The Effect of Quadriceps Weakness on Lower Extremity Muscle Function During Gait

DISSERTATION

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Abstract

Osteoarthritis (OA) is one of the leading causes of disability in the US. Quadriceps weakness, one of the most common symptoms of knee OA, has been correlated with difficulty performing activities like walking. However, the underlying mechanism relating the function of the quadriceps to gait impairments is unknown. Dynamic computer simulations are powerful tools for investigating the role of muscles during gait, but to date they have not been utilized to study the role of the quadriceps in OA gait. Furthermore, the influence of subject-specific quadriceps muscle parameters on model predictions of muscle function in simulations of OA gait has not been evaluated.

We created muscle-driven simulations of gait investigating the effect of two sources of simulated quadriceps weakness, atrophy and activation failure, on the muscle compensation strategies needed to maintain healthy gait kinematics at a self-selected speed. We found that the gluteus maximus and soleus muscles displayed the greatest ability to compensate for simulated quadriceps weakness. Our findings also suggested different compensation strategies by the lower extremity musculature in response to the different types of weakness.

To gain a better understanding of the factors that limit walking speed in individuals with weakened quadriceps, we expanded our first study to investigate the muscle compensation strategies needed to maintain healthy gait kinematics over a range of speeds in response to simulated quadriceps weakness. As with the first study, we found
that the gluteus maximus and soleus muscles displayed the greatest ability to compensate for simulated weakened quadriceps at all gait speeds; however, soleus force output decreased at faster speeds. All simulations were able to track gait kinematics at all speeds, suggesting that it is physiologically feasible for persons with quadriceps weakness to walk at fast speeds, and that other factors not simulated in our models (e.g. pain or instability) likely contribute to reduced walking speeds.

Lastly, we performed the first study incorporating subject-specific quadriceps muscle properties into simulations of OA gait. We developed models with various implementations of subject-specific quadriceps properties measured in an individual with knee OA, resulting in six different simulations: 1) generic quadriceps muscle properties (“Generic”), 2) peak isometric quadriceps forces calculated from a maximum voluntary contraction (MVC) in a dynamometer (“MVC”), 3) peak isometric quadriceps forces calculated using the burst superimposition test (“Burst”), 4) peak isometric quadriceps forces and maximum activation constraints calculated using the burst superimposition test and CAR value (“Burst+CAR”), 5) peak isometric quadriceps forces calculated using muscle volumes from magnetic resonance images (“MRI”), and 6) peak isometric quadriceps forces calculated using muscle volumes from MRI and maximum activation constraints from the burst superimposition test and CAR value (“MRI+CAR”). Gait simulations using the different models revealed large changes in quadriceps function in response to different model complexities, but small changes in other muscles. We then performed a virtual gait re-training simulation in which we estimated the changes in muscle function needed for the model with the highest degree of subject-specificity to
track healthy gait kinematics. Our findings revealed that changing kinematics had a much greater effect on muscle function than differences in model complexity, suggesting that subject-specificity of quadriceps properties in muscle-driven simulations may be secondary to kinematic changes for some individuals with knee OA.

This dissertation advances our understanding of the relationship between quadriceps weakness and gait impairment, and represents an important step towards the design of more comprehensive rehabilitation strategies. The methodology presented in these studies lays the groundwork for future research that will continue to add to our understanding of pathological gait and, more importantly, improve the function and quality of life of individuals with movement disorders.
This document is dedicated to my family.
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Chapter 1: Introduction

An estimated 49.9 million adults in the US (22.2% of the population) had doctor-diagnosed arthritis between 2007 and 2009 (2010), and that number is projected to increase to 67 million (25%) by 2030 (Hootman and Helmick, 2006), making it the leading cause of disability in the US (2010). Approximately 12% of adults aged 60 and over have symptomatic knee osteoarthritis (OA), and more than 37% present with radiographic evidence of OA (Dillon et al., 2006). An estimated 21.1 million adults in the U.S. (9.4% of the population) report activity limitations due to the symptoms of arthritis (2010). Persons with OA typically experience severe pain and disability (Badley et al., 1994; Peat et al., 2001) and report increased dependence and difficulty during activities of daily living such as rising from a chair, climbing stairs, and walking (Jette, 1980; Fisher et al., 1991; Fisher and Pendergast, 1997). Persons with OA have been shown to have altered gait (Brinkmann and Perry, 1985; Blin et al., 1990; Messier et al., 1992), including decreased knee range of motion and angular velocity (Brinkmann and Perry, 1985; Messier et al., 1992), and decreased stride length (Blin et al., 1990) compared to healthy subjects. Additionally, individuals with OA walk slowly compared to healthy individuals (Andriacchi et al., 1977; Brinkmann and Perry, 1985; Gok et al., 2002).
Quadriceps weakness is one of the earliest and most common symptoms reported by individuals with knee OA (Hurley and Newham, 1993; Fisher et al., 1997) and is a better determinant of pain and disability than radiographic changes (McAlindon et al., 1993; Hurley et al., 1997). In subjects with radiographic evidence of OA and no joint pain, quadriceps weakness predicts radiographic progression (Slemenda et al., 1997). Research in this area has led to the suggestion that quadriceps muscle dysfunction may be a factor in the development and progression of OA (McAlindon et al., 1993; Slemenda et al., 1997). Impairment of the quadriceps has been correlated with fall risk (Lord et al., 1999), slower walking speed (Gibbs et al., 1996; Connelly and Vandervoort, 1997; Moxley Scarborough et al., 1999; Yoshida et al., 2008), and decreased performance during stair climbing and sit-to-stand tasks (Walsh et al., 1998; Moxley Scarborough et al., 1999; Yoshida et al., 2008).

Muscle weakness may be a result of muscle atrophy (a decrease in the number or size of muscle fibers), or may be due to reduced voluntary activation that occurs with aging and in those with knee OA (Hurley and Newham, 1993; O'Reilly et al., 1998; Harridge et al., 1999; Stevens et al., 2001). Quadriceps strength deficits can be as high as 38% compared to the uninvolved side in individuals with OA (Petterson et al., 2007), and quadriceps activation deficits may approach 34% (Hassan et al., 2001). Failure of voluntary muscle activation is defined as a reduction in the maximal force output of a muscle resulting from an inability to recruit all of the muscle’s motor units or to attain the maximal discharge rate from the motor units that are recruited (Kent-Braun and Le Blanc, 1996). A failure of voluntary muscle activation can result from pain (O'Reilly et al.,
effusion (fluid build-up) (Fahrer et al., 1988; McNair et al., 1996), and joint damage (Hurley, 1999). However, even in the absence of pain or effusion, full activation is not always achieved, suggesting that there may be other mechanisms which reduce quadriceps activation (Hurley, 1997).

Appropriate muscle strength and activation is important for performance of activities of daily living, such as walking. The involvement of quadriceps weakness in the development of knee OA may be linked to the role of the quadriceps during gait (Lewek et al., 2004). At heel strike during normal gait, knee flexion, controlled by eccentric contraction of the quadriceps, provides shock absorption at the knee and minimizes joint stress (Jefferson et al., 1990; Radin et al., 1991). Individuals with knee OA and quadriceps weakness commonly use a limb “stiffening” movement strategy, characterized by reduced knee flexion and decreased knee extension moment during early stance (Brinkmann and Perry, 1985). Knee stiffening is often accompanied by increased co-contraction of muscles around the knee (Childs et al., 2004; Lewek et al., 2004; Schmitt and Rudolph, 2007), which can lead to higher joint contact forces (Hodge et al., 1986) and impaired movement and weakness (Busse et al., 2006). Continued use with an altered muscle activity pattern may exacerbate the symptoms of OA and lead to further joint deterioration (Fisher et al., 1997). Moreover, the relationship between muscle weakness, joint damage, and disability is complex (Figure 1.1) (Hurley, 1999). It has been suggested that quadriceps muscle dysfunction occurs first and initiates joint damage and pain in persons with OA (McAlindon et al., 1993; Hurley et al., 1997; Slemenda et al., 1997;
Hurley, 1999). However, the underlying mechanism relating the function of the quadriceps to these impairments is unknown.

Figure 1.1: The relationship between muscle dysfunction, joint damage, and disability (Hurley, 1999).

**Role of muscles during gait**

Two major motor functions used to transport the body in human walking are generation or maintenance of forward velocity and support of the upper body (Winter, 1991). Successful completion of these functions requires the coordination of muscles. An understanding of how individual muscles fulfill the requirements of walking can provide
useful insights into pathological gait, such as the role of the quadriceps in persons with OA. Determining how individual muscles contribute to observed motions is difficult because a muscle can accelerate joints that it does not span and body segments to which it does not attach due to the dynamic coupling of the body (Zajac and Gordon, 1989). The force in a leg muscle, for example, accelerates all segments in the body, including the upper body. The muscle-induced accelerations result in a flow of energy among the body segments, causing them to move (Zajac et al., 2002). An example of this principle is illustrated by the function of the soleus during walking, which decelerates the shank and thigh and accelerates the trunk during mid-stance, causing energy to flow from the leg to the trunk (Neptune et al., 2001). The complexity of the human body makes it difficult to determine the individual contributions of muscles, and therefore difficult to understand muscle coordination of movement, using experimental techniques alone (Zajac et al., 2002; Zajac et al., 2003). A theoretical framework, in combination with experiments, is needed to reveal such cause-effect relationships (Delp et al., 2007).

A powerful tool for investigating cause-effect relationships, such as how the impaired function of weakened quadriceps may be compensated by other muscles in the lower extremity, is a dynamic computer simulation. Simulations can be used to help understand muscle activations (Anderson and Pandy, 2001), joint kinematics (Anderson and Pandy, 2001) and internal joint loading (Bei and Fregly, 2004) and thereby can provide insight on mechanisms of pathological or altered kinematics (Piazza, 2006). Dynamic simulations are well-suited for performing “what if?” studies (Delp et al., 2007) in which, for example, the activation or force production of one muscle or muscle group
can be changed to observe the resulting motion and muscle forces. Simulations are also useful for predictive studies, such as how muscle function would change in response to rehabilitation, surgical procedures, or gait re-training. Forward-dynamic simulations are especially useful for studying functional tasks because they involve the application of forces to produce motions, offering potential insights into the roles played by individual muscles during a task. These simulations also permit monitoring of other variables of interest such as joint contact forces which may affect functional performance and offer insight as to the biomechanical reasons for suboptimal outcomes.

Kepple et al. (Kepple et al., 1997) used forward-dynamic simulations to evaluate the relative contributions of the lower extremity joint moments to forward progression (forward acceleration of the trunk) and support of the upper body (vertical acceleration of the trunk against gravity) during healthy gait. They concluded that forward progression was accomplished primarily by the ankle plantarflexors with assistance from the knee extensors and vertical support was provided by the plantarflexors during single limb support and by a combination of the ankle plantarflexors, knee extensors, and hip extensors during double limb support (Kepple et al., 1997).

Expanding on the investigation by Kepple et al., several studies have investigated how muscles provide support and progression during normal gait (Neptune et al., 2001; Anderson and Pandy, 2003; Neptune et al., 2004; Liu et al., 2006). Liu et al. (Liu et al., 2006) found that gluteus maximus, quadriceps (vasti), and dorsiflexors slow forward progression of the body mass center during early stance, while gluteus medius, soleus, and gastrocnemius propel the mass center forward during late stance. These same
muscles provide vertical support of the body mass center (Liu et al., 2006). These results are consistent with previous work by Neptune and colleagues (Neptune et al., 2004), who found that the uniarticular quadriceps (vasti) provide vertical support of the body while decelerating the trunk and leg in early stance. At mid-stance, however, the vasti provide forward acceleration of the trunk (Neptune et al., 2004). The biarticular quadriceps muscle (rectus femoris) was found to contribute to forward progression in late stance, and suggested to work synergistically with the plantarflexors to deliver energy to the trunk for forward progression (Zajac et al., 2003; Neptune et al., 2004).

Since individuals with OA walk slowly compared to healthy individuals (Andriacchi et al., 1977; Brinkmann and Perry, 1985; Gok et al., 2002), it is important to differentiate between the effects of pathology and the effects of walking speed. In a study of muscle contributions to support and progression over a range of walking speeds in healthy subjects, Liu et al. (Liu et al., 2008) found that gluteus maximus, gluteus medius, vasti, hamstrings, gastrocnemius, and soleus were the primary contributors to support and progression at all speeds, and the contributions from these muscles, with the exception of gluteus medius, generally increased with walking speed. During slow and very slow speeds, vertical support in early stance was provided by a straighter limb such that skeletal alignment, rather than muscles, provided support of the body mass center (Liu et al., 2008). During self-selected and fast walking speeds, greater knee flexion during stance phase caused a large increase in vasti contribution to vertical support (Liu et al., 2008). Across walking speeds, rectus femoris made only modest contributions to support
while resisting forward progression through most of stance, and was not significantly affected by changes in speed (Liu et al., 2008).

Muscle contributions to support and progression have also been examined in some impaired populations (Higginson et al., 2006; Steele et al., 2010). In crouch gait, vertical support is provided by the same muscles which provide vertical support during healthy gait (Steele et al., 2010). To propel the body forward, however, subjects walking in crouch gait rely more on proximal muscles, including gluteus medius and hamstrings, compared to unimpaired subjects (Steele et al., 2010). In a study of muscle contributions during gait in an individual with post-stroke hemiparesis, the quadriceps (vasti and rectus femoris) and gluteus maximus of the paretic leg contributed more compared to the non-paretic leg or to their contributions in healthy slow gait (Higginson et al., 2006).

While muscle contributions in healthy subjects (Liu et al., 2006; Liu et al., 2008) and impaired subjects such as those with cerebral palsy (Steele et al., 2010) and post-stroke hemiparesis (Higginson et al., 2006) have been examined, muscle contributions in the OA population remain unknown. The role of the quadriceps during healthy gait is to provide vertical support and slow forward progression during the first half of stance (Liu et al., 2006). In the presence of OA, however, other muscles may be needed to assist with knee control and stabilization, but how other muscles compensate for quadriceps weakness remains unknown. If the quadriceps in persons with OA are unable to contribute to support and progression during gait, logic and physics dictate that something else needs to “kick-in” to make up for the loss of the quadriceps. A previous study of post-stroke gait showed that in the presence of paretic muscle dysfunction, other
muscles will compensate to provide supplemental support in order to maintain upright posture (Higginson et al., 2006). However, at slow walking speeds in unimpaired subjects it has been shown that skeletal alignment (as evidenced by a straighter limb), rather than muscles, support the body mass center (Liu et al., 2008). This is in contrast to subjects who walk with a crouch gait, where less passive skeletal support of the body results in higher muscle forces during walking compared to unimpaired subjects (Steele et al., 2010).

We know that the gait kinematics and muscle activation patterns of individuals with OA are different than healthy individuals. Individuals with OA walk slowly (Andriacchi et al., 1977; Gok et al., 2002), exhibit less knee flexion during early stance (Brinkmann and Perry, 1985), and display increased co-contraction of the muscles around the knee (Lewek et al., 2004; Schmitt and Rudolph, 2007). However, we do not know how the function of the individual muscles, specifically the function of the quadriceps, directly translates to these compensation strategies. Is quadriceps weakness compensated by other muscles in the lower extremity? Does weak quadriceps cause persons with OA to walk slowly, or does walking slowly cause the quadriceps to become weak (because of disuse)? At faster walking speeds, the quadriceps provide support and braking, so it may also be that individuals with OA choose not to walk faster because their braking ability is compromised, rather than that they are unable to walk faster. Answering these questions will provide insight into the underlying mechanism relating quadriceps function to OA gait, and may help guide rehabilitation to slow the progression of the disease.
Need for a subject-specific model of OA

Quantifying muscle function during gait of an individual with OA requires a musculoskeletal model that accurately represents an individual with OA. Current models are limited because their musculoskeletal properties are based on very limited data of muscle architecture obtained from a small number of cadaver specimens (Wickiewicz et al., 1983; Delp et al., 1990; Friederich and Brand, 1990). To address this limitation, Arnold and colleagues (Arnold et al., 2010) developed a new model of the lower limb based on experimentally measured muscle architecture (i.e., muscle fiber lengths, pennation angles, and physiologic cross-sectional areas) from 21 cadavers (Ward et al., 2009). Although this model provides a more robust generic model than previous models, it does not address the differing muscle properties of persons with OA. Currently, “subject-specific” models are created by scaling the mass properties and dimensions of the model to match the subject’s body size, but no changes are made to the muscle parameters in the model. Xiao and Higginson (Xiao and Higginson, 2010) investigated the sensitivity of estimated muscle forces to perturbations in generic muscle parameters and found that the quadriceps (rectus femoris and vasti) and ankle plantar flexors were sensitive to changes in tendon slack length and optimal fiber length in simulations of healthy normal walking. Adjusting the maximum isometric forces of muscles in the generic model by ±10% had little effect on the estimated muscle forces (Xiao and Higginson, 2010). However, strength deficits in the OA population can be as high as 38% (Petterson et al., 2007), which would be more likely to have an effect on muscle function than changes of only 10%.
Determining the subject-specific muscle properties of individuals with OA and incorporating them into a computer model can be challenging. The quadriceps muscles of persons with OA have smaller cross-sectional areas, greater fatty infiltration, and greater voluntary activation failure compared to healthy quadriceps (Hurley et al., 1997; Hurley and Scott, 1998; Gur and Cakin, 2003; Lewek et al., 2004; Ikeda et al., 2005; Mizner et al., 2005; Petterson et al., 2008). Accounting for subject-specific muscle characteristics in musculoskeletal models of OA is needed if the results from dynamic simulations are to be correlated to patient function and used as a scientific basis for individualized treatment programs. These challenges have motivated this dissertation.

1.1 Focus of Dissertation

This dissertation proposes to answer the question of how weakened quadriceps affect the function of muscles in the lower extremity during gait. As a first step towards understanding the mechanism relating quadriceps weakness and gait impairment in individuals with knee OA, we developed muscle-driven simulations to investigate muscle compensations needed to maintain gait kinematics over a range of walking speeds in healthy individuals in response to two sources of simulated quadriceps weakness: atrophy and activation failure. We then developed musculoskeletal models with various implementations of subject-specific quadriceps muscle properties of an individual with knee OA to investigate the sensitivity of estimated muscle compensation strategies to model complexity. In an effort to further investigate muscles which could be potential targets in rehabilitation, we forced the model with the highest degree of subject-
specificity to track the gait kinematics of a healthy individual and analyzed changes in muscle function in response to the virtual gait re-training. The research presented in this dissertation integrates medical imaging, strength testing, gait analysis techniques and dynamic computer simulations.

1.2 Significance of Research

This dissertation represents the first effort to create simulations of OA gait incorporating subject-specific quadriceps muscle parameters and lays a foundation to determine the underlying mechanism relating the function of the quadriceps to gait impairments. To achieve this goal, we collected experimental gait data in our motion capture laboratory, which is one of only a handful in the world using the Point-Cluster Technique, a redundant set of skin-based makers to improve accuracy over more common marker sets (Andriacchi et al., 1998). Additionally, we measured subject-specific quadriceps muscle parameters from an individual with knee OA using magnetic resonance images, dynamometer strength testing, and the burst superimposition technique (Kent-Braun and Le Blanc, 1996) and used these experimental data to develop muscle-driven simulations of gait. Quadriceps muscle volumes were determined from magnetic resonance images using a semi-automated segmentation program developed at The Ohio State University (Prescott et al., 2011a).

As a first step, we investigated the muscular compensation strategies that would be needed to track the gait kinematics of healthy individuals over a range of walking speeds in response to simulated quadriceps atrophy and activation deficit, both of which
are prevalent in the OA population (Hassan et al., 2001; Petterson et al., 2007; Petterson et al., 2008). Previous studies at a self-selected speed have investigated the effect of muscle weakness by simulating atrophy only (van der Krogt et al., 2012) or activation failure only (Knarr et al., 2013) in healthy individuals. Other simulation studies have examined muscle contributions to progression and support in persons with post-stroke hemiparesis, cerebral palsy, and TKA (Higginson et al., 2006; Steele et al., 2010; Steele et al., 2012; Li et al., 2013). No study has investigated how lower extremity muscles could compensate for both quadriceps atrophy and activation failure to maintain gait kinematics of healthy subjects over a range of walking speeds. Such an investigation provides an important first step towards addressing the factors that limit walking speed in individuals with pathologically weak quadriceps.

We then developed musculoskeletal models with varying degrees of complexity in subject-specific quadriceps properties measured from an individual with knee OA. Most previous simulation studies used generic musculoskeletal models with muscle properties based on limited data of muscle architecture (Wickiewicz et al., 1983; Friederich and Brand, 1990) whose muscle properties, especially the quadriceps, may not accurately represent persons with OA. However, no study has incorporated patient-specific quadriceps muscle parameters into muscle-driven simulations of OA gait. We performed simulations of gait at a self-selected speed to investigate how model predictions of muscle force and contributions to support and progression change with different implementations of subject-specific quadriceps parameters. We then performed a “virtual gait re-training” simulation in which we estimated the changes in muscle
function needed for the model with the highest degree of subject-specificity to track healthy gait kinematics. Our pilot study lays the foundation for further investigation of the role of quadriceps weakness in OA gait, with the aim of establishing a basis for the design of more comprehensive rehabilitation strategies.

1.3 Overview of Dissertation

This dissertation contains four subsequent chapters. Chapters 2-4 are written as self-contained journal articles. Chapter 2 (published in the Journal of Biomechanics with co-authors Ajit Chaudhari, Laura Schmitt, Thomas Best, and Robert Siston) presents the results of muscle-driven simulations of healthy individuals in which we applied simulated quadriceps weakness in the form of atrophy and activation failure. Chapter 3 (in preparation for submission to the Journal of Biomechanics with co-authors Ajit Chaudhari, Laura Schmitt, Thomas Best, and Robert Siston) presents the results of our study of muscle compensations in response to simulated quadriceps weakness over a range of walking speeds in healthy individuals. Chapter 4 (in preparation for submission to the Annals of Biomedical Engineering with co-authors Ajit Chaudhari, Laura Schmitt, Metin Gurcan, Wenbo Wei, Thomas Best, and Robert Siston) presents the results of a pilot study in which we developed musculoskeletal models with different implementations of subject-specific quadriceps muscle parameters of an individual with knee OA, investigated the effects of the varying degrees of model complexity on predicted muscle function during simulations of walking at a self-selected speed, and estimated changes in muscle function in response to a virtual gait re-training in which the
model with OA-specific quadriceps parameters was forced to track healthy gait kinematics. Chapter 5, the conclusion, summarizes the key contributions of this dissertation, discusses additional applications of this research, and proposes future directions of study.
Chapter 2: Gluteus Maximus and Soleus Compensate for Simulated Quadriceps Atrophy and Activation Failure during Walking

2.1 Abstract

Important activities of daily living, like walking and stair climbing, may be impaired by muscle weakness. In particular, quadriceps weakness is common in populations such as those with knee osteoarthritis (OA) and following ACL injury and may be a result of muscle atrophy or reduced voluntary muscle activation. While weak quadriceps has been strongly correlated with functional limitations in these populations, the important cause-effect relationships between abnormal lower extremity muscle function and patient function remain unknown. As a first step towards determining those relationships, the purpose of this study was to estimate changes in muscle forces and contributions to support and progression to maintain normal gait in response to two sources of quadriceps weakness: atrophy and activation failure. We used muscle-driven simulations to track normal gait kinematics in healthy subjects and applied simulated quadriceps weakness as atrophy and activation failure to evaluate compensation patterns associated with the individual sources of weakness. We found that the gluteus maximus and soleus muscles display the greatest ability to compensate for simulated quadriceps weakness. Also, by simulating two different causes of muscle weakness, this model suggested different compensation strategies by the lower extremity musculature in response to atrophy and activation deficits. Estimating the compensation strategies that
are necessary to maintain normal gait will enable investigations of the role of muscle weakness in abnormal gait and inform potential rehabilitation strategies to improve such conditions.

2.2 Introduction

Muscle strength is important for most activities of daily living, including kneeling, stair-climbing, and walking. In particular, lower extremity muscles perform two main tasks in transporting the body during walking: generation or maintenance of forward velocity and support of the upper body (Winter, 1991). Several studies have investigated how muscles contribute to support and progression during healthy gait (Neptune et al., 2001; Anderson and Pandy, 2003; Neptune et al., 2004; Liu et al., 2006). The gluteus maximus and ankle dorsiflexors have been shown to slow forward progression of the body mass center during early stance while providing vertical support, while the gluteus medius, soleus, and gastrocnemius propel the mass center forward and provide vertical support during late stance (Neptune et al., 2004; Liu et al., 2006). The quadriceps slow forward progression and provide vertical support during early stance (Neptune et al., 2004; Liu et al., 2006; Liu et al., 2008).

Not surprisingly, muscle weakness may impair the ability to perform activities of daily living. Quadriceps weakness is a hallmark impairment following ACL injury (Eastlack et al., 1999; Rudolph et al., 2001) and in individuals with knee osteoarthritis (OA) (Hurley and Newham, 1993; Fisher et al., 1997), and is a better determinant of
functional limitations and disability in persons with OA than plain radiographic changes (McAlindon et al., 1993; Hurley et al., 1997).

Quadriceps weakness may be a result of muscle atrophy as well as reduced voluntary muscle activation (Hurley and Newham, 1993). Quadriceps strength deficits can be as high as 38% compared to the uninvolved side in individuals with OA (Petterson et al., 2007), 25% in those with ACL injuries (Williams et al., 2005), and 64% at 3-4 weeks following a total knee arthroplasty (Mizner et al., 2003). Similarly, quadriceps activation deficits may approach 34% in certain conditions (Hassan et al., 2001). In those with isolated ACL injury and recurrent knee joint instability, atrophy and activation failure explained more than 60% of the variance in quadriceps weakness (Williams et al., 2005). In persons with end-stage OA, both reduced muscle activation and lean muscle cross-sectional area contribute to quadriceps weakness, but muscle activation has been found to be the primary determinant of strength in the OA limb (Petterson et al., 2008).

While previous studies have identified the impact of quadriceps strength deficits on gait patterns, the underlying mechanism of how impaired quadriceps function contributes to altered gait remains unknown. Muscle contributions to support and progression have been examined in persons with cerebral palsy and post-stroke hemiparesis (Higginson et al., 2006; Steele et al., 2010), but not in subjects with weak quadriceps. A recent simulation study (van der Krogt et al., 2012) investigated muscle compensations due to weakness by simulating atrophy (decreasing maximum isometric force) in the muscle model. To our knowledge, no study has investigated the effects of
quadriiceps activation failure on muscle compensations and contributions to support and progression during gait.

In order to inform rehabilitation interventions that may improve the function of individuals with weakened quadriceps, it is necessary to establish the cause-effect relationships between abnormal lower extremity muscle function and patient function. As a first step towards that goal, the purpose of this study was to estimate changes in muscle forces and contributions to support and progression to maintain normal gait in response to two sources of quadriceps weakness: atrophy and activation failure. We hypothesized that, to maintain normal gait, 1) the gluteus maximus and the soleus muscles would display the largest increases in force output and contributions to progression and support in response to all types of simulated quadriceps weakness, and 2) that the increases in muscles’ forces and contributions to progression and support would be different for the different types of quadriceps weakness. We used muscle-driven simulations to track normal gait in healthy subjects and applied simulated quadriceps atrophy and activation failure to evaluate muscle compensations associated with the individual sources of weakness. Our long-term goal is to investigate how muscles weakened from pathology affect gait and function and develop targeted physical therapy strategies that may improve patient outcomes.
2.3 Methods

2.3.1 Experimental Data

Seven healthy subjects (4 male and 3 female, Age: 21.9 ± 2.3 years, Mass: 72.8 ± 11.4 kg, Height: 1.74 ± 0.08 m) provided written informed consent in accordance with the Institutional Review Board of The Ohio State University to participate in this study. Each subject walked at a self-selected speed (1.32 ± 0.13 m/s) while motion data was collected at 150 Hz using an 8-camera Vicon MX-F40 system and the Point-Cluster Technique (PCT) (Andriacchi et al., 1998). Ground reaction forces were obtained from six force plates (Bertec, Columbus, OH) sampled at 600 Hz. Muscle activation patterns from the gluteus maximus, gluteus medius, rectus femoris, vastus lateralis, biceps femoris, tibialis anterior, medial gastrocnemius, and soleus of both legs were measured with 16-channel surface EMG (Noraxon, Scottsdale, AZ) sampled at 1500 Hz. EMG data were high-pass filtered at 10 Hz, rectified, and RMS smoothed with a 20 ms window.

2.3.2 Modeling and Simulations

We generated simulations of one gait cycle for each subject, with complete ground reaction force and EMG data, using OpenSim software version 2.4 (Delp et al., 2007). A generic musculoskeletal model with 23 degrees of freedom and 92 musculotendon actuators was scaled to match the anthropometry of the individual subjects using markers located on the head, shoulders, anterior and posterior superior iliac spine, greater trochanter, medial and lateral femoral condyles, medial and lateral tibial plateaus, medial and lateral malleoli, calcaneus, and 2nd metatarsal. The dimensions
of each body segment in the model were scaled based on relative distances between pairs of markers obtained from motion capture during the static calibration trial and the corresponding virtual marker locations in the model so that the RMS marker error was no more than 2 cm. The experimental gait patterns were reproduced in the scaled model by solving an inverse kinematics problem and a weighted least-squares approach to minimize the differences between the experimental marker locations and the model’s virtual marker locations. A residual reduction algorithm (RRA) adjusted model kinematics to resolve dynamic inconsistency between model kinematics and ground reaction forces (Delp et al., 2007). Computed muscle control (CMC) (Thelen and Anderson, 2006) was used to calculate muscle excitations and forces in all lower extremity muscles that produced a coordinated muscle-driven simulation of the subject’s gait. To resolve muscle redundancy, CMC incorporates a static optimization criterion that minimizes the sum of squared muscle excitations. The results of RRA and CMC were considered acceptable if the model kinematics differed from experimentally measured kinematics by less than 2° (or 2 cm for translations) and if the peak residual forces and moments at the pelvis were less than 20 N and 50 Nm, respectively. We compared the full-strength simulated muscle activations from CMC to the subject’s experimental EMG to ensure that there was agreement between the simulated and experimental muscle activation patterns (Figure 2.1). An induced acceleration analysis (IAA) was then performed to determine the contributions of individual muscles to the support (vertical acceleration) and progression (horizontal acceleration) of the body mass center (Zajac and Gordon, 1989; Anderson and Pandy, 2003; Hamner et al., 2010).
2.3.3 Simulations with Weakened Quadriceps

After completing the simulations with the quadriceps at full-strength for each subject, we progressively weakened the quadriceps (rectus femoris and vasti) of one stance leg in three ways based on previously reported values: 1) decreasing the quadriceps’ peak isometric muscle force by 60% (“Atrophy Only”) (Mizner et al., 2003), 2) constraining the peak activations of the quadriceps to 35% less than the peak values that were calculated during the full-strength simulation (“Activation Failure Only”) (Hassan et al., 2001) and 3) a combination of simulated atrophy and activation failure (“Atrophy + Activation Failure”). Decreasing the quadriceps’ peak isometric force scales the muscles’ force-length and force-velocity curves, reflected in the simulation’s...
musculotendon contraction dynamics. Constraining the quadriceps’ peak activations decreases the upper bound of feasible muscle force that can be achieved with a given force-length-velocity relationship. We forced the simulations to track the experimentally measured “normal” gait and re-calculated muscle forces and contributions to support and progression in the weakened models.

2.3.4 Statistical Analysis

For each subject, we calculated the percentage change of a muscle’s peak force and contributions to progression and support for the three types of quadriceps weakness relative to the full-strength simulation. We then performed two-way repeated measures analyses of variance (ANOVA) to determine which muscles were used by the subjects to compensate for weakened quadriceps and maintain their normal gait. We examined the individual muscles and types of quadriceps weakness as main effects as well as the interaction effect between the muscles and the type of weakness. Additionally, we performed one-way repeated measures ANOVA to test whether the individual types of quadriceps weakness had a significant effect on peak muscle forces and contributions to progression and support compared to normal. Tukey post-hoc pairwise comparisons were further used as appropriate. All statistical tests were performed in Minitab® Statistical Software (Minitab Inc, State College, PA), and the level of significance was set at \( \alpha=0.05 \).
2.4 Results

For all subjects and types of quadriceps weakness, the simulation was able to successfully track normal gait. In response to the quadriceps weakness, most muscles in the lower extremity model changed their force output and contributions to support and progression, showing varying degrees and mechanisms by which different muscles in the model responded to the different types of simulated weakness (Tables 2.1-4 and Figures 2.2-7). Confirming previous research, different muscles produced different forces and contributions to progression and support (p<0.001 for all), although we observed a high variability across subjects. Also, the different types of weakness did not change the overall average of muscle forces (p=0.777) or overall contributions to progression and support (p=0.520 and p=0.399, respectively).

However, compared to the full-strength simulation, different muscles produced significantly different amounts of force (p=0.012) and significantly different contributions to progression and support (p<0.001 and p=0.007, respectively) with different types of weakness. Additionally, only some muscles produced significantly different amounts of force and contributions to progression and support compared to normal for the individual sources of weakness (Tables 2.2-4). Of the major muscle groups investigated, the gluteus maximus and soleus muscles displayed the greatest ability to compensate for simulated weakness in the quadriceps muscles during gait by being the only muscles which increased their peak force output and contributions to progression and support in response to all three types of quadriceps weakness.
Table 2.1: Change in muscle force and contributions to forward progression and vertical support across all types of simulated quadriceps (RF and Vasti) weakness compared to the full-strength simulation. The values represent the average and standard deviation of the peak changes in force and induced accelerations from each of the 7 subjects during stance.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Force</th>
<th>Forward Progression</th>
<th>Vertical Support</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change from Normal (N) mean (SD)</td>
<td>% change mean (SD)</td>
<td>Change from Normal (m/s²) mean (SD)</td>
</tr>
<tr>
<td>RF (early stance)</td>
<td>-152.4 (119.5)</td>
<td>-37.7 (18.8)</td>
<td>0.20 (0.17)</td>
</tr>
<tr>
<td>RF (late stance)</td>
<td>-51.9 (54.1)</td>
<td>-20.1 (19.0)</td>
<td>0.12 (0.12)</td>
</tr>
<tr>
<td>Vasti</td>
<td>-73.8 (69.3)</td>
<td>-9.0 (7.7)</td>
<td>0.16 (0.13)</td>
</tr>
<tr>
<td>Glute Max</td>
<td>95.9 (95.9)</td>
<td>26.0 (24.6)</td>
<td>-0.06 (0.05)</td>
</tr>
<tr>
<td>Soleus</td>
<td>166.6 (101.7)</td>
<td>9.8 (6.4)</td>
<td>0.06 (0.10)</td>
</tr>
<tr>
<td>MG</td>
<td>-58.1 (115.8)</td>
<td>-5.1 (11.0)</td>
<td>-0.07 (0.15)</td>
</tr>
<tr>
<td>BFih</td>
<td>-18.2 (32.8)</td>
<td>-4.4 (6.5)</td>
<td>-0.01 (0.02)</td>
</tr>
<tr>
<td>Glute Med</td>
<td>-19.7 (65.4)</td>
<td>-2.1 (5.8)</td>
<td>0 (0.01)</td>
</tr>
<tr>
<td>TA</td>
<td>4.5 (85.8)</td>
<td>4.2 (31.2)</td>
<td>0.03 (0.13)</td>
</tr>
</tbody>
</table>

*a* A positive change from normal indicates an increase in anterior/upward acceleration of the center of mass, while a negative change from normal indicates an increase in posterior/downward acceleration.

*b* A negative % change indicates a decrease in the absolute magnitude of the acceleration.
2.4.1 Muscle Forces

The quadriceps muscles showed decreases in force production that differed in magnitude depending on the mechanism of simulated weakness (Table 2.2 and Figure 2.2). The largest decrease in peak force of the vasti and rectus femoris occurred in response to “Atrophy + Activation Failure” (Table 2.2 and Figure 2.2).

To maintain a normal gait pattern in response to simulated weakened quadriceps, the gluteus maximus and soleus muscles displayed the largest average percent increase in peak force output, regardless of the type of weakness (Table 2.1), and were the only muscles which increased their force output in response to all three types of weakness (Table 2.2). The largest average percent increase in force output was displayed by the gluteus maximus muscle and was significantly greater than the response from any other muscle, regardless of the type of weakness (Table 2.1), with the largest increase in force compared to normal occurring in response to “Atrophy + Activation Failure” of the quadriceps (p=0.0003) (Table 2.2 and Figure 2.3B). The largest increase in peak force compared to normal in the soleus muscle occurred in response to “Activation Failure Only” of the quadriceps (p=0.0016) (Table 2.2 and Figure 2.3A). The gluteus maximus, soleus, and tibialis anterior were the only muscles which displayed an average increase in peak force output in response to quadriceps weakness, while all other muscles investigated displayed an average decrease in peak force (Table 2.1).
Table 2.2: Change in muscle force for each type of simulated quadriceps (RF and Vasti) weakness compared to the full-strength simulation. The values represent the average and standard deviation of the peak changes in force from each of the 7 subjects during stance. * indicates a statistically significant difference from normal (p<0.05).

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Atrophy Only</th>
<th>Activation Failure Only</th>
<th>Atrophy + Activation Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change from Normal (N) mean (SD)</td>
<td>% change mean (SD)</td>
<td>Change from Normal (N) mean (SD)</td>
</tr>
<tr>
<td>RF (early stance)</td>
<td>128.2 (108.4)*</td>
<td>-30.8 (15.6)</td>
<td>-138.7 (120.4)*</td>
</tr>
<tr>
<td>RF (late stance)</td>
<td>17.2 (63.3)</td>
<td>-10.6 (24.1)</td>
<td>-67.9 (39.4)*</td>
</tr>
<tr>
<td>Vasti</td>
<td>65.9 (53.6)*</td>
<td>-7.7 (6.0)</td>
<td>-25.9 (40.4)</td>
</tr>
<tr>
<td>Glute Max</td>
<td>61.2 (61.7)</td>
<td>15.9 (15.0)</td>
<td>63.9 (81.0)</td>
</tr>
<tr>
<td>Soleus</td>
<td>120.9 (87.6)</td>
<td>6.8 (5.0)</td>
<td>217.2 (113.9)*</td>
</tr>
<tr>
<td>MG</td>
<td>-97.7 (85.6)</td>
<td>-8.7 (8.1)</td>
<td>32.9 (82.2)</td>
</tr>
<tr>
<td>BFllh</td>
<td>-24.7 (38.4)</td>
<td>-6.2 (7.5)</td>
<td>-5.9 (13.9)</td>
</tr>
<tr>
<td>Glute Med</td>
<td>26.7 (72.7)</td>
<td>2.1 (6.5)</td>
<td>-44.2 (48.8)</td>
</tr>
<tr>
<td>TA</td>
<td>-18.7 (20.7)</td>
<td>-3.4 (3.3)</td>
<td>4.0 (8.6)</td>
</tr>
</tbody>
</table>
Figure 2.2: Force generated by the (A) vasti and (B) rectus femoris muscles in response to the 3 types of simulated weakness. The vasti peak force decreased in response to applied weakness. The response of the rectus femoris was less consistent, but generally showed decreases in force in response to simulated weakness. Each line represents the average across all 7 subjects. Shaded areas show one standard deviation for the normal simulation.

Figure 2.3: Force generated by the soleus and gluteus maximus muscles in response to the 3 types of simulated quadriceps weakness. (A) The soleus generated more force in mid to late stance in response to “Activation Failure Only” of the quadriceps, while (B) the gluteus maximus generated more force in early stance in response to “Atrophy + Activation Failure” of the quadriceps. Each line represents the average across all 7 subjects. Shaded areas show one standard deviation for the normal simulation.
2.4.2 Contributions to progression and support

The quadriceps muscles showed decreases in peak contributions to braking and support in response to the three types of weakness and differed in magnitude depending on the mechanism of simulated weakness, with the largest decreases in peak contribution to braking and support occurring in response to “Atrophy + Activation Failure” (Tables 2.3-4 and Figures 2.4-5).

To maintain a normal gait pattern, the gluteus maximus and soleus muscles displayed the largest average percent increases in peak contributions to support and fore-aft progression, regardless of the type of weakness (Table 2.1), and were the only muscles to increase their contributions to support and fore-aft progression in response to all three types of quadriceps weakness (Tables 2.3-4). The largest average percent increase in contributions to support and fore-aft progression was displayed by the gluteus maximus muscle and was significantly greater than the response from any other muscle, regardless of the type of weakness, with the exception of the contribution to support by the soleus muscle (Table 2.1). The increase in peak contributions to support and fore-aft progression compared to normal for the gluteus maximus muscle were largest in response to “Atrophy + Activation Failure” of the quadriceps (p=0.0001 and p=0.0003, respectively) and were largest for the soleus muscle in response to “Activation Failure Only” of the quadriceps (p=0.0418 and p=0.0039, respectively) (Tables 2.3-4 and Figures 2.6-7). The gluteus maximus, soleus, and gluteus medius were the only muscles which displayed an average increase in peak contributions to support and fore-aft progression in
response to quadriceps weakness, while all other muscles investigated displayed an average decrease in peak contributions (Table 2.1).
Table 2.3: Change in muscle contribution to forward progression for each type of simulated quadriceps (RF and Vasti) weakness compared to the full-strength simulation. The values represent the average and standard deviation of the peak changes in induced accelerations from each of the 7 subjects during stance. * indicates a statistically significant difference from normal (p<0.05).

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Atrophy Only</th>
<th>Activation Failure Only</th>
<th>Atrophy + Activation Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change from Normal (m/s²)</td>
<td>% change</td>
<td>Change from Normal (m/s²)</td>
</tr>
<tr>
<td>RF (early stance)</td>
<td>0.18 (0.16)*</td>
<td>-26.2 (24.8)</td>
<td>0.17 (0.18)*</td>
</tr>
<tr>
<td>RF (late stance)</td>
<td>0.04 (0.13)</td>
<td>-6.7 (29.4)</td>
<td>0.17 (0.08)*</td>
</tr>
<tr>
<td>Vasti</td>
<td>0.14 (0.10)*</td>
<td>-8.0 (5.2)</td>
<td>0.06 (0.08)</td>
</tr>
<tr>
<td>Glute Max</td>
<td>-0.05 (0.03)*</td>
<td>20.8 (9.4)</td>
<td>-0.02 (0.04)</td>
</tr>
<tr>
<td>Soleus</td>
<td>0.01 (0.11)</td>
<td>0.3 (7.1)</td>
<td>0.12 (0.12)*</td>
</tr>
<tr>
<td>MG</td>
<td>-0.11 (0.10)</td>
<td>-8.9 (8.2)</td>
<td>0.05 (0.16)</td>
</tr>
<tr>
<td>BFh</td>
<td>-0.01 (0.02)</td>
<td>-6.4 (7.4)</td>
<td>0.0 (0.01)</td>
</tr>
<tr>
<td>Glute Med</td>
<td>-0.01 (0.01)</td>
<td>1.7 (1.8)</td>
<td>0.01 (0.01)</td>
</tr>
<tr>
<td>TA</td>
<td>0.07 (0.13)</td>
<td>-3.5 (6.8)</td>
<td>-0.02 (0.05)</td>
</tr>
</tbody>
</table>

*a A positive change from normal indicates an increase in anterior acceleration of the center of mass, while a negative change from normal indicates an increase in posterior acceleration.

*b A negative % change indicates a decrease in the absolute magnitude of the acceleration.
Table 2.4: Change in muscle contribution to vertical support for each type of simulated quadriceps (RF and Vasti) weakness compared to the full-strength simulation. The values represent the average and standard deviation of the peak changes in induced accelerations from each of the 7 subjects during stance. * indicates a statistically significant difference from normal (p<0.05).

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Atrophy Only</th>
<th>Activation Failure Only</th>
<th>Atrophy + Activation Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Change from</td>
<td>% change</td>
<td>Change from</td>
</tr>
<tr>
<td></td>
<td>Normal (m/s²)</td>
<td>mean (SD)</td>
<td>Normal (m/s²)</td>
</tr>
<tr>
<td>RF (early stance)</td>
<td>-0.03 (0.18)</td>
<td>-1.9 (33.5)</td>
<td>0.12 (0.19)</td>
</tr>
<tr>
<td>RF (late stance)</td>
<td>-0.02 (0.12)</td>
<td>-3.4 (28.4)</td>
<td>-0.14 (0.08)*</td>
</tr>
<tr>
<td>Vasti</td>
<td>-0.25 (0.24)</td>
<td>-5.8 (5.0)</td>
<td>-0.01 (0.20)</td>
</tr>
<tr>
<td>Glute Max</td>
<td>0.27 (0.22)*</td>
<td>16.4 (10.1)</td>
<td>0.13 (0.17)</td>
</tr>
<tr>
<td>Soleus</td>
<td>0.51 (0.38)</td>
<td>6.6 (4.6)</td>
<td>0.87 (0.62)*</td>
</tr>
<tr>
<td>MG</td>
<td>-0.33 (0.64)</td>
<td>-6.9 (11.3)</td>
<td>0.23 (0.29)</td>
</tr>
<tr>
<td>BFh</td>
<td>-0.03 (0.05)</td>
<td>-6.1 (9.6)</td>
<td>-0.02 (0.04)</td>
</tr>
<tr>
<td>Glute Med</td>
<td>0.02 (0.13)</td>
<td>0.9 (5.4)</td>
<td>-0.02 (0.08)</td>
</tr>
<tr>
<td>TA</td>
<td>-0.24 (0.19)</td>
<td>-4.3 (3.6)</td>
<td>0.10 (0.20)</td>
</tr>
</tbody>
</table>

*A positive change from normal indicates an increase in upward acceleration of the center of mass, while a negative change from normal indicates an increase in downward acceleration.

*b A negative % change indicates a decrease in the absolute magnitude of the acceleration.
Figure 2.4: Contribution to (A) forward progression and (B) vertical support by the rectus femoris muscle in response to the 3 types of simulated quadriceps weakness. The rectus femoris contributes less to slowing forward progression in response to simulated weakness. Each line represents the average across all 7 subjects. Shaded areas show one standard deviation for the normal simulation.

Figure 2.5: Contribution to (A) forward progression and (B) vertical support by the vasti muscles in response to the 3 types of simulated quadriceps weakness. The vasti contribute less to vertical support and slowing forward progression in response to simulated weakness, with the largest decrease occurring in response to “Atrophy + Activation Failure”. Each line represents the average across all 7 subjects. Shaded areas show one standard deviation for the normal simulation.
Figure 2.6: Contribution to (A) forward progression and (B) vertical support by the soleus muscle in response to the 3 types of simulated quadriceps weakness. The soleus contributes more to vertical support than forward progression in response to “Activation Failure Only” of the quadriceps. Each line represents the average across all 7 subjects. Shaded areas show one standard deviation for the normal simulation.

Figure 2.7: Contribution to (A) forward progression and (B) vertical support by the gluteus maximus muscle in response to the 3 types of simulated quadriceps weakness. Gluteus maximus contributes more to slowing forward progression and maintaining vertical support in response to “Atrophy Only” and “Atrophy + Activation Failure” of the quadriceps. Each line represents the average across all 7 subjects. Shaded areas show one standard deviation for the normal simulation.
2.5 Discussion

The purpose of this study was to estimate changes in muscle forces and contributions to support and progression to maintain normal gait in response to two sources of quadriceps weakness: atrophy and activation failure. To our knowledge, this is the first use of muscle-driven simulations to investigate how lower extremity muscles would compensate for both quadriceps atrophy and activation failure to maintain normal gait kinematics. Confirming our hypotheses, our results indicate that the gluteus maximus and soleus muscles show the greatest potential to compensate for weakness in the quadriceps.

Muscle forces from our simulations compared well with the muscle forces of a previous study of simulated muscle atrophy (van der Krogt et al., 2012). Van der Krogt et al. found similar compensation strategies in response to quadriceps atrophy, including an increase in force of the gluteus maximus and soleus muscles, and a decrease in force of antagonistic muscles such as the gastrocnemius and biceps femoris. Muscle contributions to support and progression for our full-strength simulations generally agreed with previous studies (Kepple et al., 1997; Neptune et al., 2001; Anderson and Pandy, 2003; Neptune et al., 2004; Liu et al., 2006; Liu et al., 2008). However, while Neptune et al. (Neptune et al., 2004) found that the rectus femoris works to accelerate the body forward in late stance, we found it contributed to slowing forward progression, which agrees with Liu et al. (Liu et al., 2008).
We found that an increase in muscle force in response to quadriceps weakness did not necessarily translate to an equivalent increase in contribution to support and progression from that muscle. In an effort to relate muscle force and contributions to progression and support, we investigated muscle “instantaneous potential for acceleration (IPA)”. The IPA of each muscle was calculated by dividing the IAA results for progression and support by the muscle force from CMC (Figure 2.8). This analysis provided several key insights into our results. First, it suggests why certain muscles, such as the gluteus maximus and soleus, responded to simulated quadriceps weakness. The quadriceps act to slow progression of the body during the entire stance phase and provide vertical support throughout a majority of stance. The gluteus muscles also have the capacity to provide consistent braking during stance (Figure 2.8A) and contribute to providing vertical support, along with the ankle plantarflexors (gastrocnemius and soleus) (Figure 2.8B). Interestingly, we found that the force and contributions to progression and support decreased in the gastrocnemius with weakened quadriceps. A possible explanation could be that our simulations responded to loss of quadriceps function by decreasing forces in antagonistic muscles.
Figure 2.8: Instantaneous potential for acceleration (IPA) of each of the muscles investigated to contribute to (A) forward progression and (B) vertical support. The potential of the quadriceps (RF and Vasti) to contribute to braking is greater than any of the other muscles, with the exception of tibialis anterior (TA) in early stance.

Second, the analysis of muscle IPA further highlights the importance of the quadriceps during gait and may provide additional insight into why quadriceps weakness is strongly correlated to sub-optimal functional performance. Gait is characterized by periods of acceleration and deceleration. During weight acceptance in early stance, the eccentric contraction of the quadriceps provides energy absorption and limb stability and acts to decelerate the body. The quadriceps display the greatest potential of the major muscle groups to consistently slow forward progression (i.e., decelerate the body) during gait. Since the gluteus maximus’ potential for slowing forward progression is less than
that of the quadriceps, there is a limit to how much it could compensate for quadriceps weakness. For example, at 30% of the gait cycle, every 1 Newton decrease in force of the vasti would require an increase in force of approximately 4 Newtons from the gluteus maximus to maintain an equivalent contribution to slowing forward progression (Figure 2.8A).

Our results should be considered in light of several limitations. We forced all simulations to track normal gait, but persons with OA or ACL injury often do not use a normal gait pattern (Brinkmann and Perry, 1985; DeVita et al., 1998; Gok et al., 2002; Lewek et al., 2002). The common finding of abnormal gait in persons with pathology suggests that there are compensation thresholds beyond which an individual will choose to adapt an altered gait pattern instead of increasing muscle force to maintain normal gait. However, our results offer initial insights to what compensation strategies may be needed for a person with weak quadriceps to maintain normal gait patterns. We applied activation failure in the simulations by constraining the peak values of the quadriceps activation to 65% of the peak values from the full-strength simulation instead of applying an overall constraint on the maximum possible activation of the muscle. The quadriceps are never maximally activated during gait, so applying the constraint on the maximum activation would not have resulted in any simulated actual activation deficit. It is important to note that previous studies of activation failure in the quadriceps have been performed during experimental maximum isometric contractions with subjects seated in a dynamometer. To our knowledge, no study has investigated whether activation failure influences performance of sub-maximal activities such as gait. Therefore, while our
approach to applying quadriceps activation deficits in the simulations has not been validated through physical experiments and may not appropriately reflect in-vivo activation deficits, it represents a key step in investigating the effects of activation failure during walking and utilizes the strengths of simulations in answering “what if?” questions related to muscle function. Additionally, we chose to apply simulated weakness to both the rectus femoris and vasti because previous studies of quadriceps weakness do not differentiate between the individual quadriceps muscles. (Lewek et al., 2004; Mizner et al., 2005; Petterson et al., 2007). However, since the rectus femoris and vasti provide different contributions to progression and support, additional work is warranted to investigate individual quadriceps muscle weakness and how that weakness translates to compensation strategies in pathological gait. Our simulations also used a generic musculoskeletal model, which may not be entirely applicable to populations with weak quadriceps. For example, the quadriceps of persons with OA or ACL injury have smaller cross-sectional areas and greater activation deficits compared to healthy quadriceps (Hurley et al., 1997; Gur and Cakin, 2003; Lewek et al., 2004; Ikeda et al., 2005; Mizner et al., 2005; Williams et al., 2005; Petterson et al., 2008). Given that the amount of atrophy or activation failure present in these populations can vary greatly between individuals and may depend on other factors such as injury or disease severity, we chose to simulate what may be considered the “worst-case” for populations which commonly exhibit quadriceps weakness based on previously reported values (Hassan et al., 2001; Mizner et al., 2003). Future work should focus on simulations of pathological gait which
incorporate patient-specific muscle properties to accurately quantify variations in muscle function in impaired populations.

Our results provide an important first step in understanding the impact of the sources of quadriceps weakness on gait as well as the potential compensations by other muscles. While the gluteus maximus and soleus muscles show the greatest potential to compensate for quadriceps weakness, they may not be able to fully compensate for the loss of braking and support provided by the quadriceps. By simulating two different causes of muscle weakness, this model suggested different compensation strategies by the lower extremity musculature in response to atrophy and activation deficits. These simulation findings provide novel initial insights into specific muscle activation patterns that control the various stages of the gait cycle and further investigation is warranted to understand the mechanisms by which different sources of weakness may translate to different muscle compensation strategies. Future work with individuals with pathology will expand on these results and determine the individuals’ compensation strategies that can then be evaluated through clinical interventions.

2.6 Acknowledgements

The authors thank Mike McNally, Jay Young, Molly Mollica, Michelle Cullen, and Laura Henkel for their assistance. Funding was provided to Julie Thompson by the NSF Graduate Research Fellowship Program and the Ohio State University Graduate Fellowship Program.
Chapter 3: Muscle Compensations for Simulated Quadriceps Weakness Over a Range of Walking Speeds

3.1 Abstract

Many individuals with knee osteoarthritis (OA) and total knee arthroplasty (TKA) walk slowly compared to individuals without these conditions. Quadriceps muscle weakness, which may result from atrophy or activation failure, is typical in these patient populations and has been correlated with decreased gait speed. However, the underlying mechanism of how impaired quadriceps function contributes to reduced gait speed remains unknown. The purpose of this study was to estimate muscle compensations and changes in contribution to support and progression to maintain gait kinematics over a range of walking speeds in response to two sources of quadriceps weakness: atrophy and activation failure. We used muscle-driven simulations to track gait kinematics in young, healthy subjects and simulated quadriceps atrophy and activation failure to evaluate muscular compensation patterns over a range of speeds. We found that the gluteus maximus and soleus muscles displayed the greatest ability to compensate for simulated weakened quadriceps at all gait speeds; however, soleus force output decreased at faster speeds. All simulations were able to track gait kinematics at all speeds, suggesting it would be feasible for persons with quadriceps weakness to walk at a fast speed. Other factors not simulated by our model (e.g. pain and perceptions of instability) likely
contribute to reduced walking speeds in individuals with knee OA or TKA. This study lays the foundation for future work addressing factors that limit walking speed in pathological gait that could potentially be addressed with targeted rehabilitation programs.

3.2 Introduction

Many individuals with osteoarthritis (OA) and total knee arthroplasty (TKA) walk slowly compared to healthy individuals (Andriacchi et al., 1977; Brinkmann and Perry, 1985; Hurley et al., 1997; Walsh et al., 1998; Gok et al., 2002). Moreover, quadriceps muscle weakness is a typical impairment in these populations (Hurley and Newham, 1993; Fisher et al., 1997; Mizner et al., 2003) and has been correlated with decreased walking speed (Gibbs et al., 1996; Connelly and Vandervoort, 1997; Hurley et al., 1997; Moxley Scarborough et al., 1999; Yoshida et al., 2008). Quadriceps weakness may be a result of muscle atrophy as well as reduced voluntary muscle activation (Hurley and Newham, 1993), both of which are prevalent in knee OA and TKA populations (Hassan et al., 2001; Mizner et al., 2003; Petterson et al., 2007; Petterson et al., 2008). However, the underlying mechanism of how impaired quadriceps function contributes to reduced gait speed remains unknown.

Since persons with OA and TKA walk slowly compared to healthy individuals (Andriacchi et al., 1977; Brinkmann and Perry, 1985; Hurley et al., 1997; Walsh et al., 1998; Gok et al., 2002), it is important to differentiate between the effects of walking speed and of pathology. Previous simulation studies have investigated how muscles
contribute to support and progression over a range of speeds during healthy gait (Liu et al., 2008; Neptune et al., 2008; Hamner and Delp, 2013). Liu et al. (2008) found that the gluteus maximus, gluteus medius, vasti, hamstrings, gastrocnemius, and soleus were the primary contributors to support and progression over a range of speeds, and the contributions from these muscles, with the exception of gluteus medius, generally increased with walking speed. These findings were consistent with those of Neptune et al. (2008), who observed similar muscle contributions to trunk support and propulsion.

During running, studies of muscle contributions over a range of speeds have revealed that the quadriceps are the largest contributors to braking and support during early stance, while the plantarflexors are the largest contributors to propulsion and support during late stance (Hamner et al., 2010; Hamner and Delp, 2013), with soleus providing the greatest contribution at all running speeds (Hamner and Delp, 2013).

While previous studies have identified muscle contributions to progression and support over a range of speeds in healthy gait, less is known about muscle compensations in pathological gait. Recent studies at a self-selected speed have investigated the effect of muscle weakness by simulating atrophy only (van der Krogt et al., 2012), activation failure only (Knarr et al., 2013), and combinations of atrophy and activation failure (Thompson et al., 2013) in healthy individuals. Other simulation studies have examined muscle contributions to progression and support in persons with post-stroke hemiparesis, cerebral palsy, and TKA (Higginson et al., 2006; Steele et al., 2010; Steele et al., 2012; Li et al., 2013). To our knowledge, no study has investigated how lower extremity muscles could compensate for both quadriceps atrophy and activation failure to maintain
gait kinematics of healthy subjects over a range of walking speeds. Such an investigation would provide an important first step towards addressing the factors that limit walking speed in individuals with pathologically weak quadriceps.

The purpose of this study was to estimate the muscle compensations and changes in contribution to support and progression which could result in unchanged gait kinematics over a range of walking speeds in response to two sources of quadriceps weakness, atrophy and activation failure, in healthy subjects. We hypothesized that, to maintain gait kinematics, 1) the gluteus maximus and soleus muscles would display the largest increases in force output and contributions to progression and support in response to simulated quadriceps weakness at all gait speeds, and 2) that the muscles’ forces and contributions to progression and support would be different at different gait speeds. We used muscle-driven simulations to track gait kinematics over a range of speeds in young, healthy subjects and applied simulated quadriceps weakness as atrophy and activation failure to evaluate muscular compensation patterns associated with the individual sources of weakness.

3.3 Methods

3.3.1 Experimental Data

Six healthy subjects walked overground at three speeds (Table 3.1) while motion data were collected at 150 Hz using an 8-camera Vicon MX-F40 system and the Point-Cluster Technique (PCT) (Andriacchi et al., 1998). Each subject provided written informed consent in accordance with the Institutional Review Board of The Ohio State
University. Subjects were instructed to walk at a self-selected speed and then to walk slower and faster than their self-selected speed. Four or more trials were collected at each speed. No restrictions were placed on their walking speed other than ensuring that they were faster or slower than the self-selected pace. One representative trial at each speed for each subject, with ground reaction forces for at least one full gait cycle, was selected for analysis. Ground reaction forces were obtained from six embedded force plates (Bertec, Columbus, OH) sampled at 600 Hz. Muscle activity from the bilateral gluteus maximus, gluteus medius, rectus femoris, vastus lateralis, biceps femoris, tibialis anterior, medial gastrocnemius, and soleus were measured with 16-channel surface electromyography (EMG) (Noraxon Telemyo DTS, Scottsdale, AZ) and sampled at 1500 Hz. EMG data were high-pass filtered at 10 Hz, rectified, and RMS smoothed with a 20 ms window.

Table 3.1: Subject demographics and walking speeds

<table>
<thead>
<tr>
<th>Subject</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Mass (kg)</th>
<th>Height (m)</th>
<th>Leg length (m)</th>
<th>Slow speed (m/s)</th>
<th>Self-selected speed (m/s)</th>
<th>Fast speed (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>25</td>
<td>57.4</td>
<td>1.70</td>
<td>0.88</td>
<td>1.20</td>
<td>1.32</td>
<td>1.59</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>22</td>
<td>63.1</td>
<td>1.66</td>
<td>0.86</td>
<td>1.08</td>
<td>1.25</td>
<td>1.81</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>20</td>
<td>78.0</td>
<td>1.69</td>
<td>0.86</td>
<td>0.91</td>
<td>1.16</td>
<td>1.54</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>19</td>
<td>74.2</td>
<td>1.77</td>
<td>0.90</td>
<td>1.05</td>
<td>1.27</td>
<td>1.57</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>19</td>
<td>65.5</td>
<td>1.63</td>
<td>0.81</td>
<td>0.96</td>
<td>1.26</td>
<td>1.54</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>21</td>
<td>76.4</td>
<td>1.77</td>
<td>0.96</td>
<td>1.29</td>
<td>1.57</td>
<td>2.17</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>21.0</td>
<td>69.1</td>
<td>1.70</td>
<td>0.88</td>
<td>1.08</td>
<td>1.31</td>
<td>1.70</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td></td>
<td>2.3</td>
<td>8.3</td>
<td>0.05</td>
<td>0.05</td>
<td>0.14</td>
<td>0.14</td>
<td>0.25</td>
</tr>
</tbody>
</table>
3.3.2 Modeling and Simulations

We generated simulations of one gait cycle at each speed for each subject, using OpenSim software version 2.4 (Delp et al., 2007). A generic musculoskeletal model with 23 degrees of freedom and 92 musculotendon actuators was scaled to match the anthropometry of the individual subjects using markers located on bony anatomical landmarks. The dimensions of each body segment in the model were scaled based on relative distances between pairs of markers obtained from motion capture during the static calibration trial and the corresponding virtual marker locations in the model so that the RMS marker error was no more than 2 cm. The experimental gait patterns were reproduced in the scaled model by solving an inverse kinematics problem and a weighted least-squares approach to minimize the differences between the experimental marker locations and the model’s virtual marker locations. A residual reduction algorithm (RRA) adjusted model kinematics to resolve dynamic inconsistency between the model kinematics and the ground reaction forces (Delp et al., 2007). Computed muscle control (CMC) (Thelen and Anderson, 2006) was used to calculate the muscle excitations and forces in all lower extremity muscles that produced a coordinated muscle-driven simulation of the subject’s gait. The results of RRA and CMC were considered acceptable if the model kinematics differed from experimentally measured kinematics by less than 2° (or 2 cm for translations) and if the peak residual forces and moments at the pelvis were less than 20 N and 50 Nm, respectively. We compared the full-strength simulated muscle activations from CMC to the subject’s experimental EMG to ensure that there was agreement between the simulated and experimental muscle activation.
patterns (Figure 3.1). An induced acceleration analysis (IAA) was then performed to determine the contributions of individual muscles to the support (vertical acceleration) and progression (horizontal acceleration) of the body mass center (Zajac and Gordon, 1989; Anderson and Pandy, 2003; Hamner et al., 2010).

3.3.3 Simulations with Weakened Quadriceps

After completing the simulations with the quadriceps at full strength for each subject and gait speed, we progressively weakened the quadriceps (rectus femoris and vasti) of one stance leg using methods we have developed previously (Thompson et al., 2013). We weakened the muscles in three ways based on previously reported values: 1) decreasing the quadriceps’ peak isometric force by 60% (“Atrophy Only”) (Mizner et al., 2003), 2) constraining the peak activations of the quadriceps to 35% less than the peak values that were calculated during the full-strength simulation (“Activation Failure Only”) (Hassan et al., 2001) and 3) a combination of simulated atrophy and activation failure (“Atrophy + Activation Failure”). We forced the simulations to track the experimentally measured “normal” gait kinematics and re-calculated muscle forces and contributions to support and progression in the weakened models at each speed.
Figure 3.1: Experimental EMG (black) and simulated muscle activations (blue) averaged over 5 subjects for each gait speed (one subject was excluded from figure due to missing EMG for TA muscle). Simulated activations generally compared well with experimental EMG. Shaded areas show one standard deviation. The peak value of the Experimental EMG is normalized to the peak value of the simulated muscle activation.
3.3.4 Statistical Analysis

For each subject and gait speed, we calculated the percentage change of a muscle’s peak force and contributions to progression and support for the three types of quadriceps weakness relative to the full-strength simulation. We then performed a three-way repeated measures analyses of variance (ANOVA) to determine which muscles were used by the subjects to compensate for weakened quadriceps and maintain gait kinematics at each speed. We examined the individual muscles, types of quadriceps weakness, and speed as main effects as well as the interaction effects between the muscles, types of weakness, and speed. Additionally, we performed a two-way repeated measures ANOVA for each muscle to test the effect of individual types of quadriceps weakness and gait speed on peak muscle forces and contributions to progression and support compared to baseline. Tukey post-hoc pairwise comparisons were further used, as appropriate. All statistical tests were performed in Minitab® Statistical Software (Minitab Inc, State College, PA), and the level of significance was set at $\alpha=0.05$.

3.4 Results

For all subjects and types of quadriceps weakness, the simulation was able to successfully track the experimental baseline gait kinematics at all speeds. Different muscles and types of quadriceps weakness, as well as the interaction between muscle and type of weakness, had significant effects on the percent change in peak muscle force and contributions to progression and support relative to baseline (Table 3.2), indicating that different muscles produced significantly different peak forces and contributions to
progression and support in response to different types of quadriceps weakness. Additionally, the interaction between muscle and speed had a significant effect on the percent change in peak force and contribution to support (Table 3.2), indicating that different muscles produced significantly different forces and contributions to support as gait speed changed. When investigating speed and weakness effects in the two-way ANOVA for each muscle, gait speed and type of weakness significantly affected the peak force output and contributions to progression and support differently for each muscle (Table 3.3 and Figures 3.2, 3.5-6). Of the major muscle groups investigated, the gluteus maximus and soleus muscles displayed the greatest ability to compensate for simulated weakened quadriceps during gait. These were the only muscles which displayed increased force output and increased contributions to progression and support in response to all three types of quadriceps weakness across gait speeds (Figures 3.2, 3.5-6).

Regardless of gait speed, the gluteus maximus generated more force in early stance to compensate for quadriceps weakness and maintain the experimental gait pattern (Figure 3.3), with the largest increases in peak force output (p=0.0182) and contributions to progression (p=0.0001) and support (p=0.0084) occurring in response to “Atrophy + Activation Failure” of the quadriceps (Figures 3.3 and 3.7). The soleus generated more force in late stance to compensate for quadriceps weakness, but its compensations in response to different types of weakness varied with speed (Figures 3.2 and 3.4). As expected, the quadriceps muscles generally showed decreases in force production and contributions to braking and support in response to simulated weakness (Figures 3.2 and 3.5-6), although the reductions in vasti peak force and contribution to support were not
statistically significant (Table 3.3). Interestingly, quadriceps force and contributions were affected least by simulated activation failure, especially at the fast gait speed.

Table 3.2: P-values for the main effects and interaction effects from the three-way repeated measures ANOVA on percent change in peak force and contributions to progression and support over all muscles relative to baseline.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Force</th>
<th>Speed</th>
<th>Weakness</th>
<th>Muscle*Speed</th>
<th>Muscle*Weakness</th>
<th>Speed*Weakness</th>
<th>Muscle<em>Speed</em>Weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>&lt;0.001</td>
<td>0.703</td>
<td>&lt;0.001</td>
<td>0.006</td>
<td>&lt;0.001</td>
<td>0.899</td>
<td>0.787</td>
</tr>
<tr>
<td>Vasti</td>
<td>&lt;0.001</td>
<td>0.307</td>
<td>0.017</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.927</td>
<td>0.991</td>
</tr>
<tr>
<td>Glute Max</td>
<td>&lt;0.001</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>0.944</td>
<td>0.903</td>
</tr>
</tbody>
</table>

Table 3.3: P-values for speed and weakness main effects from the two-way repeated measures ANOVA for each muscle on peak force and contributions to progression and support

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Force</th>
<th>Speed</th>
<th>Weakness</th>
<th>Progression</th>
<th>Speed</th>
<th>Weakness</th>
<th>Support</th>
<th>Speed</th>
<th>Weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>0.001</td>
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<td>&lt;0.001</td>
<td>0.562</td>
<td>&lt;0.001</td>
<td>0.394</td>
<td>0.039</td>
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<td>0.039</td>
</tr>
</tbody>
</table>

3.4.1 *Slow to self-selected speed*

For all types of simulated weakness, the average peak force output increased significantly from the slow to the self-selected gait speed for the vasti (p<0.0001), gluteus maximus (p<0.0001), gluteus medius (p=0.0062), hamstrings (p=0.0003), and tibialis
anterior (p<0.0001). The gluteus maximus muscle displayed its largest increase in peak force relative to baseline (p<0.0001) at the slow gait speed, regardless of the type of weakness. Force compensation by the soleus muscle at the slow gait speed was largest in response to “Atrophy + Activation Failure” of the quadriceps (Figure 3.4).

The average peak contributions to progression and support over all types of weakness increased significantly from the slow to the self-selected gait speed for the vasti, gluteus maximus, hamstrings, tibialis anterior (p<0.0001 for all) and soleus (p<0.0001 and p=0.0114, respectively). At the slow gait speed, the gluteus maximus muscle displayed its largest increase in peak contribution to braking relative to baseline (p<0.0001), regardless of the type of weakness. The largest increase in peak contribution to support by the soleus muscle at the slow speed occurred in response to “Atrophy + Activation Failure” of the quadriceps, while the largest increase in peak contribution to progression occurred in response to “Atrophy Only” (Figure 3.8).

3.4.2 Self-selected to fast speed

Similar to its response when gait speed increased from slow to self-selected, the vasti muscle group displayed a significant increase in average peak force output (p<0.0001) over all types of weakness when speed increased from self-selected to fast. Furthermore, the gluteus maximus and gluteus medius muscles displayed significant increases in average peak force output (p<0.0001 and p=0.0012, respectively). Although not statistically significant, there was a trend toward a decrease in force output by the soleus muscle when gait speed increased from self-selected to fast (p=0.0575), with the
largest compensation occurring in response to “Activation Failure Only” of the quadriceps (Figures 3.2 and 3.4).

The vasti muscle group also displayed significant increases in average peak contributions to progression and support (p<0.0001 for both) when speed increased from self-selected to fast, similar to its response from the slow to self-selected speed, while the gluteus maximus and hamstring muscles displayed significant increases in average peak contributions to support (p=0.0001 and p<0.0001, respectively). In contrast to their responses from the slow to self-selected speed, the rectus femoris displayed significant increases in peak contributions to progression (p=0.0387) and support (p=0.0362), while the gastrocnemius muscle group displayed a significant increase in peak contribution to progression (p=0.0019) when speed increased from self-selected to fast (Figures 3.5 and 3.6). Additionally, peak contributions to support actually decreased significantly for the soleus (p=0.0164) and tibialis anterior (p=0.0007) muscles when going from the self-selected to the fast gait speed.
The values represent the average of the peak force from each of the 6 subjects during stance. The gluteus maximus and soleus muscles were the only muscles which increased their force output in response to all three types of weakness at each gait speed.
Figure 3.3: Gluteus maximus force output at each speed for the full-strength simulation and the simulation with the largest response to simulated quadriceps weakness. Force in the gluteus maximus muscle increased with gait speed, with the greatest compensation for weakness at each speed occurring in response to “Atrophy + Activation Failure” of the quadriceps. Each line represents the average across all 6 subjects.

Figure 3.4: Soleus force output at each speed for the full-strength simulation and the simulation with the largest response to simulated quadriceps weakness. Force in the soleus muscle decreased at the fast gait speed. The greatest compensation for weakness occurred in response to “Activation Failure Only” of the quadriceps except at the slow speed, for which compensation was greatest in response to “Atrophy + Activation Failure”. Each line represents the average across all 6 subjects.
Figure 3.5: Peak muscle contributions to forward acceleration (progression) for the normal, full-strength simulation and each type of simulated quadriceps (RF and Vasti) weakness at each gait speed. The values represent the average of the peak acceleration from each of the 6 subjects during stance. The gluteus maximus muscle increased its contribution to slowing progression (braking), while the soleus muscle increased its contribution to propulsion in response to quadriceps weakness at each gait speed.
Figure 3.6: Peak muscle contributions to vertical acceleration (support) for the normal, full-strength simulation and each type of simulated quadriceps (RF and Vasti) weakness at each gait speed. The values represent the average of the peak acceleration from each of the 6 subjects during stance. The gluteus maximus and soleus muscles were the only muscles which increased their peak contributions to support in response to all three types of weakness at each gait speed.
Figure 3.7: Gluteus maximus contributions to (A) progression and (B) support at each speed for the full-strength simulation and the simulation with the largest response to simulated quadriceps weakness. Contribution to slowing progression (braking) increased from the slow to self-selected speed, but did not change significantly from self-selected to fast. Contribution to support increased with gait speed. The greatest compensation for weakness at each speed occurred in response to “Atrophy + Activation Failure” of the quadriceps. Each line represents the average across all 6 subjects.

Figure 3.8: Soleus contributions to (A) progression and (B) support at each speed for the full-strength simulation and the simulation with the largest response to simulated quadriceps weakness. Peak contribution to progression increased from the slow to self-selected speed, but did not change from self-selected to fast. Peak contribution to support decreased from the self-selected to fast gait speed. Each line represents the average across all 6 subjects.
3.5 Discussion

To our knowledge, our study is the first use of muscle-driven simulations to investigate how lower extremity muscles could compensate for both quadriceps atrophy and activation failure to maintain gait kinematics over a range of walking speeds. Confirming our hypotheses, the gluteus maximus and soleus muscles displayed the greatest ability to compensate for simulated weakened quadriceps at all gait speeds, and the muscles’ responses were different at different gait speeds.

Muscle contributions to support and progression over a range of walking speeds for our full-strength simulations generally agreed with Liu et al. (2008), who found that contributions by the gluteus maximus, vasti, hamstrings, and gastrocnemius generally increased with gait speed. They also found that contributions by the soleus significantly increased with speed, which differs from our finding of a decrease in soleus force and contributions as speed increased from self-selected to fast, although we observed high variability between subjects. The discrepancy between our findings and those of Liu and colleagues (2008) could be attributable to differences in gait speed. The average fast gait speed in the Liu et al. study was 1.56 m/s, while the average fast speed of our subjects was 1.70 m/s. Our findings for the soleus muscle agree with a study by Neptune and Sasaki (2005), who found that muscle force increased with walking speed in all lower extremity muscles except the ankle plantarflexors. Soleus force decreased at walking speeds exceeding 1.57 m/s (80% of the average preferred walk-run transition speed of 1.96 m/s), which the authors attributed to the muscle operating at an “adverse” contractile
state (i.e. shorter fiber lengths and higher fiber shortening velocity) (Neptune and Sasaki, 2005). This speed falls between our average self-selected speed (1.31 m/s) and fast speed (1.70 m/s), which may explain why we saw a decrease in soleus force and contributions while Liu and colleagues did not.

A recent study (Arnold et al., 2013) also found that soleus force generation ability (i.e., the force generated per unit of activation) decreased with increasing walking speed. The opposite was true of the vasti, in which ability to generate force increased at fast walking speeds. We pursued this concept in our own study by investigating the normalized muscle fiber lengths and velocities from our simulations. We found that the vasti operate closer to optimal fiber length and contract more eccentrically (i.e., greater negative fiber velocity) in early stance as gait speed increases, agreeing with the findings of Arnold and colleagues (2013). These force-length-velocity properties of the vasti translate to a greater force generation capacity as gait speed increases, which may explain why there is less reduction in vasti force due to simulated weakness, particularly for the case of activation failure, at faster gait speeds. Walking at a faster speed places the vasti in a more advantageous contractile state, which may lessen the effect of atrophy and activation deficits.

The roles of the gluteus maximus and soleus muscles during gait may suggest why these muscles showed the greatest ability to compensate for deficits in the quadriceps. The quadriceps provide braking and vertical support throughout the majority of stance. The gluteus maximus muscle also provides consistent braking during stance, while both the gluteus maximus and soleus muscles contribute to vertical support.
However, at faster speeds, the contractile state of the gluteus maximus muscle is more advantageous for force production than that of the soleus muscle. Similar to the vasti, the gluteus maximus muscle produces maximum force in early stance, and contracts more eccentrically as gait speed increases. The decreased force generation of the soleus muscle at faster gait speeds, combined with the increase in gluteus maximus force generation capacity which is similar to that of the vasti, may suggest why the gluteus maximus muscle showed the greatest compensation in response to simulated quadriceps weakness. In light of this finding, the fact that the gluteus muscles have received relatively little attention in previous studies on the functional role of muscles during gait compared to the plantarflexors (Nadeau et al., 1999; Neptune et al., 2001; Neptune and Sasaki, 2005; Farris and Sawicki, 2012) may suggest that the gluteus muscles are an unrealized target in rehabilitation strategies for populations with weak quadriceps.

The limitations of our modeling approach were discussed previously (Chapter 2; Thompson et al., 2013), and the results of this current study should be interpreted in light of several additional limitations. While previous studies have controlled for walking speed by using a treadmill to collect data at fixed speed intervals for all subjects (Neptune and Sasaki, 2005; Neptune et al., 2008) or by pacing overground walking speed individually for each subject in real-time (Schmitz et al., 2009), we did not control for speed. Nevertheless, our statistical analysis revealed a significant speed effect for most muscles (Table 3.3). Additionally, the range of speeds we investigated was less than the range of speeds examined in some previous studies (Neptune and Sasaki, 2005; Neptune et al., 2008; Arnold et al., 2013). While persons with OA and TKA may walk more
slowly than the average slow speed of 1.08 m/s displayed by our subjects (Brinkmann and Perry, 1985), this value falls below the self-selected speeds reported by a previous study of gait in OA of 1.231 m/s (Mundermann et al., 2004) and in TKA of 1.17 m/s (Walsh et al., 1998), as well as the self-selected speed reported for healthy older adults of 1.32 m/s (Schmitz et al., 2009), giving us confidence that the range of speeds we investigated at least partially encompass the typical walking speeds of many persons with pathologically weak quadriceps as well as healthy older individuals.

Our findings provide important insight to the muscular compensation strategies needed to maintain gait kinematics in young, healthy individuals over a range of walking speeds in the presence of different types of quadriceps weakness. All simulations were able to track gait kinematics at all speeds, suggesting that it would be physiologically feasible for persons with quadriceps weakness to walk at a fast speed. Additionally, the contractile properties of the quadriceps in our simulations suggest that the effects of weakness may be minimized at faster gait speeds. Since persons with quadriceps weakness are known to walk slower than healthy individuals, our findings indicate that other factors not simulated by our model (e.g. pain, perceptions of instability, and cardiovascular conditioning) likely contribute to reduced walking speeds in individuals with quadriceps weakness. Our results, coupled with previous findings of changes in kinematics to compensate for pathological muscle weakness (Li et al., 2013) and the sensitivity of muscle force generation ability to gait speed and muscle architecture (Arnold et al., 2013) suggests a complex interplay between muscle forces, gait speed, kinematics, and muscle architecture in the compensation strategies during gait for persons
with weakened quadriceps. A more complete investigation of the interactions between these factors is merited. Nevertheless, our findings lay the foundation for future work addressing factors that limit walking speed in pathologies such as OA and TKA, with the aim of establishing a basis for the design of more comprehensive rehabilitation programs for individuals with weakened muscles.

3.6 Acknowledgments

The authors thank Mike McNally for his assistance with data collection. Funding was provided to Julie Thompson by The NSF Graduate Research Fellowship Program and The Ohio State University Graduate Fellowship Program.
Chapter 4: Sensitivity of Model Predictions of Muscle Function to Subject-Specific Quadriceps Muscle Parameters: Pilot Study in Osteoarthritic Gait

4.1 Abstract

Osteoarthritis (OA) is one of the leading causes of disability in the US. Quadriceps weakness, one of the earliest and most common symptoms of knee OA, has been strongly correlated with gait impairments. Dynamic computer simulations are powerful tools that can be used to investigate the relationship between impaired muscle function and gait. However, the muscle properties of generic musculoskeletal models may not accurately represent the quadriceps properties of persons with OA. The purpose of this pilot study was: 1) to investigate the effects of different implementations of subject-specific quadriceps muscle parameters on model-predicted muscle forces and contributions to support and progression from simulations of OA gait, and 2) to investigate changes in muscle function in response to a virtual gait re-training simulation of healthy gait. We developed six sets of simulations of OA gait incorporating various combinations of generic quadriceps properties and subject-specific parameters measured from magnetic resonance imaging and burst superimposition in an individual with knee OA. For the virtual gait re-training simulation, we forced the model with the highest degree of subject-specificity to track the gait kinematics of a healthy individual. We found that changing kinematics had a much greater effect on muscle forces and
contributions than differences in model complexity, suggesting that subject-specificity of quadriceps properties in muscle-driven simulations may be secondary to kinematic changes. The generalizability of our findings to individuals with different levels of function and OA severity is an area for future investigation.

4.2 Introduction

An estimated 49.9 million adults in the US had doctor-diagnosed arthritis between 2007 and 2009 (2010), and that number is projected to increase to 67 million by 2030 (Hootman and Helmick, 2006). Approximately 12% of adults aged 60 and over have symptomatic knee osteoarthritis (OA), and more than 37% present with radiographic evidence of OA (Dillon et al., 2006). Quadriceps muscle weakness, which may be a result of muscle atrophy or reduced voluntary activation (Hurley and Newham, 1993; O'Reilly et al., 1998; Harridge et al., 1999; Stevens et al., 2001) is one of the earliest and most common symptoms reported by knee OA patients (Hurley and Newham, 1993; Fisher et al., 1997). Furthermore, quadriceps weakness has been strongly correlated with decreased walking speed and performance during sit-to-stand and stair climbing tasks (McAlindon et al., 1993; Connelly and Vandervoort, 1997; Walsh et al., 1998; Moxley Scarborough et al., 1999). However, it is difficult to determine how the function of the quadriceps, and other individual muscles in the body, translate to impaired function using experiments alone.

A powerful tool for investigating how abnormal muscle function may influence movement is a dynamic computer simulation. Simulations can be used to help understand
muscle activations (Anderson and Pandy, 2001), joint kinematics (Anderson and Pandy, 2001), internal joint loading (Bei and Fregly, 2004), and muscle contributions to vertical support and forward progression of the body (Neptune et al., 2001; Anderson and Pandy, 2003; Liu et al., 2006), providing insight on mechanisms of pathological or altered kinematics (Piazza, 2006). Simulations are also useful for predictive studies, such as how muscle function would change in response to rehabilitation, surgical procedures, or gait re-training. Musculoskeletal simulations have been used to investigate gait in healthy individuals (Anderson and Pandy, 2003; Neptune et al., 2004; Liu et al., 2006; Liu et al., 2008), simulated weakness in healthy individuals (Jonkers et al., 2003; van der Krogt et al., 2012; Knarr et al., 2013; Thompson et al., 2013), and pathological populations (Higginson et al., 2006; Steele et al., 2010; Kumar et al., 2012; Steele et al., 2012; Gerus et al., 2013; Li et al., 2013). However, most of these studies used generic musculoskeletal models with muscle properties based on limited data of muscle architecture obtained from a small number of cadaver specimens (Wickiewicz et al., 1983; Delp et al., 1990; Friederich and Brand, 1990). Such generic models may not accurately represent persons with musculoskeletal disorders such as OA, whose muscle properties are often very different from healthy individuals. Most “subject-specific” models are defined as scaling the mass properties and dimensions of the model to match the subject’s body size, but no changes are made to the muscle parameters in the model. Xiao and Higginson (Xiao and Higginson, 2010) investigated the sensitivity of estimated muscle forces to perturbations in generic muscle parameters and found that the quadriceps and ankle plantar flexors
were sensitive to changes in tendon slack length and optimal fiber length in simulations of healthy walking.

Expanding on the work of Xiao and Higginson, some previous researchers have developed models which include a greater degree of subject-specificity. Tsai and colleagues (Tsai et al., 2012) found that knee moment predictions from EMG-driven models of healthy subjects were improved with direct measurements of muscle volumes and moment arms from magnetic resonance imaging. Another recent study developed models with subject-specific knee joint geometry measured from CT scans of an individual with an instrumented total knee replacement (Gerus et al., 2013). The use of the subject-specific models with minimization of peak tibiofemoral contact forces improved the accuracy of predicted contact forces compared to the generic musculoskeletal model. In simulations of post-stroke gait, Knarr et al. (2013) used the burst superimposition test to tune the maximum isometric force and maximum activation parameters of muscles in subject-specific models. The resulting changes in model-predicted force and activation led the authors to suggest that subject-specific force and activation data should be used in building musculoskeletal models of individuals post-stroke (Knarr, 2013).

Determining the subject-specific muscle properties of OA patients and incorporating them into a computer model can be challenging. Muscle activation strategies in persons with OA are significantly different from healthy individuals (Schmitt and Rudolph, 2007; Zeni et al., 2010). Magnetic resonance imaging, computed tomography, and electrical burst superimposition (Kent-Braun and Le Blanc, 1996) have
been used to show that the quadriceps muscles of persons with OA have smaller cross-sectional areas, greater fatty infiltration, and greater voluntary activation failure compared to healthy quadriceps (Hurley et al., 1997; Hurley and Scott, 1998; Gur and Cakin, 2003; Lewek et al., 2004; Ikeda et al., 2005; Mizner et al., 2005; Petterson et al., 2008). However, to our knowledge, no study has incorporated patient-specific quadriceps muscle parameters into muscle-driven simulations of OA gait.

If the results from simulations are to be used as a scientific basis for individualized treatment protocols, it is necessary to determine how much subject-specificity is needed in a musculoskeletal model of OA to ensure model predictions reflect the actual muscle function of the patient. Furthermore, since imaging and burst superimposition techniques can be expensive, time-consuming, and potentially uncomfortable for the subject, there is a need to determine which measurements have the greatest effect on simulation results.

The purpose of this pilot study was twofold: 1) to investigate the effects of different implementations of subject-specific quadriceps muscle parameters on model-predicted muscle forces and contributions to support and progression from simulations of OA gait, and 2) to investigate changes in muscle function in response to a virtual gait retraining simulation of healthy gait. We hypothesized that using subject-specific measurements of quadriceps strength would result in different model predictions of muscle forces and contributions to support and progression compared to a generic model, with the greatest differences occurring for the model incorporating subject-specific quadriceps volume and activation measurements. Furthermore, we hypothesized that the
virtual gait re-training simulation of healthy gait would result in different predictions of muscle function than the different implementations of subject-specific quadriceps properties.

4.3 Methods

One male subject (age: 52 years, mass: 85 kg, height: 1.77 m) with unilateral Kellgren/Lawrence grade II OA of his right knee provided written informed consent to participate in this study, which consisted of biomechanical testing and magnetic resonance imaging. For the biomechanical testing, the subject was instructed to walk at a self-selected (SS) speed while multiple gait trials were collected at 150 Hz using a 10-camera Vicon MX-F40 system and the Point-Cluster Technique (Andriacchi et al., 1998). Ground reaction forces were obtained from six force plates (Bertec, Columbus, OH) sampled at 600 Hz. One representative trial (1.16 m/s), with ground reaction forces for a full gait cycle of the involved limb, was selected for analysis. Muscle activation patterns from the rectus femoris, vastus lateralis, vastus medialis, biceps femoris, semitendinosus, medial gastrocnemius, lateral gastrocnemius, and soleus of both legs were measured with 16-channel surface EMG (Noraxon Telemyo DTS, Scottsdale, AZ) sampled at 1500 Hz. EMG data were high-pass filtered at 10 Hz, rectified, RMS smoothed with a 20 ms window, and normalized to the maximum EMG signal obtained from each muscle during the gait trials.
4.3.1 Quadriceps strength and volitional activation

For both limbs, quadriceps muscle strength was measured during a maximal voluntary contraction (MVC) while the subject performed isometric knee extension, and volitional quadriceps activation was measured using the burst superimposition test. The subject sat in an isokinetic dynamometer (Biodex System III) with the hip and knee flexed to 90° and the knee joint aligned with the dynamometer axis. Velcro straps across the torso, waist, and thigh secured the subject in the seat, while a padded cuff and ankle strap secured the shank to the dynamometer. Following skin preparation, two 3.0” x 5.0” self-adhesive gel electrodes (Axelgaard Manufacturing Co., Fallbrook, CA) were secured proximally over the rectus femoris muscle and distally over the vastus medialis muscle. The subject practiced producing a maximal effort isometric knee extension against the dynamometer arm while verbal encouragement was provided. Quadriceps muscle strength in each limb was defined as the maximum torque measured by the biodex during a MVC without a superimposed burst (Torque\textsubscript{MVC}). For the superimposed burst test, the subject was asked to produce a maximum contraction of his quadriceps muscle, during which a supramaximal burst of electric current (100 pulses per second, 600 μs pulse duration, 100 ms train duration, 130 V) from a Grass S48 stimulator (Grass Technologies, Warwick, RI) was delivered to the muscle. The central activation ratio (CAR) was calculated as the ratio between the torque achieved during the maximum contraction (Torque\textsubscript{volitional}; measured as the torque just prior to the electrical burst) and the torque achieved during the electrically elicited burst (Torque\textsubscript{burst}):

\[
CAR = \frac{\text{Torque}_{\text{volitional}}}{\text{Torque}_{\text{burst}}} \tag{1}
\]
4.3.2 Quadriceps muscle volume from magnetic resonance images

To measure subject-specific muscle volumes, axial MR images of both thighs were obtained using a 3.0T whole body MRI system (Achieva, Philips Healthcare, Cleveland, OH) and a 32-channel phased array cardiac coil. The cardiac coil was chosen because it is able to cover bilateral sides of the thigh and provide a better signal compared to the relatively larger 16-channel torso coil. The subject’s legs were stabilized with sand bags to prevent movement. In order to cover the full length of the quadriceps muscles, the thighs were scanned in three overlapping series starting at the distal thigh and moving to the proximal thigh. We first ran a survey sequence to review the three dimensions of the thighs with coarse resolution. An axial multiple-slice multi-shot proton density weighted turbo spin echo (PD-TSE) sequence with fat suppression was then employed to achieve high resolution images (FOV = 348(RL) x 180(AP) x 250(FH) mm², matrix size = 338 x 180, slice thickness = 2 mm, TR/TE = 6900/15 ms, TSE factor = 7, NSA = 2, SENSE factor = 2).

The images were then processed using programs we previously developed which semi-automatically detect and segment MR images of the four quadriceps muscles: rectus femoris (RF), vastus intermedius (VI), vastus lateralis (VL), and vastus medialis (VM) (Prescott et al., 2011b). The method uses an anatomically anchored, template-based initialization of the level set-based segmentation approach, and only requires the input of a single point from the user inside the rectus femoris. For this particular study, we manually segmented the four quadriceps muscles on both legs because the imaging
conditions were different from the original study used to develop the program. Since the thighs were imaged in three overlapping series, we manually aligned the series and removed the overlapping regions. Once the segmentations were completed, the total volume of each of the four muscles for each leg was computed by the trapezoidal rule (Figure 4.1).
Figure 4.1: Calculation of the quadriceps muscle volumes from MRI using the trapezoidal rule.

Approximate Volume = \( \left( \frac{A_1 + A_2}{2} \right) \cdot \Delta d \)
4.3.3 *Musculoskeletal models and simulations of OA gait*

We developed multiple models with varying degrees of complexity in subject-specific quadriceps properties and performed six sets of muscle-driven simulations (Figure 4.2) to estimate lower extremity forces and contributions to support and progression:

1. Generic quadriceps muscle properties (“Generic”)
2. Peak isometric quadriceps forces calculated from maximum voluntary contraction (MVC) in dynamometer (“MVC”)
3. Peak isometric quadriceps forces calculated using burst superimposition test (“Burst”)
4. Peak isometric quadriceps forces and maximum activation constraints calculated using burst superimposition test and CAR value (“Burst+CAR”)
5. Peak isometric quadriceps forces calculated using muscle volumes from magnetic resonance images (“MRI”)
6. Peak isometric quadriceps forces calculated using muscle volumes from MRI and maximum activation constraints from burst superimposition test and CAR value (“MRI+CAR”)

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Figure 4.2: Workflow for creating muscle-driven simulations incorporating subject-specific quadriceps properties.
1. Simulations with Generic Model

The generic model is based on a previously developed model (Arnold et al., 2010) and includes the lower limbs and torso. The model has 27 degrees of freedom, including 3 rotational degrees of freedom at the knee joint, and 94 musculotendon actuators. We generated simulations of one gait cycle using OpenSim software version 3.1 (Delp et al., 2007). The dimensions of each body segment in the model were scaled based on relative distances between pairs of markers obtained from motion capture during the static calibration trial and the corresponding virtual marker locations in the model. The experimental gait patterns were reproduced in the scaled model by solving an inverse kinematics problem and a weighted least-squares approach to minimize the differences between experimental joint angles and marker locations and the model’s joint angles and virtual marker locations. A residual reduction algorithm (RRA) adjusted model kinematics to resolve dynamic inconsistency between the model kinematics and the ground reaction forces (Delp et al., 2007). Computed muscle control (CMC) (Thelen and Anderson, 2006) was used to calculate the muscle excitations and forces in all lower extremity muscles that produced a coordinated muscle-driven simulation of the subject’s gait. An initial comparison of the simulated muscle activations from CMC to the subject’s experimental EMG revealed poor agreement (Figure 4.3). Therefore, we constrained the simulated activations to match the timing and magnitude of the normalized EMG for the 16 muscles from which EMG was recorded. An induced acceleration analysis (IAA) was then performed to determine the contributions of
individual muscles to the support (vertical acceleration) and progression (horizontal acceleration) of the body mass center (Zajac and Gordon, 1989; Anderson and Pandy, 2003; Hamner et al., 2010).
Figure 4.3: Comparison of experimental EMG data for the involved limb with the activations from the CMC algorithm with and without constraints on muscle excitations.
Simulations with subject-specific muscle parameters:

2. Quadriceps forces based on MVC in dynamometer

The “MVC” model incorporates peak isometric quadriceps forces calculated using the torque output from a MVC for each limb in the dynamometer. The joint torque measured from the dynamometer is related to muscle force ($F^m$) and moment arm (MA) by the following equation:

$$\text{Torque} = F^m \times MA \quad (2)$$

Similarly, Equation 2 can be re-written assuming the total torque measured in the dynamometer is the sum of the torque contributed by each of the individual quadriceps muscles:

$$\text{Torque}_{\text{quads}} = (F_{m1} \times MA_1) + (F_{m2} \times MA_2) + (F_{m3} \times MA_3) + (F_{m4} \times MA_4) \quad (3)$$

Table 4.1: Moment arms and maximum fiber force for each of the quadriceps muscles at 90° knee flexion in the generic model.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Max Force (N) at 90° knee flexion</th>
<th>Moment arm (m) at 90° knee flexion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>1647.6</td>
<td>0.027</td>
</tr>
<tr>
<td>VI</td>
<td>823.9</td>
<td>0.026</td>
</tr>
<tr>
<td>VM</td>
<td>1189</td>
<td>0.024</td>
</tr>
<tr>
<td>VL</td>
<td>1864.7</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Using Equation 3 and the values for muscle moment arms and maximum force at 90° knee flexion in the generic model (Table 4.1), we calculated the torque that could be produced by the quadriceps muscle group at 90° knee flexion in the generic model to be
\( \text{Torque}_{\text{generic}} = 133.6 \text{ N-m.} \) Assuming the same muscle force-length relationships for the tuned “MVC” model as in the generic model, we used the ratio of torque produced during the MVC by the subject and the torque that could be produced in the generic model to scale the peak isometric force of each quadriceps muscle of both limbs in the generic model according to the following equation:

\[
F_{0}^{m1,MVC} = F_{0}^{m1,\text{generic}} \times \frac{\text{Torque}_{\text{MVC}}}{\text{Torque}_{\text{generic}}} \quad (4)
\]

Where \( F_{0}^{m1,MVC} \) is the new peak isometric muscle force calculated using the torque from an MVC in the dynamometer, and \( F_{0}^{m1,\text{generic}} \) is the peak isometric muscle force in the generic model. After adjusting the peak isometric force parameter for each quadriceps muscle accordingly, we ran the CMC and IAA algorithms to re-calculate muscle forces and contributions to support and progression.

3. Quadriceps properties based on torque and CAR from burst superimposition test

The “Burst” model incorporates peak isometric quadriceps forces calculated using the torque output during the burst superimposition test for each limb (Figure 4.4). Using a similar equation as Equation 4 from the “MVC” case, but using \( \text{Torque}_{\text{Burst}} \) in place of \( \text{Torque}_{\text{MVC}} \), we re-calculated the individual peak isometric quadriceps muscle forces for each limb, adjusted the force parameters in the model, and ran CMC and IAA with the adjusted model. We then ran another simulation using the same model, but constrained the maximum activation of each of the quadriceps muscles to be the CAR value calculated during the burst superimposition for each limb (“Burst+CAR”). The CAR value was assumed to be the same for all four quadriceps muscles.
4. Quadriceps forces based on muscle volumes from MRI

The “MRI” model incorporates peak isometric quadriceps forces calculated from a combination of measurements from MR images and the torque output during the burst superimposition test for each limb. Using the quadriceps muscle volumes measured from the MR images, and assuming the optimal fiber length for each muscle was the same as in the generic model, we calculated the physiologic cross-sectional area (PCSA) for each quadriceps muscle by dividing muscle volume \( V^m \) by optimal fiber length \( l^m_o \) from the generic model (Arnold et al., 2010):

\[
PCSA = \frac{V^m}{l^m_o} \quad (5)
\]
The peak isometric force ($F_{o}^{m}$) can be calculated from the muscle PCSA and specific tension ($\sigma_{o}^{m}$) according to the following equation:

$$F_{o}^{m} = PCSA \times \sigma_{o}^{m} \quad (6)$$

Equation 6 can be rearranged as follows, assuming the specific tension is the same for all four muscles in the quadriceps:

$$\sigma_{o}^{m} = \frac{F_{o}^{m1}}{PCSA_{1}} = \frac{F_{o}^{m2}}{PCSA_{2}} = \frac{F_{o}^{m3}}{PCSA_{3}} = \frac{F_{o}^{m4}}{PCSA_{4}} \quad (7)$$

Since the subject was positioned with his knee at $90^\circ$ flexion during testing in the dynamometer, which may not coincide with the position at which the quadriceps produce peak isometric force, we used an adjustment equation, assuming the same muscle force-length relationships for the tuned “MRI” model as in the generic model, relating peak isometric force and the force produced at $90^\circ$ knee flexion for each quadriceps muscle:

$$F^{m} = F_{o}^{m} \times \Delta_{m} \quad (8)$$

Where $\Delta_{m}$ is a scale factor determined by dividing the maximum muscle force at $90^\circ$ knee flexion in the generic model by the peak isometric force in the generic model. Combining Equation 8 with Equation 3, we obtain an equation relating the torque measured in the dynamometer during the burst test to the peak isometric forces of each individual quadriceps muscle:

$$Torque_{\text{burst}} = [(F_{o}^{m1}\Delta_{m1} \times MA_{1}) + [(F_{o}^{m2}\Delta_{m2} \times MA_{2}) + [(F_{o}^{m3}\Delta_{m3} \times MA_{3}) + [(F_{o}^{m4}\Delta_{m4} \times MA_{4}) (9)$$

Combining Equation 7 with Equation 9 so that $F_{o}^{m1}$ is the only unknown variable:

$$Torque_{\text{burst}} =$$

$$F_{o}^{m1}\Delta_{m1}MA_{1} + \left(\frac{F_{o}^{m1}\times PCSA_{2}}{PCSA_{1}}\right)\Delta_{m2}MA_{2} + \left(\frac{F_{o}^{m1}\times PCSA_{3}}{PCSA_{1}}\right)\Delta_{m3}MA_{3} + \left(\frac{F_{o}^{m1}\times PCSA_{4}}{PCSA_{1}}\right)\Delta_{m4}MA_{4} (10)$$
Finally, Equation 10 can be rearranged to solve for $F_{0}^{m1}$:

$$F_{0}^{m1} = \frac{Torque_{\text{burst}}}{(\Delta_{m1}MA_{1}) + \left[\left(\frac{PCSA_{2}}{PCSA_{1}}\right)\Delta_{m2}MA_{2}\right] + \left[\left(\frac{PCSA_{3}}{PCSA_{1}}\right)\Delta_{m3}MA_{3}\right] + \left[\left(\frac{PCSA_{4}}{PCSA_{1}}\right)\Delta_{m4}MA_{4}\right]}$$  \hspace{1cm} (11)

Using Equation 11, we calculated the force in each of the quadriceps muscles for both limbs using the torque measured during the burst superimposition, the PCSAs calculated with the muscle volumes obtained from MRI, and the moment arms in the generic model. We adjusted the peak isometric force parameters in the model and ran CMC and IAA with the adjusted model. We also ran an additional simulation using the same model, but with constraints on the maximum activation of each of the quadriceps muscles according to the CAR value for each limb (“MRI+CAR”).

4.3.4 Virtual gait re-training simulation

We developed a virtual gait re-training simulation to investigate changes in muscle function that would be needed for a subject-specific model with the same quadriceps properties as knee OA subject to reproduce the gait kinematics of a healthy individual. Using the same generic musculoskeletal model that was used for the simulations of OA gait, we generated simulations of one gait cycle of a healthy individual walking at a self-selected speed (age: 23 years, mass: 83.6 kg, height: 1.81 m, speed: 1.17 m/s) whose body size and gait speed were very similar to our individual with knee OA. First, we generated a baseline simulation using the default quadriceps muscle properties in the generic model. We then generated a simulation in which the quadriceps muscle properties of each limb were tuned to the same values as those used in the “MRI+CAR”
Simulation of OA gait. The adjusted model was forced to track the gait kinematics of the healthy individual, and the resultant muscle forces and contributions to progression and support were compared to the baseline simulation and the “MRI+CAR” simulation of OA gait.

4.4 Results

Direct measurements of quadriceps strength, activation failure, and muscle volume resulted in different values for peak isometric force for the different models (Table 4.4). The various implementations of subject-specific quadriceps properties resulted in large differences in force output and contributions to progression and support by the involved quadriceps muscles, with the “MRI” and “MRI+CAR” simulations displaying the greatest differences compared to the generic simulation (Figures 4.6-8). However, there were relatively small changes in the force output and contributions to progression and support by any of the other lower extremity muscles investigated. Interestingly, in the virtual gait re-training simulation, there were significant changes in model predictions of muscle function in muscles other than the quadriceps, notably in the hamstrings, tibialis anterior and posterior, and gluteus muscles (Figures 4.9-11).

4.4.1 Quadriceps muscle properties from biomechanical testing

Strength testing and burst superimposition testing revealed large differences in maximum volitional torque and quadriceps activation between the involved and
uninvolved limbs of our individual with knee OA (Table 4.2). Furthermore, the involved limb displayed a large discrepancy between maximum volitional torque and the torque achieved with full activation using the superimposed burst, as illustrated by the CAR value. The quadriceps of the uninvolved limb also displayed activation deficit, but to a much lesser extent than the quadriceps of the involved limb (Table 4.2).

Table 4.2: Experimental torque measurements and CAR values

<table>
<thead>
<tr>
<th>Limb</th>
<th>Torque_{MVC}</th>
<th>Torque_{volitional}</th>
<th>Torque_{Burst}</th>
<th>CAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right (OA)</td>
<td>59.9</td>
<td>53.1</td>
<td>142.0</td>
<td>0.37</td>
</tr>
<tr>
<td>Left (non-OA)</td>
<td>159.0</td>
<td>109.1</td>
<td>169.3</td>
<td>0.64</td>
</tr>
</tbody>
</table>

The measurements of quadriceps muscle volume from MR images also revealed differences between the involved and uninvolved limbs (Figure 4.5 and Table 4.3), but the differences in muscle volume between the limbs was less pronounced than the differences in volitional strength and activation. In both limbs, the quadriceps muscle with the smallest volume was rectus femoris, while the largest muscle was vastus medialis (Table 4.3).
Figure 4.5: Quadriceps muscle segmentation from MR images. RF = rectus femoris, VI = vastus intermedius, VL = vastus lateralis, VM = vastus medialis.

Table 4.3: Quadriceps muscle volume and physiologic cross-sectional area (PCSA)

<table>
<thead>
<tr>
<th>Limb</th>
<th>Muscle</th>
<th>Volume (cm$^3$)</th>
<th>PCSA$^a$ (cm$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right (OA)</td>
<td>RF</td>
<td>99.72</td>
<td>11.27</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>393.62</td>
<td>33.31</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>537.04</td>
<td>46.67</td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>459.17</td>
<td>38.84</td>
</tr>
<tr>
<td>Left (non-OA)</td>
<td>RF</td>
<td>58.34</td>
<td>6.59</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>398</td>
<td>33.68</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>585.82</td>
<td>50.91</td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>470.88</td>
<td>39.83</td>
</tr>
</tbody>
</table>

$^a$ PCSA calculated as volume divided by optimal fiber length from generic model.

The peak isometric force of each of the quadriceps muscles varied greatly depending on the generic and subject-specific measurements used (Tables 4.4-5). For the “MVC” model, the peak isometric forces of the involved quadriceps were reduced by more than 55% compared to the values in the generic model (Table 4.5). In contrast, the peak isometric forces in the uninvolved limb increased by 19%. For the “Burst” model, the quadriceps of both the involved and uninvolved limbs increased in strength by 6.3%
and 26.7%, respectively. In the “MRI” model, which used direct measurements of muscle size instead of assuming the same distribution as the generic model, changes in peak isometric force varied between the individual muscles. In the involved limb, changes in quadriceps peak isometric force compared to the generic model ranged from -34.6% for rectus femoris to 60.1% for vastus intermedius, while changes in the uninvolved limb ranged from -52.1% for rectus femoris to 117.3% for vastus medialis (Table 4.5).

Table 4.4: Quadriceps peak isometric force values calculated for each model with different implementations of generic and subject-specific muscle parameters.

<table>
<thead>
<tr>
<th>Limb</th>
<th>Muscle</th>
<th>Generic</th>
<th>MVC</th>
<th>Burst</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right (OA)</td>
<td>RF</td>
<td>848.8</td>
<td>380.6</td>
<td>902.2</td>
<td>554.9</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>1024.2</td>
<td>459.2</td>
<td>1088.6</td>
<td>1639.9</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>1443.7</td>
<td>647.3</td>
<td>1534.5</td>
<td>2297.8</td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>2255.4</td>
<td>1011.2</td>
<td>2397.2</td>
<td>1912.2</td>
</tr>
<tr>
<td>Left (non-OA)</td>
<td>RF</td>
<td>848.8</td>
<td>1010.2</td>
<td>1075.6</td>
<td>406.3</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>1024.2</td>
<td>1218.9</td>
<td>1297.9</td>
<td>2075.0</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>1443.7</td>
<td>1718.2</td>
<td>1829.5</td>
<td>3136.7</td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>2255.4</td>
<td>2684.2</td>
<td>2858.1</td>
<td>2454.0</td>
</tr>
</tbody>
</table>

Table 4.5: Relative changes in quadriceps peak isometric force calculations for each subject-specific model compared to the generic model.

<table>
<thead>
<tr>
<th>Limb</th>
<th>Muscle</th>
<th>MVC Change from Generic</th>
<th>% Change</th>
<th>MVC % Change</th>
<th>Burst Change from Generic</th>
<th>% Change</th>
<th>Burst % Change</th>
<th>MRI Change from Generic</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right (OA)</td>
<td>RF</td>
<td>-468.2</td>
<td>-55.2</td>
<td>53.4</td>
<td>615.7</td>
<td>60.1</td>
<td>854.1</td>
<td>-293.9</td>
<td>-34.6</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>-565.0</td>
<td></td>
<td>64.4</td>
<td>90.8</td>
<td></td>
<td>854.1</td>
<td>-343.2</td>
<td>-15.2</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>-796.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>-1244.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left (non-OA)</td>
<td>RF</td>
<td>161.4</td>
<td>19.0</td>
<td>226.8</td>
<td>570.8</td>
<td>102.6</td>
<td>1693.0</td>
<td>-442.5</td>
<td>-52.1</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>194.7</td>
<td></td>
<td>273.7</td>
<td>1050.8</td>
<td>102.6</td>
<td></td>
<td>198.6</td>
<td>8.8</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>274.5</td>
<td></td>
<td>385.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>428.8</td>
<td></td>
<td>602.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.4.2 Subject-specific simulations of OA gait

The quadriceps muscles of the involved limb displayed noticeable differences in force output and contributions to slowing forward progression (braking) and providing vertical support in response to the different implementations of subject-specific muscle parameters (Figures 4.6-8). In general, the response of the quadriceps muscles of the uninvolved limb to the different model complexities was comparable to or less than the changes observed in the quadriceps of the involved limb (Table 4.6). Moreover, there were relatively small or negligible differences in the other muscles of the lower extremity in response to the different model complexities. The remaining simulation results presented in this study are for the involved limb only.

In general, the “MRI” and “MRI+CAR” simulations resulted in the greatest changes in force output (Figure 4.6) and contributions to braking (Figure 4.7) and support (Figure 4.8) of the involved quadriceps muscles compared to the generic simulation. Force output and contributions to braking and support decreased in early stance for the rectus femoris and vastus lateralis muscles in the “MRI” and “MRI+CAR” simulations, while force output and contributions increased in the vastus medialis and vastus intermedius compared to the generic simulation. For all four quadriceps muscles, the “Burst” simulation showed the smallest differences in force output and contributions to braking and providing vertical support compared to the generic simulation. For the “Burst+CAR” simulation, the rectus femoris displayed a decrease in force and contributions to braking and support in early stance compared to the generic simulation, while the vastus lateralis displayed an increase in force and contributions, and the vastus
medialis and vastus intermedius displayed small increases in force output and contributions to braking and support. For the “MVC” simulation, the rectus femoris displayed a significant decrease in force output and contributions compared to the generic simulation, while the vastus lateralis showed an increase in force output and contributions to braking and support in early stance and a decrease in force output during swing. The vastus medialis displayed a small increase in force output for the “MVC” simulation in early stance, and a decrease in force output during swing compared to the generic simulation. The vastus intermedius also displayed a small increase in force output and contributions to braking and support for the “MVC” simulation in early stance, but displayed a larger increase in force output during swing.
Table 4.6: Relative changes in peak quadriceps force of both limbs during stance for each of the subject-specific simulations compared to the generic simulation.

<table>
<thead>
<tr>
<th>Limb</th>
<th>Muscle</th>
<th>MVC</th>
<th></th>
<th>Burst</th>
<th></th>
<th>Burst + CAR</th>
<th></th>
<th>MRI</th>
<th></th>
<th>MRI + CAR</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Change from Generic (N)</td>
<td>% Change</td>
<td>Change from Generic (N)</td>
<td>% Change</td>
<td>Change from Generic (N)</td>
<td>% Change</td>
<td>Change from Generic (N)</td>
<td>% Change</td>
<td>Change from Generic (N)</td>
<td>% Change</td>
</tr>
<tr>
<td>Right</td>
<td>RF</td>
<td>-285.4</td>
<td>-54.9</td>
<td>34.7</td>
<td>6.7</td>
<td>-127.0</td>
<td>-24.4</td>
<td>-172.5</td>
<td>-33.2</td>
<td>-282.3</td>
<td>-54.3</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>39.0</td>
<td>25.7</td>
<td>-14.8</td>
<td>-9.7</td>
<td>28.7</td>
<td>18.9</td>
<td>207.0</td>
<td>136.3</td>
<td>161.1</td>
<td>106.1</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>34.0</td>
<td>16.9</td>
<td>-13.2</td>
<td>-6.6</td>
<td>42.9</td>
<td>21.4</td>
<td>218.8</td>
<td>109.1</td>
<td>202.5</td>
<td>100.9</td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>121.0</td>
<td>20.0</td>
<td>-39.7</td>
<td>-6.6</td>
<td>111.4</td>
<td>18.4</td>
<td>-186.8</td>
<td>-30.8</td>
<td>-241.9</td>
<td>-39.9</td>
</tr>
<tr>
<td>Left</td>
<td>RF</td>
<td>59.8</td>
<td>9.8</td>
<td>67.4</td>
<td>11.1</td>
<td>60.7</td>
<td>10.0</td>
<td>-286.3</td>
<td>-47.1</td>
<td>-310.6</td>
<td>-51.0</td>
</tr>
<tr>
<td></td>
<td>VI</td>
<td>-0.1</td>
<td>-0.1</td>
<td>-4.8</td>
<td>-3.5</td>
<td>-7.1</td>
<td>-5.1</td>
<td>146.8</td>
<td>106.5</td>
<td>197.6</td>
<td>143.3</td>
</tr>
<tr>
<td></td>
<td>VM</td>
<td>-8.7</td>
<td>-4.6</td>
<td>-7.9</td>
<td>-4.2</td>
<td>-8.7</td>
<td>-4.6</td>
<td>241.7</td>
<td>127.3</td>
<td>282.9</td>
<td>149.1</td>
</tr>
<tr>
<td></td>
<td>VL</td>
<td>-18.7</td>
<td>-3.2</td>
<td>-42.2</td>
<td>-7.2</td>
<td>-30.8</td>
<td>-5.3</td>
<td>-239.2</td>
<td>-40.9</td>
<td>-193.1</td>
<td>-33.0</td>
</tr>
</tbody>
</table>
Figure 4.6: Force output from the involved quadriceps muscles for each of the subject-specific simulations. In general, the largest differences compared to the generic simulation were for the “MRI” and “MRI+CAR” simulations.
Figure 4.7: Contributions to braking (slowing forward progression) during stance from the involved quadriceps muscles for each of the subject-specific simulations.

Figure 4.8: Contributions to vertical support during stance from the involved quadriceps muscles for each of the subject-specific simulations.
4.4.3 Virtual Gait Re-training Simulations

Similar to the simulations of OA gait, there were relatively small changes in force output and contributions to progression and support for most muscles of the lower extremity between the generic and “MRI+CAR” simulations of healthy gait kinematics, with the exception of the quadriceps muscles (Figures 4.9-11). The quadriceps in the healthy gait simulation with subject-specific quadriceps properties displayed similar changes in force output and contributions to braking and support compared to the generic model as the changes displayed in the simulation of OA gait incorporating the same quadriceps muscle properties.

Comparison of the simulations tracking OA gait kinematics and the simulations tracking healthy gait kinematics, however, revealed large differences in force output and contributions to progression and support in muscles of the lower extremity, including the quadriceps (Figures 4.9-11). The gluteus muscle group and the tibialis posterior muscle displayed significant decreases in force output for the “MRI+CAR” simulation of healthy gait compared to the “MRI+CAR” simulation of OA gait, while the vasti muscle group and the soleus muscle displayed increases in force output (Figure 4.9).

Contributions to braking by the quadriceps muscles showed relatively little change between the healthy and OA gait simulations (Figure 4.10). The tibialis anterior and tibialis posterior muscles decreased their contributions to braking in the healthy gait simulation compared to the OA gait simulation. The gluteus muscles also decreased their contributions to braking in early stance, but slightly increased their contributions to braking in late stance. The soleus muscle slightly decreased its contribution to forward...
progression in early stance, and increased its contribution to progression in late stance compared to the OA gait simulation. The hamstrings muscle group, especially biceps femoris long head, increased its contribution to forward progression.

Contributions to vertical support by the quadriceps muscles increased in the healthy gait simulation compared to their contributions in the OA gait simulation (Figure 4.11). The tibialis anterior muscle displayed a decrease in contribution to vertical support in early stance, while the soleus muscle displayed an increase in contribution to support in late stance. The biceps femoris long head and short head muscles acted to reduce vertical support compared to the OA gait simulation, especially in the first half of stance.
Figure 4.9: Force output from muscles of the involved limb for the generic and MRI+CAR simulations tracking OA gait, and the generic and MRI+CAR simulations tracking healthy gait. Compared to OA gait, the force output decreased for the gluteus and tibialis posterior muscles and increased for the vasti and soleus muscles in the healthy gait simulations.
Figure 4.10: Contributions to forward progression during stance by the muscles of the involved limb for the generic and MRI+CAR simulations tracking OA gait, and the generic and MRI+CAR simulations tracking healthy gait. Compared to OA gait, the contributions to progression decreased for the soleus muscle in early stance, and increased for the hamstring muscle group and for the soleus muscle in late stance in the healthy gait simulations. Contributions to slowing progression (braking) decreased for the tibialis anterior and posterior muscles and for the gluteus muscle group in early stance.
Figure 4.11: Contributions to vertical support during stance by the muscles of the involved limb for the generic and MRI+CAR simulations tracking OA gait, and the generic and MRI+CAR simulations tracking healthy gait. Compared to OA gait, the contributions to support decreased for the tibialis anterior and posterior muscles and increased for the vasti and soleus muscles in the healthy gait simulations. The hamstring muscle group acted to decrease vertical support in the healthy gait simulations.

4.5 Discussion

The purpose of this study was: 1) to investigate the effects of different implementations of subject-specific quadriceps muscle parameters on model-predicted muscle forces and contributions to support and progression from simulations of OA gait, and 2) to investigate changes in muscle function in response to a virtual gait re-training simulation of healthy gait. To our knowledge, this is the first study to incorporate patient-
specific quadriceps muscle parameters into muscle-driven simulations of OA gait. Partially confirming our hypothesis, we found that there were large differences in force output and contributions to progression and support by the involved quadriceps muscles for the different implementations of subject-specific quadriceps properties, with the “MRI” and “MRI+CAR” simulations resulting in the greatest differences compared to the generic simulation. However, we saw relatively small changes in the force output and contributions to progression and support by any of the other lower extremity muscles investigated. Interestingly, when we forced a model with the same quadriceps properties as the “MRI+CAR” simulation of OA gait to track the gait kinematics of a healthy individual in our virtual gait re-training simulation, we observed significant changes in model predictions of muscle function in muscles other than the quadriceps. Moreover, the changes in quadriceps force output and contributions to progression and support that resulted from changing gait kinematics were generally greater than the changes that resulted from different implementations of subject-specific quadriceps properties.

A possible explanation for why we saw little change in muscle function for any muscles besides the quadriceps when using different implementations of subject-specific quadriceps properties may be due to the default strength of the generic model. Using the muscle parameters in the generic model, we calculated the maximum torque achievable by the quadriceps at 90° knee flexion in the generic model to be 133.6 N-m. However, burst superimposition of the quadriceps of our OA subject revealed that both his involved and uninvolved limbs were capable of achieving more torque than the default model, producing 142.0 N-m and 169.3 N-m, respectively (Table 4.2). Since we used the torque
achieved during the burst test to calculate peak isometric force in four of the five subject-specific simulations, the quadriceps muscle group in most of our models was actually stronger than in the generic model. Furthermore, the quadriceps generally do not reach their peak isometric force during gait, which may explain the lack of “compensation” by other muscles. Even in the “MVC” simulation, the only case in which the involved quadriceps muscle group was weaker than the generic model, the rectus femoris was the only muscle to reach its peak isometric force, and was compensated by increased forces in the vasti. The fact that the quadriceps were stronger in most of our simulations of OA gait compared to the generic model, combined with the apparent ability of the individual quadriceps to compensate for one another, may suggest why we saw no compensations by any other lower extremity muscles for our individual with knee OA. These findings highlight the need to investigate the strength of the model as a whole, as well as determine how much strength testing is necessary to appropriately tune the model to the individual subject.

The virtual gait re-training simulation expanded on our investigation of the sensitivity of model predictions to changes in subject-specific quadriceps muscle properties. Even though the quadriceps muscle properties were identical between the virtual gait re-training simulation of healthy gait and the “MRI+CAR” simulation of OA gait, there were noticeable differences in the force output and contributions to progression and support by the quadriceps, as well as other muscles of the lower extremity. A comparison of the sagittal plane joint kinematics revealed differences between our OA subject and healthy individual (Figure 4.12). The individual with knee
OA displayed less hip, knee, and ankle range of motion than the healthy individual. The OA subject walked with a more extended knee during weight acceptance, which agrees with previous findings (Kaufman et al., 2001), and significantly less ankle plantarflexion in late stance. Additionally, the OA subject walked with a more flexed hip than the healthy individual, and in fact never exhibited hip extension during the gait cycle (Figure 4.12). Since the OA subject and healthy individual were walking at the same self-selected speed, the differences in their joint kinematics cannot be attributable to differences in walking speed. An analysis of fiber operating lengths revealed that the gluteus muscle group and the tibialis posterior muscle, which displayed the largest decreases in force output for healthy gait compared to OA gait, operate closer to their optimal fiber lengths during OA gait. The differences in joint kinematics between healthy and OA gait, and the corresponding differences in the contractile state of the gluteus and tibialis posterior muscles, may suggest why these muscles displayed large changes in force output and contributions to progression and support in the virtual gait re-training simulation compared to the simulations of OA gait.
Figure 4.12: Sagittal plane joint kinematics for the individual with knee OA and the healthy individual whose gait kinematics were used in the virtual gait re-training simulation.

Our findings should be interpreted in light of several limitations. This pilot study used one subject with moderate knee OA (K-L grade II), who may not be representative of the general OA population. He maintains a high level of physical activity, and the quadriceps muscle group of both of his limbs is stronger than the generic model, although he did exhibit large activation deficits. Less physically active individuals with knee OA, and those with more severe OA, would likely have more atrophy of their quadriceps, which, if combined with measurable activation deficits, could be expected to have a greater impact on model predictions of muscle function and compensatory strategies. Additionally, there are other subject-specific muscle parameters we could measure and incorporate into the model besides peak isometric force and maximum activation, such as optimal fiber length, tendon slack length, pennation angle, and moment arm. Since we did not have direct measurements of these parameters, we assumed the same values as those in the generic model. A sensitivity study by Xiao and Higginson (Xiao and Higginson, 2010) investigating perturbations in generic muscle parameters found that the force output of the quadriceps and ankle plantar flexors were sensitive to changes in
tendon slack length and optimal fiber length in simulations of healthy normal walking. It is possible that our OA gait simulation results would also be sensitive to changes in these parameters, but whether the tendon slack length or optimal fiber length of muscles in the OA population are different than healthy individuals is unknown. When Xiao and Higginson adjusted the peak isometric forces of muscles in their generic model by ±10%, it had little effect on estimated muscle forces (Xiao and Higginson, 2010). However, our previous study investigating muscle compensations needed to maintain healthy gait kinematics in response to larger amounts of simulated quadriceps atrophy, as well as activation failure, found that not only did the estimated forces of the quadriceps decrease significantly, but the gluteus maximus and soleus muscles increased their force output to compensate for the weakened quadriceps (Thompson et al., 2013). In the current study, the lack of changes in estimates of muscle function when adjusting peak isometric force parameters is likely due to the fact that our OA subject had stronger quadriceps than the generic model. Another possible limitation of our study is the fact that we measured quadriceps strength and activation deficit at a single position: with the subject’s knee flexed to 90°. By assuming the same muscle force-length relationships as in the generic model, we were able to use the torque output in this position to calculate the corresponding peak isometric force in the quadriceps muscles. A more accurate approach may have been to do strength testing over a range of knee angles to determine the peak forces in the quadriceps. However, given the possibility of fatigue, we chose to restrict the strength testing to one joint angle. Despite this potential limitation, we have greater confidence in the validity of the peak isometric force values calculated using burst
superimposition than from volitional effort alone because the burst test ensures full activation of the muscles. It is also important to note that the CAR values we calculated in this study are sensitive to the value we chose to use for the maximum volitional torque. For consistency, we picked the point just before the superimposed burst as the volitional torque. However, our subject was able to produce higher torques during his non-burst MVC trials (Table 4.2). Due to the discomfort experienced by the subject during the superimposed burst, we chose not to repeat the test even though he may not have been producing a true maximum contraction. While our CAR values did fall within the range of values measured in a population of individuals with knee OA (Petterson et al., 2008), they are lower than the average values reported in some previous studies of 0.87 (Mizner et al., 2005) and 0.66 (Hassan et al., 2001). Finally, the healthy individual whose kinematics were used for the virtual gait re-training simulation was not age-matched to our OA subject. Older individuals have been shown to exhibit reduced peak hip extension and ankle plantarflexion compared to young individuals (Kerrigan et al., 1998; DeVita and Hortobagyi, 2000), which agrees with our kinematic findings. We may have observed smaller differences between the kinematics of our healthy individual and OA subject if they were age-matched, however, this study provides important initial insight to the possible changes in muscle function needed for an individual with knee OA to walk with normal gait kinematics.

We established a robust modeling technique which incorporates measurements of subject-specific quadriceps parameters from magnetic resonance imaging and burst superimposition in simulations of OA gait. Using our modeling technique, we were able
to elucidate subtle differences in quadriceps muscle force output and contributions to progression and support in response to different implementations of subject-specific quadriceps properties. We found that changing kinematics had a much greater effect on muscle forces and contributions than differences in model complexity, suggesting that subject-specificity of quadriceps properties in muscle-driven simulations may be secondary to kinematic changes. How much change in model predictions of muscle function is clinically significant, and whether the findings of our pilot study are generalizable to individuals with different levels of function and OA severity, warrants further investigation.

4.6 Acknowledgments

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Chapter 5: Conclusion

Osteoarthritis (OA) is a very common musculoskeletal disorder, and its prevalence is expected to increase significantly in the coming years. Quadriceps weakness, which is one of the earliest and most common symptoms of knee OA, has been correlated with difficulty performing activities of daily living such as walking. However, the mechanism relating impairment of the quadriceps to functional impairment remains unknown. Dynamic computer simulations are powerful tools for investigating the role of individual muscles during movements such as gait, but to date they have not been utilized to study the role of the quadriceps in OA gait, and the effect of weakened quadriceps on other muscles in the lower extremity. Furthermore, the influence of subject-specific quadriceps muscle parameters on model predictions of muscle function in simulations of OA gait has not been evaluated.

We created muscle-driven simulations of gait in healthy individuals and investigated the effect of different types of simulated quadriceps weakness on the muscle compensation strategies needed to maintain healthy kinematics at a self-selected walking speed. We then expanded this study to investigate the muscle compensation strategies needed to maintain healthy gait kinematics over a range of speeds in response to simulated quadriceps weakness. We collected gait data and subject-specific measurements of quadriceps volume, strength, and activation deficit from an individual with knee OA and investigated the effect of different implementations of the subject-
specific quadriceps parameters on model predictions of muscle function during gait. We then forced a model with the highest degree of subject-specificity to track the gait kinematics of a healthy individual to explore changes in muscle function in response to a virtual gait re-training.

5.1 Contributions

The main contributions of the research presented in this dissertation are:

Development of muscle-driven simulations investigating muscle compensations in response to both quadriceps atrophy and activation failure. While previous studies have investigated simulated muscle atrophy, we developed the first simulations investigating the effects of both atrophy and activation failure on muscle forces and contributions to progression and support during gait. Our findings suggested different compensation strategies by the lower extremity musculature in response to atrophy and activation deficits. Developing these simulations and establishing a method for investigating different sources of quadriceps weakness laid the groundwork for the other research presented in this dissertation.

Estimation of muscle compensations needed to maintain normal gait kinematics in response to simulated quadriceps atrophy and activation failure over a range of walking speeds. Many individuals with OA walk slowly compared to healthy individuals, which has been correlated with quadriceps muscle weakness. However, the mechanism relating impaired quadriceps function to reduced gait speed is unknown. As a
first step towards a better understanding of the factors that limit walking speed in individuals with weakened quadriceps, we investigated the muscle compensations needed to maintain healthy gait kinematics over a range of walking speeds in response to simulated quadriceps atrophy and activation failure. The results from this study suggest that it is physiologically feasible for persons with quadriceps weakness to walk at fast speeds and that other factors not simulated in our models (e.g. pain or instability) likely contribute to reduced walking speeds.

Development of musculoskeletal models incorporating subject-specific quadriceps muscle properties of an individual with knee OA. The generic musculoskeletal models used in many simulation studies have muscle properties that are based on limited data of cadaver muscle architecture. However, the muscle properties of individuals with OA are often significantly different from healthy individuals. No previous study had incorporated subject-specific quadriceps muscle properties into simulations of OA gait. We developed models with peak isometric force and maximum activation parameters that were calculated from direct measurements of muscle volume and activation deficits using magnetic resonance imaging and the burst superimposition technique in an individual with knee OA. Our modeling technique allowed us to detect subtle changes in force output and contributions to progression and support by the quadriceps in response to different model complexities and emphasizes the need for further investigation in a larger population of individuals with OA.
Evaluation of a virtual gait re-training simulation for an individual with knee OA.

Individuals with knee OA walk differently compared to healthy individuals. In an effort to investigate the effects of changes in gait kinematics on model predictions of muscle function, we forced a model with subject-specific quadriceps properties measured from an individual with OA to track the gait kinematics of a healthy individual. The simulations revealed that changing kinematics had a much greater effect on muscle forces and contributions to progression and support than differences in model complexity, suggesting that subject-specificity of quadriceps properties in muscle-driven simulations may be secondary to kinematic changes for some individuals with knee OA. These findings emphasize the need to investigate kinematic factors in addition to muscle factors in impaired gait and lays the groundwork for further investigation of the interplay between the different potential mechanisms of impaired function in persons with OA.

5.2 Additional Applications

This dissertation presents the development of dynamic musculoskeletal simulations investigating the effect of quadriceps weakness on muscle function during gait and lays the groundwork for additional investigations that capitalize on the capabilities of muscle-driven simulations.

Estimation of muscle forces and contributions to progression and support in persons with varying levels of function and OA severity. Our pilot study investigating the sensitivity of model predictions to different implementations of subject-specific
quadriiceps muscle properties revealed changes in quadriiceps force and contributions for
the different model complexities, but small or negligible changes in other muscles. However, our OA subject was a high-functioning individual with moderate OA (K-L grade II) whose quadriiceps muscles were stronger than in the generic model, and so is not representative of the general OA population. The modeling technique we developed can be applied to a larger number of subjects with varying levels of function and OA severity to gain a more complete understanding of muscle function in persons with knee OA. Such an investigation would also provide a more conclusive analysis of the sensitivity of model predictions to different subject-specific parameters, and may even reveal important differences in model predictions for individuals with different levels of function and OA severity.

**Evaluation of additional subject-specific parameters.** We developed a robust modeling technique incorporating subject-specific quadriiceps muscle properties measured using magnetic resonance images and burst superimposition. These measurements were used to tune the quadriiceps peak isometric force and maximum activation parameters of a musculoskeletal model to reflect the properties of an individual with knee OA. We focused on these properties because they have been shown to be different in the OA population compared to healthy individuals (Hassan et al., 2001; Mizner et al., 2003; Petterson et al., 2008). However, there are other subject-specific muscle parameters that could be measured and used to develop models with an even higher degree of subject-specificity, including tendon slack length, optimal fiber length, pennation angle, and
moment arm. Whether these parameters are significantly different in individuals with OA compared to healthy individuals, and how perturbations in these parameters would influence model predictions in simulations of OA gait, is an area that should be explored.

**Investigation of function in additional muscle groups of persons with OA.** The prevalence of quadriceps weakness in the OA population motivated our investigation of its role in gait and its effect on other muscles of the lower extremity. However, other muscles of the lower extremity may also play an important role in OA gait. We found that the gluteus maximus and soleus muscles compensated for simulated quadriceps weakness to maintain the gait kinematics of healthy, young individuals. However, these simulations assumed unimpaired function of all other muscles of the lower extremity besides the quadriceps. If persons with OA experience weakness or impaired function in other muscles of the lower extremity, especially in muscles that might otherwise compensate for weakness in the quadriceps, it might significantly influence model predictions of muscle function. Whether individuals with OA have impairment in other muscle groups, and how that impairment may influence abnormal function and movement, is currently unknown. The same methods that we used to obtain patient-specific measurements of quadriceps parameters could also be applied to other muscle groups such as the gluteus and plantarflexor muscles.

**Estimation of muscle function in other pathological populations using subject-specific modeling parameters.** Muscle-driven simulations have been used to investigate
pathological populations such as post-stroke hemiparesis, cerebral palsy, and TKA (Higginson et al., 2006; Kumar et al., 2012; Steele et al., 2012; Gerus et al., 2013; Li et al., 2013). While some studies have incorporated subject-specific measurements, many employed generic musculoskeletal models with muscle properties that may not represent changes in muscle due to disease or altered function. The sensitivity of model predictions of muscle function to changes in muscle properties and implementation of patient-specific measurements of muscle parameters in these populations should be investigated, especially if simulation results are used to inform treatment. Estimation of muscle function in populations that are known to be at a higher risk for OA, such as persons with cartilage defects or ACL injuries, also warrants further investigation. An analysis of muscle forces and contributions to progression and support in these populations would provide a more complete understanding of the mechanism of progression from injury to OA.

**Investigation of muscle function in other activities of daily living.** Walking is an important activity of daily living that is commonly impaired in individuals with OA. However, other activities of daily living are also difficult for persons with OA, including kneeling, stair climbing, and rising from a chair. Difficulty in performing these activities has been correlated to quadriceps impairment. In order to address the factors that limit performance in activities such as stair climbing, there is a need to investigate the effect of muscle weakness on compensation strategies during these activities. It may be that the
compensatory strategies for such activities are different than those in walking and would suggest different targets for rehabilitation.

**Development and evaluation of simulations with subject-specific knee joint properties.** Many simulation studies employ models which not only have generic muscle properties based on limited data and averages, but also have generic joint properties. The knee joint in most generic models does not account for subject-specific differences in bony geometry, nor does it include models of ligaments, cartilage, meniscus, or any other soft tissues within the joint. These limitations restrict the use of generic models for accurately predicting quantities such as joint contact forces, which are believed to be an important factor in the development and progression of OA. Incorporating detailed models of subject-specific bony geometry (Gerus et al., 2013), cartilage, ligaments, and other soft tissues into dynamic simulations would provide a higher level of confidence in model predictions of variables such as articular contact forces during gait. Such models could shed important insight on the role of changes in joint structure and soft tissues on impaired function in pathologies such as OA.

**Implementation and evaluation of more detailed muscle properties.** Most current musculoskeletal models represent muscles in the body as a series of lines and wrapping surfaces and do not distinguish between different muscle compositions and fiber type. Structural changes in muscle are common in the OA population due to aging and disuse, including atrophy of type II muscle fibers, transformation of type II fibers to type I fibers,
and fatty infiltration. Image-based musculoskeletal modeling (Blemker et al., 2007) has led to the development of more detailed 3D muscle models which include fiber lengths for many fibers within a muscle, distribution of fibers, tendon aponeuroses, and tissue stresses and strains. The tradeoff between muscle model complexity and computational time may limit the applicability of such detailed muscle models in simulations of gait, but an investigation of how much subject-specificity in muscle structure is necessary to relate impaired muscle function to impaired gait in the OA population may be warranted.

**Investigation of perturbations in kinematic variables.** The first two studies presented in this dissertation investigated the muscle compensations that would be needed to maintain healthy gait kinematics in the presence of simulated quadriceps weakness. In our pilot study of OA gait, we investigated changes in muscle function as a result of a virtual gait re-training by forcing a model with OA-specific quadriceps properties to track the gait kinematics of a healthy individual. The common finding of abnormal gait in persons with OA, however, suggests that many individuals will choose to adapt an altered gait pattern instead of changing their muscle function to maintain normal gait. The initial findings from our virtual gait re-training simulation also suggest that changes in subject-specific quadriceps properties may be secondary to kinematic changes. A more thorough investigation of the role of kinematic variables on muscle function in the OA population is needed. The development of experimental protocols which systematically perturb gait kinematics, such as on a treadmill or through the use of biofeedback, would provide data
that could be fed into simulations and allow for a better understanding of the role of kinematic changes on altered muscle function.

**Analysis of EMG-driven simulations of OA gait.** EMG-driven models have been employed by previous researchers as a means of using subject-specific muscle activation patterns to inform simulations (Lloyd and Besier, 2003; Buchanan et al., 2004; Sartori et al., 2011; Kumar et al., 2012). It has been suggested that using EMG data as model input may provide better physiological estimation of muscle forces (Gerus et al., 2013). In our study of OA gait, we constrained the simulated muscle activations to match the general timing and magnitude of the normalized EMG data from our OA subject, but did not use the experimental EMG to drive our simulations of gait (i.e., to generate purely forward dynamic simulations of gait). Since the muscle activation patterns of persons with OA can be significantly different from healthy individuals, developing and analyzing forward simulations that are informed directly by patient-specific activation patterns may provide a higher degree of confidence in model predictions of muscle function.

**Exploration of neural factors in dynamic simulations.** Assessing the influence of muscle activation deficits on gait poses a unique challenge that is an important area for further research. Measurements of volitional muscle activation are commonly made with the subject seated in a dynamometer and performing maximal isometric contractions. Some previous studies have gone a step further by investigating activation failure during slow isokinetic contractions (Babault et al., 2001), as well as over a range of knee flexion
angles (Pietrosimone et al., 2008). However, to our knowledge, no study has investigated how, and if, activation failure measured during testing in a dynamometer influences performance of sub-maximal activities such as gait. We applied activation deficits in our simulations by directly constraining peak quadriceps activation or by applying an overall constraint on maximum activation based on CAR values from a superimposed burst, which may not appropriately reflect in-vivo activation deficits during gait. Furthermore, there is evidence to suggest that volitional activation deficits are a systemic problem and not simply a local problem of the muscle (Heroux and Tremblay, 2006; Pietrosimone et al., 2012; Fisher et al., 2013). The CAR is a measure of the local excitability of the muscle, but muscle inhibition may also be a result of spinal or cortical factors that are not captured with the CAR via superimposed burst. Additional measurements of muscle activation deficits which include local, spinal, and cortical factors (e.g. H-reflex and spinal reflex) may provide a better understanding of muscle inhibition in OA.

The challenge then becomes how best to incorporate such measurements into a modeling and simulation framework. Many current models do not model the central nervous system, so simulations assume ideal or “normal” neural control. This assumption highlights the importance of comparing model predictions of muscle activation to experimental EMG. However, EMG measurements may include errors due to cross-talk, impedance between the electrode and muscle, and difficulties measuring the activity of deep muscles. Furthermore, the CMC algorithm within OpenSim does not take muscle synergies into account, but treats each muscle as an independently controlled actuator. Persons with pathologies may have different muscle synergies and use different muscle
recruitment strategies than healthy individuals. Simulations which are able to model the specific neural control strategies of an individual may provide more accurate predictions of the effects of muscle inhibition or abnormal recruitment patterns in persons with neuromusculoskeletal pathologies. Such models would help shed light on the role of neural factors in the development and progression of pathologies such as OA.

5.3 Future Work

Future work linking dynamic simulations with individualized treatment strategies will extend the work presented in this dissertation.

**Development and evaluation of clinical interventions using simulations.** Simulations are powerful tools for asking “what if” questions and performing predictive studies, such as how muscle function would change in response to rehabilitation, surgical interventions, or gait re-training. Using the methods presented in this dissertation, we are able to input subject-specific measurements of muscle properties and experimental gait kinematics to estimate changes in muscle forces and contributions to progression and support, variables that provide important insight to the mechanisms relating muscle function and patient function. The findings from our studies could have important implications for personalized physical therapy strategies.

If the results from these simulations are to provide a scientific basis for the treatment of individuals with OA, we need to correlate model predictions with patient function and validate the results from simulations with physical experiments. For
example, our investigation of muscle compensations needed to maintain healthy gait kinematics in the presence of simulated quadriceps weakness revealed the gluteus maximus and soleus muscles to be compensatory muscles. A follow-up study could investigate the efficacy of targeted strengthening of the gluteus and plantarflexor muscles on improving gait kinematics in individuals with OA. The same study also revealed different compensation mechanisms in response to the different sources of quadriceps weakness: atrophy and activation failure. This finding might suggest different rehabilitation protocols depending on the type of quadriceps weakness that is more prevalent in a specific patient. An individual with more atrophy than activation deficit might benefit more from traditional strength training, while someone with more activation failure may respond more to interventions designed to address volitional activation such as electrical stimulation or biofeedback. To validate the findings from our virtual gait re-training simulation, we could investigate whether altering the gait of individuals with OA to walk with normal gait patterns via experimental gait training leads to similar changes in muscle function as those predicted in our simulation. Physical experiments such as those described here would help provide validation for model predictions.

Validated dynamic simulations could then become powerful tools for predicting the functional outcome of individual patients. If we could establish relationships between model predictions of function and experimental measures of subject-specific parameters such as strength, activation, kinematics, and functional performance, we could potentially use simulations to tailor rehabilitation strategies to an individual patient that would lead
to a desired functional outcome. The development of predictive real-time simulations (Chadwick et al., 2009) could further capitalize on the integration of simulations with clinical interventions by providing real-time feedback to patients and researchers. Such simulations could allow for the development and analysis of different treatment strategies in a single testing session, and allow researchers and clinicians to evaluate the effectiveness of interventions in real time.

5.4 Summary

Osteoarthritis (OA) is one of the most common musculoskeletal disorders in the US, and many individuals with OA report activity limitations due to the symptoms of the disease. Musculoskeletal simulations are becoming more widely used to gain a greater understanding of the mechanisms relating muscle impairment with functional outcome, however, research remains to be done to rigorously test their ability to accurately predict pathological muscle function and patient outcome. Additional opportunities exist to use muscle-driven simulations as tools to help inform personalized treatment strategies for individuals with pathological muscle weakness. This dissertation represents a step towards realizing those opportunities. I hope that the research presented here will guide future research by suggesting a methodology for developing subject-specific models of individuals with knee OA and by presenting some of the different investigations and questions that can be addressed with dynamic simulations.

I believe that muscle-driven simulations are an important tool in biomechanics research, as they allow researchers to ask “what if?” questions, explore cause-effect
relationships, and estimate quantities that are otherwise not possible or extremely difficult with purely experimental techniques. Simulations have been used to investigate muscle activations, joint kinematics, internal joint loading, and muscle forces and contributions to progression and support, providing insight on mechanisms of pathological movement. The studies presented in this dissertation expand on the excellent work of previous researchers, and it is my hope that the work I have presented here lays the groundwork for future studies that will continue to add to our understanding of pathological gait and, more importantly, improve the function and quality of life of individuals with movement disorders.
References


Appendix A: Supplementary data for Chapter 2
Figure A.1: Force output for major lower extremity muscles in response to each type of simulated quadriceps weakness. Line colors: Black = Normal, Red = Activation Failure Only, Blue = Atrophy Only, Green = Atrophy + Activation Failure.
Figure A.2: Contributions to forward progression for major lower extremity muscles in response to each type of simulated quadriceps weakness. Line colors: Black = Normal, Red = Activation Failure Only, Blue = Atrophy Only, Green = Atrophy + Activation Failure.
Figure A.3: Contributions to vertical support for major lower extremity muscles in response to each type of simulated quadriceps weakness. Line colors: Black = Normal, Red = Activation Failure Only, Blue = Atrophy Only, Green = Atrophy + Activation Failure.
Appendix B: Supplementary data for Chapter 3
Figure B.1: Normalized fiber lengths for major lower extremity muscles at each gait speed. Line colors: Red = slow speed, Green = self-selected speed, Blue = fast speed. The colored circles represent the point of maximum total force generation for each type of simulated quadriceps weakness at each gait speed. Circle colors: Black = Normal, Red = Activation Failure Only, Blue = Atrophy Only, Green = Atrophy + Activation Failure. Fiber lengths were normalized by the optimal fiber length for each muscle.
Figure B.2: Normalized fiber velocities for major lower extremity muscles at each gait speed. Line colors: Red = slow speed, Green = self-selected speed, Blue = fast speed. The colored circles represent the point of maximum total force generation for each type of simulated quadriceps weakness at each gait speed. Circle colors: Black = Normal, Red = Activation Failure Only, Blue = Atrophy Only, Green = Atrophy + Activation Failure. Fiber velocities were normalized by maximum fiber contraction velocity, set at 15 optimal fiber lengths per second, for each muscle.
Appendix C: Supplementary data for Chapter 4
Figure C.1: Force output for major lower extremity muscles of the involved limb in response to the different subject-specific models. The quadriceps muscles displayed the largest differences between the different models, while there were relatively small changes in the other muscles.
Figure C.2: Force output for major lower extremity muscles of the uninvolved limb in response to the different subject-specific models. The quadriceps muscles displayed the largest differences between the different models. The force output for each muscle is displayed as a function of % Gait Cycle of the involved (right) limb.
Figure C.3: Contributions to forward progression for major lower extremity muscles of the involved limb in response to the different subject-specific models. The quadriceps muscles displayed the largest differences between the different models, while there were relatively small changes in the other muscles.
Figure C.4: Contributions to forward progression for major lower extremity muscles of the uninvolved limb in response to the different subject-specific models. The quadriceps muscles displayed the largest differences between the different models. The contribution for each muscle is displayed as a function of % Gait Cycle of the involved (right) limb.
Figure C.5: Contributions to vertical support for major lower extremity muscles of the involved limb in response to the different subject-specific models. The quadriceps muscles displayed the largest differences between the different models, while there were relatively small changes in the other muscles.
Figure C.6: Contributions to vertical support for major lower extremity muscles of the uninvolved limb in response to the different subject-specific models. The quadriceps muscles displayed the largest differences between the different models. The contribution for each muscle is displayed as a function of % Gait Cycle of the involved (right) limb.
Figure C.7: Comparison of joint kinematics between the involved limbs of the healthy subject and osteoarthritic (OA) subject. In general, the OA subject displayed less joint range of motion than the healthy subject, including decreased hip extension, decreased knee flexion and abduction, and decreased ankle plantarflexion.
Figure C.8: Comparison of internal joint moments between the involved limbs of the healthy subject and osteoarthritic (OA) subject. Compared to the healthy subject, the OA subject displayed a greater hip abduction moment, less hip internal rotation moment, and less knee extension moment in early stance.
Figure C.9: Comparison of normalized fiber lengths for major lower extremity muscles of the involved limb between the healthy subject and osteoarthritic (OA) subject. Fiber lengths were normalized by the optimal fiber length for each muscle.
Figure C.10: Comparison of normalized fiber velocities for major lower extremity muscles of the involved limb between the healthy subject and osteoarthritic (OA) subject. Fiber velocities were normalized by maximum fiber contraction velocity, set at 15 optimal fiber lengths per second, for each muscle.