduction

Three dimensional (3D) gait analysis is widely used to assess functional performance and clinical outcomes, and it is affected by many sources of variability, such as intra and inter-subject intrinsic variations, extrinsic variations introduced by raters, instrumentation, marker sets, models and algorithms for data analysis (Schwartz et al., 2004).

One of the most common models used in clinical 3D gait analysis is Plug-in-Gait (PiG) (Davis III et al., 1991; Kadaba et al., 1990). In the PiG model, hip joint centers are calculated through regression equations, while knee and ankle joint centers and their frontal planes definitions rely on the lateral technical thigh and shank markers placement (Kadaba et al., 1990). Slight misplacements of these markers can cause great frontal and transverse plane deviations (Kadaba et al., 1990). This is particularly evident for knee angles, where marker misplacements can create cross-talk between degrees of freedom and unrealistic frontal and transverse ranges of motion (Kadaba et al., 1990). Since the placement of anatomical skin markers is more accurate than the placement of technical skin markers (Cappozzo et al., 1996), a modified version of PiG was developed, so called the University of Ottawa motion analysis model (UOMAM) (Lamontagne et al., 2009a). Rather than relying on the technical skin markers of the thigh and shank, in UOMAM the medial knee and ankle markers are used to define knee and ankle joint centers and frontal planes together with the lateral knee and ankle markers. Two extra markers at the pelvis are placed on the mid-point between the anterior and posterior iliac crests to help tracking the other pelvic markers during occlusions, which occur often during movements such as squatting. Anatomical skin markers are necessary to define repeatable coordinate systems; however, sometimes they do not comply with the ideal characteristics for tracking markers, such as visibility from cameras and low soft tissue artifacts (Cappozzo et al., 1995). Cluster marker sets were introduced to solve these problems: additional technical skin markers are placed where they are less affected by skin movements (Borhani et al., 2013; Cappozzo et al., 1996; Manal et al., 2000; Stagni et al., 2005), and then the technical markers are calibrated with respect to the anatomical coordinate system (Chiari et al., 2005). Analyses of kinematic results obtained with different marker sets and models exist with the purpose of understanding to what extent such outcomes are comparable (Benedetti et al., 2013; Duffell et al., 2014; Ferrari et al., 2008; Gorton Iii et al., 2009). The validity of such marker sets and models can be assessed by comparison with gold standard results, such as bone pin studies (Benoit et al., 2006; Lafortune et al., 1992; Ramsey and Wretenberg, 1999).

Studies comparing kinematic variables obtained from different marker sets showed that cluster marker sets usually perform better (i.e., more accurate and reliable kinematics), especially if used together with soft tissues artifact reduction techniques (Andriacchi et al., 1998; Dumas and Cheze, 2009 ;

Söderkvist and Wedin, 1993). These studies used a classic “direct kinematics” (DK) approach, where the anatomical markers directly defined joint axes and body segment orientations (Wu et al., 2002). However, joint kinematic sensitivity to marker sets in an “inverse kinematics” (IK) framework is not known yet, even though marker configurations originally developed for DK are commonly used in IK (e.g., PiG in Steele (2012)). Joint angles are estimated in IK by maximizing the overlapping between experimental and model-determined (also called virtual) markers of a model with joint constraints (Lu and O'Connor, 1999). In this case the local coordinate system of one body segment depends on the whole marker set (for this reason is also known as “global optimization” approach), rather than just on specific joint-defining markers like in direct kinematics. Moreover, the model characteristics (e.g., joint definition, axis orientation, etc.) are independent from the marker set, and different combinations of markers can be used on the same kinematic model. Because of these substantial differences, it cannot be assumed that the results drawn from marker set comparison studies in DK can be extended to IK.

Therefore, the purpose of this study was to examine the reliability and sensitivity of kinematic outcomes to inter-marker set variability, comparing three marker sets applied to the same kinematic model with a IK approach during level walking. The three marker sets were: 1) PiG as commonly used in the literature and represents the minimum set of markers to model three-dimensional kinematics, 2) UOMAM, which uses PiG markers configuration with additional markers for improving the joint center definitions, and 3) Cluster (three-marker clusters on thighs, shanks and feet) as commonly used to reduce the effects of soft tissue artifacts. We hypothesized that PiG would overestimate the knee frontal and transverse ranges of motion with respect to the two other marker sets. Since PiG had a different definition of knee and ankle joint centers than UOMAM and Cluster marker sets, we hypothesized that reliability measures would show more consistency between UOMAM and Cluster than when compared to PiG.

4.3. Methods

4.3.1. Instrumentation

The motion capture system included: ten infrared cameras (MX-13, VICON, Oxford, UK), two fixed Bertec force plates (models FP4060-08, Bertec Corporation, Columbus OH) and two mobile Kistler force plates (models 9286BA, Kistler Instruments Corp, Winterhur, Swtz). Marker trajectories were captured at 200Hz and ground reaction forces at 1000Hz. Scaling and inverse kinematics were performed in OpenSim 3.1 (Stanford University, Stanford CA).

4.3.3. Data processing

The three-dimensional marker trajectories and the ground reaction forces were filtered with a zero-lag fourth order Butterworth filter (cut-off frequency at 6Hz). The data were converted into OpenSim compatible formats through a custom made Matlab (R2014a, MathWorks, MA, USA) program.

The model scaling procedure was divided in two steps, dimensional scaling and marker adjustment. The dimensional scaling simply resized the original body segments to the actual anthropometric dimensions of the participant by comparing the virtual with the experimental anatomical markers (e.g., anterior superior iliac crests, femoral epicondyles, and malleoli). All limbs were scaled isotropically, while two different scaling factors (vertical and transversal) were used to scale the pelvis and trunk anisotropically. The second step of scaling consisted of replacing the original locations of the virtual markers with the experimental coordinates, once the whole body pose had been estimated through global optimization. For both scaling and inverse kinematics, the weights were distributed so that every segment was equally weighted during inverse kinematics (Supplementary material, Markers weights for scaling and inverse kinematics

Table 4-5).

The hip joint center was calculated according to the regression equation presented in Davis III (1991). The knee and ankle joint centers were calculated as midpoint between the lateral and medial markers at the knee and ankle, respectively. In PiG there were no medial markers, therefore, the joint centers were identified based on the lateral thigh marker as suggested by Davis III (1991) and Kadaba (1990). The joint centers were treated as additional experimental markers in OpenSim. The kinematic model was adapted from the one proposed by Hamner et al. (2010); originally this model had a three-degree of freedom (DOF) hip modelled as ball-and-socket joint, a one-DOF knee (with prescribed translation dependent on flexion/extension angle), and one-DOF ankle modelled as revolute joint. To comply with the characteristics of the original PiG model (Davis III et al., 1991; Kadaba et al., 1990), knee abduction/adduction, knee internal/external rotation and ankle eversion/inversion degrees of freedom were added to the model.

The eight kinematic variables from the right side (hip and knee flexion/extension, abduction/adduction, internal/external rotations, and ankle flexion/extension, eversion/inversion) during gait were time normalized over 101 points. For every kinematic variable, max range of motion (ROM), peak max (MAX), and peak min (MIN) were calculated. Since the use of different marker sets directly affects the kinematic results, it was deemed sufficient to only include results and discussions relative to the kinematic variables. However, the kinetic analysis was also performed, and its results are reported in the Supplementary material for completeness.

4.3.4. Data analysis and statistics

The indices used to establish reliability and sensitivity of kinematic outcomes to marker sets were the intra-class correlation coefficient (ICC) (Beckerman et al., 2001; Ferber et al., 2002; McGraw and Wong, 1996; Monaghan et al., 2007; Weir, 2005; Wilken et al., 2012), and the coefficient of multiple correlation (CMC) (Borhani et al., 2013; Duffell et al., 2014; Ferrari et al., 2010; Kadaba et al., 1989; Røislien et al., 2012). ICC looked at the correlation of scalar parameters extracted from the kinematic waveforms (e.g., peaks, range of motion, value at foot-strike), while CMC evaluated the overall similarity between waveforms. These two indices used together provide a comprehensive measure of correlation among variables. Both ICC and CMC carried intrinsic limitations as they normalized measurement error to the heterogeneity of subjects (Weir, 2005); therefore, absolute reliability indices such as mean absolute variation (MAV) (Ferrari et al., 2008) and minimum detectable changes (MDC) (Beckerman et al., 2001; Weir, 2005; Wilken et al., 2012) were also needed. MAV and MDC are particularly common in 3D gait analysis and provide a large base for comparison among studies.

Given the available dataset, the proper choice of ICC was a two-way model, single measurement, absolute agreement, ICC(A,1) (McGraw and Wong, 1996). ICC was calculated for ROM, MAX and MIN of every kinematic variable. ICC varies between 0 (no correlation) and 1 (perfect correlation).

CMC was calculated as suggested by (Ferrari et al., 2010):

$$CMC^j = \sqrt{1 - \frac{\sum_{g=1}^G \sum_{p=1}^P \sum_{f=1}^F (Y_{gpf}^j - \bar{Y}_{gf}^j)^2 / GF_g(P-1)}{\sum_{g=1}^G \sum_{p=1}^P \sum_{f=1}^F (Y_{gpf}^j - \bar{Y}_g^j)^2 / G(F_g P - 1)}}$$

where Y_{gpf}^j is the g^{th} repetition of the kinematic variable j , at frame f (a.k.a. time), for protocol p (a.k.a. marker set). $\bar{Y}_{gf}^j$ is the average curve of the same kinematic variable j for different marker sets, $\bar{Y}_g^j$ is the average of $\bar{Y}_{gf}^j$ over time f . G , F_g and P are the number of gait repetitions, frames and protocols respectively. One of CMC's drawbacks is that, if the protocol variability is similar or higher than the intrinsic variability of the curve, the result could be an imaginary number. To the purpose of this study, this result would be equivalent to no correlation, thus, imaginary results were forced to zero. Also, to account for the dependence of CMC on sampling rate (Røislien et al., 2012), the time normalization was kept over 101 points so that no further correlation was introduced by a higher sampling rate.

MAV was measured as described in Ferrari (2008), according to the following formula $MAV = \frac{1}{N} \sum_{f=1}^N (\max_p \bar{Y}_p^f - \min_p \bar{Y}_p^f)$, where $\bar{Y}_p^f$ is the average of the five repetitions for protocol (i.e., marker set)

p, and at frame f, and N is the total number of frames. MDC was calculated as $MDC = 1.96 \cdot \sqrt{2} \cdot SEM$ (Beckerman et al., 2001; Haley and Frigala-Pinkham, 2006). SEM was defined as $SEM = SD \cdot \sqrt{(1 - ICC)}$ (Weir, 2005), where SD is the standard deviation of the values for all the subjects and can be determined from the same ANOVA model employed to calculate ICC as $SD = \sqrt{SS_{TOT}/(N - 1)}$, where SS_{TOT} is the total variance.

4.4. Results

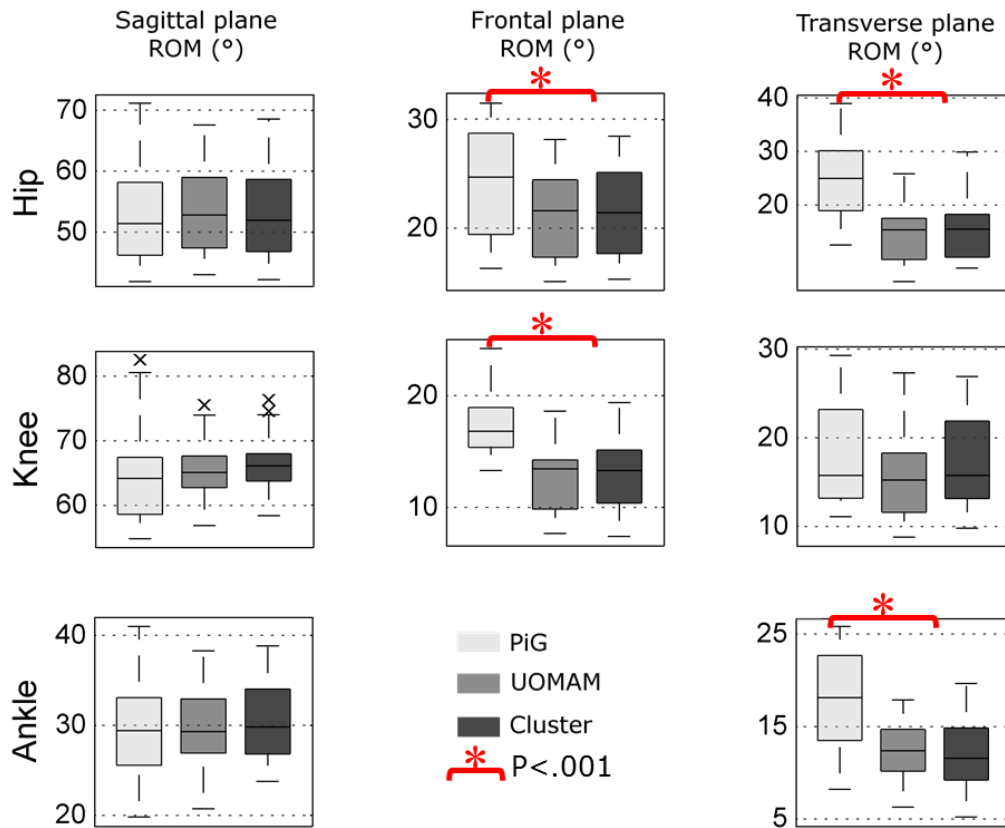


Figure 4-2. Range of motion for the different marker sets

Box plots of the range of motion (ROM) distributions over the 8 kinematic variables for every marker set. Repeated measures ANOVA showed that the three marker sets were significantly different ($P < .001$) for hip and knee ab/adduction angles, and hip and ankle rotations. The symbol 'X' indicates outliers

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Table 4-1. Inter-marker set coefficient of multiple correlation (CMC)

Since the distributions were not normal, median, 25 and 75 percentile values were reported in the table. CMC were calculated comparing all three marker sets, and for pairs comparison.

CMC inter-markersets		All markersets			PiG vs UOMAM			PiG vs Cluster			UOMAM vs Cluster		
		Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	0.99	0.98	0.99	0.99	0.97	0.99	0.99	0.97	0.99	1.00	1.00	1.00
	Knee	1.00	0.99	1.00	1.00	0.98	1.00	1.00	0.98	1.00	1.00	1.00	1.00
	Ankle	0.99	0.98	0.99	0.98	0.98	0.99	0.98	0.95	0.99	0.99	0.99	1.00
Ab/Add	Hip	0.97	0.96	0.99	0.96	0.95	0.98	0.97	0.94	0.98	1.00	0.99	1.00
	Knee	0.92	0.88	0.96	0.91	0.82	0.94	0.89	0.83	0.94	0.97	0.96	0.99
	Ankle												
Rotation	Hip	0.72	0.00	0.87	0.66	0.00	0.88	0.69	0.00	0.84	0.92	0.84	0.94
	Knee	0.89	0.84	0.92	0.88	0.81	0.92	0.86	0.77	0.93	0.96	0.93	0.97
	Ankle	0.73	0.57	0.81	0.73	0.47	0.79	0.67	0.46	0.77	0.86	0.78	0.93

Table 4-2. Inter-marker set intra-class correlation coefficients (ICC²) for ROM, peak MAX and peak MIN parameters

Since the distributions were not normal, median, 25 and 75 percentile values were reported in the table. ICC were calculated comparing all three marker sets, and for pairs comparison.

ICC inter-marker sets (ROM)		All markersets			PiG vs UOMAM			PiG vs Cluster			UOMAM vs Cluster		
		Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	0.98	0.94	0.99	0.97	0.89	0.99	0.97	0.90	0.99	0.99	0.98	1.00
	Knee	0.66	0.36	0.87	0.65	0.19	0.88	0.54	0.03	0.84	0.95	0.81	0.99
	Ankle	0.93	0.83	0.98	0.94	0.79	0.98	0.90	0.71	0.97	0.95	0.77	0.99
Ab/Add	Hip	0.78	0.33	0.94	0.73	-0.08	0.94	0.72	0.05	0.92	0.96	0.87	0.99
	Knee	0.48	0.02	0.81	0.33	-0.08	0.75	0.38	-0.10	0.78	0.94	0.81	0.98
Rotation	Hip	0.37	0.00	0.73	0.27	-0.10	0.68	0.28	-0.12	0.70	0.90	0.71	0.97
	Knee	0.80	0.56	0.93	0.64	0.17	0.88	0.87	0.61	0.96	0.89	0.47	0.97
	Ankle	0.40	0.01	0.75	0.31	-0.11	0.72	0.33	-0.11	0.74	0.92	0.75	0.98
ICC inter-marker sets (MAX)													
Flex/Ext	Hip	0.87	0.67	0.96	0.77	0.33	0.93	0.83	0.49	0.95	0.99	0.94	1.00
	Knee	0.56	0.20	0.83	0.48	-0.05	0.81	0.49	-0.03	0.81	0.96	0.84	0.99
	Ankle	0.83	0.61	0.94	0.83	0.36	0.95	0.76	0.37	0.92	0.95	0.83	0.98
Ab/Add	Hip	0.82	0.60	0.94	0.84	0.53	0.95	0.72	0.26	0.91	0.94	0.80	0.98
	Knee	0.43	0.05	0.76	0.30	-0.13	0.70	0.32	-0.13	0.72	0.94	0.71	0.98
Rotation	Hip	0.57	0.25	0.83	0.51	-0.02	0.82	0.51	-0.01	0.83	0.87	0.62	0.96
	Knee	0.71	0.36	0.90	0.56	-0.05	0.86	0.66	0.09	0.89	0.89	0.67	0.97
	Ankle	0.73	0.36	0.91	0.74	0.34	0.92	0.56	-0.04	0.86	0.88	-0.03	0.98
ICC inter-marker sets (MIN)													
Flex/Ext	Hip	0.93	0.75	0.98	0.87	0.37	0.97	0.92	0.63	0.98	0.99	0.91	1.00
	Knee	0.87	0.43	0.97	0.79	-0.05	0.95	0.88	0.18	0.97	0.96	0.43	0.99
	Ankle	0.84	0.55	0.95	0.87	0.20	0.97	0.74	0.10	0.93	0.91	0.74	0.97
Ab/Add	Hip	0.77	0.35	0.93	0.71	-0.06	0.93	0.74	0.12	0.93	0.96	0.75	0.99
	Knee	0.79	0.55	0.92	0.72	0.30	0.91	0.73	0.33	0.91	0.93	0.78	0.98
Rotation	Hip	0.34	0.01	0.70	0.22	-0.12	0.63	0.34	-0.12	0.74	0.79	0.44	0.93
	Knee	0.89	0.75	0.96	0.86	0.59	0.96	0.86	0.59	0.96	0.96	0.83	0.99
	Ankle	0.45	0.10	0.77	0.28	-0.14	0.69	0.38	-0.13	0.76	0.81	0.15	0.95

² In theory, ICC coefficients should not be below zero. When this happens, it means the variability inter-marker set was higher than the variability intra-marker set. Therefore, this indicates a non-existent correlation. For those variables, the reader should refer to the other indices for a more appropriate characterization of the variability

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Table 4-3. Inter-marker sets mean absolute variation (MAV)

Since the distributions were not normal, median, 25 and 75 percentile values were reported. MAV were calculated comparing all three marker sets, and for pairs comparison

MAV (°)		All markersets			PiG vs UOMAM			PiG vs Cluster			UOMAM vs Cluster		
Inter-markersets		Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	4.5	3.4	6.5	4.2	3.3	6.4	3.3	2.2	5.6	1.2	0.8	1.8
	Knee	2.4	1.8	5.4	2.0	1.5	5.3	1.9	1.6	4.5	0.7	0.5	0.9
	Ankle	2.4	2.0	3.0	1.7	1.4	2.1	1.9	1.4	2.8	1.3	0.9	1.5
Ab/Add	Hip	2.8	1.9	3.5	2.2	1.9	2.8	2.2	1.5	3.1	0.8	0.6	1.0
	Knee	2.8	2.2	3.4	2.2	1.6	3.2	2.6	1.8	3.1	0.8	0.7	1.0
	Ankle												
Rotation	Hip	5.2	4.3	10.7	4.4	3.1	9.9	4.6	3.6	7.9	1.5	1.2	2.5
	Knee	4.1	2.3	5.1	2.9	1.7	3.9	2.9	1.8	4.7	1.8	1.4	1.9
	Ankle	4.9	4.0	7.0	3.8	2.8	5.0	4.4	2.8	5.8	2.1	1.4	3.0

Table 4-4. Minimum detectable change (MDC)

MDC were obtained comparing ROM, peak MAX and peak MIN parameters for all three marker sets and for pairs comparison

inter-markerset MDC (ROM)		All markersets	PiG vs UOMAM	PiG vs Cluster	UOMAM vs Cluster
Flex/Ext	Hip	3.0	3.7	3.5	1.6
	Knee	7.8	8.8	10.0	2.2
	Ankle	3.2	3.2	4.0	2.4
Ab/Add	Hip	5.5	6.5	6.6	2.0
	Knee	7.6	8.9	8.4	2.2
	Ankle				
Rotation	Hip	16.6	19.1	18.6	4.7
	Knee	6.4	8.7	5.2	4.5
	Ankle	10.1	11.4	11.8	2.5
inter-markerset MDC (MAX)					
Flex/Ext	Hip	7.9	10.4	8.5	2.7
	Knee	9.4	11.6	11.0	2.0
	Ankle	4.4	4.8	5.4	2.1
Ab/Add	Hip	3.9	4.0	5.2	2.0
	Knee	7.4	8.8	8.3	1.9
	Ankle				
Rotation	Hip	11.3	13.7	13.4	4.5
	Knee	5.5	6.5	5.5	3.8
	Ankle	6.5	5.9	8.3	4.5
inter-markerset MDC (MIN)					
Flex/Ext	Hip	8.2	10.9	8.6	3.1
	Knee	3.9	5.2	3.6	2.1
	Ankle	4.3	4.0	5.4	3.2
Ab/Add	Hip	5.7	6.9	6.5	1.9
	Knee	4.1	4.8	4.8	2.2
	Ankle				
Rotation	Hip	13.2	15.5	14.5	4.9
	Knee	5.3	6.1	6.1	3.3
	Ankle	10.1	12.0	11.0	5.2

Kinematic variables in the sagittal plane showed better agreement than in the frontal and transverse planes, where peaks and range of motion differed noticeably among the three marker sets. The overall similarity of the sagittal curves was reflected in CMC values above 0.99 (Table 4-1). The variables in frontal plane showed slightly worse agreement (0.97 for hip and 0.92 for knee), with most of the differences to be attributed to PiG, since UOMAM vs Cluster comparison produced CMC values of 1.00 and 0.97 for hip and knee, respectively. Transverse plane angles demonstrated the worst agreement, especially at the hip (0.72) and ankle (0.73). The curves for one “typical” participant (whose CMC and MAV were the closest to the median values) were reported in the Supplementary material, Figure 4-3.

The ROM values of all kinematic variables are shown in Figure 4-2. The hip and knee abduction/adduction angles, and hip and ankle rotations showed significant differences among the three marker sets (repeated measure ANOVA $P < 0.001$), with PiG always producing larger ROMs. The variables reporting significant differences were also those with the worst inter-marker sets ICC values (Table 4-2). ICC values calculated between Cluster and UOMAM were good ($ICC > 0.79$), but the comparison of these marker configurations to PiG largely decreased the ICC, especially in the frontal and transverse planes.

The MAV values for all kinematic variables are reported in Table 4-3. Overall, MAV indices showed a good absolute repeatability in knee and ankle sagittal plane, and hip and knee frontal plane ($MAV < 2.8^\circ$), while rotational variables had MAV above 4.1° . However, when the comparison was restricted to UOMAM and Cluster, MAV values improved considerably (0.7 - 2.1°).

MDC values were higher when PiG was included in the marker set comparison. When PiG was excluded from the analysis, all kinematic variables produced MDC values below 5.2° (Table 4-4).

Intra-marker set (inter-trial) variability measured the reliability of kinematic variables when the same marker set was used to capture multiple trials for the same subject. The results are reported in the Supplementary material, Intra-marker set variability

Table 4-6 and showed very similar inter-trial variability, with knee flexion/extension being the most variable angle and knee abduction/adduction the least.

4.5. Discussions

This study analyzed the sensitivity of kinematic outcomes to inter-marker set variability when using an inverse kinematic framework. ICC, CMC, MAV and MDC values for lower limb kinematic variables subject to marker set variability were provided, and the results were compared to previous literature.

PiG marker set differed the most from the other two reporting the lowest ICC and CMC and the highest MAV values. Moreover, PiG produced significantly larger ROM, as previously found for DK by

Ferrari (2008). *In vivo* bone-pins studies showed a stable 1.2° abduction during stance phase and a peak abduction of 6.4° during swing, with an overall average ROM of about 5.0° (Lafortune et al., 1992; Ramsey and Wretenberg, 1999). Even considering the standard error of estimate of 3.6° for knee abduction/adduction due to skin artifacts (Benoit et al., 2006), all marker sets still overestimated the frontal plane ROM (Figure 4-2). Among the three, PiG demonstrated to be the least accurate marker set with an interquartile range for knee frontal ROM of 15.5° - 18.9° , while UOMAM and Cluster produced 10.5° - 14.4° and 11.2° - 15.4° , respectively.

The overall reliability as expressed by CMC was good in sagittal and frontal planes, but not in the coronal plane. MAV indices in the frontal and coronal planes were below 5.2° , but these values reflected poor repeatability if considering that abduction/adduction and internal/external rotations are characterized by low ROMs. Similar trends were found in previous inter-rater and inter-session reliability results for studies using DK (Duffell et al., 2014; Ferber et al., 2002; Kadaba et al., 1989; McGinley et al., 2009). The inter-marker set MAV values were lower than those presented in Ferrari (2008) obtained from a 5-protocol comparison, consistent with the fact that the only source of variability in the present study was the marker set, while the different protocols in Ferrari's paper involved different models and/or data processing.

Both CMC and MAV analyze the entire curve and average the results over the whole cycle, so that differences in specific regions of interest might not emerge. The comparison of curve parameters (e.g. ROM and peaks) demonstrated that overall repeatability of curves does not necessarily lead to repeatability of relevant parameters. Only hip and ankle sagittal ROM produced good reliability over the three different marker sets ($ICC > 0.8$). However, when limiting the comparison to just UOMAM and Cluster, ICC values for all variables exceed 0.80, therefore, these two marker sets produced consistent relevant parameters.

Both relative and absolute reliability indices indicated that Cluster and UOMAM produced very similar results, with MDC values below 2.4° for sagittal and frontal plane angles, and below 5° for transverse (fourth column in Table 4-4). This shows that, with the global optimization approach, the addition of cluster markers does not considerably change the outcomes of the analysis. On the other hand, the variability increased drastically when PiG was included in the comparison, with MDC values up to four times higher (first three columns in Table 4-4). Since the only major difference between PiG and UOMAM was the joint centers definition, it can be concluded that the kinematic outcomes are highly sensitive to anatomical markers, especially those used to define joint centers (Ferrari et al., 2008; Kainz et al., 2014).

In a similar study comparing different approaches to inverse kinematics Lathrop et al. (2011) concluded that marker weighting did not cause relevant changes in kinematic outcomes, but only root mean square values were reported and no MDC analysis was conducted. From this study, however, it emerged that even when absolute repeatability indices (i.e., MAV) are low for overall curves comparison, relevant parameters (e.g., ROM) could still cause large MDC values, and therefore invalidating small differences among studies. Further analyses on weighting differences are therefore warranted.

In this study the use of different marker sets was the only source of variability, since data processing and modeling were identical. Nevertheless, the MDC obtained when comparing all three marker sets exceeded 5° for most variables, even in the sagittal and frontal plane angles that are usually the most reliable, with the worst results recorded at hip internal/external rotation ROM (16.6°). This should warn researchers to use caution when comparing studies that use different marker sets in an inverse kinematic framework, especially if joint centers are not identified consistently. The MDC to be considered in these cases should be the highest between test-retest (Wilken et al., 2012) and inter-marker set studies since the total variability will be a combination of the single sources of variability.

The inter-trial variability of the three marker configurations was also examined. Relative reliability indices could not be used since ICC and CMC are ‘context-specific’ (Weir, 2005), and are not appropriate when the population variability changes systematically like with PiG (see larger interquartile ranges with respect to UOMAM and Cluster results in Figure 4-2). Therefore, inter-trial variability was assessed with MAV index, and is reported in the Supplementary material, Intra-marker set variability

Table 4-6. The three marker sets produced comparable inter-trial repeatability in line with Duffell’s (2014) and Ferrari (2008) studies. Therefore, the inter-trial variability captured probably represents the biological variability and the presence soft tissue artifacts.

Few limitations should be noted. No knee alignment device was used for more accurate lateral marker identification, which would have helped reducing the differences between PiG and the other two marker sets, especially in non-sagittal plane variables. Moreover, subjects were not recalled for a re-test, and therefore it was not possible to calculate the total variability when combining both inter-marker set and inter-session variance. Future studies could complete the analysis by providing MDC reference values in such situation. The population used for this study was not homogenous: one woman was included in the analysis, and five out of twelve participants were affected by femoroacetabular impingement. Femoroacetabular impingement subjects reported no differences in knee kinematics with respect to healthy participants (Brisson et al., 2013); thus, the large knee ROM found in the present study was probably not caused by the population characteristics. However, differences in hip kinematics were noted (Alshameeri and Khanduja, 2014; Brisson et al., 2013). This possible increase in the total variability does not invalidate the results obtained in this study since we focused on the inter-marker set and not inter-

subject variability, and the sample was the same for all three marker sets. Lastly, the results of this analysis are valid within the limits of the characteristics of the chosen kinematic model; it is possible that adopting different modelling choices (e.g., using one-DOF knee) could reduce the dependency of the joint kinematics on the choice of marker set.

In summary, this study established MDC values for comparisons of kinematic outcomes when using different marker sets on the same model in an inverse kinematic framework. The inter-marker set repeatability was good for sagittal angles, intermediate for frontal angles, and worse for internal/external rotation, similarly to what was found in inter-rater and inter-session variability studies. The Cluster and UOMAM marker sets produce comparable curve parameters, while PiG produces larger ranges of motion and inter-subject variability. Lastly, the large differences introduced by PiG with respect to the other two marker sets depends on the higher sensitivity of kinematic outcomes to anatomical markers that define joint centers rather than changes in number and/or location of technical markers.

Conflict of interest statement

All the authors have no financial or personal conflicts to disclose

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4.7. Supplementary material

4.7.1. Graphical representation of the marker set variability

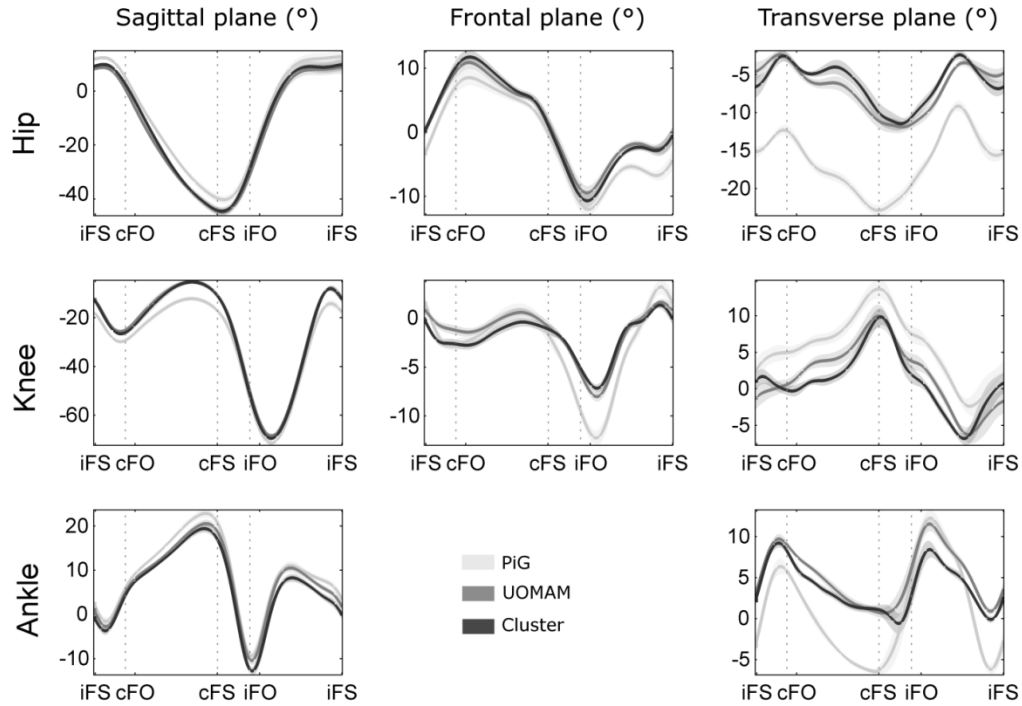


Figure 4-3. Curves variation over the three marker sets

Average curves (bold line) and standard deviation (shadow) over 5 repetitions of subject 5 who shows a "typical" behavior (MAV and CMC closest to the group median)

4.7.2. Markers weights for scaling and inverse kinematics

Table 4-5. Markers' weights for scaling and inverse kinematics

The sum of weights for every segment in both static and inverse kinematics is 100, so that every segment is equally considered. When a markerset has larger number of markers in a segment (e.g., Cluster), the weight is distributed among the markers of the segment. When a marker is present bilaterally, the side letter ('R' or 'L') is omitted

Segment	Markers	Weight					
		Scaling			Inverse Kinematics		
		PiG	UOMAM	Cluster	PiG	UOMAM	Cluster
Trunk	C7		20			20	
	T10		10			10	
	CLAV		20			20	
	STRN		10			10	
	SHO		19.5			15	
	RBAK		1			10	
Upper Arm	SJC		33			5	
	UPA		1			45	
	ELB		33			45	
	EJC		33			5	
Forearm	FRA		1			45	
Hand	WRA		25			10	
	WRB		25			10	
	WJC		25			40	
	FIN		25			40	
Pelvis	ASI, PSI	20	19.75	19.75	20	13	13
	LAS	n.a.	0.5	0.5	n.a.	14	14
	HJC	10	10	10	10	10	10
Thigh	THI	1	1	0.33	50	50	22
	TH1, TH2	n.a.	n.a.	0.33	n.a.	n.a.	22
	KNL	49.5	33	33	25	25	20
	KNM	n.a.	33	33	n.a.	10	4
Shank	KJC	49.5	33	33	25	15	10
	TIB	1	1	0.33	50	50	22
	TB1, TB2	n.a.	n.a.	0.33	n.a.	n.a.	22
	ANL	49.5	33	33	25	25	20
Foot	ANM	n.a.	33	33	n.a.	10	4
	AJC	49.5	33	33	25	15	10
	HEE	50	50	33.3	50	50	33.3
	TOE	50	50	n.a.	50	50	n.a.
	MT1, MT5	n.a.	n.a.	33.3	n.a.	n.a.	33.3

4.7.3. Intra-marker set variability

Table 4-6. Intra-marker set (inter-trial) mean absolute variation (MAV)

Since the distributions were not normal, median, 25 and 75 percentile values were reported.

MAV (°)										
Intra-markerset (inter-trial)		PiG			UOMAM			Cluster		
		Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	3.5	(3.0	3.9)	3.4	(2.9	3.9)	3.4	(2.9	3.8)
	Knee	4.4	(3.2	4.9)	4.2	(3.4	5.3)	4.2	(3.5	5.2)
	Ankle	2.3	(2.1	2.8)	2.5	(2.1	2.7)	2.5	(2.1	2.8)
Ab/Add	Hip	2.2	(1.7	2.7)	2.0	(1.6	2.3)	2.0	(1.6	2.3)
	Knee	1.7	(1.6	2.0)	1.3	(1.1	1.5)	1.5	(1.1	1.6)
Rotation	Hip	2.9	(1.8	3.7)	3.1	(1.9	3.5)	2.4	(2.0	2.9)
	Knee	2.5	(2.1	2.6)	2.3	(2.0	2.5)	2.4	(2.1	2.6)
	Ankle	2.4	(2.1	2.7)	2.2	(1.8	2.7)	2.1	(1.8	2.8)

4.7.4. Inverse kinetics results

Table 4-7. Inter-marker set coefficient of multiple correlation (CMC) for torques

Since the distributions were not normal, median, 25 and 75 percentile values were reported in the table. CMC were calculated comparing all three marker sets, and for pairs comparison

CMC inter-marker sets		All markersets			PiG vs UOMAM			PiG vs Cluster			UOMAM vs Cluster		
		Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	1.00	1.00	1.00	1.00	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Knee	0.99	0.95	1.00	0.99	0.93	0.99	0.99	0.94	1.00	1.00	1.00	1.00
	Ankle	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Ab/Add	Hip	0.99	0.99	1.00	0.99	0.98	1.00	0.99	0.98	1.00	1.00	1.00	1.00
	Knee	0.95	0.91	0.98	0.93	0.89	0.97	0.92	0.89	0.97	1.00	0.99	1.00
	Ankle												
Rotation	Hip	0.98	0.94	0.99	0.97	0.91	0.98	0.97	0.94	0.98	1.00	0.99	1.00
	Knee	0.97	0.94	0.99	0.97	0.92	0.99	0.96	0.91	0.98	1.00	1.00	1.00
	Ankle	0.98	0.96	0.98	0.97	0.95	0.98	0.97	0.92	0.98	1.00	0.99	1.00

Table 4-8. Inter-marker set intra-class correlation coefficients (ICC) for peak MAX and peak MIN parameters of the torques

Since the distributions were not normal, median, 25 and 75 percentile values were reported in the table. ICC were calculated comparing all three marker sets, and for pairs comparison

		All markersets			PiG vs UOMAM			PiG vs Cluster			UOMAM vs Cluster		
ICC inter-markersets (MAX)		Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	0.99	0.94	1.00	0.98	0.57	1.00	0.99	0.86	1.00	0.99	0.96	1.00
	Knee	0.90	0.76	0.97	0.84	0.54	0.95	0.85	0.56	0.95	0.99	0.97	1.00
	Ankle	0.92	0.80	0.98	0.90	0.65	0.97	0.88	0.58	0.97	1.00	0.99	1.00
Ab/Add	Hip	0.67	0.37	0.88	0.55	-0.02	0.85	0.47	-0.10	0.81	0.98	0.93	0.99
	Knee	0.79	0.56	0.93	0.67	0.22	0.89	0.72	0.29	0.91	0.98	0.92	0.99
	Ankle												
Rotation	Hip	0.94	0.66	0.98	0.89	0.04	0.98	0.92	0.46	0.98	0.99	0.85	1.00
	Knee	0.98	0.95	0.99	0.97	0.90	0.99	0.98	0.93	0.99	1.00	0.99	1.00
	Ankle	0.82	0.61	0.94	0.74	0.33	0.92	0.74	0.30	0.92	0.98	0.94	0.99
ICC inter-markersets (MIN)													
Flex/Ext	Hip	0.99	0.93	1.00	0.98	0.64	1.00	0.98	0.79	1.00	1.00	0.99	1.00
	Knee	0.93	0.84	0.98	0.90	0.70	0.97	0.90	0.70	0.97	1.00	1.00	1.00
	Ankle	0.99	0.98	1.00	0.99	0.97	1.00	0.99	0.96	1.00	1.00	1.00	1.00
Ab/Add	Hip	0.97	0.89	0.99	0.95	0.71	0.99	0.95	0.76	0.99	1.00	0.99	1.00
	Knee	0.84	0.62	0.95	0.78	0.35	0.94	0.78	0.33	0.93	0.99	0.96	1.00
	Ankle												
Rotation	Hip	0.70	0.35	0.89	0.62	0.09	0.87	0.54	-0.02	0.84	0.96	0.87	0.99
	Knee	0.90	0.51	0.97	0.88	0.06	0.97	0.85	0.03	0.97	1.00	0.98	1.00
	Ankle	0.96	0.91	0.99	0.97	0.89	0.99	0.94	0.80	0.98	0.99	0.98	1.00

Table 4-9. Inter-marker sets mean absolute variation (MAV) for torques

Since the distributions were not normal, median, 25 and 75 percentile values were reported. MAV were calculated comparing all three marker sets, and for pairs comparison

MAV (Nm/BW)		All markersets			PiG vs UOMAM			PiG vs Cluster			UOMAM vs Cluster		
Inter-markersets		Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Flex/Ext	Hip	0.0057	0.0039	0.0070	0.0050	0.0034	0.0063	0.0043	0.0034	0.0050	0.0011	0.0010	0.0028
	Knee	0.0057	0.0038	0.0123	0.0047	0.0036	0.0119	0.0046	0.0030	0.0115	0.0009	0.0009	0.0013
	Ankle	0.0024	0.0015	0.0039	0.0021	0.0011	0.0032	0.0020	0.0008	0.0039	0.0004	0.0002	0.0006
Ab/Add	Hip	0.0055	0.0040	0.0078	0.0048	0.0037	0.0062	0.0044	0.0031	0.0070	0.0019	0.0013	0.0022
	Knee	0.0065	0.0055	0.0075	0.0059	0.0045	0.0067	0.0059	0.0039	0.0067	0.0015	0.0013	0.0017
	Ankle												
Rotation	Hip	0.0021	0.0018	0.0026	0.0020	0.0016	0.0024	0.0018	0.0014	0.0024	0.0006	0.0005	0.0006
	Knee	0.0013	0.0010	0.0014	0.0011	0.0009	0.0013	0.0012	0.0008	0.0014	0.0002	0.0002	0.0002
	Ankle	0.0013	0.0010	0.0018	0.0011	0.0008	0.0016	0.0012	0.0007	0.0016	0.0003	0.0002	0.0004

Table 4-10. Minimum detectable change (MDC) for torques

MDC were obtained comparing ROM, peak MAX and peak MIN parameters for all three marker sets and for pairs comparison

inter-markerset MDC (MAX) (Nm/BW)		All markersets	PiG vs UOMAM	PiG vs Cluster	UOMAM vs Cluster
Flex/Ext	Hip	0.0078	0.0103	0.0058	0.0068
	Knee	0.0252	0.0310	0.0305	0.0068
	Ankle	0.0050	0.0058	0.0062	0.0012
Ab/Add	Hip	0.0171	0.0196	0.0221	0.0044
	Knee	0.0063	0.0080	0.0073	0.0021
	Ankle				
Rotation	Hip	0.0047	0.0060	0.0051	0.0019
	Knee	0.0009	0.0011	0.0010	0.0003
	Ankle	0.0063	0.0077	0.0076	0.0020
inter-markerset MDC (MIN) (Nm/BW)					
Flex/Ext	Hip	0.0070	0.0085	0.0082	0.0031
	Knee	0.0064	0.0078	0.0079	0.0008
	Ankle	0.0095	0.0109	0.0121	0.0032
Ab/Add	Hip	0.0120	0.0148	0.0146	0.0027
	Knee	0.0162	0.0197	0.0196	0.0041
	Ankle				
Rotation	Hip	0.0054	0.0061	0.0068	0.0018
	Knee	0.0055	0.0063	0.0070	0.0010
	Ankle	0.0012	0.0013	0.0017	0.0005

Chapter 5. On the pelvic orientation

Sensitivity of kinematic and kinetic parameters to pelvic tilt variation in an inverse kinematic framework

Submitted to Gait & Posture

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5.1. Abstract

The joint angles calculated in a motion analysis study are affected by the marker locations with respect to the underlying bones; in an inverse kinematic framework, in particular, all joint angles are influenced by virtual markers' locations in the kinematic model. This study examines the sensitivity of joint angles, moments and hip contact forces to simulated inaccurate pelvic tilt, caused by an inconsistency between virtual and experimental markers or by markers misplacement, which are problems of interest for musculoskeletal model users. Joint angles for a walking trial of one healthy male participant were estimated while varying the pelvic tilt orientation between 0° and 26.5° by perturbing the virtual posterior-superior iliac spine markers by 10 cm in the vertical direction. Mean absolute variation (MAV) values were reported for joint angles, moments and hip contact forces finding large variations in the sagittal planes of the pelvis (MAV = 21.0°) and hip (27.4°), which propagated into the frontal and transverse planes. The instantaneous variations in hip contact forces reached 1.3 times the body weights at contra-lateral foot-strike in the anterior-posterior component.

Lower limb kinematic variables calculated using an inverse kinematic approach are highly sensitive to variations in pelvic tilt. Kinematic variations propagated non-linearly to all planes and joints, showing the importance of adjusting possible pelvic misalignment errors. A methodology was presented to correct the pelvic alignment when the relative positions of surface pelvic markers with respect to bony landmarks are known from medical images, and an example based on Computed Tomography images was offered.

5.2. Introduction

Motion capture can be used to derive body kinematics, and a common technique to calculate joint angles consists in decomposing the relative orientation of two adjacent body segments into Cardan angles. In direct kinematics the body orientation is constructed directly from experimental markers coordinates, as described in Wu (2002) and Cappozzo (1995). In inverse kinematics (also called “global optimization”), the experimental markers are tracked by virtual markers placed in a pre-existing kinematic model, by adjusting the joint angles to minimize the tracking error (Lu and O'Connor, 1999). In this second case the body reference systems are defined a priori and they might not be aligned with marker-based reference systems. For instance in Delp (1990) and Arnold (2010) the neutral position of the pelvis is set to the anatomical pose, close to the Lewinnek plane (Lewinnek et al., 1978), resulting in a forward pelvic tilt of about 14° with respect to the marker based ISB reference system.

The pelvis segment is the “root” of the lower limb kinematic chain, and its orientation and position is crucial to obtain accurate kinematics (Winter, 2009). In direct kinematics, an incorrect location of the pelvic experimental markers generates orientation errors, and directly affects only the adjacent joints (Della Croce et al., 1999; Groen et al., 2012). In inverse kinematics, errors can be introduced by an initial inconsistency between positions of the pelvic virtual and experimental markers, still liable to misplacements as in the traditional techniques (El Habachi et al., 2015; Myers et al., 2015). This discrepancy can cause an offset in the pelvic orientation not detectable by commonly used tracking metrics with errors propagating non-linearly to the whole kinematic chain (Della Croce et al., 2005).

The effect of the pelvic tilt offset caused by inconsistencies between experimental/virtual marker locations in inverse kinematic frameworks has never been specifically addressed by previous literature, although representing an important source of error in gait analysis applications. Therefore, the purpose of this study was to examine the sensitivity of the lower limb joints angles, moments and hip contact forces to simulated incorrect pelvic tilt, during walking, when using an inverse kinematic framework. An approach to correct the pelvic tilt based on information from medical images is also described.

5.3. Methods

5.3.1. Experimental data

A walking trial of one healthy participant (height 171 cm, weight 69.2 Kg) was collected with ten infrared cameras (MX-13, VICON, Oxford, UK, sampling: 200 HZ) and two force plates (FP4060-08, Bertec Corporation, Columbus OH, sampling: 1000 Hz). The participant was instrumented with the University of Ottawa Motion Analysis Model marker set (Plug-in-Gait including medial knee and ankle

markers). The trajectories and ground reaction forces were filtered with a zero-lag low-pass Butterworth filter (4th order, 6Hz cut-off). The subject was enrolled in a larger clinical study for which Computed Tomography (CT) scans were approved by the hospital's and university's ethic boards. The participant provided written informed consent.

CT images (64-slice CT, Aquilion, Toshiba; 1-mm axial slice thickness, 0.72-0.98 mm in-plane resolution, 120 kV and 200 mA radiation level) of the participant's pelvis and hip region were collected with radiopaque surface markers (reflective markers with a metallic core) prior to motion capture. From the CT images two trained readers identified the coordinates of the anterior (R/LASI) and posterior superior iliac spines (R/LPSI) bony landmarks and the position of the four correspondent radiopaque surface markers. The readings were performed in a multi-planar reconstruction view in ITK-SNAP 2.4 (PICSLS, USA). Each reader performed three evaluations, with near-perfect inter- and intra-observer reliability (interclass correlation coefficient >0.90).

5.3.2. Musculoskeletal simulations

All simulations were performed in OpenSim 3.1 (Delp et al., 2007), using the model of Hamner et al. (2010) where the hip is represented as a ball and socket joint, the knee as a custom joint (Yamaguchi and Zajac, 1989) and the ankle as a hinge. The model scaling procedure consisted of a dimensional scaling followed by markers adjustment. The dimensional scaling resized the segments of the generic model to the anthropometric dimensions of the participant by using pairs of the virtual and experimental markers to compute scaling ratios. In particular, the pelvis was scaled isotropically by using pelvic width as reference dimension. The second step consisted of registering the virtual marker locations to their experimental coordinates, after estimating static pose through inverse kinematics.

To simulate the altered pelvic tilt, R/LPSI virtual markers were symmetrically displaced in the vertical direction, where the largest error in locating pelvic markers has been reported (Della Croce et al., 2005; White et al., 1989). Perturbations of increasing magnitude were applied to one experimental walking trial, from -3 to +6 cm of the R/LPSIS nominal position (corresponding to 0 and 26.5° of inclination, respectively) with 1-cm steps (Figure 5-1).

After the model had been scaled³, inverse kinematics, inverse dynamics, static optimization and joint reaction analyses (Steele et al., 2012) were performed for each of the ten virtual R/LPSI positions. Mean absolute variation (MAV) index was calculated as the average over time of the maximum instantaneous

³ As suggested by OpenSim guidelines, the weights for the pelvic, knee and ankle markers were 100, while the weights for any other marker were 1

variation between curves. MAV percentage (MAV%) with respect to the maximum range of motion was also reported.

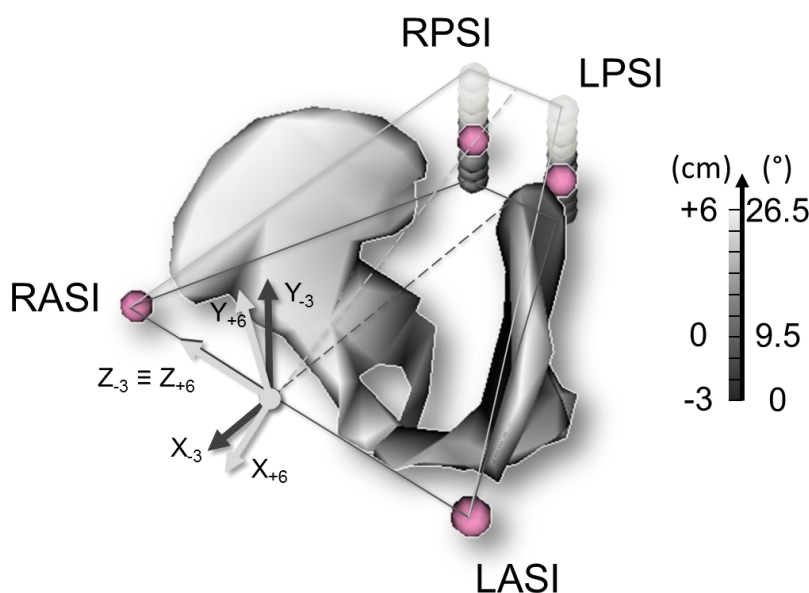


Figure 5-1. Three-dimensional view of the 10 perturbed pelvic marker positions and their respective coordinate systems defined according to ISB guidelines for pelvis

RASI/LASI = right and left anterior superior iliac spine markers, RPSI/LPSI = right and left posterior superior iliac crest markers. XYZ_{-3} is the coordinate system corresponding to -3 cm of perturbation (0° of inclination), and it is aligned with the musculoskeletal model pelvic coordinate system. As the RPSI/LPSI markers are moved upward, the pelvic coordinate system is inclined forward (XYZ_{+6} is the coordinate system corresponding to +6 cm of perturbation and 26.5° of inclination). All the perturbed positions of the RPSI/LPSI markers are illustrated with gray markers

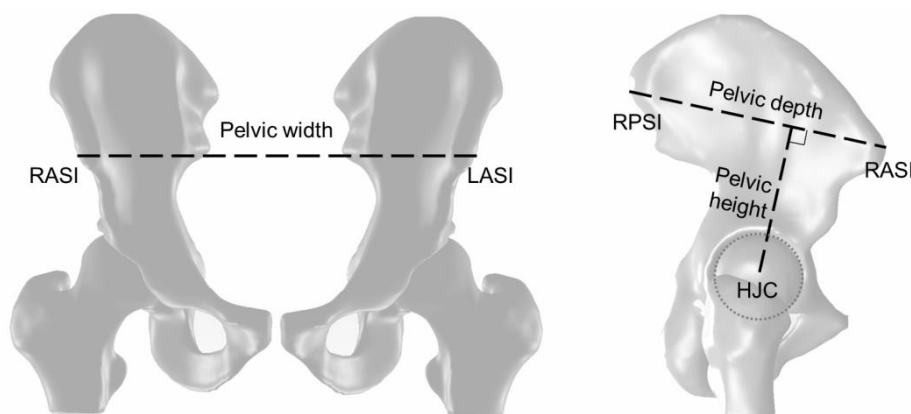


Figure 5-2. Three pelvic measurements (pelvic width, depth and height)

The pelvic measurements were used for anisotropic scaling of the pelvis. Pelvic width is the distance between right and left anterior superior iliac crest; pelvic depth is the distance between the mid-points of the two anterior and the two posterior superior iliac crests; pelvic height is the distance between the hip joint center and the plane passing through right and left superior iliac crests and the mid-point of the two posterior superior iliac crests

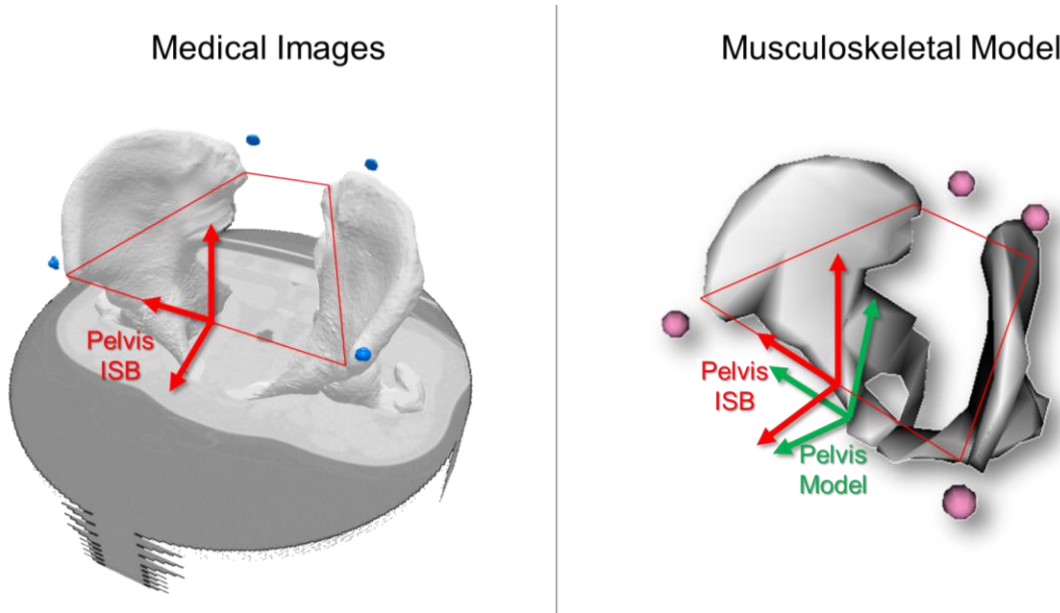


Figure 5-3. Computed Tomography images of the pelvis versus the model representation

On the left, the segmented pelvis and surface radiopaque markers (in blue) from the CT images. The CT included the pelvis and the proximal femur, delimited by the lesser trochanter. The reference systems defined from the radiological image and on the musculoskeletal model are represented. The coordinates of the bony landmarks from the medical images were located through virtual palpation; instead, the coordinates of the model bony landmarks were found from the segmented pelvic geometry of the model. The model pelvic coordinate system does not rely on bony landmarks according to ISB recommendations, therefore the coordinate system "Pelvis ISB" may not be aligned with "Pelvis Model". In "Pelvis ISB", the center coincides with the mid-point between RASI and LASI. The medial-lateral axis consists of the line from the LASI to RASI; the anterior-posterior axis is orthogonal to the medial-lateral axis from the midpoint between RPSI and LPSI, and the superior-inferior axis is perpendicular to the other two

The coordinates of the pelvic bony landmarks and the hip joint centers available from the CT scans were used to calculate pelvic width, depth and height (Figure 5-2). The same lengths were calculated for the pelvic bone geometry of the generic model, which was then scaled anisotropically in the three dimensions. The rest of the scaling process remained unchanged from the previous simulations. Because of the difference between the ISB's and model's pelvic reference systems (15.1° in this specific case), a common coordinate system was defined both in the musculoskeletal model and in the CT bone geometries based upon bony landmarks and ISB guidelines (Pelvis ISB, Figure 5-3). As the relative position of the surface (radiopaque) experimental markers (blue markers in Figure 5-3) with respect to the underlying bone anatomy was known from the medical images, they were mapped onto the musculoskeletal model (from Pelvis ISB to Pelvis Model) using the following transformation:

$$M^{Model} = R_{ISB}^{Model} \cdot M^{ISB} + O_{ISB}^{Model} \quad (1)$$

where M^{Model} and M^{ISB} are the marker coordinate vectors in the Model and the ISB coordinate systems respectively, R_{ISB}^{Model} (3×3 matrix) is the rotation matrix between the two pelvic reference systems, and O_{ISB}^{Model} (3×1 vector) is the origin of Pelvis Model with respect to Pelvis ISB.

5.4. Results

Across the 10 perturbations, the experimental markers were tracked with a maximum error of 53 ± 1 mm (found in medial knee or thigh markers), but the largest RMSE was 15 mm, suggesting a globally satisfactory tracking.

The pelvic kinematics changed progressively with the perturbation of R/LPSIS (Figure 5-4), affecting all lower limb joint angles, as compared to the corrected pelvic virtual markers based on medical images (see MAV and MAV% reported in Table 5-1).

Hip and pelvic kinematics both presented a larger perturbation in the sagittal plane, which propagated into the frontal and transverse planes. Figure 5-5 shows how the perturbations affected hip joint kinetics and contact forces; the MAV% was lower than 15% for both these variables. However, the MAV was 0.37 body weights (BW) for the vertical hip contact force over the whole gait cycle, reaching instantaneous variations of 1.3 and 1.2 BW at contra-lateral foot-strike in the anterior-posterior and superior-inferior contact forces, respectively.

Table 5-1. Mean absolute variation (MAV) for hip, knee and ankle variables, and their percentage with respect to the maximum range of motion

		Sagittal		Frontal		Transverse	
		MAV	%	MAV	%	MAV	%
Pelvis	Angle (°)	21.0	>100.0%	2.4	18.9%	1.1	9.3%
Hip	Angle (°)	27.4	72.4%	2.0	9.4%	1.4	8.4%
	Moment (Nm/BW)	0.016	8.7%	0.004	2.9%	0.002	12.1%
	Contact Force (N/BW)	0.25	8.2%	0.37	10.1%	0.09	14.4%
Knee	Angle (°)	6.95	10.5%	-	-	-	-
	Moment (Nm/BW)	0.006	7.0%	-	-	-	-
Ankle	Angle (°)	2.46	5.6%	-	-	-	-
	Moment (Nm/BW)	0.001	0.5%	-	-	-	-

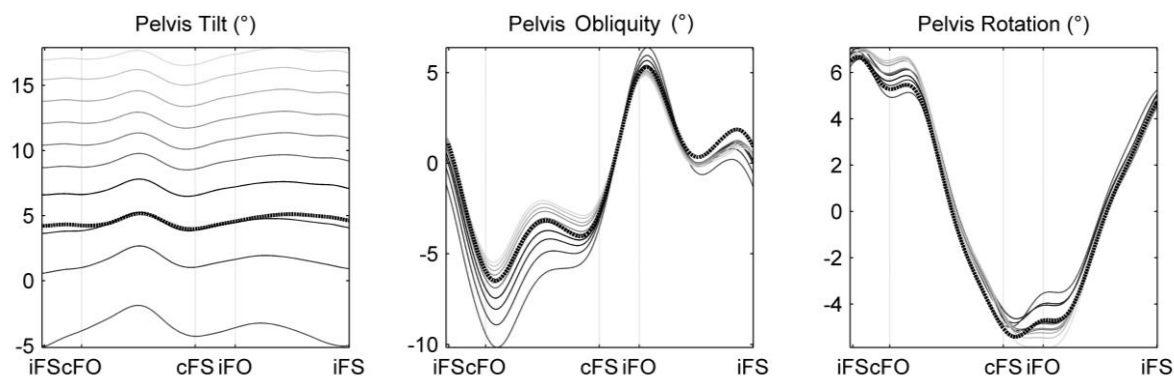


Figure 5-4. Pelvic kinematics for the 10 different marker perturbations

The darkest gray curve represents the most inferior position of R/LPSI (-3 cm perturbation), the lightest gray curve represents the most superior position (+6 cm perturbation). The bold dotted line is the result of the correction method. iFS = ipsi-lateral foot strike, cFO = contra-lateral foot off, cFS = contra-lateral foot strike, iFO = ipsi-lateral foot off

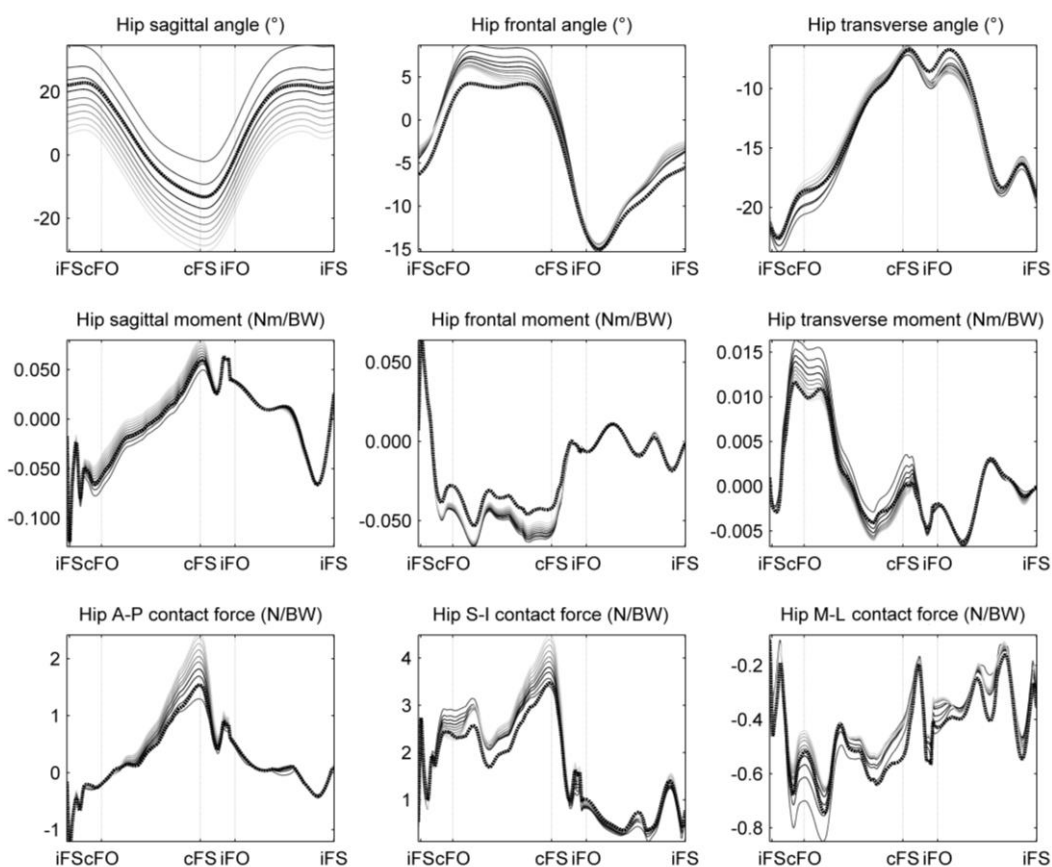


Figure 5-5. The curves represent the hip kinematics, kinetics and contact forces for the 10 different marker perturbations

The darkest gray curve represents the most inferior position of R/LPSI (-3 cm perturbation), the lightest gray curve represents the most superior position (+6 cm perturbation). The bold dotted line is the result of the correction method. Moments and contact forces are normalized by body weight (BW). A-P = antero-posterior direction, S-I = superior-inferior direction, M-L = medio-lateral direction. iFS = ipsi-lateral foot strike, cFO = contra-lateral foot off, cFS = contra-lateral foot strike, iFO = ipsi-lateral foot off

5.5. Discussions

The objectives of this study were to show the sensitivity of kinematics (estimated using global optimization) and kinetic variables and contact forces to variations in pelvic tilt generated by inconsistencies between virtual and experimental markers, and to present a approach for correcting the pelvic orientation when medical images including visible skin surface markers are available.

In an inverse kinematic framework, all joint angles are estimated at the same time by minimizing the weighted distance between experimental and virtual markers, while respecting joint constraints (Lu and O'Connor, 1999). Since joint angle optimization is dependent on all body markers, local variations can cause kinematic alterations globally. This explains why pelvic changes propagated into not only the hip, but also the knee and ankle joints, even if the MAV values were smaller as the kinematic chain reached the foot (Table 5-1). Given the non-linear nature of joint kinematic calculations, predicting the variations is difficult and a correction prior to the analysis is preferable.

The perturbation of the pelvic markers produced an offset in pelvic tilt (Figure 5-4); in 10-cm variation this angle reported a MAV of 21° , which is larger than some clinically relevant differences. The variation was not limited to this plane, but propagated to the other two degrees of freedom (Della Croce et al., 2005).

The increase of hip contact forces at cFS can be explained by the kinematic and kinetic results. At cFS, hip adduction and rotation were close to zero for all conditions, while hip extension went from zero (dark grey) to -30° (light grey). With a more extended hip, the flexion moment increased. At the same time, hip flexor muscles moment arms greatly decreased from 0° to -30° of hip extension. To generate larger flexion moments with lower moment arms, flexor muscle forces increased, contributing to the larger anterior and superior hip contact forces of the more tilted pelvis (Figure 5-5). This resulted in a substantial difference in the maximum instantaneous hip contact force (above 1 BW), which is close to the variation between walking and jogging measured *in vivo* by Bergmann et al. (1993).

The 10-cm perturbation in the R/LPSIS location was larger than the 2.5 cm inter-examiner variation found for pelvic marker placement (Della Croce et al., 1999; Della Croce et al., 2005). However, accuracy with respect to bony landmarks could be quantified with larger errors. Therefore, the variations reported in our results represented the worst-case-scenario, and exacerbated the variability introduced in the analysis when no correction for pelvic orientation is used. This study did not analyze other perturbations (e.g., asymmetric), but the reported simulations were deemed sufficient to demonstrate the need for pelvic adjustment methods in inverse kinematic frameworks.

Medical images of the pelvis, including radiopaque or MRI-visible markers, reveal the relative position of landmarks on the bone and reflective skin markers, allowing a correction of the estimated pelvis angles. While this has been proposed as solution for direct kinematics (Della Croce et al., 2005), it had never been applied to an inverse kinematic framework. Inclusion of visible markers in clinical imaging is essential to avoid the limitations of a posteriori registration between gait markers and bone geometry, like in Bartels (2015).

The pelvis orientation correction obtained through marker registration is affected by some methodological limitations. Firstly, the bony landmark locations in the model were affected by uncertainty due to the simplified bone geometry representation. Secondly, equation (1) assumes equivalent Pelvic ISB coordinate systems from medical images and in the scaled model, which was not completely accurate since pelvis asymmetries or non-rigid deformations cannot be accounted for with a linear scaling. Also, the CT were acquired in a supine position, which could cause some skin movement (Hara et al., 2014), therefore, the proposed correction method would work better with imaging technologies such as EOS (Illés and Somoskeöy, 2012). When no medical images are available, three-dimensional pointers could be used instead.

Furthermore, this study only considered inconsistent virtual marker locations on the musculoskeletal model, but similar results can be expected from inaccurate experimental marker placement, since both sources of variation affect inverse kinematics at the same time. Unsatisfactory personalization of the generic musculoskeletal model due to inaccurate scaling or joint parameter estimation is likely to also produce similar kinematic variations.

Although implemented in OpenSim, both the sensitivity analysis and the correction method are platform independent, and therefore are valid for any study using the inverse kinematic approach described by Lu and O'Connor (1999). Other implementations of the inverse kinematic approach (Andersen et al., 2010b; Andersen et al., 2009) may require different adjustments.

Conclusions

This study showed that lower limb kinematic variables calculated using an inverse kinematic approach are highly sensitive to variations in pelvic tilt. 10-centimeter perturbation of the virtual markers caused up to 21°-MAV in pelvic sagittal angle, with kinematic variations propagating non-linearly to the other planes and to the entire kinematic chain. The observed kinematic alterations can cause over 1 BW-difference in hip contact forces. An approach was described to locate pelvic virtual markers in the musculoskeletal model when the relative position of surface pelvic markers with respect to bony landmarks is known from medical images.

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Chapter 6. On the subject-specific hip joint center

Customization of Hip Joint Center Location for Contact Forces Estimation

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6.1. Abstract

Different degrees of customization are possible when using musculoskeletal models for kinematic and kinetic analyses. However, clinical studies require a certain level of simplicity and efficiency which limits the customization possibilities. The Hip Joint Center (HJC) is a crucial parameter of the analysis, especially when the focus of the investigation is the hip joint. The objectives of this study were 1) evaluate the error in HJC estimation when using a generic scaled model with respect to common regression and the geometrical HJC measured from CT; and 2) evaluate the possibility of using subject-specific HJC in an otherwise generic musculoskeletal model during a functional task (i.e., walking).

Ten participants underwent CT scan and motion analysis investigation. The geometrical HJC was measured from the CT, and estimated from Harrington and Davis regression equations. Moreover, 2-cm perturbations in every perpendicular direction were also applied to the original HJC, for a total of ten different HJC conditions, including the HJC from the generic scaled model. For every HJC, inverse kinematics, kinetics, static optimization and joint reaction forces were calculated, and the results compared by means of a sensitivity index.

The accuracy of the HJC from the generic scaled model was comparable with the best regression equation (Harrington), with 14.7 mm of linear error with respect to the geometrical HJC measured from CT. With the exception of the frontal plane, kinematic and kinetic variables demonstrated a medium to low sensitivity to HJC variations. On the contrary, hip contact forces were highly sensitive, especially because of the muscle moment arms dependency to HJC changes. The variation of HJC without consistent muscle anatomy customization introduced artifacts that could potentially produce inaccurate muscle and joint contact forces estimation by static optimization.

In conclusion, subject-specific HJC without a consistent customized muscle anatomy can create artifacts in muscle and contact force estimation; therefore, it is suggested to rely on a carefully scaled generic model anatomy rather than compromising the internal consistency of the model when subject-specific muscle anatomy cannot be modelled.

6.2. Introduction

When a generic musculoskeletal model is used on experimental data of a specific participant, a certain degree of approximation is accepted. In recent years techniques for musculoskeletal models customization have been developed in an attempt to increase model accuracy (Blemker et al., 2007; Scheys et al., 2011; Schmid J. et al., 2009; Valente et al., 2014); however, the high computational requirements and long manual processing times still prevent their use in clinical studies. Therefore, the generic musculoskeletal models available from repositories are often used, which are based on cadaveric data of single average subjects (Delp et al., 1990; Klein Horsman et al., 2007; Modenese et al., 2011), scaled to match the experimental anthropometric dimensions (Lund et al., 2015; Rasmussen et al., 2005).

Motion analysis and musculoskeletal modelling are highly sensitive to the location of the hip joint center (HJC). Inverse dynamics studies reported differences of up to 22% in hip flexion-extension moments, with discrepancies of 3 cm in HJC location (Stagni et al., 2000). Muscles' capacity to generate hip torque is most sensitive to vertical displacements of HJC: a 2-cm superior displacement decreases hip abduction moment by about 50% (Delp and Maloney, 1993) and, consequently, leads to inaccurate muscle and hip contact force estimations.

Radiological images represent the gold standard for accurate HJC measurements; the hip is modelled as a ball-and-socket joint, and the HJC is assumed to be the geometrical center of the sphere interpolating the femoral head and acetabulum contours (Harrington et al., 2007; Hicks and Richards, 2005; Leardini et al., 1999). Alternatively, HJC can be estimated from regression equations, where anthropometric measurements are used as model parameters (Andersen et al., 2013; Bell et al., 1990; Davis III et al., 1991; Harrington et al., 2007). When using musculoskeletal models, the HJC is estimated with neither of these methods, but its location depends on the scaling factors applied to the pelvis, and, as with the regression methods, will generate some errors (Bartels et al., 2015).

Given the importance of HJC, the purpose of this preliminary investigation was twofold: 1) to quantify the inaccuracy in HJC location when using scaled generic models, and 2) to investigate the possibility of HJC customization based on CT images available from clinical studies, to improve the accuracy of the contact force estimation. For the first objective, the coordinates of the scaled HJC were compared to the geometrical centers measured from CT and two popular regression equations (Davis and Harrington), all expressed in the same reference system. The initial hypothesis was that the regression equations would be more accurate than the scaled HJC, since they are developed from larger populations and are, supposedly, more generic. For the second objective, a sensitivity analysis was conducted on the

variables dependent on HJC that most affected the contact forces estimation: kinematics, kinetics and muscle moment arms.

6.3. Methods

6.3.1. Equipments and participants

Medical images of pelvis and femoral head were acquired by Computed Tomography (CT) (64-slice CT, Aquilion, Toshiba; Tokyo, Japan). Four radiopaque surface markers were placed on the skin in correspondence of bony anatomical landmarks (left and right anterior and posterior superior iliac spines) to be able to register the location of the HJC with the musculoskeletal model.

The motion capture system included: ten infrared cameras (MX-13, VICON, Oxford, UK), two fixed Bertec force plates (models FP4060-08, Bertec Corporation, Columbus OH) and two mobile Kistler force plates (models 9286BA, Kistler Instruments Corp, Winterhur, Swtz). Marker trajectories were captured at 200Hz and ground reaction forces at 1000Hz.

Ten healthy male participants took part in the study (height 177.7 ± 3.2 cm, weight 83.2 ± 13.8 Kg and age 32 ± 6 years). Participants were instrumented with reflective markers for motion capture according to University of Ottawa Motion Analysis Model (UOMAM) marker set, which consists in a Plug-in-Gait model with additional medial knee and ankle markers. Every participant performed a static acquisition, followed by five repetitions of walking trials performed at a self-selected pace. The subjects were enrolled in a larger clinical study for which CT scans were approved by the hospital's and university's ethic boards. The participant provided written informed consent.

6.3.2. Data processing

6.3.2.1. *Hip Joint Center*

The CT images were processed in ITK-SNAP 3.0 (PICS�, USA) that can provide semi-automatic threshold-based segmentation. The coordinates of the bony landmarks, radiopaque markers and hip geometric centers were recorded by three readers, each performing three readings, with near-perfect inter- and intra-observer reliability ($ICC > 0.90$). The hip geometric centers were located on CT images as the center of a maximum-radius circumference fitting the contour of the femoral head on the three planes, and were considered as the actual HJC (from now on referred to as GC – geometric center). The local pelvic coordinate system was defined according to ISB guidelines (Wu et al., 2002): the center coincided with the mid-point between ASIS; the medial-lateral axis (ML) consisted of the line from the left to the right

ASIS; the anterior-posterior (AP) axis was orthogonal to ML from the midpoint of the two PSIS, and the superior-inferior axis (SI) was perpendicular to ML and AP.

HJCs were estimated in this common coordinate system from two regression models: Davis and Harrington (Davis III et al., 1991; Harrington et al., 2007). Davis model was chosen because is a very popular method, and is embedded in some motion analysis software, whereas Harrington was chosen because it has been shown to outperform other commonly used regression methods (Andersen et al., 2013; Sangeux et al., 2011; Sangeux et al., 2014). The Harrington regression equations (from now on referred to as rH) depend on two parameters (pelvic width $-PW$ and depth $-PD$ expressed in mm) (Harrington et al., 2007), where $x = -0.24PD - 9.9$, $y = -0.30PW - 10.9$, and $z = 0.33PW + 7.3$. The Davis regression equations (from now on referred to as rD) depend on PW , leg length (L) and another anthropometric parameter indicated as D that represents the antero/posterior component of the distance between a point approximating the hip center and the homolateral ASIS: $x = -0.95D + 0.031L - 4$, $y = -0.31D - 0.096L + 13$ and $z = 0.5PW - 0.055L + 7$. The regression equations from both models were applied directly to the pelvic bony landmarks to increase the accuracy of the result.

Additionally, six perturbed HJCs were also included to investigate the outcomes of the analysis in more extreme conditions. The perturbation consisted of moving the original hip center of the model (OC) by 2 cm in every direction relative to the three major axes. In conclusion, for every participant there was a total of ten different HJC: the original from the musculoskeletal model (OC), the one measured from CT (GC), the two regressions (rH and rD) and the 6 perturbations (Sup, Inf, Lat, Med, Ant and Pos).

Once the HJC were all expressed in the same coordinate system, the errors between GC and the other three HJC estimation methods (OC, rH and rD) were calculated in the three orthogonal directions (e_{ML} , e_{AP} e_{SI}) together with the linear distance (e_L), calculated as $e_L = \sqrt{e_{ML}^2 + e_{AP}^2 + e_{SI}^2}$.

6.3.2.2. Modelling

The three-dimensional marker trajectories and the ground reaction forces were filtered in Vicon Nexus with a zero-lag fourth order Butterworth filter (cut-off frequency at 6Hz). A custom made Matlab pipeline converted maker trajectories and ground reaction forces into a format compatible with OpenSim 3.1 (Stanford University, Stanford CA), where inverse kinematics, kinetics, static optimization and contact forces estimation were carried out. The musculoskeletal model was adapted from the ‘gait2392’ model (Delp et al., 1990); to reduce computational costs only pelvis and right leg were included. The hip was modelled as a ball and socket joint, the knee as a custom joint (Yamaguchi and Zajac, 1990) and the ankle as a hinge joint, with a total of 43 musculotendon actuators.

The scaling procedure is carefully described in Chapter 5: firstly, a dimensional scaling resized the original body segments to the actual anthropometric dimensions of the participants by comparing pairs of virtual and experimental markers. For the pelvis, the scaling factors (*i.e.*, pelvic width, depth and height ratios) were computed by directly comparing CT measurements with the model pelvic dimensions, rather than using surface markers. At this stage, the pelvic virtual markers were repositioned according to the experimental coordinates by means of a registration between model and CT coordinate systems, to prevent artifacts due to marker mismatches. In the last step of scaling, the virtual markers are adjusted according to the experimental coordinates, once the whole body pose had been estimated through inverse kinematics. The registration between the model and CT coordinate systems allowed the replacement of the original HJC location of the model with the alternative joint centers (GC, rH and rD).

After the scaling, inverse kinematics and dynamics were run. The kinematic outcomes were used for the static optimization tool to estimate muscle forces. The redundancy problem was solved with a quadratic cost function (Glitsch and Baumann, 1997; Modenese et al., 2011) for a system with n muscle actuators and d degrees of freedom: $\min J(F_i) = \min \sum_{i=1}^n \left(\frac{F_i}{F_{i,MAX}} \right)^2$, subject to the constraints $\sum_{i=1}^n \vec{r}_{ij} \times \vec{F}_i = \vec{M}_j$ and $0 \leq F_i \leq F_{i,MAX}$ where $i = 1, \dots, n$ and $j = 1, \dots, d$, F_i was the force of the i th muscle, $F_{i,MAX}$ was the maximal force that the i th muscle can produce. $\vec{r}_{ij}$ was the i th muscle's moment arm with respect to the j th degree of freedom, and $\vec{M}_j$ was the torque acting on the j th degree of freedom. $F_{i,MAX}$ of every muscle was scaled by $(M_{exp} \cdot H_{exp}) / (M_{mod} \cdot H_{mod})$, where M is the mass, H the height, and *exp* and *mod* indicate the experimental and model measurements, respectively (Handsfield et al., 2014). No force-length-velocity relationship was used in the model. Finally, hip contact forces applied on the pelvis were calculated by means of joint reaction analysis as sum of muscular, inertial and external forces, and expressed in the pelvic reference system.

6.3.3. Data analysis

To verify if there was statistical difference between the measured and estimated HJC, the errors in the three directions (anterior-posterior, superior-inferior and medial-lateral– e_x , e_y , e_z) plus the linear error (e_L) were analyzed with Wilcoxon signed rank tests, given the non-normality of the data distribution and the reduced sample size.

The analyzed variables were hip angles, moments and contact forces. They were averaged over the trial repetitions. For each of the ten HJC locations, intra and inter-HJC variations of hip angles, moments and contact forces were calculated, as shown in Figure 6-1. Percentage of maximum variation

(*Max var%*) quantifies the impact of using different HJCs with respect to the average range of variation of that variable, and can be interpreted as a sensitivity index.

Muscle moment arms for all modelled hip muscles with respect to the three hip degrees of freedom were calculated (Sherman et al., 2013). For simplicity, *Max var%* of opposite perturbations is reported in Figure 6-4.

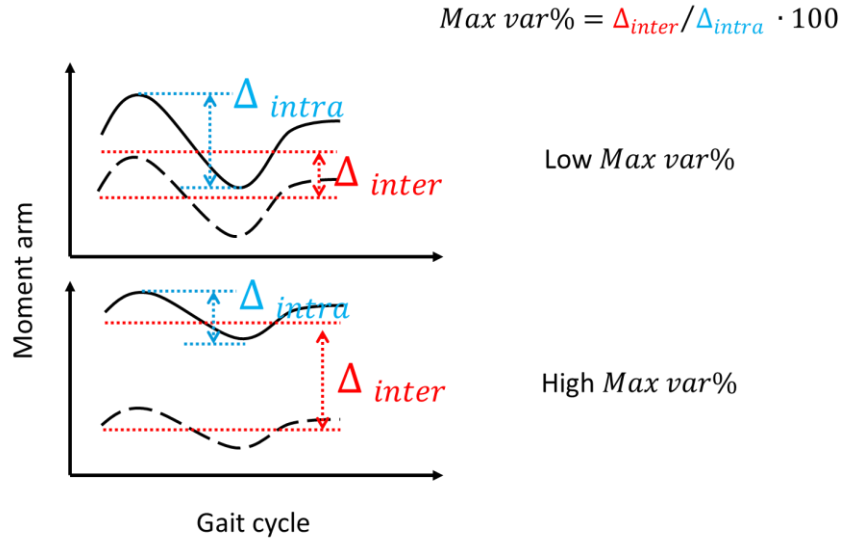


Figure 6-1. Graphical explanation of *Max var%* calculation

Intra-method variation (Δ_{intra}) is the maximum variation within the curve (e.g., Gluteus Medius flexion/extension moment arm over gait cycle). Every time a different HJC is used, Δ_{intra} changes, therefore an average value over all HJC locations is used. Inter-method variation (Δ_{inter}) is the average change in the curve when a different HJC locations are used. The percentage of maximum variation is the ratio between these two values (***Max var%*** = $\Delta_{inter} / \Delta_{intra} \cdot 100$)

6.4. Results and discussions

6.4.1. Hip joint center

The Wilcoxon signed rank tests showed that all three HJC estimation methods (rD, rH and OC) were statistically different from GC (the geometrical HJC measured from CT images) at a 95% significance level. The median errors are reported in Figure 6-2. Harrington model had an overall accuracy of 13.2 mm, and represented the best estimation. However, e_L for OC was very close to Harrington, with 14.7 mm error. Davis model demonstrated the lowest accuracy with 29.5 mm error with respect to GC.

A similar investigation was previously conducted by Bartels et al. (2015); the error presented in that study is considerably higher than the one reported here, due to an offset in the vertical direction (median 18.7 mm, up to 33.6 mm). The differences could be due to the scaling approaches and registration

methods employed by the present and Bartels' studies. Bartels scaled the pelvis by using surface marker measurements, and, therefore, is less accurate than the one employed in this study. Moreover, the absence of persistent markers between the CT and motion analysis forced the authors to use an alternative registration procedure, which can also contribute to the differences observed between the results.

Our initial hypothesis stated that the regression equations would be more accurate than the scaled HJC. The hypothesis was not confirmed by the results presented in Figure 6-2; in fact, the accuracy of OC was comparable to the best available regression method, with the median error only 1.5 mm different from rH. Davis model, instead, performed very poorly compared to the other two methods. Therefore, when pelvic scaling was accurately performed by means of CT measurements, the error on the HJC estimation from the scaled generic musculoskeletal model (in particular, 'gait2392') was comparable to the best available regression equations (Harrington et al., 2007), and it was confined within the 2cm radius around the true geometrical HJC.

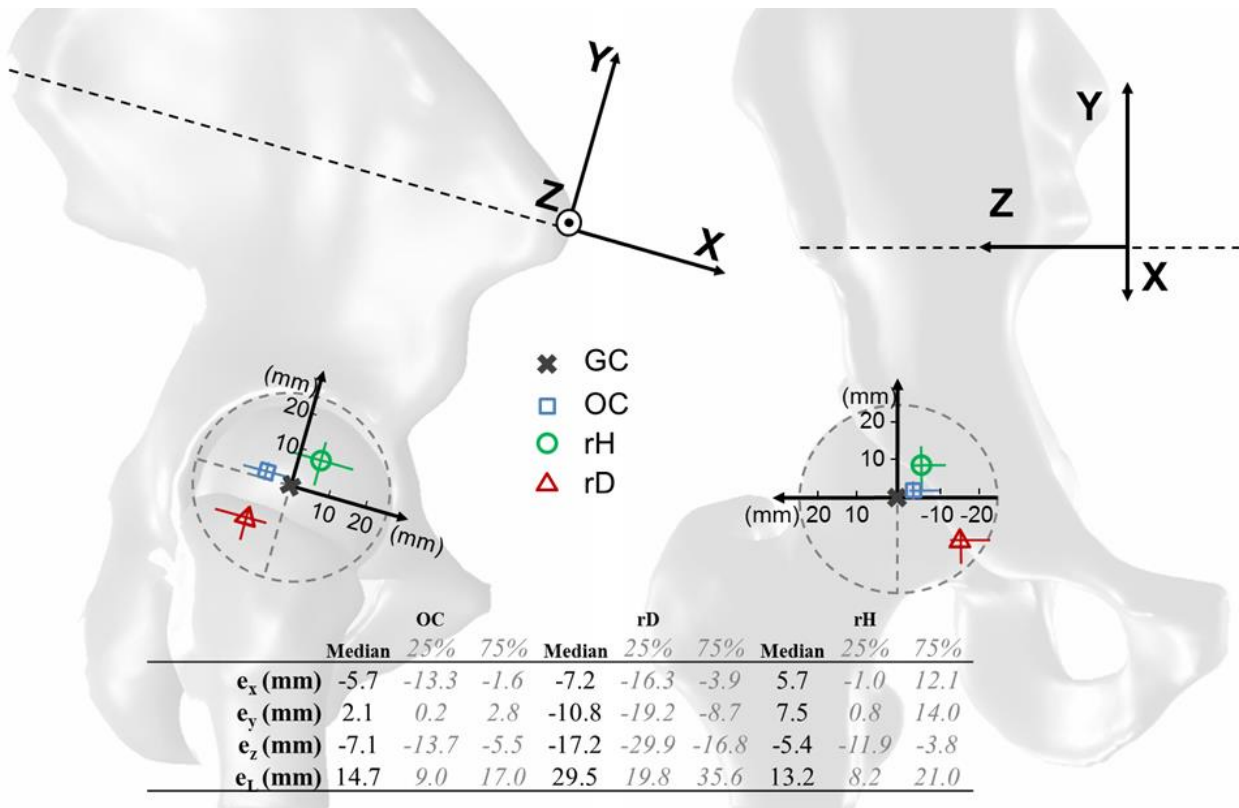


Figure 6-2. Modelled versus measured hip joint centers

The figure shows the two hip joint centers calculated from the regression equations (rH and rD), and the model original joint center (OC) with respect to the geometric center (GC), and their respective 25 and 75 percentile bars for the ten participants. The table reports the errors in the three axes plus the distance between GC and the other methods

6.4.2. Variables sensitivity to hip joint center

The group average curves of the hip kinematics, kinetics and contact forces for every HJC method plus the six perturbations are shown in Figure 6-3 A,B, while the relative maximum and minimum peaks, maximum variation and percentage of maximum variation are reported in Table 6-1. The variables that were more sensitive to HJC variation were the frontal angles ($Max\ var\% > 41\%$), and the maximum peak of the vertical hip contact force ($Max\ var\% > 51\%$ corresponding to 2.7 times the body weights of maximum variation) together with the minimum peak of the mediolateral contact force ($Max\ var\% > 88\%$ corresponding to 1.5 times the body weights of maximum variation).

For simplicity, $Max\ var\%$ values for muscle moment arms were reported in Figure 6-4. Overall, hip muscle moment arms were the most sensitive to the HJC perturbations in the ML direction, with a total average over all three degrees of freedom of 100% (*i.e.*, on average, muscle moment arms had an inter-method variation one time bigger than the intra-method variation). Moment arms were also globally 76% sensitive to HJC perturbations in the AP direction, and only 47% to HJC perturbations in the SI direction.

The muscles whose moment arms that had the highest sensitivity to the HJC location were the Iliacus, Psoas and Pectineus. This is not surprising, since these muscles are very close to the HJC, and, consequently, highly affected by the perturbation of its location. This finding suggests that these muscles should be given priority when medical images for customized anatomical models (and in particular muscle moment arms) are available. This is especially true for the Iliacus and Psoas that play a primary role in any hip movement.

The absence of a gold standard prevents a clear understanding about whether the introduction of subject-specific HJC improved the accuracy of the results or not. However, it seems reasonable to state that the kinematic and the kinetic results can only benefit from the use of a more accurate HJC, and to consider the curves associated to the GC model as the most accurate.

The situation is more complex for the contact forces. Contact forces depend on muscle forces and inverse kinetic calculations, which in turn depend on the inverse kinematic results. Several muscle parameters are affected by the HJC variation, first of all the muscle moment arms. Consequently, part of the contact forces sensitivity is passed down from the kinematics and kinetics dependency, and part is related to the muscle moment arms sensitivity to HJC variation, as shown in Figure 6-4. In fact, in the present study the muscle anatomy was not customized because complete Magnetic Resonance Images of the hip muscles were not available, and the intent was to customize the model with the accessible information from the clinical investigation (CT images). Consequently, this introduced an inconsistency between the skeletal and muscular model, *e.g.*, hip dislocation and consequent penetration of muscles into

the bone geometries (Figure 6-5). Such inconsistency is not quantifiable, and potentially caused inaccurate muscle and joint contact forces estimation by static optimization.

The use of wrapping surfaces did not improve the situation. Wrapping surfaces are OpenSim entities that interact with the muscles only, and can help creating a more realistic line of action. In attempt to prevent the muscle/bone penetration introduced by HJC dislocation, wrapping were used surfaces as described in (van Arkel et al., 2013) and then customized for the specific problem. However, it emerged that the muscle paths are unpredictable once the HJC is moved. With the original HJC location, wrapping surfaces produced realistic moment arm curves over the range of motion of the different hip degrees of freedom, and comparable to the *in-vivo* measurements (Arnold et al., 2000; Visser et al., 1990). After the HJC is adjusted to a new location (*e.g.*, as estimated from CT measurements), moment arm curves are completely altered and assume non-physiological shapes. The muscles are forced to work under non-tested conditions; therefore, their behaviour becomes unpredictable.

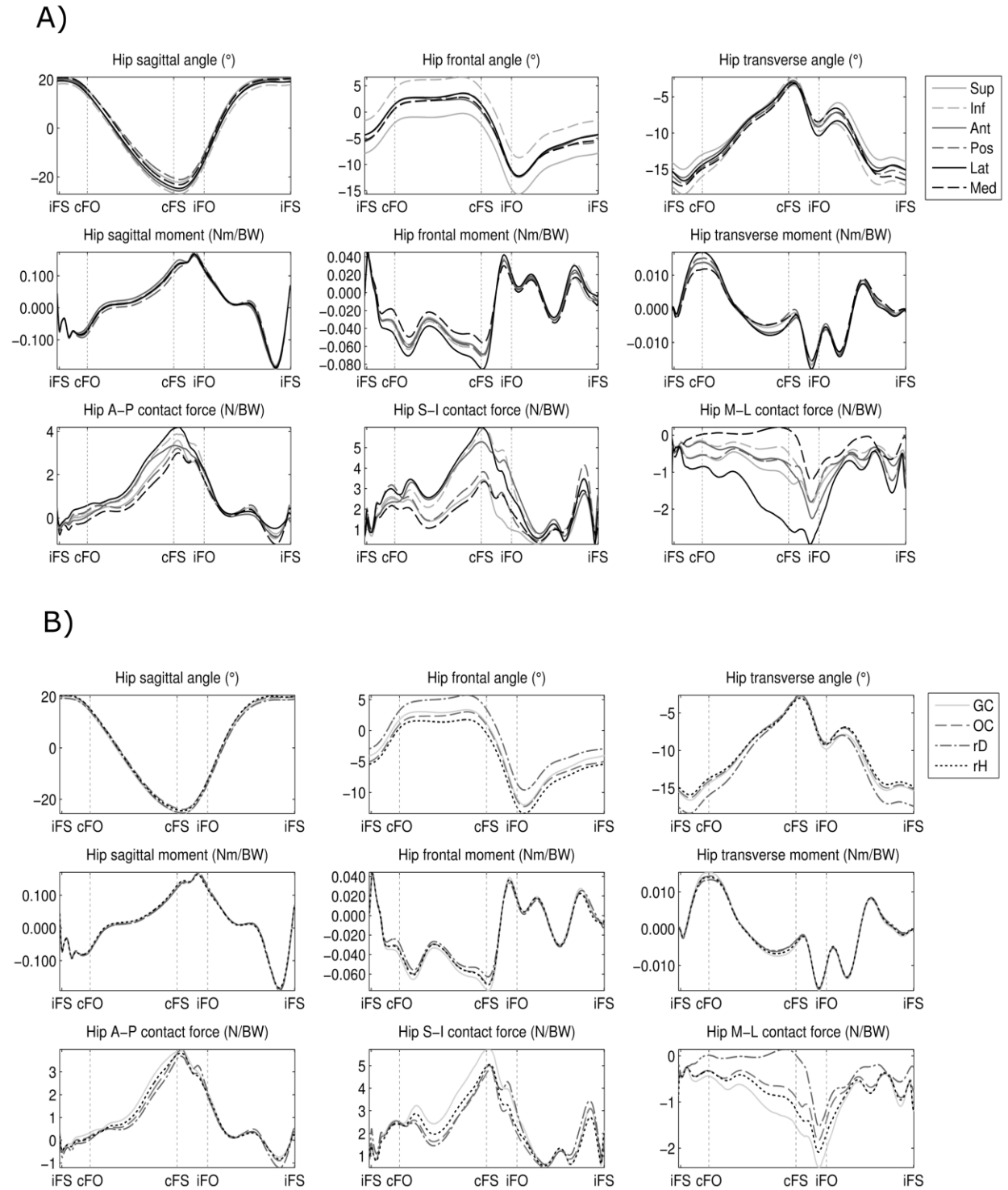


Figure 6-3. Average curves for the HJC perturbations

In (A) the curves represent the six directional perturbations, and in (B) the four HJC prediction methods. Gait cycle events: ipsilateral foot-strike (iFS), contralateral foot-off (cFO), contralateral foot-strike (cFS), ipsilateral foot-off (iFO). A-P = anterior-posterior, S-I = superior-inferior, M-L = medial-lateral

Table 6-1. Curve peaks for HJC perturbations

Maximum and minimum curve peaks of the group average curves for the ten different HJC methods and their respective maximum variation and percentage of maximum variation

		Sup	Inf	Ant	Pos	Lat	Med	OC	GC	rD	rH	Max var %
Kinematics (°)												
Sagittal	max	21.6	18.9	20.8	20.9	20.1	21.4	20.8	20.1	19.9	21.2	6.0
	min	-22.5	-27.3	-26.0	-21.4	-25.0	-23.5	-24.2	-25.8	-25.6	-24.7	13.2
Frontal	max	0.4	7.4	3.8	3.9	4.2	3.5	3.8	4.3	6.3	2.8	41.9
	min	-16.1	-9.2	-12.9	-12.7	-12.7	-12.7	-12.8	-12.5	-10.1	-13.9	41.6
Transv	max	-2.7	-2.0	-2.4	-2.7	-2.7	-2.7	-2.3	-2.5	-2.3	-2.6	4.5
	min	-17.4	-20.5	-18.5	-19.1	-18.9	-19.4	-18.5	-18.9	-20.5	-18.2	19.3
Kinetics (N*m/BW)												
Sagittal	max	0.172	0.178	0.172	0.183	0.177	0.175	0.175	0.175	0.179	0.172	2.9
	min	-	-	-	-	-	-	-	-	-	-	2.9
Frontal	max	0.065	0.071	0.069	0.066	0.071	0.065	0.067	0.070	0.067	0.067	4.6
	min	-	-	-	-	-	-	-	-	-	-	16.1
Transv	max	0.016	0.017	0.016	0.017	0.019	0.014	0.016	0.017	0.016	0.016	11.5
	min	-	-	-	-	-	-	-	-	-	-	6.0
Contact Forces (N/BW)												
A-P	max	3.7	4.0	3.4	3.4	4.3	3.2	4.1	4.0	3.8	3.9	23.2
	min	-0.8	-1.0	-0.9	-0.9	-0.6	-1.2	-0.8	-0.9	-1.2	-0.9	13.2
S-I	max	3.7	6.1	5.4	4.5	6.1	3.6	6.0	5.0	5.3	5.3	52.5
	min	0.1	0.4	0.3	0.3	0.1	0.2	0.2	0.3	0.4	0.3	6.5
M-L	max	-0.2	-0.1	-0.1	-0.2	-0.2	0.3	-0.2	-0.2	0.2	-0.2	23.4
	min	-1.9	-1.9	-2.4	-2.0	-3.1	-1.4	-2.5	-2.0	-1.7	-2.2	87.0

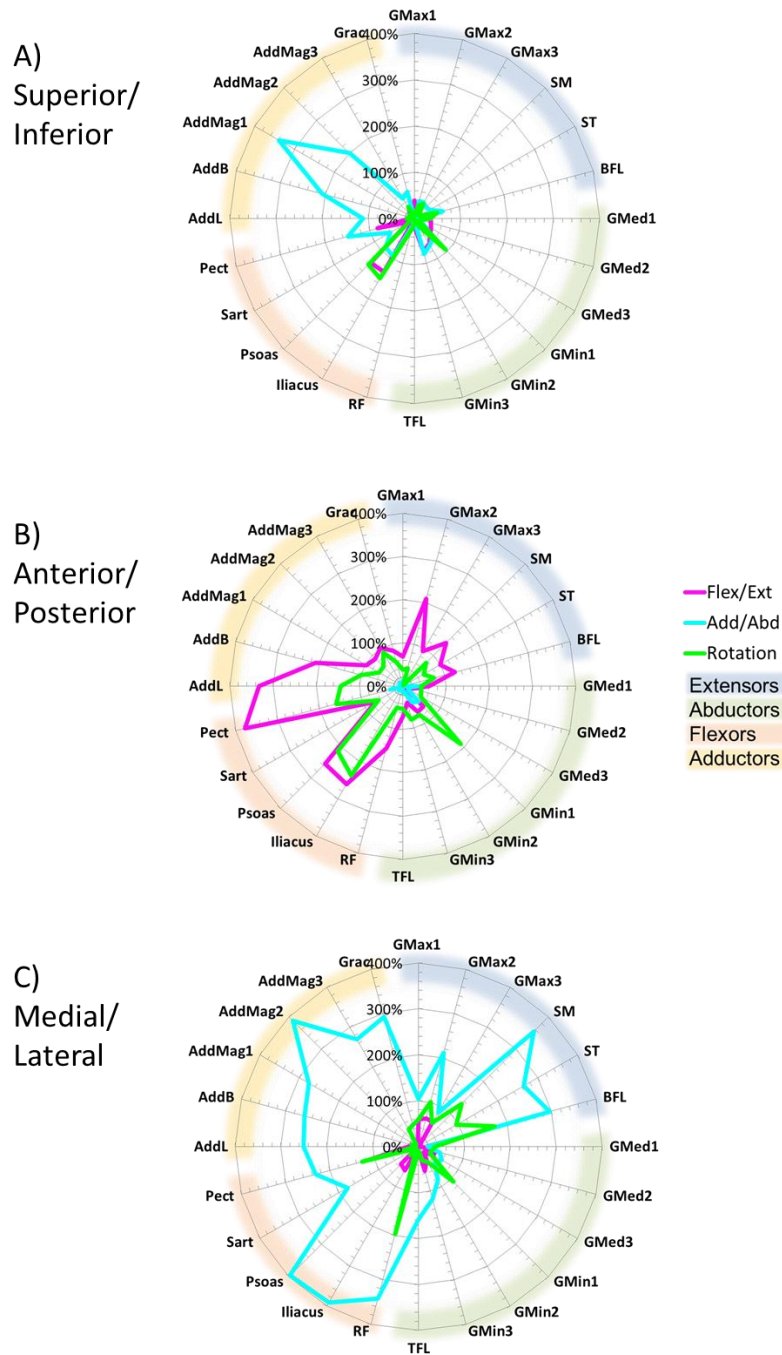


Figure 6-4. Percentage of maximum variation of the muscle moment arms

The values were calculated during gait cycle for all modelled hip muscles with respect to the three hip degrees of freedom (Flexion/extension = violet, Adduction/Abduction = cyan, Internal/External Rotation = green). The sensitivity indices are divided by Superior/Inferior (A), Anterior/Posterior (B) and Medial/Lateral (C) perturbations of the HJC. GMax = gluteus maximus, SM = semimembranosus, ST = semitendinosus, BFL = biceps femoris caput longus, GMed = gluteus medius, GMin = gluteus minimus, TFL = tensor fasciae latae, RF = rectus femoris, Sart = Sartorius, Pect = pectineus, AddL = adductor longus, AddB = adductor brevis, AddMag = adductors magnus, Grac = gracilis. The numbers in the names indicate muscles that have been divided into subgroups for modelling purposes, see the original 'gait2392' model for further details

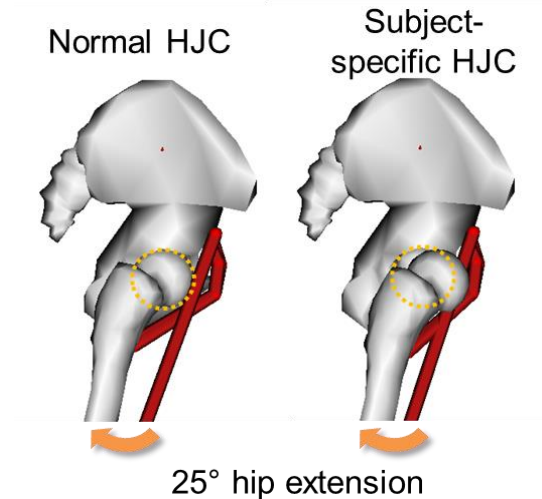


Figure 6-5. The normal and subject-specific hip joint centers, with hip flexor muscles at 25° hip extension

The dotted line highlights the position of the acetabulum, and shows that in the subject-specific HJC the hip results anteriorly dislocated of 11 mm in this specific subject, causing the muscles to penetrate the bone geometries

The only situation where HJC location varies but the muscle anatomy remains intact is in prosthetic reconstruction. The results reported in this study show how superior and medial displacement in the HJC causes a considerable hip contact force reduction, consistently with what has been previously shown by Depl et al. (Delp and Maloney, 1993; Delp et al., 1996). However, this consideration goes beyond the objectives of the present study.

6.5. Conclusions

In conclusion, subject-specific HJC can be used in generic musculoskeletal models if only kinematic and kinetic variables are the focus of the analysis. If radiological images are not available, the best option is using Harrington regression equations. However, an accurate manual scaling of the pelvis from a generic musculoskeletal model can also produce quite accurate HJC estimates.

When muscle and contact forces are included in the analysis, however, the results of this study highly discourage the use of subject-specific HJC without a consistent adjustment of muscle anatomy, because of the inconsistencies that are created in the muscle moment arms. In this case, it is best to rely on the scaled generic model anatomy that, even if not tailored for the specific subject, is at least internally consistent.

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Chapter 6. On the subject-specific hip joint center

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6.7. Supplementary material: Functional Hip Joint Center

It is deemed important to report the results obtained from the estimation of the Hip Joint Center (HJC) using a functional method.

When available, ISB (International Society of Biomechanics) recommends using functional methods for HJC estimation (Wu et al., 2002). In fact, functional methods do not rely on the correct placement of markers, and are shown to be more repeatable to inter-trial and inter-operator variability (Besier et al., 2003).

The star plus circumduction task covers the full functional range of motion and allows for the most accurate 3-dimensional location of the HJC (Camomilla et al., 2006). This is a large movement executed with the free leg reproducing the trajectory reported in Figure 6-6 (Camomilla et al., 2006; Hicks and Richards, 2005). Using these functional trials, the HJC was estimated as in Piazza (2001). The algorithm was implemented in MATLAB (R2014a, MathWorks, Natick, MA, USA) using the optimization function *fminunc* (unconstrained nonlinear optimization). The initial conditions were set to the results of the Harrington regression equations.

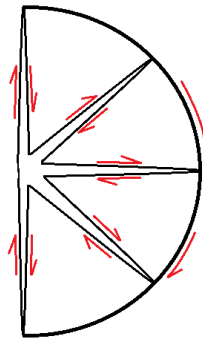


Figure 6-6. Task for the estimation of the functional Hip Joint Center

The figure describes the 'Star plus circumduction' movement. The black lines represent the trajectory that the free leg follows during the execution of the hip swing task

The functional HJC was first tested on artificial data, using ideal marker trajectories as produced from OpenSim for the same star+arc movement. These data had no noise or soft tissue artifacts, and the estimated HJC was expected to be perfectly matched with the one from the OpenSim model. This preliminary test gave perfect results, and the algorithm was then applied to the experimental data of 12 subjects.

The results are reported in Figure 6-7. The accuracy of the functional HJC estimates was very low, with a median distance between estimates and CT-measured (geometrical) HJC of 35.5 mm, which is worse than Davis regression method.

This poor performance can be partially explained by the high sensitivity of functional methods to soft tissue artifacts. In fact they are often used in conjunction with soft tissue artifact reduction algorithms (Heller et al., 2011). However, given the nature of the available dataset, it was not possible to apply such techniques.

According to the presented results, functional HJC produces poor results when compared to CT-measured HJC. It should always be advised to use soft tissue artifact reduction techniques when functional HJC are to be used. If that is not a possibility given the nature of the study, then Harrington regression equations should be used.

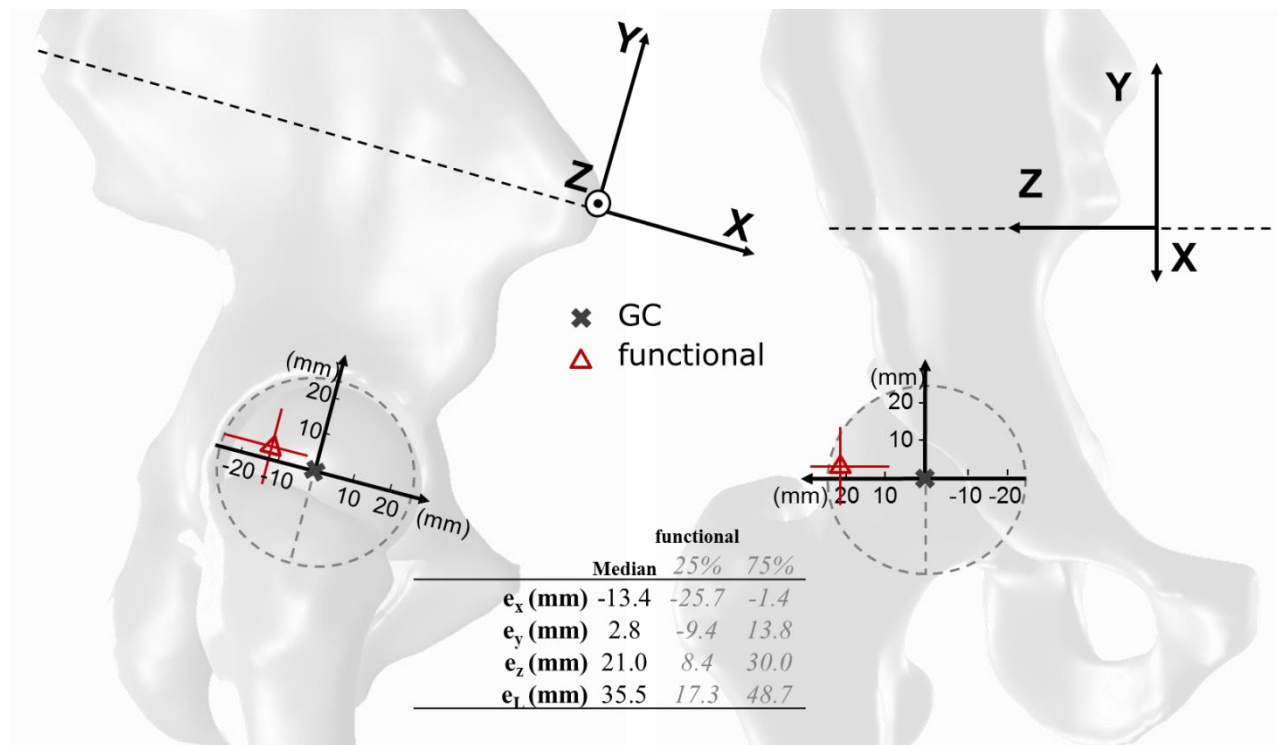


Figure 6-7. Functional Hip Joint Center

The figure shows the hip joint center estimated from the functional method (functional) with respect to the geometric center (GC), and their respective 25 and 75 percentile bars for the twelve participants. The table reports the errors in the three axes plus the distance between GC and the functional estimates

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Regression Models to Predict Hip Joint Centers in Pathological Hip Population

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6.9. Abstract

The purpose was to investigate the validity of Harrington and Davis hip joint center (HJC) regression equations on a population affected by a hip deformity, (i.e., femoroacetabular impingement). Sixty-seven participants (21 healthy controls, 46 with a cam-type deformity) underwent pelvic CT imaging. Relevant bony landmarks and geometric HJCs were digitized from the images, and skin thickness was measured for the anterior and posterior superior iliac spines. Non-parametric statistical and Bland-Altman tests analyzed differences between the predicted HJC (from regression equations) and the actual HJC (from CT images). The error from Davis model (25.0 ± 6.7 mm) was larger than Harrington (12.3 ± 5.9 mm, $p < 0.001$). There were no differences between groups, thus, studies on femoroacetabular impingement can implement conventional regression models. Measured skin thickness was 9.7 ± 7.0 mm and 19.6 ± 10.9 mm for the anterior and posterior bony landmarks, respectively, and correlated with body mass index. Skin thickness estimates could be considered to reduce the systematic error introduced by surface markers. New adult-specific regression equations were developed from the CT dataset, with the hypothesis that they could provide better estimates when tuned to a larger adult-specific dataset. The linear models were validated on external datasets and using leave-one-out cross-validation techniques; Prediction errors were comparable to those of Harrington model, despite the adult-specific population and the larger sample size, thus, prediction accuracy obtained from these parameters could not be improved.

6.10. Introduction

Motion analysis and musculoskeletal modelling are highly sensitive to the location of the hip joint center (HJC). Inverse dynamics studies reported differences of up to 22% in hip flexion-extension moments, with discrepancies of 3 cm in HJC (Stagni et al., 2000). Muscles' capacity to generate moment at the hip joint is most sensitive to vertical displacements of HJC; a 2-cm superior displacement decreases the hip abduction moment by about 50% (Delp and Maloney, 1993) and, consequently, leads to inaccurate muscle and hip contact force estimations.

Although the gold standard to identify HJC is medical images, regression equations can be used when imaging data are not available (Bell et al., 1989; Bell et al., 1990; Davis III et al., 1991; Harrington et al., 2007; Seidel et al., 1995). Among other factors, the regression equation parameters depend upon the sample size and its characteristics. Several established HJC regression models were developed from specific demographics, however, their abilities to represent populations with different characteristics (from those on which they have been developed) and are often disputed. An early model by Bell (1989) was established from 39 healthy children and 31 healthy adults (Bell et al., 1989; Bell et al., 1990), whereas a conventional model by Davis (1991) provided no specific information about the original cohort data as to which the regression equations were developed from (Davis III et al., 1991). Seidel's study later analyzed 65 healthy cadaveric pelvises, but the use of pelvic height as a predictor prevents the clinical use of this model (Seidel et al., 1995). More recently, a model by Harrington and associates (2007) examined a mixed population of 14 healthy children, 10 cerebral palsy children, and 8 adults (Harrington et al., 2007). They also investigated the validity of models developed from adult populations when applied to children and young cerebral palsy patients, and found that the prediction errors were similar in all three groups (Harrington et al., 2007). Andersen and colleagues investigated patients who underwent hip resurfacing, where the geometrical features of the pelvis were known to be different from the normal population, and found significant differences in these two groups according to the type of regression equation used (Andersen et al., 2013). Among the available HJC regression models, recent studies showed that the Harrington equations provided the highest accuracy (Andersen et al., 2013; Kainz et al., 2015; Sangeux et al., 2011; Sangeux et al., 2014), although this set of equations was developed from a non-homogeneous and relatively small size sample.

Cam femoroacetabular impingement (FAI) is the result of bone overgrowth on the femoral head and neck, characterized by an elevated alpha angle, femoral retro-torsion and acetabular retro-version, and decreased femoral neck-shaft angle (Ng et al., 2015), thus it cannot be assumed a priori that the same regression equations can properly locate HJCs in individuals with a cam deformity. However, no study

has investigated the accuracy of these regression equations applied to subjects with hip deformities such as cam-type FAI.

Therefore, the objective was to evaluate the validity of HJC regression models for a population characterized with a cam-type deformity (FAI) compared to a healthy, control population; where the actual geometric HJC was measured using Computed Tomography (CT) images. Two models were compared: 1) Harrington, as it is considered to be the most accurate (Kainz et al., 2015); and 2) Davis, as it is still one of the most used and a standard in some commercial software. Moreover, new regression equations were proposed to verify if the predictors used by Harrington (2007) could provide better estimates in adults when tuned on a larger and adult-specific dataset. Lastly, skin thickness was measured to provide reference values to account for a source of error, when regression equations are applied to surface markers instead of bony landmarks.

6.11. Methods

6.11.1. Experimental data

Sixty-seven subjects consented to participate in the study approved by the Research Ethics Board of the institution: 21 control participants (CON) and 46 affected by FAI. Gender composition, age, height, and body mass index (BMI) were comparable in the two groups (Table 6-5, Supplementary Material). Pelvic CT images were acquired from each participant using either the Toshiba Aquilion (Toshiba Medical Systems Corporation, Otawara, Japan) or the Discover CT750 (GE Healthcare, Mississauga, ON, Canada). The scan was executed in a supine position, with a pillow underneath the lumbar vertebra to mimic the natural lordosis of the standing position. FAI participants were selected based on their hip deformity, quantified by an alpha angle larger than 50.5° in the axial or 60° in the radial 1:30 view on CT data (Beaulé et al., 2012; Khanna et al., 2014; Nötzli et al., 2002). CON participants did not show any sign of hip deformity and both groups were not affected by any other lower limb musculoskeletal disorder. The hips of every participant were divided into highest and lowest alpha angles (labelled ‘low alpha’ and ‘high alpha’ in Table 6-2).

The CT data were blinded and read using ITK-SNAP 2.4 (PICS, USA), in a multi planar reconstruction view (2007). For every participant, the 3D coordinates of the bony landmarks for left and right, anterior and posterior superior iliac spines were recorded, and the skin thicknesses were measured as the distance between these bony landmarks and the skin surface in the transverse plane. The local pelvic coordinate system was based on these coordinates and defined according to ISB guidelines (2002). The hip geometric centers were located as the center of a maximum-radius circumference fitting the contour of the femoral head on the three planes, and considered as the actual HJC (Taddei et al., 2007).

The CT measurements were completed by two readers, each performing three readings, with near-perfect inter- and intra-observer reliability (ICC>0.90).

6.11.2. Data analysis

The HJCs were estimated from the two regression models in the common pelvic coordinate system. Harrington regression equations depend on pelvic width (PW - the distance between right and left anterior superior iliac crest) and pelvic depth (PD - the distance between the mid-points of the two anterior and the two posterior superior iliac crests) (Harrington et al., 2007): $x = -0.24PD - 9.9$, $y = -0.30PW - 10.9$, and $z = 0.33PW + 7.3$ (expressed in mm), where x, y and z are the anterior-posterior (AP), superior-inferior (SI) and medial-lateral (ML) coordinates, respectively. Davis regression equations depend on PW, leg length (L) and the AP distance between the HJC and the ipsilateral anterior-superior iliac spine (denoted as D): $x = -0.95D + 0.031L - 4$, $y = -0.31D - 0.096L + 13$ and $z = 0.5PW - 0.055L + 7$. The regression equations from both models were applied directly to the pelvic bony landmarks.

The errors between the estimated and the actual HJC were calculated in the three orthogonal directions (e_{ML} , e_{AP} , e_{SI}) together with their linear distance (e_L). HJCs from each regression model were directly compared to the actual HJC, using: 1) Bland-Altman scatter plots (Bland and Altman, 1986) to calculate the limits of agreement; and 2) the Wilcoxon signed-rank test to determine whether measurements and estimates were statistically different. One-way Kruskal-Wallis tests were used to identify significant differences between groups and sides (independent variables), by using errors as dependent variables. In order to increase the possible differences between FAI and CON, the hips with the highest deformity from the FAI group were compared to the hips with lowest alpha angles from the CON group. A paired t-test compared the average error over all participants between the two models. All statistical tests were conducted with a 5% significant level with a Bonferroni correction to account for dependencies between variables (i.e., errors in three directions plus linear distance), thus P-values less than 0.013 were considered significant.

New regression equations were also developed based on the available dataset. The prediction variables were PD, PW, L, and body height (H). A linear model of the form $HJC = a + b \cdot PD + c \cdot PW + d \cdot L + e \cdot H$ was chosen (Harrington et al., 2007). A forward stepwise regression method based on R^2 criterion automatically selected the predictors that best described the dataset variability. Linear regression equations using only one predictor at a time or all predictors together were also calculated. The model validation was done using leave-one-out cross-validation, and applying the new set of equations to other independent datasets (Harrington et al., 2007; Leardini et al., 1999).

6.12. Results

The differences between evaluators in the bony landmarks identification on the CT images are shown in Figure 6-10 of the Supplementary material; the median error on HJC location was 1.8 mm, with a maximum of 5 mm. Notably, the asymmetry found between contralateral HJC locations was 5.0 ± 2.0 mm, calculated as linear distance between left and right coordinates (after flipping the ML axis). The average skin thickness for the anterior superior iliac spine bony landmarks was 9.7 ± 7.0 mm, while the posterior superior iliac spine reported 19.6 ± 10.9 mm. More information about the relationship between skin thickness and BMI is reported in the Supplementary material (Figure 6-11).

6.12.1. Differences in groups and sides for Davis and Harrington models

Table 6-2. HJC prediction errors

Median (and 25/75 percentile-range) of prediction errors in antero-posterior (e_{AP}), superior-inferior (e_{SI}), medial-lateral (e_{ML}) directions and relative linear distance (e_L). The results are divided by prediction method (Davis, Harrington), group (CON, FAI), side (Low alpha, High alpha)

Davis								Harrington								
Low α side	CON				FAI			CON				FAI				
	Md	25%	75%		Md	25%	75%	Md	25%	75%		Md	25%	75%		
e_{AP}	-0.8	-9.9	1.3		-1.4	-4.7	3.0	0.1	-4.3	3.2		2.9	-0.2	4.8		
e_{SI}	-13.5	-15.9	-9.1	**	-15.7	-19.0	-10.7	**	4.0	2.4	11.3	*	6.2	-0.7	9.8	**
e_{ML}	-15.7	-21.6	-11.8	**	18.2	12.2	24.3	**	-4.8	-7.2	-1.5	**	5.6	2.6	9.7	**
e_L	22.3	17.9	28.6	**	26.1	21.0	29.2	**	10.3	6.7	17.9	**	11.7	8.2	16.3	**
High α side																
e_{AP}	-2.0	-8.5	1.1		-2.5	-6.0	3.1	-0.3	-4.8	2.7		1.6	-1.5	4.8		
e_{SI}	-13.2	-16.2	-10.2	**	-14.5	-19.3	-11.3	**	5.1	1.1	13.3	*	5.4	1.4	11.4	**
e_{ML}	14.4	10.0	21.5	**	-18.4	-22.4	-13.4	**	2.0	0.3	8.3	*	-6.0	-10.4	-2.5	**
e_L	24.7	19.0	27.1	**	26.3	21.3	29.2	**	11.0	8.6	15.7	**	12.3	8.5	15.5	**

** Wilcoxon signed rank test, P-value<0.001

* Wilcoxon signed rank test, $0.001 \leq P\text{-value} < 0.013$

Kruskal-Wallis test was non-significant for group and side comparisons

The Kruskal-Wallis test found no significant differences between groups (Table 6-2), therefore, participants from the two groups were pooled together when testing the performance of the two regression equations, for a total of 67 hips. Given the dependency from the same anthropometric measurements, the contralateral hips were not pooled together even though there was no significant difference between the two sides (symmetric error) (Table 6-2).

Overall, the paired t-tests showed a significantly lower e_L for Harrington equations (12.3 ± 5.9 mm) than Davis (25.0 ± 6.7 mm, $p < 0.001$), mostly given by the higher error in the ML direction of the latter model.

The prediction for both Davis and Harrington models was more accurate in AP direction, where the Wilcoxon signed rank test found no significant difference between estimates and the actual HJC (Table 6-2). Both models demonstrated poor accuracy in every other direction, where errors were significantly different from a zero-median distribution (Table 6-2). The errors in the vertical dimension were similar in magnitudes but opposite in directions. Both models estimated the HJC too medially, but Davis error was three times larger than Harrington.

In the Bland-Altman tests, some variables showed a linear relationship between error and mean. In such cases, the limits of agreements (LOA) were corrected to adjust for this linear relationship (Bland and Altman, 1999) (Figure 6-8). Davis model (A-C) showed larger LOA (i.e., worst reliability) than Harrington (D-F).

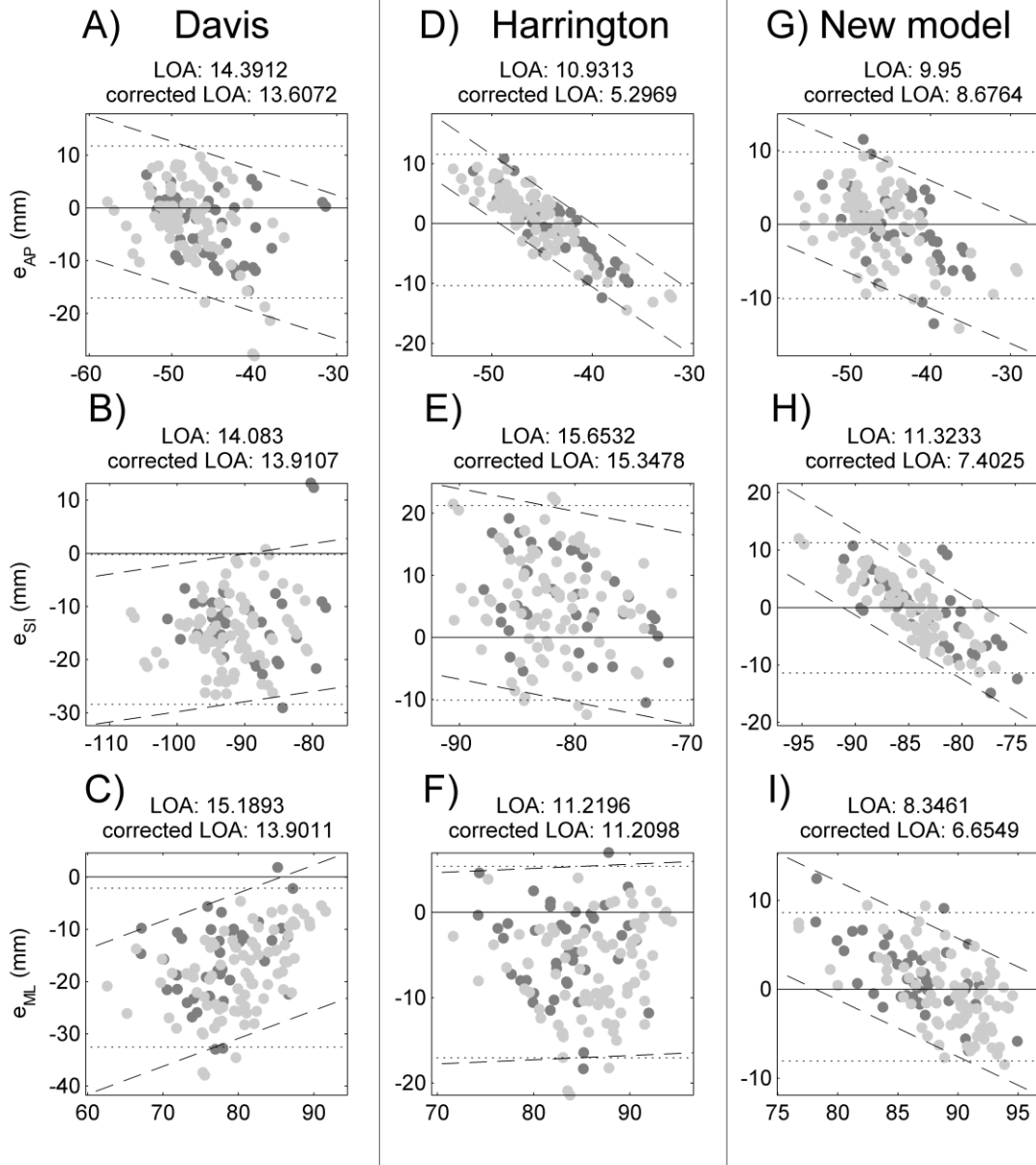


Figure 6-8. Bland-Altman scatter plots of HJC estimates

The plots were calculated for the actual hip joint center coordinates versus the regression equation predictions in the three directions (e_{AP} = error in antero-posterior direction, e_{SI} = superior-inferior, e_{ML} = medio-lateral) and for the three models ('Davis', 'Harrington' and the 'New model' proposed in the present study). The solid line is the zero-error line, the dotted lines are the limits of agreements (LOA), the dashed lines are the corrected LOA as calculated from the regression line ($b_0 + b_1 \cdot avg \pm 1.96 \text{ residual std}$). Dark grey markers = CON, Light grey markers = FAI subjects

6.12.2. New regression equations and validation analysis

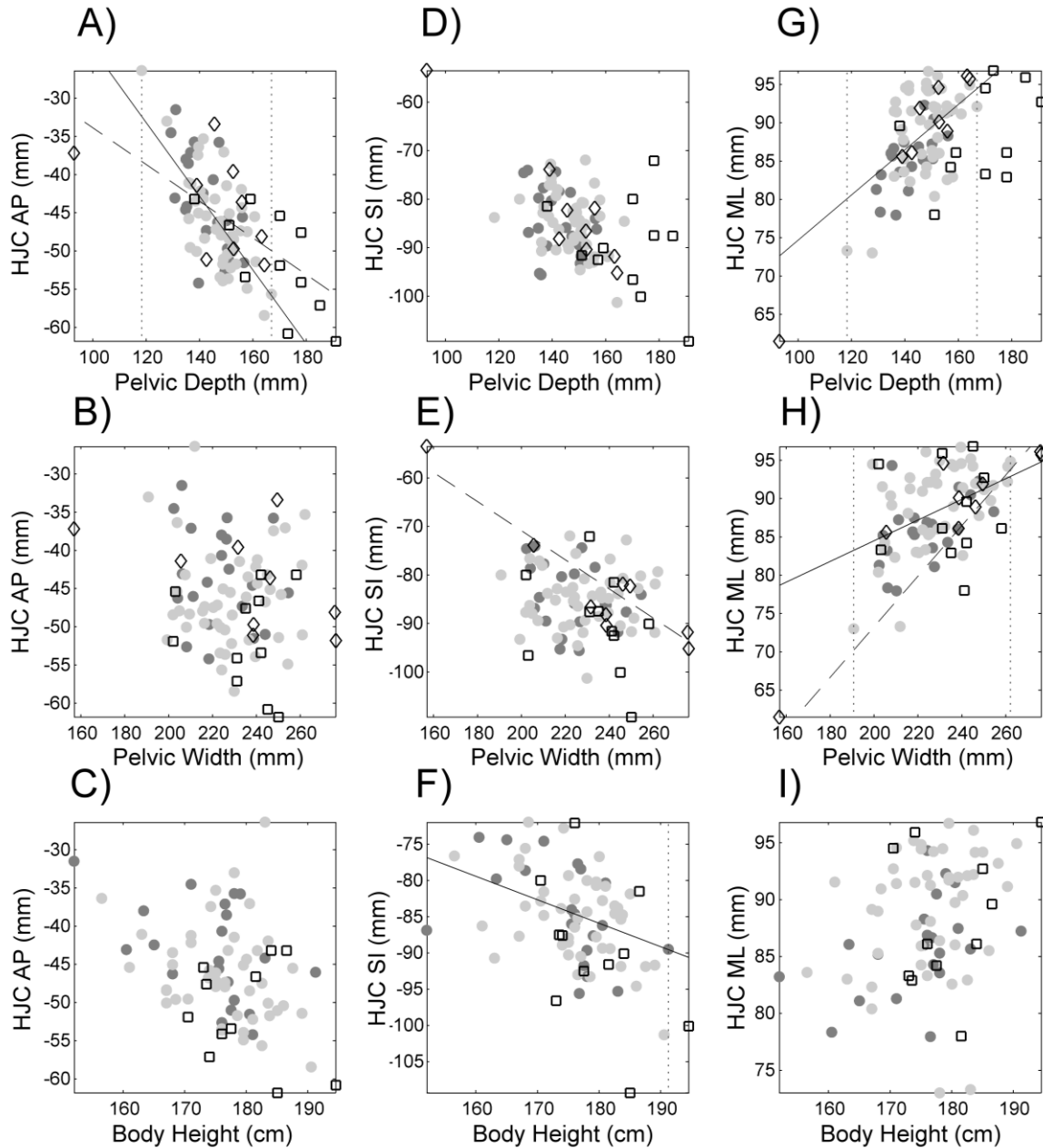


Figure 6-9. HJC predictors versus predictive variables

The scatterplots of the correlations between predictive (PD = pelvic depth, PW = pelvic width, H = body height) and predicted (HJC AP = antero-posterior hip joint center coordinate, SI = superior-inferior, ML = medial-lateral) variables are shown. Leg length (L) was omitted from the figure given its poor performance in the single-predictor equations (Table 6-3). The solid lines represent the 'New model'. The dashed lines represent 'Harrington' regression equations. The vertical dotted lines indicate the boundaries of the current dataset on which the 'New model' equations have been developed. Dark grey markers = CON, Light grey markers = FAI subjects, diamonds = Harrington 2007 adult dataset, and squares = Leardini 1999 dataset

Table 6-3. Linear regression analysis for HJC prediction

The results are reported when using 1) 'All predictors', 2) only one predictor at the time ('Single predictor'), and 3) the 'Stepwise regression' method. The model parameters as calculated in the different approaches are reported in the first five columns (Intercepts and all coefficients for PD = pelvis depth, PW = pelvis width, L = leg length, H = body height). The right part of the table reports the performance indices: R^2 is the coefficient of determination, which indicates the percentage of variability explained by the model. F-statistics tests for a significant linear regression relationship between the response variable and the predictor variables, and the relative P-values for the F-test on the model are reported in the line underneath F. The last column reports the square root of the leave-one-out cross validation (LOOCV) error. The calculations were executed in MATLAB (R2014a, MathWorks, Natick, MA, USA), and the function 'stepwiselm' was used with R^2 -entry (improvement parameter to add terms to the prediction) set to 0.01, while the R^2 -remove (improvement parameter to remove terms) was 0.005

		Intercept	PD	PW	L	H	R^2	F	P-value	LOOCV error ⁽²⁾
All predictors	AP	0.6	-0.505	0.043	0.148	0.022	0.46	13.0	0.000	5.04
	SI	-30.4	-0.116	0.034	0.048	-0.281	0.19	3.8	0.008	5.53
	ML	41.3	0.200	0.100	-0.165	0.058	0.45	12.8	0.000	3.56
Single predictors	AP	24.6	-0.482				0.42	48.0	0.000	
	SI	-52.2	-0.222				0.11	8.0	0.006	
	ML	45.2	0.295				0.32	30.4	0.000	
	AP	-38.6		-0.031			0.01	0.4	0.534	
	SI	-78.2		-0.028			0.01	0.4	0.536	
	ML	57.5		0.135			0.23	19.2	0.000	
	AP	-72.3			0.292		0.05	3.5	0.067	
	SI	-90.0			0.060		0.00	0.2	0.680	
	ML	102.7			-0.160		0.03	2.1	0.157	
	AP	-2.0				-0.248	0.08	5.5	0.022	
	SI	-27.6				-0.324	0.16	12.8	0.001	
	ML	44.3				0.249	0.16	12.3	0.001	
Stepwise regression⁽¹⁾	AP	24.6	-0.482	-	-	-	0.42	48.0	0.000	5.17
	SI	-27.6	-	-	-	-0.324	0.16	12.8	0.001	5.64
	ML	31.6	0.241	0.095	-	-	0.42	23.2	0.000	3.67

⁽¹⁾ R^2 criterion, P-entry 0.1, P-remove 0.05

⁽²⁾LOOCV error = (sqrt (MSE))

Table 6-4. HJC prediction errors

Errors were calculated in the anterior-posterior (e_{AP}), superior-inferior (e_{SI}), medial-lateral (e_{ML}) directions and relative linear distance (e_L). The three different models were: 1) 'New model' including H parameter, 2) 'New model' excluding H parameter, and 3) 'Harrington model'. The three sets of equations were applied on 1) the 'Current' dataset (all subjects, no group distinction), 2) 'Harrington 2007' dataset (restricted to 8 adults subjects), and 3) 'Leardini 1999' dataset (11 adult subjects). Since no H values were provided in Harrington 2007, the errors of 'New model (with H)' could not be calculated on this dataset

Dataset		New model (with H)			New model (w.out H)			Harrington model		
		Md	25%	75%	Md	25%	75%	Md	25%	75%
Current	e_{AP}	0.5	-3.0	3.4	0.5	-3.0	3.4	2.0	-2.8	4.3
	e_{SI}	0.4	-4.6	4.2	0.1	-4.5	4.7	5.8	-0.2	12.2
	e_{ML}	0.4	-2.1	3.6	0.4	-2.1	3.6	-5.3	-9.7	-1.6
	e_L	8.3	6.3	10.7	8.1	6.0	10.0	11.6	8.4	16.9
Harrington 2007 (adults only)	e_{AP}				-2.7	-7.5	2.3	-1.0	-4.5	3.6
	e_{SI}	n.a.			0.5	-5.9	4.3	1.4	-3.0	5.9
	e_{ML}				1.0	-1.1	2.8	-2.3	-5.7	0.4
	e_L				9.2	7.2	10.8	9.1	4.5	11.1
Leardini 1999	e_{AP}	-5.7	-8.5	0.6	-5.7	-8.5	0.6	1.2	-3.6	5.1
	e_{SI}	3.7	-1.4	9.0	2.6	-5.3	6.5	8.4	2.9	14.0
	e_{ML}	8.3	0.4	9.9	8.3	0.4	9.9	-2.6	-8.9	2.7
	e_L	12.5	8.9	19.1	12.4	9.8	17.5	12.2	8.3	21.8

The results for the multiple regression analysis are reported in Table 6-3: PD was the best predictor in the AP and ML directions, PW and H provided limited prediction power for ML, and SI, while L (leg length) was discarded because non-significant. The scatter plots show the dependencies between predictors and measurements compared with Harrington's and Leardini's datasets (Figure 6-9).

The final equations according to the stepwise regression approach were:

$$x = 24.6 - 0.482PD,$$

$$y = -27.6 - 0.324H$$

$$z = 31.6 + 0.241PD + 0.095PW$$

All residuals followed a normal distribution. The leave-one-out cross validation errors for these regressions in AP, SI, and ML were 5.17, 5.64, and 3.67 mm, respectively. These equations were applied to the current dataset, the adult population in Harrington (2007) and Leardini's studies (1999), and the prediction errors were reported in Table 6-4. The proposed model performed as well as Harrington's on both Harrington's and Leardini's datasets.

A Bland-Altman test on the new proposed model indicated that the LOA in AP was comparable to Harrington model, while slightly better values for the new proposed equations were found in the other two directions (Figure 6-8, G-I).

6.13. Discussions

The objective of the study was to investigate the validity and application of two popular HJC regression models on participants with a hip deformity (e.g. FAI), and to develop new adult-specific regression equations based on a larger sample than previous studies,

6.13.1. Differences between groups and sides for Davis and Harrington models in hip deformity population

No differences from the Kruskal-Wallis test for either set of regression equations indicated that the anatomical characteristics of the FAI group did not significantly alter the estimation HJC location with respect to the CON group. No significant difference was found between sides (larger versus smaller deformity) either; therefore, motion analyses on FAI populations can use the same HJC regression equations used for the healthy population. The absence of a significant difference in the prediction errors between sides implies that the 5.0 ± 2.0 mm asymmetry found cannot be predicted; this could be the result of measurement errors and intrinsic anatomical variability between hips.

The average errors in HJC estimations for both models were consistent with previous studies (Harrington et al., 2007; Leardini et al., 1999; Sangeux et al., 2011; Sangeux et al., 2014). Davis model produced an eL two times higher than Harrington, confirming the overall superiority of the latter model in predicting accurate HJCs. Both models showed accurate measurement in the AP direction, demonstrated by the statistical consistency between the predicted and actual HJCs. However, the LOA for the Davis model were larger, demonstrating less reliability than Harrington (Figure 6-8 A,H). Since the two models performed similarly in the SI direction, Davis model's poorer results were mostly attributed to the ML component. AP and SI are considered the most critical axes for HJC estimation, as inverse dynamics and moment-generating capacity of muscles are more sensitive to these directions (Delp and Maloney, 1993; Stagni et al., 2000), therefore Davis model's poor performance in ML is less critical. In any case, Harrington model should be preferred.

6.13.2. New regression equations and validation analysis

Since FAI and CON were not different in HJC location, the new regression equations were developed from the entire dataset, pooling together participants from both groups. Similar to Harrington's

(2007) and Seidel's (1995) findings, PD was the best predictor for HJC in the AP and ML axes (Table 6-3). In contrast with Harrington (2007) and similarly to Seidel's findings (1995), PW did not show a large predictive power for the AP and SI directions, and the stepwise regression model used PW only as a second predictive variable for HJC in the ML axis (Table 6-3).

The use of L as HJC predictor is limited by the reliability of this measurement (e.g., errors in bony landmarks location, instrument used) (Badii et al., 2014). Moreover, some subjects might have non-standard anthropometric proportions. Lastly, in the current dataset, L prediction power was very low for all variables. Therefore, contrary to previous studies that used L (Davis III et al., 1991; Harrington et al., 2007), we suggest relying on body height for HJC prediction.

The developed model is demographics-specific, thus, its performance cannot be guaranteed when applied outside the boundaries on which the model has been trained. Figure 6-9 A,G,H show how the error on the prediction increases notably when the predictors exceed the original dataset (vertical dotted lines). Because of this limitation, the proposed model cannot be used with confidence in children, for example. On the contrary, Harrington model's biggest advantage is that the original dataset covered larger range of ages. This allowed the authors to reveal new relationships between variables (such as PW versus HJC SI) not visible in a smaller range. However, this 'macroscopic' relationship might not demonstrate great accuracy when zooming into a particular range of the dataset, exactly like shown in Figure 6-9 E. Therefore, we tuned the same predictors to more restricted demographics to verify whether the prediction accuracy would increase. Our model demonstrated good accuracy on independent datasets, however, the prediction did not considerably improve with respect to Harrington regression equations.

For clinical gait analysis applications, the regression equations are applied to surface markers. This represents a further source of error (Lalonde et al., 2003; Lalonde et al., 2007); in fact, even with the assumption that the markers are properly placed, there is a consistent layer of skin that offsets the location of the markers with respect to the bony landmarks, and its thickness is highly correlated to the BMI (Figure 6-11). The regression parameters that are mostly affected by this problem are PD and the origin of the pelvic reference system (as defined by ISB guidelines). Therefore, we strongly suggest to account for this systematic error, as suggested by Sangeux (2015).

Some limitations of the study have a potential impact on the findings. Firstly, all measurements of bony landmark location were affected by errors; although the error on the single measurement might not be large (median < 2 mm), their combined effects on local reference systems cause a larger baseline uncertainty. Also, the 9 female participants might have added unwanted variability. However, Seidel's study (1995) found no significant differences between female and male HJC, and concluded that both genders could be represented by the same model. Skin thickness measurements would not have been

possible without the use of CT; however, they could be affected by skin movement errors due to the supinated position used during the scans, which could partly explain the large difference between the anterior and posterior averages.

6.14. Conclusions

This study confirmed the better accuracy of Harrington model (Harrington et al., 2007) with respect to Davis (Davis III et al., 1991), mostly given by Davis poor prediction in the medial-lateral direction. The asymmetry index measured as absolute difference between hips was negligible because it was very close to the measurement errors. Also, the prediction errors found for both Harrington and Davis models were the same between the controls and hip deformity group; therefore, the anatomical features characterizing FAI did not significantly alter HJC location, and regular regression models can be used on this population.

New adult-specific regression equations were developed from a 67 hip CT-dataset using pelvic depth, width, leg length and body height as predictors. The new model performed as well as Harrington, in terms of validation on all the available sets of data (leave-one-out cross validation error, and prediction error on an independent dataset), despite the fact that our equations were developed from a larger adult-specific population. Therefore, it can be concluded that the prediction accuracy obtainable from using these predictors cannot be further increased, and that the errors found from the newly proposed model or from Harrington equations are due to intrinsic subject variability and measurement errors.

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Conflict of interest statement

All the authors have no financial or personal conflicts to disclose

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6.16. Supplementary material

The supplementary material is organized in three parts: the first reports some reliability measurements on the bony landmarks localization procedure, the second reports a brief analysis on the relationship between the skin thickness and the body mass index, and the third contains the table with all available raw data for the regression model.

1. Bony landmark localization reliability

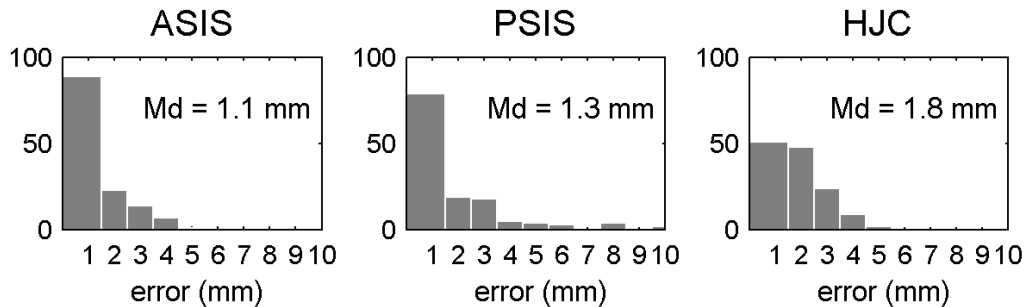


Figure 6-10. Distribution of localization errors of the bony landmarks on the Computed Tomography images
The errors were calculated as linear distance between the two raters measurements. Errors from contralateral sides were pooled together, and the median value is reported. ASIS = anterior-superior iliac spines, PSIS = posterior-superior iliac spines, HJC = hip joint centers

2. Skin thickness and BMI regression models

The skin thickness found for the anterior superior iliac spine bony landmarks was 9.7 ± 7.0 mm, while the posterior superior iliac spine reported 19.6 ± 10.9 mm. These values are averaged between left and right bony landmarks.

There appeared to be a strong relationship between body mass index (BMI) and skin thickness (ST) in both the anterior and posterior locations. The linear regression equations (and relative coefficient of determination R^2 , root-mean-squared error RMS, F-statistics and P-value) are:

$$ST_A = -24.45 + 1.30 \cdot BMI, \text{ with } R^2 = 0.527, \text{ RMS} = 4.83, F = 72.5, \text{ P-value} < 0.001$$

$$ST_P = -35.53 + 2.09 \cdot BMI, \text{ with } R^2 = 0.579, \text{ RMS} = 7.00, F = 89.3, \text{ P-value} < 0.001$$

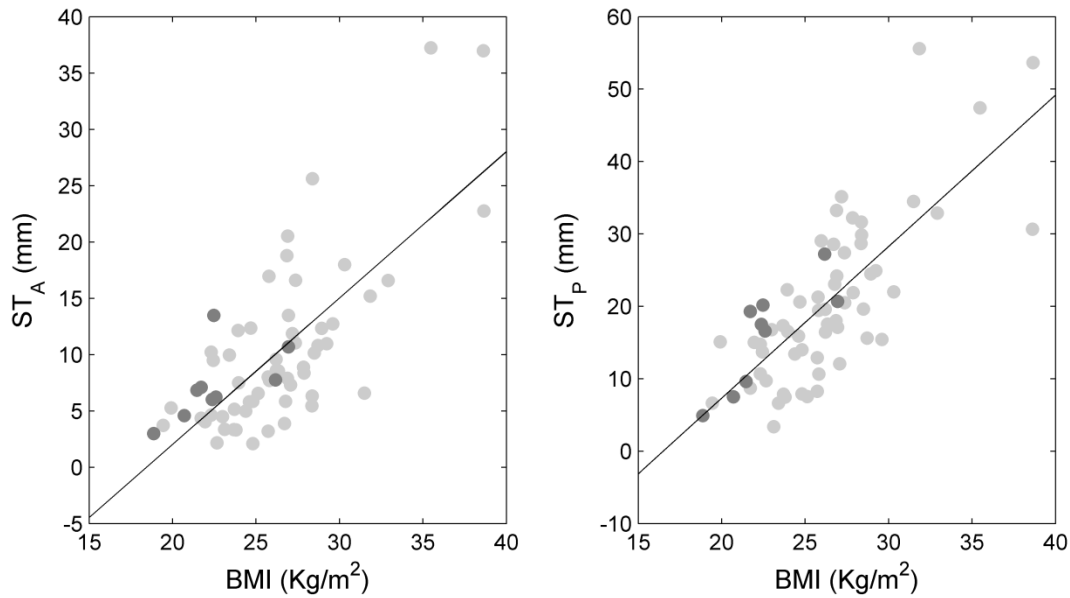


Figure 6-11. Scatter plots: body mass index versus skin thickness

The darker dots are the female participants

3. Raw data for future reference

Leg Length was measured with a measuring tape as the distance between anterior superior iliac spine and ipsilateral medial malleolus. Pelvis Width and Depth were measured from CT images; Pelvic Width is the distance between right and left anterior superior iliac crest; Pelvic Depth is the distance between the mid-points of the two anterior and the two posterior superior iliac crests.

Table 6-5. Participants' demographics information, anthropometric measurements and CT HJC measurements

Participant code	Gender	Age	Height	Leg Length	Pelvis Width	Pelvis Depth	X	HJC Y	Z
CON1	M	28.6	191.2	95.8	211.1	150.0	-46.0	-89.5	87.2
CON2	M	41.2	179.0	92.0	247.6	147.2	-35.8	-87.6	92.3
CON3	F	32.9	165.0	85.3	227.4	141.2	-42.5	-74.4	81.1
CON4	M	36.7	176.0	96.0	224.0	145.0	-40.7	-85.9	86.9
CON5	F	42.1	152.0	82.5	205.9	131.0	-31.5	-86.9	83.2
CON6	M	36.9	180.5	92.8	238.6	156.5	-51.5	-86.2	91.5
CON7	M	30.2	175.5	95.0	254.4	156.0	-45.6	-84.0	88.3
CON8	F	43.7	163.3	91.0	224.0	134.8	-38.0	-79.8	86.1
CON9	M	31	168.0	92.0	204.0	146.7	-46.2	-78.6	85.2
CON10	M	37.4	177.5	90.8	243.9	150.7	-51.0	-91.8	90.5
CON11	M	26.4	178.0	97.0	218.3	150.4	-49.7	-93.2	85.3
CON12	M	25.4	181.0	94.5	218.2	139.6	-54.2	-80.4	87.5
CON13	M	31.8	183.0	85.0	217.5	135.1	-44.2	-95.3	85.7
CON14	M	26.4	177.0	93.3	233.4	142.5	-47.3	-78.4	84.3

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CON15	M	47.7	176.0	73.0	208.1	149.5	-52.6	-84.6	94.3
CON16	M	23.7	160.5	93.5	206.1	130.7	-43.1	-74.1	78.3
CON17	M	25.8	175.5	103.5	238.0	134.7	-44.6	-86.0	86.0
CON18	M	37	178.0	96.8	226.5	137.9	-35.7	-89.6	83.6
CON19	M	36.7	176.8	92.3	226.3	135.7	-38.5	-95.6	86.7
CON20	M	32.5	176.5	95.0	210.1	136.6	-37.1	-77.7	78.0
CON21	M	27.4	171.0	94.0	202.3	129.2	-34.5	-74.6	81.3
FAI1	F	27.5	161.0	88.5	203.7	142.4	-46.9	-87.3	86.9
FAI2	M	43.2	181.8	84.5	207.5	145.7	-42.0	-92.1	90.0
FAI3	M	30.6	178.5	91.5	199.2	153.6	-56.1	-92.7	94.0
FAI4	M	30.6	173.8	96.0	244.0	148.0	-45.8	-82.5	92.6
FAI5	M	30.4	177.0	88.0	244.9	141.3	-48.0	-90.2	92.0
FAI6	M	33.4	185.0	91.7	260.8	148.9	-51.3	-79.5	90.9
FAI7	M	44.3	178.0	88.5	232.2	150.1	-43.7	-81.9	83.3
FAI8	M	31.2	181.0	95.8	228.6	151.6	-48.8	-82.2	87.3
FAI9	M	25	180.5	93.0	228.9	152.7	-49.8	-87.0	90.6
FAI10	M	28.2	170.5	88.5	216.2	136.4	-49.7	-85.3	85.9
FAI11	M	29	176.0	89.5	225.6	150.7	-48.1	-90.9	94.9
FAI12	M	28.4	182.5	91.0	224.1	166.9	-53.6	-87.0	95.2
FAI13	M	23.9	179.5	92.0	239.4	148.7	-49.5	-86.6	90.1
FAI14	M	31.8	174.0	94.8	251.2	135.9	-46.5	-89.2	92.0
FAI15	M	29.7	190.5	89.0	229.8	164.2	-56.8	-100.3	92.3
FAI16	M	31.3	179.5	91.3	254.2	157.7	-51.1	-80.4	88.9
FAI17	F	45.4	171.0	94.5	239.6	140.2	-46.1	-82.1	94.6
FAI18	F	23.2	156.5	101.5	203.8	139.6	-33.6	-78.8	83.5
FAI19	M	28.8	178.0	98.0	190.7	127.7	-27.4	-75.2	78.3
FAI20	M	31	187.5	86.5	228.0	160.6	-43.4	-89.5	92.1
FAI21	M	29	179.5	94.5	246.1	151.1	-42.7	-81.2	87.4
FAI22	M	32.7	183.5	91.5	223.6	152.2	-48.9	-87.5	94.1
FAI23	M	44.7	183.0	91.0	211.8	118.2	-26.0	-81.0	79.8
FAI24	M	26.3	189.0	90.5	250.0	161.0	-53.8	-93.8	94.9
FAI25	M	25.3	183.5	80.0	260.7	155.6	-44.1	-87.1	93.6
FAI26	M	38.2	183.8	94.0	236.5	148.6	-53.8	-79.9	89.5
FAI27	M	29.4	168.0	89.0	236.1	138.5	-46.1	-84.8	88.0
FAI28	M	31.1	176.5	88.0	216.3	155.3	-49.7	-92.9	96.9
FAI29	M	46.5	168.0	81.8	224.7	139.5	-48.3	-77.5	88.1
FAI30	M	40.3	186.0	92.3	225.5	150.3	-48.8	-93.8	91.2
FAI31	M	51.7	182.5	96.5	220.3	157.8	-50.4	-80.1	90.3
FAI32	M	42.8	176.5	96.0	215.4	152.2	-50.7	-87.7	88.1
FAI33	M	41.9	174.2	90.0	247.7	139.3	-40.3	-74.2	92.1
FAI34	M	33	175.0	85.0	204.8	148.0	-49.3	-82.3	86.2
FAI35	M	35.5	175.0	94.0	235.3	148.0	-50.3	-90.1	98.1
FAI36	M	48.2	176.0	91.6	223.3	147.6	-51.8	-84.8	82.8
FAI37	F	36.7	163.0	91.5	219.1	135.9	-42.1	-90.1	81.6
FAI38	M	46.4	180.0	85.0	240.3	155.7	-48.1	-78.3	85.9

Chapter 6. On the subject-specific hip joint center

FAI39	M	23.1	167.0	93.3	209.4	141.8	-53.0	-77.8	82.5
FAI40	M	49	167.0	84.5	208.0	138.8	-48.1	-74.7	90.1
FAI41	M	39.4	175.0	98.0	262.0	141.3	-29.4	-80.9	93.7
FAI42	F	46.7	168.5	83.0	222.0	152.3	-49.4	-71.6	90.1
FAI43	F	21.4	167.0	89.0	201.9	151.0	-51.4	-85.1	77.7
FAI44	M	40.3	171.0	99.0	240.3	136.7	-43.5	-82.6	89.7
FAI45	M	27.6	180.5	101.5	253.0	149.0	-35.6	-81.1	86.6
FAI46	M	33.4	175.0	95.0	222.1	146.1	-49.5	-86.9	84.7

Chapter 7. On the hip muscle and contact forces in FAI

***In-silico* assessment of Muscle and Contact Forces provides New Insights into FAI Pathomechanisms**

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7.1. Abstract

Femoroacetabular Impingement (FAI) is an anatomical deformity of the hip, associated with groin pain and reduced hip range of motion. The objective was to analyze and link the functional alterations observed in FAI population during level walking to anatomical alterations, muscle and the hip contact forces. Inverse kinematics, kinetics, static optimization and joint reaction analyses were performed, and the differences between the FAI and a healthy control group were examined during walking trials. The FAI group showed a significantly reduced normalized walking speed and step length, with slight reductions in pelvic and hip ranges of motion, and hip flexion moment. At contralateral foot-strike the hip contact force in the FAI group was lower than the control, and the Iliacus and Psoas muscles showed a reduced force production. These results could be interpreted as a protective mechanism developed by FAI patients to prevent high compression at the site of the impingement. In fact, at contralateral foot-strike the hip was extended, and the compressing hip contact force was directed towards the anterior-superior quadrant of the acetabulum, consistent with the localization of the cam-type deformity and the cartilage and labrum damages. In hip extension, the tension is further aggravated by the hip capsule and Iliopsoas tendon actions on the bone overgrowth, which becomes more anteriorly exposed.

Based on these findings, a possible FAI pathomechanism was proposed, which could be used to support the development of preventive treatment and intervention for symptomatic FAI patients.

7.2. Introduction

Cam type Femoroacetabular Impingement (FAI) is an anatomical deformity of the hip, associated with groin pain and reduced hip range of motion limiting activities of daily living (Ganz et al., 2003). With a prevalence of 17% in men and 4% in women, cam type FAI is characterized by a decreased femoral head-neck offset and/or asphericity of the lateral femoral head (Gosvig et al., 2008; Hack et al., 2010; Laborie et al., 2011). Studies suggested that FAI is a leading factor for the development of hip osteoarthritis (OA), particularly in younger adults (Agricola et al., 2013; Ganz et al., 2008), but its etiology is still unclear (Ganz et al., 2008).

From a functional point of view, the biomechanics of the hip joint are also altered, with reduced range of motion in both the sagittal and frontal planes during everyday activities such as walking, squatting and stairs climbing (Hunt et al., 2013; Kennedy et al., 2009; Lamontagne et al., 2009b; Rylander et al., 2013; Rylander et al., 2011). The kinematics of level walking is characterized by a general reduction of the range of motion that involves specifically the hip frontal and sagittal planes, and frontal pelvic angles (Hunt et al., 2013; Kennedy et al., 2009; Rylander et al., 2013), and also the hip internal rotation (Hunt et al., 2013; Rylander et al., 2013). Differences in kinetics were only noticed by Hunt et al. (2013), who found reduced hip flexion and external rotation moments.

Some of the functional alterations found for FAI cannot be directly related to the impingement caused by the bony deformity. Hypotheses have been suggested that functional alterations are linked to muscle properties and soft tissue characteristics. In particular, one study showed that FAI population is affected by a reduced muscular strength during maximal isometric voluntary contractions in hip adduction/abduction, flexion and external rotations (Casartelli et al., 2011b). This was deemed important especially because FAI is considered an OA precursor (Ganz et al., 2003), and is associated with the presence of other pathologies, such as labral tear, for which muscle weakness and altered recruitment patterns have been found (Mendis et al.). Altered neuromuscular activation in FAI has been hypothesized and linked to the differences found in activities of daily living (Casartelli et al., 2011b; Kennedy et al., 2009). Muscle activity during dynamic tasks for FAI has only been investigated during squatting (Lamontagne et al., 2015); however, no significant differences were found with respect to the control population. No studies exist that have investigated electromyography (EMG) in FAI during walking.

Joint loading from inverse dynamics only consider external forces, however muscles are speculated to produce more than 70% to the total hip contact forces (HCF) (Lu et al., 1998; Ng et al., 2012), and therefore, their contributions cannot be overlooked. Since *in vivo* measurements are invasive, computational models of the musculoskeletal system (musculoskeletal models) are the most ethically

acceptable approach to estimate muscle forces and HCF. For instance, static optimization estimates muscle forces by minimizing an appropriate cost function, e.g. sum of muscle stresses or muscle activations squared (Crowninshield and Brand, 1981) while satisfying dynamic equilibrium at the joints.

Therefore, our objective was to examine the functional alterations observed in FAI population during level walking by analyzing the relationships between FAI anatomical alterations, neuromuscular function as observed through EMG measurements and muscle and hip contact forces. In particular, since an overall reduction at the hip range of motion has been previously found, we hypothesized a lower muscle force production and, consequently, lower hip contact forces for FAI population compared to healthy population.

7.3. Methods

7.3.1. Participants

Table 7-1. Anthropometric information and alpha angles for the two groups

	CON mean $\pm$ std	FAI mean $\pm$ std	P-values
# participants	18 males	18 males	
Height (m)	1.76 $\pm$ 0.06	1.76 $\pm$ 0.06	0.401
BMI (Kg/m²)	25.9 $\pm$ 3.2	27.0 $\pm$ 4.3	0.428
Age (year)	32 $\pm$ 6	38 $\pm$ 9	0.050
Axial Alpha (°)	42 $\pm$ 5	56 $\pm$ 9	<0.001
Radial Alpha (°)	51 $\pm$ 3	64 $\pm$ 6	<0.001

Two groups were included: 19 symptomatic FAI male patients, and 18 healthy male participants (CON), who gave written consent to participate in the study approved by the Research Ethics Board of the institution. FAI subjects were selected based on: 1) their cam deformity, quantified by alpha angle higher than 50.5° in the axial view, and higher than 60° in the radial view (Nötzli et al., 2002; Rakhra et al., 2009), 2) a visible convex ridge at the femoral head-neck junction on radiographs, 3) a positive impingement test, and 4) persistence of pain longer than 6 months near the groin/lateral aspect of the hip.

All participants from the FAI group underwent FAI corrective surgery after participating in the study, one participant was removed from the analysis because the intra-surgical observation revealed a prevalent pincer-type deformity.

The healthy controls were recruited from the general population, and matched for gender and body mass index (BMI) to the FAI group (Table 7-1). The leg of interest corresponded to the symptomatic side

for the FAI group, and to the side with the lowest combined (axial and radial) alpha angle for the CON one.

7.3.2. Protocol

Pelvic CT images were acquired from each participant while lying supine, using either the Toshiba Aquilion (Toshiba Medical Systems Corporation, Otawara, Japan) or the Discover CT750 (GE Healthcare, Mississauga, ON, Canada). Four radiopaque surface markers (reflective markers with a metallic core) were placed on the skin in correspondence of bony anatomical landmarks (left and right anterior and posterior superior iliac spines) in order to register the location of the surface landmarks with respect to the bones. Then, the participants were transferred to the Human Movement Research Laboratory, and instrumented with retro-reflective markers according to the UOMAM marker set (similar to Plug-in-Gait with additional medial knee and ankle markers). After a static trial in neutral standing pose, five repetitions of walking trials (at a self-selected pace) were acquired for every participant with a motion capture system including ten infrared Vicon MX-13 cameras (VICON, Oxford, UK, sampling: 200 Hz), and two fixed Bertec force plates (models FP4060-08, Bertec Corporation, Columbus OH, UK, sampling: 1000 Hz).

Synchronized EMG signals were acquired from the leg of interest with FreeEMG300 (BTS BioEngineering, Milan, Italy) and Bagnoli Desktop EMG System (Delsys, Boston, MA), both sampling at 1000 Hz. The muscles of interest were Gluteus Maximus and Medius, Tensor Fasciae Latae, Rectus Femoris, Biceps Femoris and Semitendinosus, identified by palpation and following SENIAM guidelines (Hermens et al., 1999).

7.3.3. CT measurements

Alpha angles in the axial and radial views were computed by expert radiologists from CT scans as described by Beaulé et al. (2005). Three trained readers identified the coordinates of bilateral superior anterior and posterior iliac spines (bony landmarks), the geometrical center of the hip joint, and the position of four radiopaque surface markers (RASI, LASI, RPSI and LPSI). The readings were performed in a multi-planar reconstruction view in ITK-SNAP 2.4 (PICSLS, USA).

7.3.4. Musculoskeletal model and simulations

The three-dimensional marker trajectories and the ground reaction forces were filtered with a zero-lag fourth order Butterworth filter (cut-off frequency at 6Hz). All simulations were performed in OpenSim 3.1 using the ‘gait2392’ model based on (Delp et al., 1990), which includes the lower body

segments plus torso. The hip and the lumbar articulations were modelled as a ball and socket joint, the knee as a custom joint (Yamaguchi and Zajac, 1990) and the ankle as a hinge joint.

Consistently with the tool available in OpenSim, the generic musculoskeletal model dimensions were linearly scaled, comparing the distance between pairs of virtual and experimental markers. Since CT images of the pelvis were available, accurate pelvic width, depth and height were measured and used for the manual scaling of the pelvic segment. Then, the virtual marker positions were adjusted by registering their locations to their experimental coordinates, after estimating static joint angles through inverse kinematics. The locations of the pelvic virtual markers with respect to the correspondent bony landmarks were adjusted based on the CT images, in order to prevent inclusion of offsets in pelvic orientation.

The muscle properties of Delp's model were based on cadaveric measurements of a 74.2 Kg and 1.67 male. The maximum isometric force of every muscle was scaled by $(M_{exp} \cdot H_{exp}) / (M_{mod} \cdot H_{mod})$, where M is the mass, H the height, and *exp* and *mod* indicate the experimental and model measurements respectively (Handsfield et al., 2014).

After the model had been scaled, inverse kinematics, inverse dynamics, static optimization and joint reaction analyses (Steele et al., 2012) were performed. The static optimization tool for muscle force estimation was set to use a quadratic cost function (Crowninshield and Brand, 1981), and without considering muscle contraction dynamics (force-length-velocity relationship) as they have been shown not to influence muscle predictions for walking (Anderson and Pandy, 2001b). Hip contact force vectors were finally calculated as forces acting on the acetabulum and expressed in the pelvic coordinate system.

The variables of interest computed from the simulations were: hip angles, torques, contact forces and muscle forces. The last three variables were normalized by body weight (BW) to enable the comparison of participants with different body masses.

7.3.5. Gait analysis data

The analysis was limited to the stance phase (from foot-strike to foot-off); all variables were time-normalized to the stance cycle by means of a quintic natural spline function. Relevant curve parameters such as peak and range of motion (ROM) were extracted for the statistical analysis. Gait cycle parameters such as walking speed, step length and cadence were also calculated using the built-in function in Nexus 1.8.5 (VICON, Oxford, UK). Walking speed and step length were normalized to the participant leg length.

7.3.6. Electromyography

EMG data were high-pass filtered (cut-off frequency 10 Hz, zero-lag fourth-order Butterworth filter) to remove bias and skin motion artifacts, full-wave rectified, and low-pass filtered at 6 Hz (zero-lag fourth-order Butterworth filter). The linear envelopes so obtained were time-normalized to the stance cycle, and amplitude-normalized to the maximum isometric voluntary contraction (MVIC) values. All data processing was done in Matlab (R2014a, MathWorks, MA, USA).

7.3.7. Statistical analysis

Between-group differences for demographic and anatomical variables, and gait parameters were examined using independent samples t-tests. Those kinematic, kinetic and force variables that demonstrated a significant interaction with walking speed have been analyzed with an analysis of covariance (ANCOVA). A 5% significant level was used to reveal differences between the two groups (independent variable). All statistical analyses were done with the Statistic Toolbox in Matlab (R2014a, MathWorks, MA, USA).

Despite the borderline significant difference in age, this variable was not considered as co-variate. In fact, within the age range examined in this article, there is no known interaction with the variables of interest (Bohannon and Andrews, 2011).

7.4. Results

7.4.1. Gait Cycle Parameters

The anthropometrics, alpha angles and gait cycle parameters for the two groups are reported in Table 2. The statistical tests confirmed the significant difference in both measured alpha angles ($P < 0.001$). Walking speed and step length measurements were normalized by leg length. Both the normalized step length and walking speed were significantly smaller for the FAI group, while the cadence was not.

Table 7-2. Gait cycle parameters

The walking speed and step length were normalized by leg length (LL)

	CON	FAI	
	mean $\pm$ std	mean $\pm$ std	P-values
Cadence (steps/min)	116.4 $\pm$ 6.6	111.9 $\pm$ 7.9	0.074
Walking Speed/LL (m/m/s)	1.63 $\pm$ 0.17	1.44 $\pm$ 0.16	0.001
Step Length/LL (m/m)	0.85 $\pm$ 0.07	0.77 $\pm$ 0.07	0.004

7.4.2. Kinematics, kinetics, muscle and contact forces

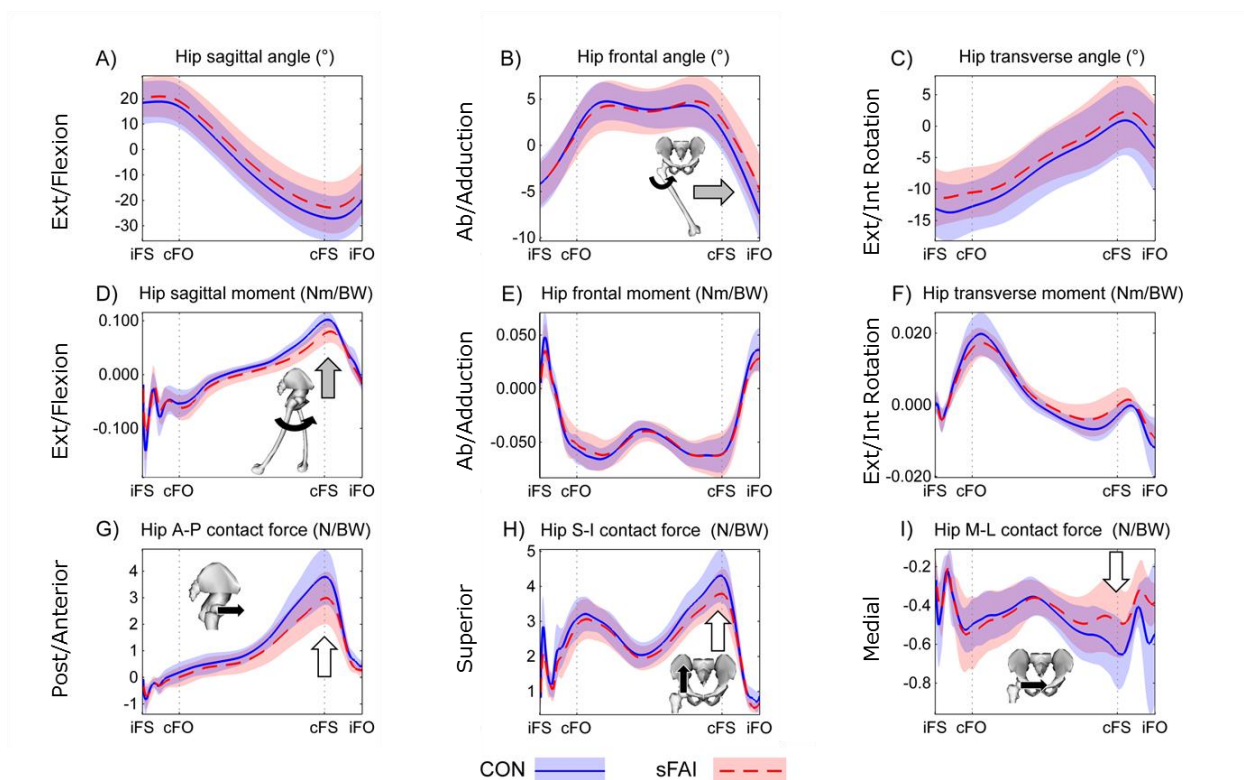


Figure 7-1. Curve comparison between FAI and CON groups

A-C) Kinematic variables, D-F) kinetic variables, and G-I) contact forces for the hip joint during the stance phase of the affected side for CON (blue) and FAI (red). The gray arrow indicates the statistically significant difference; the white arrows point to the curves' peaks that were significantly different without normalized walking speed as covariate. iFS = ipsilateral foot-strike, cFO = contralateral foot-off, cFS = contralateral foot-strike, iFO = ipsilateral foot-off. The shaded areas represent +/- one standard deviation

Hip angles, moments and contact forces curves are reported in Figure 7-1. The hip extension peak angle at contralateral foot-strike was $-23.1 \pm 10.2^\circ$ for the FAI group, and $-27.3 \pm 8.8^\circ$ for CON (P-value = 0.187, Figure 7-1, A). No reversals (also called “hesitations”, i.e., a second order change in the slope of the curve observed typically in OA (Hunt et al., 2013)) were noted in any of the participants. The hip adduction at ipsilateral foot-off was $-4.8 \pm 3.8^\circ$ for FAI group, $-7.5 \pm 2.9^\circ$ for CON (P-value = 0.027, Figure 7-1, B). Pelvic rotation range of motion was slightly lower for the FAI group ($12.0 \pm 3.4^\circ$) with respect to the CON ($14.3 \pm 4.6^\circ$), but the t-test was not significant (P-value = 0.098). No other relevant difference was noted in the kinematics of the lower limb.

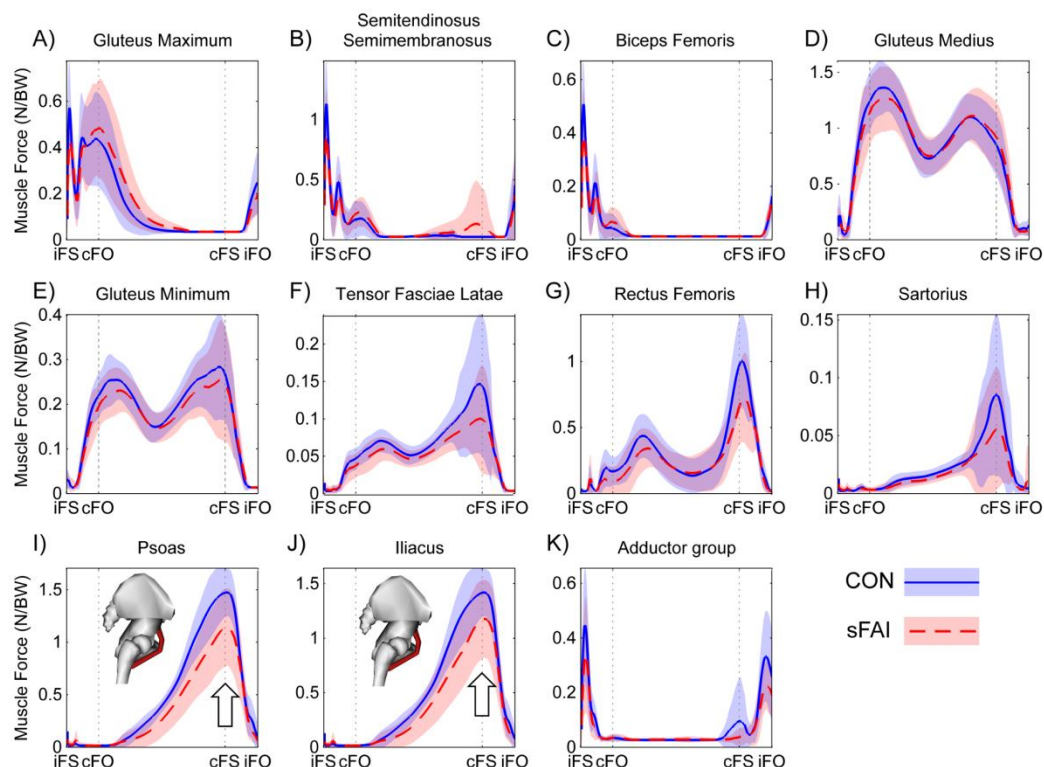


Figure 7-2. Muscle force as estimated by static optimization

The white arrows point to the curves' peaks that were significantly different without normalized walking speed as covariate. iFS = ipsilateral foot-strike, cFO = contralateral foot-off, cFS = contralateral foot-strike, iFO = ipsilateral foot-off. The shaded areas represent $\pm$ one standard deviation

The hip sagittal moment peak at contralateral foot-strike was 0.084 ± 0.024 Nm/BW for FAI group and 0.103 ± 0.014 Nm/BW for CON (P-value = 0.020, Figure 7-1, D), which was significantly different despite the interaction of this variable with the walking speed.

At contralateral foot-strike the anterior-posterior component of the contact force, expressed in pelvic reference frame, was 3.01 ± 0.99 N/BW for FAI group, 3.80 ± 1.04 N/BW for CON (P-value = 0.245, Figure 7-1, G); in the superior-inferior direction it was 3.86 ± 0.70 N/BW for the FAI group and 4.36 ± 0.73 N/BW for CON (P-value = 0.701, Figure 7-1, H); in the medial-lateral direction was -0.48 ± 0.19 N/BW for the FAI group and -0.64 ± 0.19 N/BW for the CON (P-value = 0.099, Figure 7-1, I). The non-significant P-values were mostly due to the strong interaction between these variables and the normalized walking speed.

The estimated muscle forces are reported in Figure 7-2. The muscles that showed the biggest difference in force production between FAI and CON groups were the Iliacus (FAI = 1.20 ± 0.35 N/BW, CON = 1.43 ± 0.22 N/BW, Figure 7-2, J) and Psoas (FAI = 1.18 ± 0.35 N/BW, CON = 1.48 ± 0.22

N/BW, Figure 7-2, I). However, given the dependencies of these variables on the normalized walking speed, no significant difference was found.

7.4.3. Electromyography

Due to defective equipment, one control and two FAI subjects had to be removed from the EMG analysis. The EMG curves showed no differences between the two groups (Figure 7-3). All muscles but the Gluteus Medius showed low level of activation during walking.

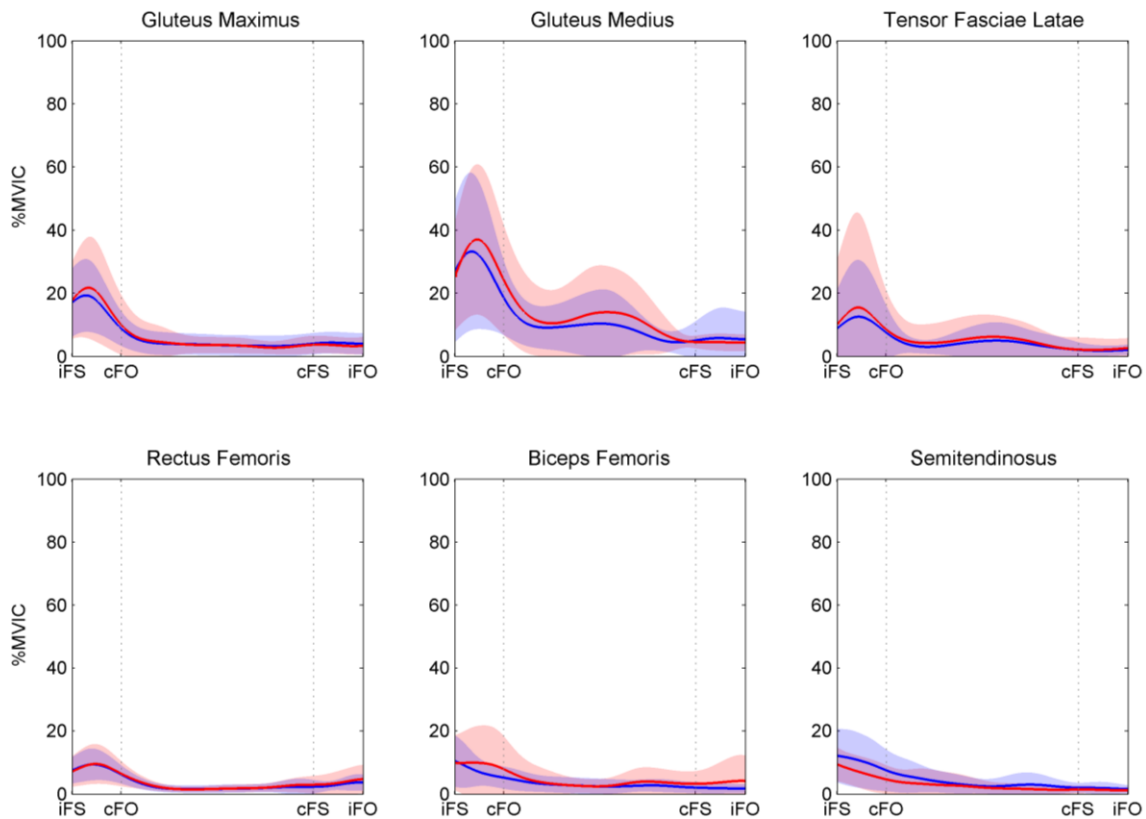


Figure 7-3. Electromyography curves comparison between FAI and CON groups

The curves were calculated during the stance phase of walking, and amplitude normalized to maximum voluntary isometric contraction (MVIC)

7.5. Discussions

Previously, FAI motion studies assumed that the limited range of motion could be directly related to the bone-on-bone impingement caused by the bone deformity (Kubiak-Langer et al., 2007). However, only squatting revealed a reduction of functionality during hip flexion directly related to the impingement (Lamontagne et al., 2011; Lamontagne et al., 2009b). From gait, stair climbing and maximum range of motion studies, it emerged that most of the functional limitations of the FAI hip is due to limits in extension and abduction (Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2011). Specifically for level walking, some found reductions in peak hip abduction angle (Hunt et al., 2013; Kennedy et al., 2009), others also a reduced peak extension, and internal rotation angles (Hunt et al., 2013; Rylander et al., 2013; Rylander et al., 2011). Only one study found alterations in the kinetic results (reduced hip flexion and external rotation moment) (Hunt et al., 2013). Therefore, it has been speculated that mechanisms other than bone impingement were responsible for such functional limitations.

In this study, the kinematic outcomes were in line with previous results, with a statistically significant reduction of hip abduction angle at ipsilateral foot-off, and a decreased hip extension at contralateral foot-strike (not statistically significant). Combined with the smaller pelvic rotation, the reduced hip range of motion was amplified into a significantly shorter normalized step length for the FAI group (Figure 7-4, A). Therefore, the slower walking speed for the pathological group, also found in Hunt et al. (Hunt et al., 2013), seems to be caused mostly by a shorter step length, rather than by a difference in walking cadence.

The different walking speeds influenced the kinetic and force variables. In fact, beside the hip flexion moment, the results of the ANCOVA for muscle and contact forces were not significant in spite of the differences noted from the curves. To gain insights into the FAI pathomechanism, we had hence to investigate the causes of the kinematic differences (reduced hip and pelvic mobility) at contralateral foot-strike, which led to a reduced step length and walking speed, and why these differences occur in extension, where no bone-on-bone impingement is present. Muscle and contact forces estimated through a musculoskeletal model can help answering these questions. In particular, we focused on the resultant contact force and the force production of the hip flexor muscles.

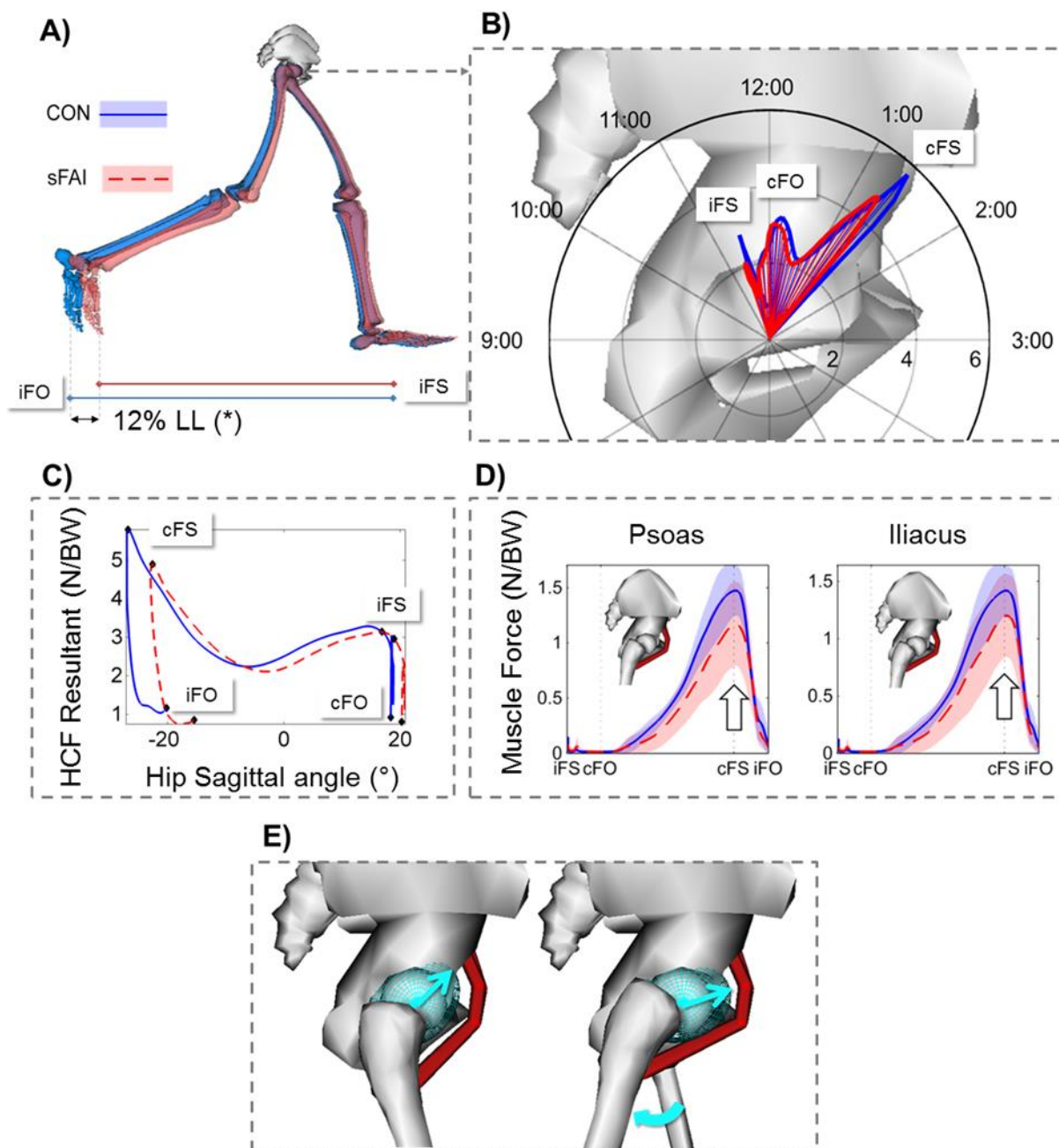


Figure 7-4. Scheme of the proposed FAI pathomechanism

A) The small differences in hip extension and pelvic rotation translated into a significantly shorter normalized step length. B) The resultant average HCF are reported with a 'butterfly' graph showing magnitude and direction of the forces with respect to the pelvic coordinate system and the clock-face representation of the acetabulum. The magnitude indicated by the concentric circles is expressed in body weights. C) The resultant HCF is reported as a function of hip sagittal angle, where the black diamond marks represent the gait cycle events. The graph shows that the HCF of the two groups are similar for similar hip flexion/extension angles. D) Iliacus and Psoas muscle forces are reported since they are the two major contributors to the peak HCF at contralateral foot-strike. E) The extension of the femur exposes the bony bulge anteriorly, towards the Iliacus and Psoas tendon

HCF can be represented with a ‘butterfly’ graph (Figure 7-4, B) that shows the magnitude and direction of the resultant force at the different stages of the stance phase. The butterfly curves for CON and FAI groups show that the major differences happen at transitioning phases (from single to double stance phase and vice versa). At contralateral foot-strike, the compression force acting from the femur onto the pelvis (and expressed in the pelvic reference system) was directed towards the anterior-superior quadrant of the acetabulum, approximately 1:30 in the clock-face reference system. This is consistent with intra-operative observations of the cartilage and labrum damages in patients with cam-type FAI population (Beck et al., 2005; Ganz et al., 2008; Ito et al., 2004; Khanna et al., 2014). When visualizing the resultant HCF versus hip sagittal angle, it is evident that the HCF increased with hip extension (Figure 7-4, C). Therefore, the reduced step length and walking speed could be associated with a preventive mechanism to reduce the load applied on these damaged structures. The fear of pain induces reduced flexor muscle forces and, consequently, lower contact loads (Neptune et al., 2008), similarly to what has been proposed for FAI and labral tear populations (Alshameeri and Khanduja, 2014; Mendis et al., 2014).

In walking, FAI hip extension approaches the angles that this population can extend during maximum range of motion tasks (Kennedy et al., 2008; Kennedy et al., 2009). At these extremes, both the anterior-superior components of the hip capsule and the iliopsoas tendon are in tension to resist a hip anterior displacement (Philippon et al., 2014; Weidner et al., 2012), and generate flexion moment (Figure 7-1, D, Figure 7-4, D). In fact, Iliacus and Psoas muscles are the principal contributors to the peak resultant HCF in hip extension, and their tendon directly overlies the capsulolabral complex at the 2 to 3 o’clock position (Figure 7-4, E) (Alpert et al., 2009). The tension at the hip capsule interface generated by ligaments and tendons is further aggravated by the cam deformity, which is exposed more anteriorly with leg/femur extension (Figure 7-4, E). Therefore, while the tissue damages are developed at the impingement site during movements like flexion and internal rotation, extension and abduction might lead to a further load concentration on the damaged tissues. The altered hip biomechanics could be interpreted as a protective mechanism to prevent such high compression between the bony bulge and the tensed iliopsoas tendon. The proposed mechanism also supports the high hip capsule pressure theory proposed by Daenen et al. about the insurgence of the herniation pits, whose prevalence in FAI male population is 36% (Daenen et al., 1997; Leunig et al., 2005).

Hip ligaments and flexor muscles tightness has been hypothesized as a possible explanation for the observed reductions in hip range of motion (Alshameeri and Khanduja, 2014; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2013). In case of tighter muscles, the passive component of the muscle force (and consequently the total fiber force) would increase, preventing the hip from a full extension and abduction. The present study cannot provide confirmation for such theory since direct

measurements of hip passive properties are not available. However, it is plausible to conclude that the resultant HCF would increase in presence of tighter flexor muscles (Neptune et al., 2008), exacerbating the load on the hip capsule previously described. Future studies should measure hip flexor stiffness, and adjust the model characteristics to account for experimental measurements, in the attempt to validate this theory.

The previously discussed mechanisms seem to be accentuated in presence of OA signs. In fact, the resultant peak contact forces at contralateral foot-strike of the four FAI patients who demonstrated cartilage damages in the intra-surgical observations fell in the lower 50% percentile of the group, therefore, strongly contributing to the reduced muscle forces and hip contact load observed in the FAI group. A significant reduction of walking speed and hip range of motion were also found in mild to moderate hip osteoarthritic patients (Eitzen et al., 2012; Watelain et al., 2001). These observations seem to corroborate the hypothesis that FAI is associated to an early stage of hip osteoarthritis.

Despite the lower walking speed of FAI participants and the aforementioned gait alterations, no difference in the neuromuscular function was found when comparing the EMG curves. This could be justified by the variability of the EMG signal, and by smaller speed differences compared to those inducing EMG alterations reported in other studies (Schwartz et al., 2008; Shiavi et al., 1986).

The self-selected pace was asked to avoid alterations to the normal walking patterns of the participants. Since FAI walking speed was significantly different from the control group, walking speed was used as covariate in the statistical analysis. However, walking speed is affected by the main effect (presence of FAI), and it is not an independent disturbing variable. Therefore, reporting and discussing adjusted and unadjusted results only strengthened the analysis (Asthen Wilson, 2012).

This study is affected by some limitations. Due to the strict inclusion criteria, the sample size was relatively small, which might have caused some type II errors, especially for the EMG where the number of subjects was further reduced for technical problems. The pelvis reference system of the adopted musculoskeletal model presents an offset of 14 degrees in the sagittal plane with respect to the standard ISB reference system (Wu et al., 2002) that must be taken into account when comparing the pelvic and hip flexion/extension angles to previous FAI literature. The joint angles calculated in this study are consistent with previous literature once this offset is considered. The musculoskeletal model used in this study was generic; however, the results obtained from the current simulations are realistic when qualitatively assessed by comparison against instrumented prostheses data for similar walking speeds (Bergmann et al., 1993). Moreover, the model was used in a comparative way to simulate the kinematics and kinetics of healthy and pathologic populations within a consistent framework. The static optimization technique was adopted for estimating muscle forces, since for walking simulations it has been shown to

yield muscle activations consistent with EMG measurements at different walking speeds (Modenese and Phillips, 2011), and it does not require EMG from deeper muscles like EMG-driven models (Buchanan et al., 2004). The absence of statistical differences between the EMGs of the two groups considered in the study further justifies the use of static optimization in FAI gait simulations. In future studies, muscle and contact force estimations could be improved by using specific measurements of muscle anatomy (e.g., muscle attachments and lines of action), muscle contraction properties (e.g., muscle tightness, physiological cross-sectional area) and developing fully subject-specific models (Scheys et al., 2009) in order to improve accuracy of HCF directions (Modenese et al., 2013).

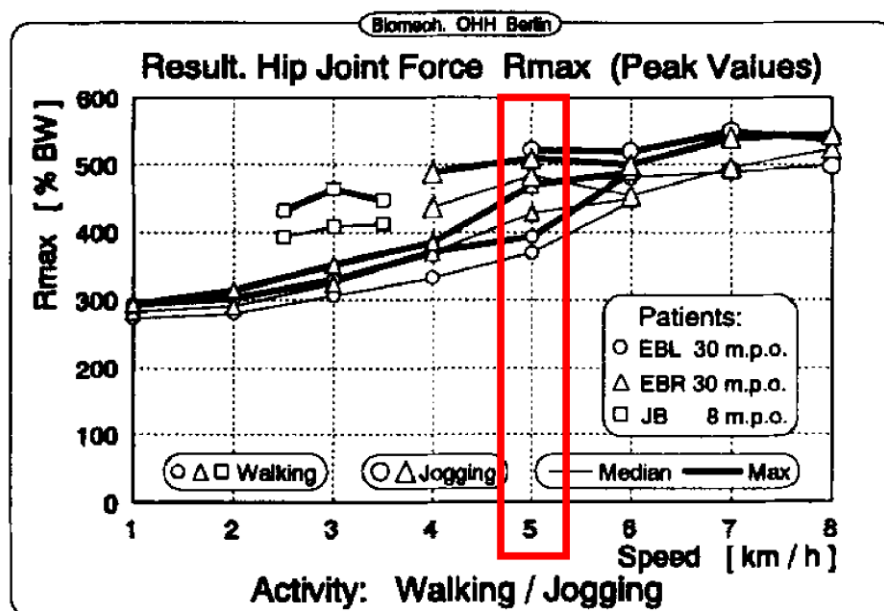


Figure 7-5. Hip Contact Forces from instrumented prosthesis

This figure is taken from (Bergmann et al., 1993) to demonstrate that for comparable walking speeds, the hip contact forces can reach up to 5 BW

This study is the first to provide insights into the link between FAI and hip muscle and contact forces. The results suggested that the kinematic alterations noticed in FAI group during gait (especially in hip extension) might be due to a protective mechanism to prevent higher loads on the hip capsule where tissue damages are concentrated, and/or tightness of anterior hip ligaments and flexor muscles, which would also contribute to an increase in soft tissue loading at the hip. The proposed FAI pathomechanism could be used to support the development of preventive treatment and intervention for symptomatic FAI patients as well as optimizing rehabilitation after surgical intervention.

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Chapter 8. General discussions

The FAI aetiology is still unclear (Ganz et al., 2008; Hartofilakidis et al., 2011; Imam and Khanduja, 2011; Leunig et al., 2009; Pollard et al., 2010), and the mechanisms of development, progression and degeneration of FAI need to be largely investigated in order to develop appropriate measurements for early diagnosis and treatment, and to prevent the degeneration of the pathology into osteoarthritis.

Musculoskeletal modeling can support the development of a biomechanical framework to advance the research on FAI pathomechanisms, and expand the knowledge about hip contact load distribution in FAI population, and relate the muscle and hip contact forces to the alterations observed during functional tasks. Therefore, this thesis was composed of two main aspects: the development of appropriate methodologies, and the investigation of the methods sensitivity to address the clinical problem under investigation.

In the following, the results and conclusions of every study presented in this thesis will be summarized addressing: the main findings, the relevance for biomechanics research in general, and the relevance with respect to the present thesis.

Methodological studies

Marker sets variability has not been investigated in an inverse kinematic framework, which is becoming largely used for musculoskeletal modelling. Researchers in clinical gait analysis tend to use simpler settings with respect to pure research applications. This explains the popularity of Plug-in-Gait (PiG) model, which represents the minimum set of markers that can be used to model lower limb kinematics. There exist variations of this model that try to overcome some of its limitations. UOMAM (University of Ottawa Motion Analysis Model) marker set is one example, where medial markers are added at the knee and ankle to improve the definition of the frontal planes at these two joints. However, there is a tendency to prefer marker sets that place a redundant number of markers per segment (cluster of markers) with the purpose of mitigating the errors due to soft tissues artifacts (Cappozzo et al., 1995; Peters et al., 2010; Stagni et al., 2005). With cluster marker sets the complexity increases because the higher number of markers causes longer acquisition and processing times.

Objective: the main objective of Chapter 4 was to examine the reliability and sensitivity of kinematic outcomes to inter-marker set variability using an inverse kinematic approach.

Main findings: the sensitivity analysis was conducted on three marker sets (PiG, UOMAM, and Cluster) applied to the same kinematic model and walking data to isolate inter-marker set as the only

source of variability. The reliability indices were chosen to capture the level of overall similarity among curves (coefficient of multiple correlation - CMC) and curve parameters (intra-class correlation coefficient - ICC), and to provide absolute comparison values (mean absolute variation – MAV, and minimum detectable change - MDC). The chosen reliability indices are also commonly used in the literature, so that comparison with previous sensitivity studies could be carried out.

Both relative and absolute reliability indices indicated that Cluster and UOMAM produced very similar results, with MDC values below 2.4° for sagittal and frontal plane angles, and below 5° for transverse. This shows that, with the inverse kinematic approach, the addition of cluster markers does not considerably change the outcomes of the analysis. On the other hand, the variability increased drastically when PiG was included in the comparison, with MDC values up to four times larger. Since the only major difference between PiG and UOMAM was the joint centers definition, it can be concluded that the kinematic outcomes are highly sensitive to anatomical markers, especially those used to define joint centers (Ferrari et al., 2008).

In this study the use of different marker sets was the only source of variability. Nevertheless, the MDC obtained when comparing all three marker sets exceeded 5° for most variables, with values up to 16.6° at hip internal/external rotation. This should warn researchers to use caution when comparing studies that use different marker sets in an inverse kinematic framework, especially if joint centers are not identified consistently.

Summarizing, MDC values were presented for comparisons of kinematic outcomes when using three different marker sets on the same model in an inverse kinematic framework. The inter-marker set repeatability was good for sagittal angles, intermediate for frontal angles, and worse for internal/external rotation, similarly to what was found in inter-rater and inter-session variability studies. The Cluster and UOMAM marker sets produce comparable curve parameters, while PiG produces larger ranges of motion and inter-subject variability. Lastly, the large differences introduced by PiG with respect to the other two marker sets depends on the higher sensitivity of kinematic outcomes to anatomical markers that define joint centers rather than changes in number and/or location of technical markers.

Relevance for biomechanics research: investigating the sensitivity of kinematic outcomes to the use of different marker sets provided suggestions to clinical gait analysis researchers who work with inverse kinematics in finding the compromise between complexity of marker set and reliability of the outcomes.

Moreover, the comparison among different gait analysis studies is possible when these are conducted with similar methodologies. The marker set choice represents a considerable source of variability among studies, and establishing the acceptable thresholds for comparison (the so called, minimum detectable

change) can help researchers to understand their results with respect the available literature, and avoid misinterpreting their data.

Relevance for this thesis: since this thesis is part of a larger research program on FAI population, part of the data that have been analyzed had already been collected from a previous investigator with the UOMAM marker set. The study described in Chapter 4 enabled the confident use of previously collected data, since the UOMAM marker set proved to perform consistently with the cluster marker set, but more reliably than PiG.

Medical images can be used to improve the subject-specificity of musculoskeletal models. However, clinical gait analysis studies do not often provide information for a complete subject-specific model. Therefore, the available data can still be used to inform and partially customize a generic model. Lower limb kinematic and kinetic variables are highly sensitive to the location of the hip joint center (Delp and Maloney, 1993; Stagni et al., 2000), therefore, using subject-specific hip joint center measured from medical images would certainly improve the accuracy of the outcomes. An accurate registration (and therefore, proper local reference system orientation) between the medical images and gait analysis settings is necessary to import subject-specific hip joint centers into the model. Chapters 5 and 6 aimed to explore this aspect.

Objective: Chapter 5 examined the consequences of pelvic misalignments on the gait analysis outcomes. Thereafter, a possible approach to correct pelvic misalignments if information from medical images is available was suggested.

Main findings: the lower limb kinematics is highly sensitive to pelvic tilt misalignments introduced by errors in the marker placement, as demonstrated by the differences in all lower limb joint angles, with smaller MAV as the kinematic chain reached the foot. The MAV values are large (21.0° in pelvic tilt, 27.4° in hip flexion/extension), but they represent the worst-case scenario as they consider the extreme perturbations imposed in the study. However, even the variations obtained with smaller perturbations were comparable to clinically relevant differences, and therefore, require attention. Given the non-linear nature of joint kinematic calculations, predicting the variations is difficult and a correction prior to the analysis is preferable.

Relevance for biomechanics research: this study is relevant to all clinical gait analysis researchers that want to use subject-specific pelvic data to inform a generic musculoskeletal model. By isolating this specific source of variability, showing its propagation along the kinematic chain and in kinetic variables, we were able to demonstrate the importance of correcting for pelvic misalignments. Although

implemented in OpenSim, both the sensitivity analysis and the correction method are platform independent, and therefore are valid for any study using the inverse kinematic approach described by Lu and O'Connor (1999). By using the proposed correction approach to integrate medical image information into the generic musculoskeletal model, and correctly register the pelvic markers with respect to the underlying bone (*i.e.*, correct the pelvic orientation), the variability explained in the sensitivity study can be partially removed. Since the joint that was majorly affected by such variability is the hip, this is especially important for studies focusing on this joint.

Relevance for this thesis: from the presented sensitivity analysis it emerged that, in a worst-case scenario, there could be substantial differences in the maximum instantaneous hip contact force (above 1 BW), when pelvic misalignments are unaccounted for, which is close to the variation between walking and jogging measured *in vitro* by Bergmann et al. (1993). The correction approach was crucial to remove such variability from the dataset, especially considering that hip contact forces are principal variables of interest in this thesis for the investigation of FAI pathomechanisms.

The correction approach presented in Chapter 5 was a necessary methodological adjustment to apply the subject-specific hip joint centers (HJC) measured from Computed Tomography to the musculoskeletal models. The results of this study were presented in the first part of Chapter 6.

Objective: part one of Chapter 6 presented a feasibility study on the use of subject-specific HJC within a generic musculoskeletal model during a functional task (*i.e.*, walking).

Main findings: subject-specific HJC produced more accurate kinematic and kinetic outcomes, but introduced an inconsistency between the skeletal and muscular model, compromising muscle properties such as moment arms, which could not be adjusted according to the subject-specific characteristics for lacking of soft tissues images. Therefore, using a subject-specific HJC without customizing the muscle attachments and paths led to an artificial alteration of muscle parameters, which caused unrealistic muscle and joint contact force estimation by static optimization. Considering that the error in HJC estimation obtained by an accurate geometrical scaling of the pelvis in the generic musculoskeletal model is 14.7 mm on average (comparable to the best regression equation), the results of this study suggest not to alter the internal consistency of the model when subject-specific muscle anatomy cannot be modelled.

Relevance for biomechanics research: this study is relevant to all clinical gait analysis researchers that want to use subject-specific HJC data to inform a generic musculoskeletal model.

Chapter 8. General discussions

Relevance for this thesis: the clinical investigation presented in Chapter 7 aimed to obtain the most accurate hip contact force possible from the available motion analysis and imaging data for the FAI population, therefore, using subject-specific HJC was initially considered an improvement in comparison to the scaled generic HJC. Given the results previously discussed, however, the inconsistencies introduced in the model by this customization were deemed more harmful than using the generic HJC with an accurate pelvic scaling. Therefore, the results from this investigation provided the justification for some modelling choices in Chapter 7.

FAI studies available from the literature use generic regression equations for HJC estimation. However, significant pelvic anatomical alterations have been found in FAI patients (Ng et al., 2015), which questioned the validity of generic HJC regression equations for this population.

Objective. The objective of Chapter 6 was to evaluate the validity of HJC regression models for a population characterized with a cam-type deformity (FAI). Moreover, new regression equations were proposed to verify if the predictors could provide better estimates in adults when tuned on a larger and adult-specific dataset.

Main findings. The pelvic anatomical alterations in FAI subjects did not invalidate the use of generic regression equations for HJC estimation, as demonstrated by the non-significantly different prediction errors between FAI and control subjects. Therefore, motion analyses on FAI populations can use the same HJC regression equations than the healthy ones.

Davis model errors were two times higher than Harrington (median errors between 22.3-26.3 mm and 10.3-12.3 mm, respectively), confirming the overall superiority of the latter model in predicting accurate HJCs (Harrington et al., 2007; Leardini et al., 1999; Sangeux et al., 2011; Sangeux et al., 2014). Davis model's poorer results were mostly attributed to the medial-lateral component, which appeared to be less critical for accurate inverse dynamics and muscle force estimation models (Delp and Maloney, 1993; Stagni et al., 2000) than the other two directions. In any case, Harrington model should be preferred.

The newly developed regression equations performed as well as Harrington model, in terms of validation on all the available sets of data (leave-one-out cross validation error, and prediction error on an independent dataset) despite the fact that our equations were developed from a larger adult-specific population. Therefore, it can be concluded that the prediction accuracy obtainable from using such predictors (pelvis width, depth, leg length and body height) cannot be further increased, and that the

errors found from the newly proposed model or from Harrington equations are due to intrinsic subject variability and measurement errors.

In a standard clinical gait analysis, the regression equations are applied to surface markers. This represents a further source of error (Lalonde et al., 2003; Lalonde et al., 2007); in fact, even without considering marker placement errors, there is a consistent layer of skin that mostly affects the measurements of pelvic width and origin. A regression model has been provided to estimate anterior and posterior pelvic skin thickness from body mass index, so that pelvic depth and origin can be corrected according to Sangeaux's suggestions (Sangeaux, 2015).

Relevance for biomechanics research. The clinical gait analysis studies investigating FAI biomechanics can use generic hip joint center regression equations without introducing unwanted bias due to differences in HJC location.

The fact that our newly developed model was not able to improve the prediction accuracy despite the bigger and population-specific training dataset demonstrates that the 12.5 mm of median HJC prediction error represents a convergence value due to intrinsic subject variability and measurement errors. This suggests that, to better the predictions, future studies should introduce new and more informative predictors, or different forms of regression equations (e.g., geometrically based, or non-linear equations).

Lastly, the introduction of regression equations for estimating skin thicknesses will improve the HJC prediction in clinical gait analysis studies where the regressions are applied on skin markers rather than bony landmarks.

Clinical application

The second part of this doctoral project focused on the clinical application of the methodological framework to detect changes between FAI and healthy control populations.

In particular, a growing body of literature exist on the biomechanics of FAI patients. These studies generally show differences in a variety of functional tasks between symptomatic cam FAI and healthy control population (Alradwan et al., 2014; Alshameeri and Khanduja, 2014; Ayeni et al., 2013; Brisson et al., 2013; Diamond et al., 2014; Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Lamontagne et al., 2011; Lamontagne et al., 2009b; Rylander et al., 2013; Rylander et al., 2011). Initially, these functional alterations were directly attributed to the bone-on-bone impingement between the anterior-superior portion of the femoral head and acetabular rim caused by the bone deformity (Audenaert

et al., 2011; Audenaert et al., 2012; Kubiak-Langer et al., 2007), but the research revealed alterations that were beyond this explanation, such as limited range of motion in hip extension and abduction (Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2011). Therefore, other hypotheses were proposed: soft tissue tightness (Brisson et al., 2013; Hunt et al., 2013; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2011), pain inhibition mechanisms (Brisson et al., 2013; Hunt et al., 2013), and muscle weakness (Casartelli et al., 2011a; Casartelli et al., 2011b) are the most popular. However, there is limited evidence to support such hypotheses, since muscle contribution and neuromuscular activations have never been investigated during functional tasks in FAI population.

Objective: the main objective of Chapter 7 was to investigate the functional alterations in FAI population compared to healthy controls by estimating hip muscle and contact forces with musculoskeletal modelling during level walking. FAI hip muscle contribution and neuromuscular activation could provide information to support or connect the hypotheses that have been formulated to explain FAI pathomechanisms.

Main findings: in this study, the kinematic findings were in line with previous results, with a significantly reduced hip abduction angle at ipsilateral foot-off, and a reduced (but not significantly) hip extension at contralateral foot-strike. Combined with the smaller pelvic rotation, the reduced hip range of motion was amplified into a significantly shorter normalized step length and slower walking speed for the FAI group. The reduced walking speed and the kinematic configuration were consistent with the smaller hip flexor muscle and contact forces found for the FAI group. However, the study does not have the means to identify which one is the cause, and which the effect; whether the reduced muscle force (*i.e.*, muscle weakness) caused a slower walking speed, or the pain protection mechanism described in the article induced the reduced muscle force.

The findings could be interpreted as a protective mechanism developed by FAI patients to prevent high compression at the site of the impingement. In fact, at contralateral foot-strike the hip was extended, and the compressing hip contact force was directed towards the anterior-superior quadrant of the acetabulum, where the cam-type deformity is most likely to be localized (Ganz et al., 2008; Khanna et al., 2014), and most cartilage and labrum damages were reported from surgical observation in this population (Beck et al., 2005; Ito et al., 2004). In hip extension during walking, FAI subjects approach their maximum active hip extension (Kennedy et al., 2008; Kennedy et al., 2009), further aggravating the tension between the hip capsule and iliopsoas tendon (Philippon et al., 2014; Weidner et al., 2012) on the bone overgrowth, which becomes more anteriorly exposed with hip extension.

The proposed pathomechanism would also explain why most of the functional alterations occur far from bone-on-bone impingement conditions; the tissue damages are developed at the impingement site during extreme movements like hip flexion and internal rotation, but extension and abduction movements lead to a further load concentration on the damaged soft tissues, and therefore, to pain.

Hip ligaments and flexor muscles tightness was also suggested as a possible cause of the reduced hip range of motion (Alshameeri and Khanduja, 2014; Kennedy et al., 2008; Kennedy et al., 2009; Rylander et al., 2013). It was not possible to provide confirmation for such hypothesis since direct measurements of hip passive properties were not available. However, it is plausible to conclude that the resultant hip contact force would increase in presence of tighter flexor muscles, exacerbating the load on the hip capsule previously described. We warrant further studies to measure hip flexor stiffness in FAI population, and include it in the model to assess its contribution to the total contact force.

Relevance for biomechanics research: by analyzing hip contact and muscle forces, this study provided an understanding of how FAI deformity is linked to the functional alterations found during walking. The described pathomechanisms provided a link between (and a partial confirmation of) the hypotheses previously proposed for explaining functional differences and onset of pain. The outlined results could also be used for clinical recommendations, to support the development of preventive treatment and intervention for symptomatic FAI patients.

In the proposed pathomechanism, the neuromuscular adaptation is a protective reaction to the cartilage and labrum damages caused by the bone impingement; according to this hypothesis, muscles would not have a direct impact on the degenerative pathway of cam-type FAI, but the pain could be managed by reducing activities requiring large hip extensions and abduction, such as fast walking, or stair climbing. Non-surgical management such as muscle balancing and/or strengthening exercises may not be able to reverse the pain; however, maintaining healthy muscles and normal neuromuscular activation is likely to prevent the onset of other alterations and side effects. Thus, such non-surgical managements might have validity as preventative measures, rather than to relieve the symptoms.

8.1. Limitations and mitigations

It is important to address the limitations of the present thesis to define the validity of the results and conclusions previously discussed. Firstly, a generic list of limitations that affect all musculoskeletal models will be addressed, and then limitations more specific to the studies conducted in this thesis will be discussed, together with the adopted mitigation strategies.

Chapter 8. General discussions

Musculoskeletal models are simplified representations of the musculoskeletal system and its functionalities (Hicks et al., 2015). Bodies are considered rigid and connective tissues are often omitted. The joint kinematics are simplified, and some degrees of freedom are neglected. The muscles are geometrically represented as massless lines, and the complex interaction between muscle volumes (i.e., friction between fascicles) is lost. Some assumptions on which muscle models are built are known to be false (e.g., homogeneity of the fiber type, scalable sub-maximal activation force-length curve), and some phenomena ignored (e.g., muscle fatigue, viscous properties of tendons). Soft tissues artifacts and dynamics inconsistencies due to errors in the estimated inertial properties are also inevitable.

The static optimization assumes an optimal neuromuscular strategy, and pathological patterns cannot be represented. Moreover, co-contraction is not properly modelled by the static optimization approach. If co-contraction increases in the pathological populations, as shown for osteoarthritic patients, static optimization would not be able to detect this alteration. FAI individuals are considered pre-osteoarthritis, and could show an increase in co-contraction similar to osteoarthritis patients. In presence of increased co-contraction, hip contact forces would also increase.

The limitations listed above are common to all musculoskeletal models. Validation studies demonstrated that, despite such limitations, the models are capable of estimating contact forces with a certain level of accuracy (Hamner et al., 2010; Kim et al., 2009; Kinney et al., 2013; Lundberg et al., 2013; Manal and Buchanan, 2013; Martelli et al., 2011; Modenese et al., 2011), which can be considered sufficient if the conclusions of the clinical investigation do not rely so much on the exact numbers provided, as on the relative relationship between variables.

Specifically to Chapter 4, it should be noted that the MDC values provided for comparison among marker sets in inverse kinematics are valid for the specific model and framework used in the study. Moreover, it was not possible to directly assess which marker set was the most accurate, as no gold standard was provided. Almost half of the participants used for this study were affected by FAI. This added variability to the dataset, although the reliability indices used in the study were isolating the intra-subject rather than the inter-subject variability.

The major methodological limitations of the correction approach proposed in Chapter 5 are linked to the use of a pelvic linear scaling, and the supine CT scan. The simple linear scaling approach was not sufficient to create an accurate registration between the generic model and the medical images due to pelvis asymmetries or non-rigid deformations, although the markers can be considered properly corrected with respect to the model-defined pelvic reference system (which was the purpose of the transformation). The CT were acquired in a supine position, which could cause some vertical skin movement (Hara et al., 2014), therefore, the proposed correction method would work better with imaging technologies such as

EOS (Illés and Somoskeöy, 2012). However, to mitigate this source of error, a pillow was placed under the lumbar spine of the participant, to mimic the natural curvature of the spine.

The major limitations in Chapter 6 were the measurement errors on bony landmark location from CT images. To mitigate such source of error, two readers and three readings were performed for each CT, and the reliability analysis indicated good repeatability ($ICC > 0.90$). However, the nature of the bony landmark geometry (an area rather than a precise point) limits the measurement accuracy, and justifies the rather small differences between readers (median < 2 mm).

In Chapter 7, the statistical analysis could have type II errors due to the relatively small sample size caused by the difficulties of recruiting FAI subjects with strict criteria like the ones used in this study. Some of the variables were not statistically significant when the walking speed was used as co-variate. This could not be avoided, since the choice of a self-selected pace was done to avoid alterations to the normal walking patterns. The model was only partially validated against data from instrumented prostheses available from the literature, and EMG activations acquired from the participants. The musculoskeletal model used in this study was generic, and improved muscle and contact force estimations could be provided by using specific measurements of both muscle properties (e.g., muscle tightness) and anatomy (e.g., muscle attachments, physiological cross-sectional area). However, as stated at the beginning of this paragraph, all the conclusions drawn from the findings relied on the relative comparison between groups, rather than on the absolute values of the force estimates, which should mitigate the effect of force estimation errors.

8.2. General conclusions

The main objective of this thesis was to provide a biomechanical contribution to the understanding of FAI pathomechanisms. Methodological and clinical investigations were carried out to achieve this objective. From the methodological studies a gait analysis framework for clinical analyses was outlined, investigating the sensitivity of some modelling choices.

Such framework consisted in the use of a musculoskeletal model with UOMAM marker set for motion capture, which represented a good compromise between marker set complexity and reliability of the results. Pelvic orientation correction with information from medical images was a crucial step to remove the variability due to markers misplacement. Subject-specific HJC obtained from CT scans could not be integrated in a generic model for muscle force estimation, without risking introducing inconsistency due to non-subject-specific muscle attachments and paths; however, the use of generic HJC regression equations was validated for FAI population thanks to the availability of such large CT dataset.

Once the methodological framework was applied to the specific clinical investigation of FAI pathomechanism, relevant observations could be made on the magnitude and orientation of hip contact forces, the hip muscles majorly involved, and the link with functional alterations and pain, which led to clinically relevant considerations.

8.3. Future directions

This represents the first study done on hip contact force estimation for FAI population. However, there are several possible improvements that can be applied to the methodological framework. A better subject-specific customization can be achieved by introducing MRI-based models. These models are still very expensive and time-consuming, therefore, not yet practical for clinical uses. However, the technology is developing very fast, and it will soon be possible to apply such models to clinical set-ups.

We also discussed how static optimization has several limitations, among which its inability to detect alterations in the neuro-muscle pattern activations. The use of EMG-driven musculoskeletal models could be an answer to this limitation. However, some of the hip's major muscles are deep in the tissues, and therefore cannot be detected with surface EMG systems. Therefore, an interesting suggestion is the use of indwelling EMG to measure the muscle activities of the major hip deep muscles, to enable the use of EMG-driven models. Some level of optimization would still be required, as the full instrumentation of hip muscles with indwelling EMG is not achievable, but even the use of hybrid models would represent a step forward to overcome the previously mentioned limitation.

FAI patients have been demonstrated to show some level of hip tightness. Whether this is the result of an induced range of motion limitation, or *vice versa*, it would be important to include this alteration in the muscle model. Similarly, FAI patients are characterized by muscle weakness in adduction/abduction, flexion and external rotations, which could be modelled by an ad-hoc scaling of the maximum isometric muscle force.

The analysis of walking is certainly important since this is the primary functional daily task for every individual. However, better insights could be drawn from the analysis of more challenging tasks, such as squatting, stair-climbing, sit-to-stand and stand-to-sit movements. These movements require larger ranges of motion, where the effect of bone-on-bone contact could also have an impact, and could further clarify the origin of the functional alterations. However, caution is warned on the methodological side when modelling more extreme ranges of motion: proper model adjustments are necessary to avoid the operation of the model outside its validity boundaries.

Chapter 8. General discussions

Future studies could assess the impact of muscular training and balancing exercises on the degenerative status of FAI, and provide suggestions for non-surgical treatments.

Finally, finite element models will have a crucial contribution to the understanding of FAI pathomechanisms. The muscle and contact forces estimated with the developed methods could be applied as external forces to investigate the mechanical behaviour of the hip tissues.

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Appendices

Subjects description

Table A-1 reports a detailed list of all participants, and the necessary information to justify the inclusion or exclusion of certain participants from the specific studies reported in Chapters 4 to 7.

Table A-1. Complete list of all participants used in the thesis

The list includes basic demographic information, the group they belonged, a brief description of the issue that caused the exclusion from the study, and the marker set protocol used for the motion analysis. FAI = participants diagnosed as pathological, aFAD = asymptomatic femoroacetabular deformity participants who did not report any symptom but for whom the radiological investigations revealed a hip deformity consistent with FAI, CON = healthy control participants

Code	Gender	Height (cm)	Age (y)	BMI (Kg/m ²)	Group	Issues	Marker set
FAI 001	M	191.2	28.6	24.7	CON	-	UOMAM
FAI 002	M	179	41.2	29.6	CON	-	UOMAM
FAI 003	F	165	32.9	22.6	CON	-	UOMAM
FAI 004	M	183.5	25.3	24.8	FAI	-	UOMAM
FAI 005	F	161	27.5	21.4	aFAD	-	UOMAM
FAI 006	M	181.75	43.2	27.4	aFAD	-	UOMAM
FAI 007	M	183.75	38.2	25.8	FAI	-	UOMAM
FAI 008	M	168	29.4	22.4	FAI	-	UOMAM
FAI 009	M	178.5	30.6	19.4	aFAD	-	UOMAM
FAI 010	M	173.8	30.6	28.3	aFAD	-	UOMAM
FAI 011	M	176.5	31.1	23.9	FAI	-	UOMAM
FAI 012	M	177	30.4	24.4	aFAD	-	UOMAM
FAI 013	M	168	46.5	35.5	FAI	-	UOMAM
FAI 014	M	176	36.7	26.0	CON	-	UOMAM
FAI 015	F	152	42.1	22.4	CON	-	UOMAM
FAI 016	M	180.5	36.9	27.8	CON	-	UOMAM
FAI 017	M	186	40.3	26.8	FAI	-	UOMAM
FAI 018	M	185	33.4	24.0	aFAD	-	UOMAM
FAI 019	M	178	44.3	26.7	aFAD	-	UOMAM
FAI 020	M	182.5	51.7	38.6	FAI	-	UOMAM
FAI 021	M	176.5	42.8	30.3	FAI	-	UOMAM
FAI 022	M	175.5	30.2	31.5	CON	-	UOMAM
FAI 023	F	163.3	43.7	22.5	CON	-	UOMAM
FAI 024	M	181	31.2	32.9	aFAD	-	UOMAM
FAI 025	M	180.5	25.0	23.1	aFAD	-	UOMAM
FAI 026	M	168	31.0	23.7	CON	-	UOMAM
FAI 027	M	174.2	41.9	29.2	FAI	-	UOMAM
FAI 028	M	170.5	28.2	27.3	aFAD	-	UOMAM
FAI 029	M	175	33.0	22.3	FAI	-	UOMAM
FAI 030	M	177.5	37.4	27.9	CON	-	UOMAM
FAI 031	M	176	29.0	25.1	aFAD	-	UOMAM
FAI 032	M	175	35.5	21.7	FAI	-	UOMAM
FAI 033	M	182.5	28.4	28.7	aFAD	Force plates problems	UOMAM

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FAI 034	M	178	26.4	22.7	CON	-	UOMAM
FAI 035	M	179.5	23.9	25.8	aFAD	-	UOMAM
FAI 036	M	176	48.2	28.9	FAI	Force plates problems	UOMAM
FAI 037	M	174	31.8	25.7	aFAD	-	UOMAM
FAI 038	M	181	25.4	31.8	CON	-	UOMAM
FAI 039	M	190.5	29.7	26.8	aFAD	-	UOMAM
FAI 040	M	183	31.8	26.2	CON	-	UOMAM
FAI 041	F	163	36.7	18.9	FAI	-	UOMAM
FAI 042	M	179.5	31.3	24.8	aFAD	-	UOMAM
FAI 043	M	177	26.4	23.0	CON	-	UOMAM
FAI 044	M	176	47.7	28.4	CON	-	UOMAM
FAI 045	M	180	46.4	26.2	FAI	-	UOMAM
FAI 046	M	160.5	23.7	27.2	CON	-	UOMAM
FAI 047	M	175.5	25.8	22.3	CON	-	UOMAM
FAI 048	F	171	45.4	21.7	aFAD	-	UOMAM
FAI 049	M	167	23.1	28.4	FAI	-	UOMAM
FAI 050	F	156.5	23.2	26.2	aFAD	-	UOMAM
FAI 051	M	178	28.8	25.7	aFAD	-	UOMAM
FAI 052	M	187.5	31.0	25.8	aFAD	-	UOMAM
FAI 053	M	179.5	29.0	21.9	aFAD	-	UOMAM
FAI 054	M	178	37.0	26.9	CON	-	UOMAM
FAI 055	M	167	49.0	24.6	FAI	-	UOMAM + Cluster
FAI 056	M	176.75	36.7	23.4	CON	-	UOMAM + Cluster
FAI 057	M	176.5	32.5	19.9	CON	-	UOMAM + Cluster
FAI 058	M	175	39.4	27.1	FAI	-	UOMAM + Cluster
FAI 059	F	168.5	46.7	26.9	FAI	-	UOMAM + Cluster
FAI 060	M	183.5	32.7	26.3	aFAD	-	UOMAM + Cluster
FAI 061	F	167	21.4	20.7	FAI	Not collaborative	UOMAM + Cluster
FAI 062	M	183.00	44.7	28.5	aFAD	-	UOMAM + Cluster
FAI 063	M	171	40.3	38.6	FAI	Recent surgical treatment	UOMAM + Cluster
FAI 064	M	171	27.4	23.7	CON	-	UOMAM + Cluster
FAI 065	M	180.5	27.6	23.8	FAI	-	UOMAM + Cluster
FAI 066	M	189	26.3	26.9	aFAD	-	UOMAM + Cluster
FAI 067	M	175	33.4	26.9	FAI	-	UOMAM + Cluster
FAI 068	M	181	32.9	24.0	FAI	CT problem	UOMAM + Cluster

Model validation

These results refer to the data shown in Chapter 7.

For model validation purposes, electromyography (EMG) signals from lower limb muscles were measured Table A-2 reports the list of muscles included in the protocol.

Table A-2. List of the 16 monitored muscles and their relative placement

Muscle	Placement
Rectus Femoris	50% on the line from the anterior spina iliaca superior to the superior part of the patella, in the direction of the line from the anterior spina iliaca superior to the superior part of the patella §
Vastus Lateralis	Electrodes need to be placed at 2/3 on the line from the anterior spina iliaca superior to the lateral side of the patella, in the direction of the muscle fibers §
Vastus Medialis	80% on the line between the anterior spina iliaca superior and the joint space in front of the anterior border of the medial ligament, almost perpendicular to the line between the anterior spina iliaca superior and the joint space in front of the anterior border of the medial ligament §
Sartorius	30% on the line between the anterior spina iliaca superior and the medial tibial condyle, parallel to this line
Gluteus Medius	50% on the line from the crista iliaca to the trochanter, in the direction of the line from the crista iliaca to the trochanter §
Tensor Fasciae Latae	On the line from the anterior spina iliaca superior to the lateral femoral condyle in the proximal 1/6, in the direction of the line from the anterior spina iliaca superior to the lateral femoral condyle §
Gluteus Maximus	50% on the line between the sacral vertebrae and the greater trochanter, In the direction of the line from the posterior superior iliac spine to the middle of the posterior aspect of the thigh §
Biceps Femoris	50% on the line between the ischial tuberosity and the lateral epicondyle of the tibia, in the direction of the line between the ischial tuberosity and the lateral epicondyle of the tibia §
Semintendinosus	at 50% on the line between the ischial tuberosity and the medial epycondyle of the tibia, in the direction of the line between the ischial tuberosity and the medial epycondyle of the tibia §
Gracilis	50% of the line between the inferior border of pubic body and medial tibial condyle, parallel to this line
Adductor Group	Approximately one palm below the pubic tubercle, parallel to the line going from the superior aspect of pubis to the middle third of linea aspera of femur
Gastrocnemius Lateralis	Electrodes need to be placed at 1/3 of the line between the head of the fibula and the heel, in the direction of the line between the head of the fibula and the heel §
Gastrocnemius Medialis	Electrodes need to be placed on the most prominent bulge of the muscle, in the direction of the leg§
Tibialis Anterior	The electrodes need to be placed at 1/3 on the line between the tip of the fibula and the tip of the medial malleolus, in the direction of the line between the tip of the fibula and the tip of the medial malleolus §
Peroneus Longus	Electrodes need to be placed at 25% on the line between the tip of the head of the fibula to the tip of the lateral malleolus, in the direction of the line between the tip of the head of the fibula to the tip of the lateral malleolus §
Soleus	The electrodes need to be placed at 2/3 of the line between the medial condylis of the femur to the medial malleolus, in the direction of the line between the medial condylis to the medial malleolus §

§Seniam guidelines

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EMG data were high-pass filtered (cut-off frequency 10 Hz, zero-lag fourth-order Butterworth filter) to remove bias and skin motion artifacts, full-wave rectified, and low-pass filtered at 6 Hz (zero-lag fourth-order Butterworth filter). A first order differential equation (1) (He et al., 1991; Zajac, 1989) representing the muscle activation dynamics was also applied to the linear envelopes to have a signal consistent with the muscle activations estimated by the model. In equation (1), $u(t)$ is the linear envelope, $a(t)$ is the muscle activation, and c_1 and c_2 are two constants linked to the activation and deactivation rates.

$$\dot{a}(t) = (u(t) - a(t))(c_1 u(t) + c_2) \quad (1)$$

$$c_1 + c_2 = \text{activation rate}$$

$$c_2 = \text{deactivation rate}$$

The muscle activation data so obtained were time-normalized to the stance cycle, and then compared to the muscle activation curves obtained from static optimization analysis. Since such comparison is qualitative, the amplitude of the curves was not deemed relevant, and both the muscle activation and EMG curves were amplitude-normalized to their maximum value across the trial. Pearson's correlation coefficients were calculated between the two curves to quantify the level of agreement.

The comparison between the muscle activations predicted by the model and those predicted by EMG data through activation dynamics is represented in Figure A-1. The Pearson's correlation coefficients between them is reported in the graph, and it varied between -0.76 (Sartorius), to 0.87 (Gastrocnemius Medialis).

The majority of the monitored muscles showed correlations with $R > 0.25$ between the muscle activations estimated by static optimization and those obtained from EMG signals. However, five of the fifteen muscles reported a correlation coefficient equal or below zero. These were the Adductor group muscles, Gracilis, Sartorius, Tensor Fasciae Latae and Rectus Femoris. The poor results of the Adductor muscles and Gracilis can be blamed on the difficulty of properly recording EMG activity on these muscles, especially in individuals with higher fat composition; the probe movement given by the soft tissues, and the rubbing between legs during walking could have caused unwanted and undetectable noise on the EMG signals. Also the model might poorly represent the musculoskeletal behavior in the frontal plane given the simplification adopted, such as a purely 1 degree-of-freedom knee joint, which might have altered the kinematics in this plane. However, the behavior of other muscles acting on this plane (Gluteus Medius) and those muscles responsible for knee stability (Vastii and Hamstrings) was good, which made us lean toward a faulty EMG signal theory. On the other hand, Tensor Fasciae Latae, Rectus Femoris and Sartorius's poor results might be simply caused by the difficulty of modelling biarticular

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muscles: spanning two articulations add errors to the estimation of muscles parameters such as moment arms and fiber lengths.

No assessment can be made on the deeper hip muscles, which is the principal reason for using static optimization over other possible solutions (e.g., EMG-driven models).

A direct validation of musculoskeletal models is not possible because muscle forces cannot be measured *in vivo* (Hicks et al., 2015), however, extensive literature exist providing indirect validation through measured contact forces (instrumented prostheses) (Bergmann et al., 1993; Heller et al., 2005; Kim et al., 2009; Lin et al., 2010), and by comparing muscle forces to EMG profiles (Crowninshield and Brand, 1981; Glitsch and Baumann, 1997; Martelli et al., 2011; Modenese et al., 2011).

The contact forces obtained from joint reaction calculations and presented in the manuscript was consistent with the literature and the available data on instrumented prostheses. The peak resultant contact force for individuals walking at 5-6 Km/h (about 1.4-1.7 m/s) from Bergmann (1993) was comparable to the results obtained in this study. Beside inevitable errors due to modelling assumptions, the differences between the reference data and these results could be also explained by considering that the population analyzed in Bergmann et al was older and had undergone hip replacement surgery, which might justify a certain degree of muscle weakness and, consequently, reduced contact forces. Also, THA studies showed that certain placement of the prosthesis can reduce contact forces (e.g., more lateral HJC relocation) by reducing the required torque.

In the authors' opinion, the results can be considered overall acceptable, especially because we are comparing two populations, and the value of the analysis reside more on the comparison than on the absolute values.

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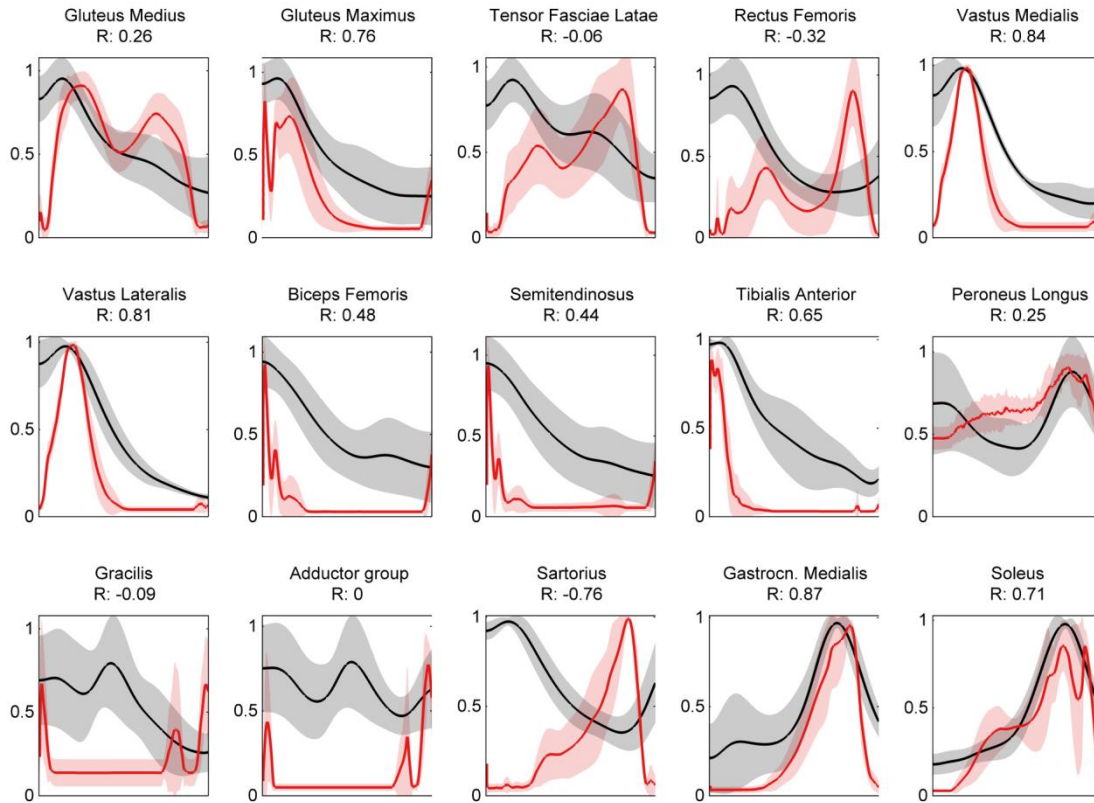


Figure A-1. Muscle activation comparison: modelled versus measured

Comparison of muscle activations as obtained from EMG signals (black) and static optimization (red) during the stance phase

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