Metabolic Cost and Stability of Locomotion in People with Lower Limb Amputation

METABOLIC COST AND STABILITY OF LOCOMOTION IN PEOPLE WITH LOWER LIMB AMPUTATION

A Dissertation Presented

By

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DEDICATION

I dedicate this to my children, Haley Jade and Jackson Ryan, and my supportive and loving wife, Amy.

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I would not be where I am today without help from many people who have supported and motivated me to get to this point.

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ABSTRACT

METABOLIC COST AND STABILITY OF LOCOMOTION IN PEOPLE

WITH LOWER LIMB AMPUTATION

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It is generally accepted that metabolic energy expenditure and gait stability are key factors that influence the selection of able-bodied locomotor patterns. It is unclear how energy expenditure and gait stability are prioritized during walking in people with lower limb amputation. People with lower limb amputation generally have greater metabolic energy expenditure during walking and increased incidence of falls. People with unilateral lower limb amputation spend more time on the intact limb compared with the prosthetic limb, while able-bodied individuals generally walk with symmetrical timing between limbs. Restoring symmetry is often a goal of rehabilitation and assistive devices, yet the gait differences for people with unilateral amputation relative to able-bodied walkers could in fact be optimal for metabolic energy expenditure and stability. The purpose of this dissertation was to determine how metabolic energy expenditure and

gait stability are affected by inter-limb gait asymmetry in people with and without unilateral transtibial amputation. To the best of my knowledge, this is the first set of studies to have people with amputation walk with preferred (i.e., asymmetrical) and non-preferred (i.e., symmetrical and greater asymmetry) inter-limb stance timing in order to understand how metabolic energy expenditure and gait stability are affected by asymmetry. Results from the first study found that subjects with amputation walked with more time on intact side compared with the prosthetic side, while able-bodied subjects walked with near symmetry (<1% difference between limbs) on average. Although the study may not have been adequately powered, the asymmetries predicted to yield the minimum-cost of transport for both groups were in the same direction (i.e., greater asymmetry for subjects with amputation compared with able-bodied subjects) as the preferred asymmetries. Results from the second study found that all stability metrics exhibited minima within the experimental range, expect for medial-lateral margin of stability, for which linear trends were found. These results indicate that during preferred conditions, subjects may minimize stability while walking with preferred inter-limb stance timing, and therefore many of the stability metrics had their lowest values near the preferred conditions. Even though we need to be cautious about some of the interpretations, these findings warrant further investigation into how preferred patterns emerge in people with amputation. Understanding why preferred patterns are asymmetrical in people with unilateral transtibial amputation may provide insights for rehabilitation and assistive device design, and also show that an asymmetric gait may be the best result after some injuries and do not represent a problem that should be fixed.

TABLE OF CONTENTS

LIST OF TABLES

Table Page

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

1.1 General Introduction

Humans optimize locomotion. It is generally accepted that metabolic cost and stability are optimized with able-bodied self-selected locomotor patterns, but it is unclear if people with lower limb amputation do the same. People with lower limb amputation usually have greater metabolic cost of locomotion (Waters & Mulroy, 1999; Waters et al., 1976) and higher rates of falling (Miller et al., 2001(b); Kulkarni et al., 1996) compared with able-bodied individuals. Even though gait patterns of people with lower limb amputation have been studied since World War II, the causes for greater metabolic cost and decreased stability have not been fully determined. People with unilateral amputations typically have asymmetries between the prosthetic and intact sides for temporal-spatial, kinematic, and kinetic stride measures. For people with lower limb amputation, the impacts of inter-limb asymmetries on metabolic cost and stability have been addressed by few studies. Gait asymmetries in people who use a passive prosthesis unilaterally may simply result from the altered anatomy of the residual limb and a passive prosthesis not functioning like a biological limb. The gait differences relative to able-bodied walkers could in fact be optimal for metabolic cost and stability, but this is presently unknown. Therefore, the focus of this dissertation is to determine how metabolic cost and gait stability are affected by inter-limb gait asymmetry in people with unilateral below knee amputation.

1.2 Motivation

The number of people with amputation was estimated to be 1.6 million in 2005, and is expected to reach 3.6 million by 2050, with approximately two thirds being of the lower limb (Ziegler-Graham et al., 2008). The number of people with amputation continues to increase from both traumatic causes (e.g., blast injury) and impaired vasculature (e.g., diabetes), with the economic cost of lower limb amputation due to impaired vasculature alone estimated at $4.6 billion in 1996 (Dillingham, 2005). People with lower limb amputation have decreased mobility and subsequently decreased quality of life (Pell et al., 1993), even though after receiving a prosthesis they are expected to regain mobility and return to activities of daily living. Two potential reasons why they may not return to previous levels of functional mobility are greater metabolic cost and decreased stability during locomotion. People with lower limb amputation consistently have greater metabolic cost (Waters & Mulroy, 1999) and decreased stability (Hak et al., 2013) compared with able-bodied people. The altered residual limb anatomy and passive prosthesis does not mimic the biomechanics of a biological limb. When using prostheses that inject power into the gait cycle (i.e., active prostheses), metabolic cost is lower compared with the use of passive prostheses (Herr & Grabowski, 2012), but active prostheses are less prevalent than passive prostheses. Even though passive prostheses have improved dramatically (Norton 2007), it might be reasonable to expect that there will be inter-limb stride asymmetries due to the asymmetrical morphology. From this perspective, asymmetrical gait patterns might represent the new optimal form of locomotion for people with lower limb amputation; however, the effects of inter-limb asymmetry on metabolic cost and stability have not yet been established.

Inter-limb asymmetries have been consistently observed in unilateral lower limb amputees with temporal-spatial (i.e., stride and stance time) (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997), kinematic (Sanderson & Martin, 1997), and kinetic (Sadeghi et al., 2001; Sanderson & Martin, 1997; Silverman et al., 2008; Winter & Sienko, 1988) gait characteristics. When able-bodied individuals walk with varying degrees of stride asymmetry, metabolic cost increases (Ellis et al., 2013) and gait stability decreases (Ducharme & van Emmerik, 2016) directly with the degree of gait asymmetry. Surprisingly, few studies (Dingwell et al., 1996; Davis et al., 2004) have trained people with lower limb amputation to walk with symmetrical stride characteristics in a research setting. Only one of these studies included measures of metabolic cost (Davis et al., 2004), and none have included measures of stability. Dingwell et al. (1996) demonstrated that people with lower limb amputation can improve stride (i.e., stance plus swing on one side) time and push-off force symmetry with real time visual feedback. Davis et al. (2004) found decreased metabolic cost while walking without real time feedback after training for push off force symmetry, but not after stride time training; however, their study had a small, non-homogenous sample so there is a need to confirm the generality of their initial findings. There have been efforts to match mass and inertial properties of the prosthetic limb to the intact limb, removing the inertial asymmetry (Mattes et al., 2000), but doing so actually resulted in greater temporal-spatial asymmetry and metabolic cost. A computer simulation and modeling approach was used with an amputee musculoskeletal model that emulated able-bodied walking kinematic and ground reaction force data (Zmitrewicz et al., 2007) to determine prosthetic foot and individual muscle contributions for forward propulsion. The prosthetic-side hip muscles and intact-side hip and ankle muscles had increased mechanical energy contribution to maintain forward propulsion compared to a non-amputee musculoskeletal model. This result would imply greater mechanical demand, and probably greater metabolic cost, for a person with unilateral limb loss to walk symmetrically. Therefore, the effect of inter-limb stride asymmetry on metabolic cost and stability is not fully known.

Although biological organisms are believed to find an optimal locomotor pattern, subject to constraints that act upon the system (Sparrow & Newell, 1998), people with lower limb amputation have greater metabolic cost (Waters & Mulroy, 1999; Waters et al., 1976) and a higher incidence of falls (Miller et al., 2001(a); Kulkarni et al., 1996) compared with able-bodied individuals. They walk subject to different constraints due to altered residual limb anatomy and a prosthesis's design and function, and may have an optimal locomotor pattern characterized by inter-limb asymmetries. Having people with unilateral lower limb amputation walk with varying degrees of stride asymmetry, including a symmetrical condition, while measuring metabolic cost and gait stability could provide insights on the adaptations that are made to walk effectively with a prosthesis.

1.3 Concepts and Background

People with lower limb amputation have altered morphology and must rely on a (usually) passive (i.e., no external power injected into device from an actuator) prosthesis in place of the missing anatomy. Depending on the cause of the amputation, there may be more deficits affecting overall health, especially with people who have an amputation due to dysvascular causes (Roberts et al., 2006). No matter the reason for amputation, there is altered proprioception (Liao & Skinner, 1995) and muscle function (Huang & Ferris, 2012) in the residual limb. The sensory feedback from an intact foot and ankle is lost, and muscles that were used to generate most of the ground reaction force in late stance (Anderson & Pandy, 2003) have been removed or wrapped around the distal end of the residual limb. Due to the altered anatomy and reliance on a prosthesis, the person will adapt their gait pattern in order to walk. Based on the anatomical and device constraints, an asymmetrical gait may work within the new system and be the new optimal for metabolic cost and stability, but this has not been clearly established in the literature.

People with unilateral transtibial amputation demonstrate increased stance time on the intact side compared to the prosthetic side (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson and Martin, 1997), though the stance time asymmetry decreases as walking speed increases above preferred speed (Nolan et al., 2003). In able-bodied subjects, Ellis et al. (2013) found greater metabolic cost with inter-limb stride time asymmetry, with metabolic cost increasing proportionally with the degree of asymmetry. They proposed that in the case of people with pathologically asymmetrical gait, the asymmetries may be more favorable metabolically. Two experimental studies (Davis et al., 2004; Dingwell et al., 1996) and one computer simulation study (Zmitrewicz et al., 2007) have constrained people with lower limb amputation to walk with inter-limb temporal symmetry. Davis et al. (2004) found decreased metabolic cost after training for stride time symmetry, but they had a small, non-homogenous, sample size. The subjects had a mix of lower limb amputations, including above- and below-knee, as well as different causes of amputation, traumatic and dysvascular. Even though this was a promising finding, general conclusions about metabolic cost and gait asymmetry cannot be made because of the varied subject sample. Therefore, the difference in metabolic cost between symmetrical and asymmetrical stride patterns is not fully understood for people with unilateral lower limb amputations.

People with an amputation as a result of trauma (e.g., blast injury, car accident) generally have a lower metabolic cost of walking compared with people who have lost a limb from vascular (i.e., diabetes) causes (Waters et al., 1976). Also, it has been shown that metabolic cost at preferred walking speed is greater with increasing level of amputation, and preferred walking speed is lower for people with vascular compared with traumatic amputations (Waters et al., 1976). In the case of highly-functioning military service members with unilateral below knee amputation using an elastic storage and return prosthetic foot, one study showed no significant difference in metabolic cost compared to able-bodied people (Esposito et al., 2014).

One way to link energy expenditure at different speeds is cost of transport (energy expended per unit distance traveled). The cost of transport curve for people with lower limb amputation looks like the characteristic U-shape as seen in able-bodied walkers, but the minimum cost is greater with increasing level of amputation and the speed at the minimum decreases with increasing amputation level (Genin et al., 2008). When a powered robotic ankle that can provide external energy is used, the preferred walking speed and cost of transport curves were similar between people with transtibial amputation from trauma using the powered ankle compared with matched non-amputees (Herr & Grabowski, 2012). This result is exciting, and holds considerable promise, but the majority of people with a lower limb amputation will continue to use a passive prosthesis for the foreseeable future due to the financial cost of actuated prostheses.

People with lower limb amputation of all levels have an increased incidence of falls, more commonly for people with above knee amputation than below knee (Miller et al., 2001(a); Kulkarni et al., 1996). Due to an increased incidence of falls, there is an increased fear of falling (Miller et al., 2001(a); Kulkarni et al., 1996), which may contribute to decreased mobility. With decreased mobility and overall physical activity, people are at greater risk for many other pathologies, such as heart disease and diabetes (Booth et al., 2012). Measures used to compare fallers and non-faller, include local measures that focus on a single segment or joint (e.g., horizontal trunk acceleration and global measures that account for stability of the whole body center of mass (Bruijn et al., 2013). One global measure of stability is margin of stability (MoS), which has been used in people with unilateral transtibial amputation (Hak et al., 2013). When compared to able-bodied individuals, people with lower limb amputation have increased stability when perturbed, as evident by showing a larger margin of stability (Beltran et al., 2014; Hak et al., 2013). Traditional measures of stability, such as step width and step width variability have also been used, demonstrating a larger step width and greater variability in people with amputation compared with able-bodied individuals (Hak et al., 2013;

Beurskens et al., 2014). People with lower limb amputation consistently demonstrate poor stability compared with able-bodied individuals, yet how gait stability is affected by temporal-spatial asymmetry is largely unknown. In a recent study, it was found that when able-bodied individuals walk with asymmetry, local stability, that is the system's resistance to very small perturbations across strides (Dingwell et al., 2001), decreases (Ducharme & van Emmerik, 2016). People with lower limb amputation consistently demonstrate inter-limb asymmetries, and the asymmetries may occur to improve stability (Hak et al., 2014), but this has not been determined.

The gait patterns people with lower limb amputation choose may be optimized for metabolic cost, stability or a combination of the two. Monsch et al. (2012) theorized there is a trade-off between metabolic cost and stability depending on task goals. When their able-bodied subjects walked at a set speed with a more conservative, stable pattern, it led to greater metabolic cost, while walking with a more risky, less stable pattern led to less metabolic cost (Monsch et al., 2012). Different gait parameters have previously been linked to optimizing metabolic cost, such as speed (Ralston, 1958), stride rate (Zarrugh & Radcliffe, 1978), and mechanical power and efficiency (Umberger & Martin, 2007). People with lower limb amputation consistently demonstrate stride asymmetries, unlike able-bodied individuals who walk and run symmetrically (Hamill et al., 1983; Hannah et al., 1984). If able-bodied individuals optimize gait for metabolic cost and stability, the asymmetrical gait patterns may represent the conditions that optimize metabolic cost and stability for people with lower limb amputation. Alternatively, there may be inherent trade-offs involved in walking with a prosthesis, such as maintaining gait stability at the expense of greater metabolic cost.

1.4 Problem Statement and Purpose

People with unilateral transtibial amputation have greater metabolic cost and decreased stability in locomotion, while demonstrating inter-limb differences with temporal-spatial parameters (i.e., stride and stance time), kinematics, and kinetics. The effects of these inter-limb asymmetries on metabolic cost and stability remain largely undetermined. When able-bodied individuals voluntarily walk with asymmetrical strides, metabolic cost increases as the amount of asymmetry increases (Ellis et al., 2013). When able-bodied individuals deviate from preferred stride characteristics, local stability decreases (Ducharme & van Emmerik, 2016) but the effects on global stability, that is the system's ability to accommodate larger perturbations (Dingwell et al., 2001), are unknown. The effect of inter-limb asymmetry on the trade-offs between metabolic cost and gait stability for people with lower limb amputation remains unclear, and understanding this relationship will provide insight on how people with lower limb amputation regulate their locomotion.

The purpose of the dissertation is to determine the effects of inter-limb asymmetry on metabolic cost and stability in people with unilateral transtibial amputation. In study one, whole body energy expenditure will be measured in people with unilateral transtibial amputation and able-bodied subjects. Each group will walk using their self-selected stride characteristics, and then will be constrained to walk with symmetry and varying degrees of asymmetry. The subjects will receive real time visual feedback of a stance time symmetry index. In study two, stability will be measured with global and traditional measures under the same conditions as study one. These two studies will provide important information on how people with lower limb amputation self-select stride characteristics in light of metabolic cost and gait stability.

1.5 Significance of this Dissertation

The studies within this dissertation are significant because they will help answer the question of whether self-selected locomotor patterns used by people with unilateral transtibial amputation are optimal for metabolic cost, stability or of some combination thereof. Inter-limb temporal-spatial stride asymmetries might be optimal for unilateral amputees because of altered residual limb anatomy and the dynamics of the prosthesis, which is considerably lighter than the intact limb and restricts push-off against the ground. If able-bodied individuals choose symmetrical gait patterns, while potentially optimizing metabolic cost and stability, then why people with lower limb amputation choose inter-limb asymmetry remains of interest.

Knowledge of the impact of stride symmetry on metabolic cost and stability could influence future rehabilitation paradigms and the design of assistive devices. Improving rehabilitation should lead to increased mobility and subsequently quality of life for people with lower limb amputation. Also, the trend with prosthesis design is to mimic biological characteristics with respect to kinetic output. Yet, if inter-limb asymmetry is optimal because of altered anatomy and device constraints, future devices should not be designed in an effort to force a symmetrical gait. Results from this dissertation will help drive rehabilitation and device design, and ultimately may improve the quality of life for people with lower limb amputation.

1.6 Proposed Experimental Designs

1.6.1 Study One – Stride Symmetry and Metabolic Cost of Locomotion in People with Unilateral Transtibial Amputation

People with unilateral transtibial amputation generally have greater metabolic cost compared with able-bodied individuals (Waters & Mulroy, 1999; Waters et al., 1976) and consistently demonstrate temporal-spatial inter-limb stance asymmetry (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997), whereas able-bodied individuals tend to walk symmetrically (Gundersen et al., 1989; Hamill et al., 1983; Hannah et al., 1984). Ellis et al. (2013) found greater metabolic cost when able-bodied participants voluntarily walked with inter-limb stride time asymmetry and speculated that pathological asymmetry may lead to less metabolic cost in some populations, such as people with an amputation. Few studies have evaluated the effects of gait asymmetry on the cost of walking in people with unilateral transtibial amputation. The difference in metabolic cost between symmetrical and asymmetrical stride conditions may help explain why people with lower limb amputations self-select asymmetrical gait patterns.

The first aim of this study is to confirm previously shown greater stance time on the intact side versus the prosthetic side for people with unilateral lower limb amputation, and equal inter-limb stance time for able-bodied. After evaluating preferred characteristics, the second aim is to determine the effect of temporal asymmetry on metabolical energy expenditure in both groups. Real time visual feedback of inter-limb stance symmetry while walking on a treadmill will be provided to the subjects while whole body energy expenditure is determined via pulmonary gas exchange.

I will test the following hypotheses related to purpose one:

Hypothesis 1.1: The subjects with unilateral transtibial amputation will exhibit greater stance time on the intact side compared with the prosthetic side with their preferred gait pattern.

Hypothesis 1.2: Able-bodied subjects will exhibit symmetrical stance times with their preferred gait pattern.

I will test the following hypotheses related to purpose two:

Hypothesis 1.3: Metabolic cost versus inter-limb asymmetry will demonstrate a U-shaped curve for both groups.

Hypothesis 1.4: Metabolic cost will be the lowest at the preferred stride characteristics for both groups.

A direct consequence of hypotheses 1.1-1.3 is that subjects with unilateral lower limb amputation are predicted to have an elevated cost of walking when required to walk symmetrically, compared with the cost for walking for their preferred, asymmetrical gait pattern.

1.6.2 Study Two – Stride Symmetry and Global Stability of Locomotion in People with Unilateral Transtibial Amputation

People with lower limb amputation have higher rates of falls compared with able-bodied individuals (Miller et al., 2001(a); Kulkarni et al., 1996), as well decreased global stability when perturbed (Beltran et al., 2014; Hak et al., 2013). One consistent difference between people with unilateral amputation and able-bodied individuals is asymmetrical inter-limb stance time, with greater stance time on the intact side (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997). Asymmetries, such as asymmetrical stride characteristics, are often viewed as a negative consequence of disease or injury that should be reduced through therapeutic interventions. However, another possibility is that inter-limb stride asymmetry, such as in people with unilateral lower limb amputation, may be an adaptation that serves to increase gait stability and avoid falling (Hak et al., 2014). Unfortunately, the relative lack of research on the effects of asymmetry on gait stability in people with unilateral amputation precludes drawing firm conclusions. In able-body participants, some measures of local stability have been shown to decrease with increasing gait asymmetry (Ducharme & van Emmerik, 2016), but the effects on global gait stability measures are unknown.

The protocol will be identical to that of study one. Global gait stability will be evaluated using the backwards and medial-lateral margin of stability measures because they relate whole body center of mass kinematics to individual limb strides. Global measures, like margin of stability, may be more closely related to falls than local measures that evaluate single marker, segment or joint characteristics in the time domain. Traditional stability metrics will also be quantified; specifically stride length variability, stride time variability, step width and step width variability, to permit comparisons with the literature. The purpose of this study is to determine the effect of temporal asymmetry on gait stability in both groups. In evaluating that purpose, it will be determined if gait stability is greatest during walking using preferred stride characteristics. Whole body kinematics will be collected during treadmill walking while subjects receive real time visual feedback about inter-limb stance time symmetry to evaluate gait stability

I will test the following hypothesis:

Hypothesis 2.1: Gait stability, measured by backwards and medial-lateral margin of stability, step width and step width variability, versus inter-limb asymmetry will demonstrate an inverted U-shaped curve.

Hypothesis 2.2: Gait stability, measured by backwards and medial-lateral margin of stability, step width and step width variability, will be the greatest at the preferred stride characteristics for both groups.

Similar to Study One, this hypothesis implies that subjects with unilateral lower limb amputation are most stable walking with their preferred, asymmetrical gait patterns, and being required to walk symmetrically will reduce measures of gait stability.

CHAPTER 2

REVIEW OF LITERATURE

The number of people with lower limb amputation continues to rise (Ziegler-Graham et al., 2008), most commonly from traumatic and vascular causes (Owings & Kozak, 1998). People with lower limb amputation usually have greater metabolic cost of locomotion (Waters & Mulroy, 1999; Waters et al., 1976) and higher rates of falling (Miller et al., 2001(a); Kulkarni et al., 1996) compared with able-bodied individuals. Even though gait patterns of people with lower limb amputation have been studied since World War II, the causes for greater metabolic cost and decreased stability have not been fully determined. People with unilateral amputations typically have asymmetries between the prosthetic and intact sides for temporal-spatial, kinematic, and kinetic stride measures. For people with lower limb amputation, the impacts of inter-limb asymmetries on metabolic cost and stability have been addressed by few studies. The gait differences relative to able-bodied walkers could in fact be optimal for metabolic cost and stability, but this is presently unknown.

2.1 Limb Loss

2.1.1 Number of people with an amputation

The number of people with a lower limb amputation was estimated at 1.6 million in 2005 and is expected to rise to 3.6 million by 2050 (Ziegler-Graham et al., 2008). There are an estimated 185,000 amputations in the United States every year (Owings & Kozak, 1998). The two most common causes of amputation are trauma (e.g., blast injury, car accident) and vascular problems (e.g., diabetes) (Owings & Kozak, 1998). The third primary cause of amputation is cancer but accounts for less than 2% of amputations (Owings & Kozak, 1998). From 1988 to 1996, trauma was the cause of 82% of amputations, and over that same time period, there was a 27% increase in the amount of vascular amputations, with black people more likely to have a vascular amputation than non-black (Dillingham et al., 2002). Coincidentally during that time period, the prevalence of diabetes rose sharply in the United States, and is more common in black compared to non-black people (Geiss et al., 2014). One common problem with people who have an amputation due to poor vasculature is re-occurrence of amputation. In an analysis of people with lower limb amputation in 1996, 26% of people had another amputation within 12 months of the initial amputation. Reoccurrence of amputation is a major concern because higher amputation level leads to greater metabolic cost (Waters et al., 1977) and higher incidence of falls (Gauthier-Gagnon et al., 1999). Dillingham et al. (2002) evaluated the number of amputations from 1988 to 1996, and found that there were 953,367 in the United States. Of the 953,367 lower limb amputations, 31.5% were of the toe, 10.5% of the foot, 0.8% through the ankle, 27.6% below the knee, 0.4%

through the knee, 25.8% above the knee, 0.4% hip disarticulations, and 0.1% pelvic amputations.

2.1.2 Mobility post amputation

Even though people are given a prosthesis after an amputation, the amount of usage varies across populations, and many use an assistive device in addition to a prosthesis for mobility. People with unilateral transtibial amputation progress more quickly compared with transfemoral, and walk more at the end of rehabilitation, as well as after one year and two years post-amputation (Holden & Fernie, 1987). Even though people with transtibial amputation progress walking ability more quickly, there are high amounts of sedentary time for people with transtibial amputation from vascular causes (Samuelsen et al., 2016). Providing an initial prosthetic dressing and fitting is supposed to encourage early mobility, but people who have an amputation from vascular causes may have other physical disabilities that limit mobility and lead to prosthesis disuse (Bilodeau et al., 2000).

Most people (nearly 95%) with a trauma-related lower limb amputation wear a prosthesis 80 hours per week, even though only 43% reported being satisfied with prosthesis comfort (Dillingham et al., 2001). 85% of people with unilateral transtibial and transfemoral amputation use a prosthesis, with 53% using one for locomotion indoors and 64% using one for locomotion outdoors (Gauthier-Gagnon et al., 1999). Age is a significant factor in determining usage of a prosthesis (Burger et al., 1997), as well as possession of a wheelchair (Bilodeau et al., 2000). Elderly people with above and through knee amputation choose to use a wheelchair, and 9% decide to stop using their prosthesis entirely after being prescribed one (Beekman & Axtell, 1987). It is surprising how frequent prosthesis disuse is considering most bouts of activity for people with amputation are short. Most activities are 1-2 minutes long and at a low intensity of 17 steps/minutes. Activities that last more than 15 minutes are rare for people with lower limb amputation (Klute et al., 2006). People with lower limb amputation who limit physical activity have worse physical function and satisfaction with participation in social roles compared to able-bodied (Amtmann et al., 2015). The reasons for decreasing physical function may be because of the greater metabolic cost, higher incidence of falls or because of other disabilities that commonly occur after amputation.

2.1.3 Other disabilities related to amputation

Even among people who use a prosthesis 80 hours per week, only 43% reported being satisfied with prosthesis comfort (Dillingham et al., 2001). There are problems with socket fit in 59% of people with transtibial amputation and 78% with transfemoral amputation, leading to skin irritations in 41% and 22%, respectively (Chatterjee et al., 2016). Aside from skin irritations, ulcers, cysts and calluses are the most common skin problems for prosthesis users (Dudek et al., 2006). 95% of people with lower limb amputation reported amputation-related pain, with the most common being phantom limb (79.9%), residual limb (67.7%), and back (62.3%) pains (Ephraim et al., 2005). The high prevalence of back pain has been associated with moderate to severe disability, and further limits overall function aside from the amputation (Hammarlund et al., 2011). There is a decreased knee moment on the prosthetic side (Sanderson & Martin, 1997), potentially due to residual limb pain, and the intact side knee has higher loads (Fey &

Neptune, 2012; Sadeghi et al., 2001) to compensate for decreased prosthetic side loading. The asymmetric loading is one reason to explain the occurrence of significantly more knee osteoarthritis on the intact side and osteoporosis on the amputated side (Burke et al., 1978).

2.1.4 Economic costs due to amputation

Acute and post-acute medical care costs associated with care for people with lower limb amputation from dysvascular causes exceeded $4.3 billion in 1996 (Dillingham et al., 2005). Veterans that underwent lower limb amputation from 2001 to 2008 had a mean cost per year of $14,700 and $18,700 for unilateral and bilateral amputation, respectively (Bhatnagar et al., 2015). In that same time, people with both unilateral and bilateral amputation had costs double 3-5 post-amputation.

2.2 Gait

2.2.1 Able-bodied

Locomotion has been of interest for many years, but how and why humans organize locomotion the way they do is not fully understood. The gait cycle is a series of strides with one stride of the gait cycle typically defined as heel strike to heel strike of the same foot (Gage, 1990). The gait cycle is divided into two main phases, stance and swing phases, comprising 60% and 40% of a full gait cycle, respectively (Gage, 1990). The stance phase is when the foot is in contact with the ground, and the swing phase is when the foot is in the air and ends when the next stance phase begins at heel strike. The stance phase is typically further divided into double support phase and single support phase. The double support phase is when both feet are in contact with the ground, and single support is when only one foot is in contact with the ground. The double support phase is during the first 10% (0-10%) of a stride and then the last 10% (50-60% of a stride) of stance.

The gait cycle is typically further divided into other sections to make it possible to reference bodily actions in smaller periods of time (Gage, 1990). Stance phase is divided into 5 sub-phases, initial contact (0%), loading response (0-10%), mid-stance (10-30%), terminal stance (30-50%) and pre-swing (50-60%). Swing phase is divided into 3 sub-phases, early swing (60-70%), mid-swing (70-85%) and terminal swing (85-100%). Initial contact is when the foot first strikes the ground.

Able-bodied individuals generally choose symmetrical walking patterns with both kinematics and kinetics. The hip (Hannah et al., 1984), knee (Gundersen et al., 1989; Hannah et al., 1984) and ankle (Gundersen et al., 1989; Hannah et al., 1984) joint kinematics demonstrate high levels of kinematic symmetry in the sagittal plane, as well as in the transverse and frontal plan at the hip (Hannah et al., 1984). The ground reaction forces between the right and left limbs have been described as both symmetrical (Hamill et al., 1983; Seeley et al., 2008) and asymmetrical (Herzog et al., 1989). Seeley et al. (2008) found that the vertical and propulsive impulses were symmetrical at slow and preferred speeds, but the propulsive impulse was asymmetrical at a fast speed. In the case of asymmetrical ground reaction forces, Herzog et al. (1989) noted that the amount of asymmetry was variable specific. As an example, the combined positive and negative impulses in the anterior-posterior direction are near zero, and small differences between limbs could indicate a large asymmetry even though the actual value differences are small. Muscle activity of the soleus and rectus femoris measured with electromyography (EMG) in healthy subjects showed high correlations between limbs and nearly identical shapes (Arsenault et al., 1986).

2.2.2 People with lower limb amputation-symmetry and asymmetry

People with lower limb amputation have the same gait cycle as able-bodied, but there are many inter-limb asymmetries in temporal-spatial, kinematic and kinetic variables. People with lower limb amputation no longer have an intact biological limb and must rely on a prosthesis to walk without any other assistive device aside from the prosthesis. The residual limb tissues were not designed to bear loads of the socket-residual limb interaction. The residual limb has altered proprioception, and is missing joints distal to the amputation that are designed to provide kinesthetic awareness, requiring increased reliance on the remaining joints proprioception (Eakin et al., 1992;

Liao & Skinner, 1995). Preferred walking speed is slower for people with amputation when using a passive prosthesis (Genin et al., 2008, Hak et al., 2013; Herr & Grabowski, 2012; Waters et al., 1976) compared with able-bodied people, and is lower for people with an amputation from vascular causes compared with traumatic causes (Waters et al., 1976). Preferred walking speed decreases as amputation level increases (Figure 1) (Waters & Mulroy, 1999).

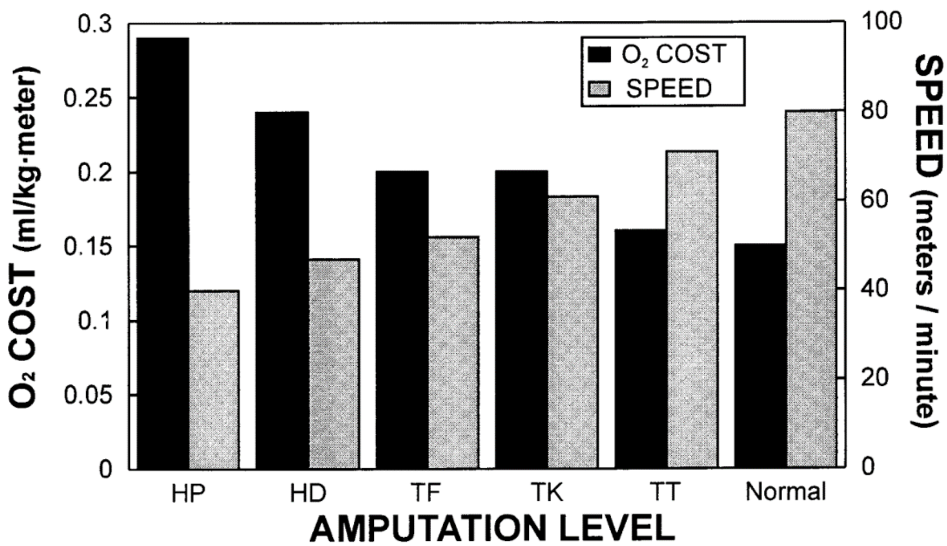

Figure 2.1: Metabolic cost and PWS by Amputation Level. The figure from Waters & Mulroy (1999) depicts O_2 cost of walking and preferred walking speed for people with different levels of unilateral amputation. Speed decreases and O_2 cost of walking increases as amputation level increases. HP = hemipelvectomy, HD = hip disarticulation, TF = transfemoral, TK = amputation at knee, TT = transtibial.

People with unilateral transtibial amputation demonstrate stance time asymmetries at slower and preferred speeds. Increased stance time on the intact side compared to the prosthetic side is commonly found (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997). The degree of inter-limb stance time asymmetry decreases with increased walking speed at the expense of increasing loading on the intact limb (Nolan et al., 2003).

Even though there is less asymmetry with increasing gait speed, people with lower limb amputation have a slower preferred walking speed compared to able-bodied people. The temporal-spatial asymmetries may be the result of the prosthetic ankle not having the same power capability as a biological ankle (Sanderson & Martin, 1997; Winter & Sienko, 1988; Zelik et al., 2011) and not being able to accelerate the center of mass at push-off as well as the intact limb (Hak et al., 2014).

The ankle is a large contributor to center of mass acceleration during late stance, and a decrease in force capability could be a reason for the subsequent asymmetries at other joints and in the time domain. A simple dynamic walking model (two rigid pendula-like legs with curved feet) with decreased push off work similar to a transtibial amputee predicted asymmetries (Adamczyk & Kuo, 2015). Beyond the predictions from a simple walking model, decreased ankle work led to inter-limb asymmetry and can result in greater metabolic cost (Collins & Kuo, 2010). Caputo and Collins (2014) used an ankle emulator with able-bodied people to simulate increased ankle push off work, similar to a powered robotic ankle for a person with an amputation, and found a reduced metabolic rate (Caputo & Collins, 2014). People with unilateral transtibial amputation who use a traditional flex foot, which is a carbon composite foot designed for energy storage at heel strike and return at push off, demonstrate decreased power (Zelik et al., 2011) and moment (Winter & Sienko, 1988) at push off across increasing speeds. The prosthetic ankle produces less mechanical work during stance than the intact limb, and able-bodied limbs (Silverman et al., 2008). Zelik et al. (2011) manipulated prosthetic foot stiffness to determine the optimal stiffness for minimizing metabolic cost, and found that maximizing push off work did not optimize metabolic cost. The deficit in ankle power can be eliminated with a powered robotic device that delivers external positive power to the ankle. Ferris et al. (2012) found that even when ankle power from the device is slightly greater than a normal biological limb, asymmetries at hip and knee joints persist. The capacity to produce power at the ankle is limited by the prosthetic device being utilized, and may be the main contributing factor to inter-limb asymmetries between the intact and prosthetic sides. Yet, even when the prosthetic and intact limbs have similar capabilities, there are compensations made by people with lower limb amputation.

During level walking, able-bodied individuals typically have a knee extensor moment at initial contact as part of loading response with a slightly flexed knee (Gage, 1990). People with unilateral transtibial amputation consistently demonstrate a decreased knee extensor moment at initial contact across walking speeds (Fey & Neptune, 2012; Sanderson & Martin, 1996; Silverman et al., 2008; Winter & Sienko, 1988). People with transtibial amputation may decrease the knee extensor moment to limit the loading at the residual limb-socket interface because the tissues are not designed to bear the contact loads. Due to the altered loading on the prosthetic side, the intact side knee moment is typically larger than the prosthetic side (Fey & Neptune, 2012; Sadeghi et al., 2001). An increased intact side sagittal plane knee moment has been linked to the prevalence of knee osteoarthritis on the intact side for unilateral transtibial amputees (Norvell et al., 2005). The peak internal abduction moment, which is commonly associated with knee pathology, is 46% and 17% greater on the intact side compared to the prosthetic side and able-bodied controls, respectively (Royer & Wasilewski, 2006). The knee abductor moment on the intact side is lowered when using a powered prosthesis compared to a passive prosthesis (Royer & Wasilewski, 2006). The consistent presence of an increased knee moment on the intact side is supported by the finding of higher quadriceps muscle activation on the intact side compared to the prosthetic side during braking (Fey et al., 2010) and may contribute to the higher energetic cost of locomotion for people with lower limb amputation.

The hip joint demonstrates the largest kinetic compensations for people with unilateral transtibial amputation. They produce a larger hip flexor moment (Winter & Sienko, 1988) and power (Sadeghi et al., 2001) at push off on the prosthetic side compared to the intact side to compensate for the decreased capability of the ankle to produce mechanical power. Across speeds, people with unilateral transtibial amputation produce more positive sagittal plane work on both prosthetic and intact sides compared to able-bodied controls (Silverman et al., 2008). The greater work and power being performed at the hip in the sagittal plane to compensate for prosthetic limitations may be a large factor in the greater metabolic energy expenditure for people with lower limb amputation. Asymmetries in frontal plane hip moment are exhibited by a larger moment on the intact side compared to the prosthetic side and able-bodied controls (Royer & Wasilewski, 2006). The larger frontal plane moment may be necessary to improve stability during gait.

2.2.3 Organismal Symmetry

Evolution has predisposed more than 1.5 million species, from fruit flies to humans, with bilateral structural symmetry (Collins & Valentine, 2001). Bilateral symmetry is when the body is divided into two symmetrically opposed parts on opposite sides of an axis (Brusca et al., 2016). As organisms have developed through evolution, a third germ layer emerged (mesoderm) and perhaps simultaneously, bilateral symmetry (Brusca et al., 2016). The mesoderm gives rise to human musculature and the circulatory system. Fossils dating back 600-630 million years show the first signs of bilateral symmetry in Ediacarans. Human's symmetrical morphology is the result of evolution, and may be the basis for why humans walk and run symmetrically. Even though humans have evolved to be symmetrical and restoring symmetry is a goal of rehabilitation for people with lower limb amputation, it may be unrealistic because of differences between biological limbs and prosthetic devices.

2.3 Metabolic Cost of Walking

2.3.1 Able-bodied

Metabolic energy expenditure can be calculated with exhaled carbon dioxide and inhaled oxygen via indirect calorimetry (Weir, 1949; Brockway et al., 1987). Metabolic energy expenditure increases directly with walking speed, but if you normalize the energy expended to distance covered, there is an energetically optimal speed. The energetically optimal speed relative to energy cost per unit distance is known as the cost of transport (Ralston, 1958). The most energetically optimal speed is between 1.2 and 1.3 m s^{-1} (Ralston, 1958; Zarrugh et al., 1974). At slower and faster walking speeds, cost of transport increases, and human's preferred walking typically falls in this range of economical speeds (Finley & Cody, 1970; Ralston, 1958).

Walking speed is the end result of a chosen stride length and stride frequency. Given that humans choose a preferred walking speed that is optimized for cost of transport, humans also demonstrate a preferred stride frequency that is coincident with minimized metabolic energy expenditure (Molen et al., 1972; Zarrugh & Radcliffe, 1978). Metabolic energy expenditure increases when stride frequency increases or decreases away from preferred and speed is held constant (Cotes and Meade, 1960; Minetti et al., 1995; Zarrugh & Radcliffe, 1978). The minimization of mechanical power usually occurs below (i.e., long slow steps) the preferred stride frequency (Cavagna & Franzetti, 1986; Minetti et al., 1995). The net mechanical efficiency is optimal at higher stride frequency (i.e., short fast steps) (Umberger & Martin, 2007).

2.3.2 Locomotion across species

All animals expend energy during locomotion. Animals swim through water, fly through the air, and run on land. Even though these forms of locomotion are very different, different species with these forms of locomotion can be compared when expressing metabolic energy expenditure over a unit distance (cost of transport) relative to body weight (Schmidt-Nielsen, 1972). Running, flying and swimming demonstrate a similar relationship across species sizes, with a lesser net cost of transport for larger animals than smaller animals (Schmidt-Nielsen, 1972). Running has a greater cost of transport than flying (Tucker, 1970), and flying has a greater cost than swimming when comparing similarly sized animals (Schmidt-Nielsen, 1972). Even though it is not the focus of this dissertation, being able to compare the energy expenditure of insects to elephants is of great interest.

2.3.3 People with Lower Limb Amputation

People with unilateral transtibial and transfemoral amputation have greater net energy expenditure rate than able-bodied people while walking at various walking speeds (Figure 2) (Genin et al., 2008; Waters et al., 1976).

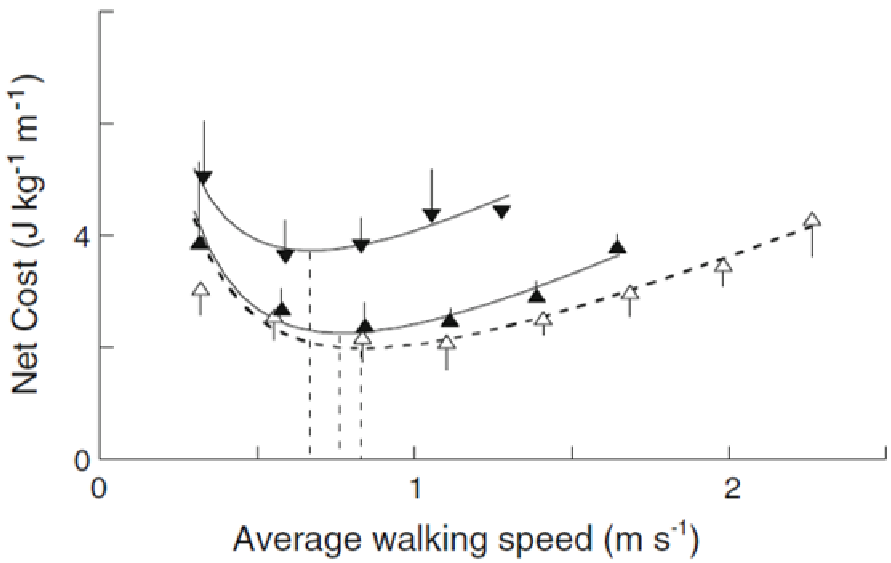

Figure 2.2: Cost of Transport with walking speed. The figure from Genin et al. (2008) represents cost of transport (Net Cost (J kg^{-1} m^{-1}) versus walking speed (m s^{-1}) for able-bodied participants (open upward triangles), people with unilateral transtibial amputation (filled upward triangles) and people with unilateral transfemoral amputation (filled downward triangles). The figure depicts increased cost of transport for the two groups of people with amputations compared with the able-bodied across walking speeds, and a slower predicted optimal walking speed for people with amputation as well, with the people with transfemoral amputation having the slowest optimal walking speed and greatest cost of transport.

Net energy expenditure increases directly with increasing amputation level (Waters et al., 1976; Waters & Mulroy, 1999). Net energy expenditure is also influenced by the cause of amputation (Waters et al., 1976; Waters & Mulroy, 1999). A person with an amputation due to trauma (e.g., improvised explosive device (IED), car accident) frequently has a lesser metabolic cost of walking compared to a person with an amputation from vascular (e.g., diabetes) causes (Waters et al., 1976). The cost of transport curve for people with lower limb amputation looks like the characteristic U-shape but the minimum cost has been shown to increase with increasing level of amputation and the speed at the minimum decreases with increasing amputation level (Genin et al., 2008).

In one recent study, Esposito et al. (2014) showed no significant differences in metabolic cost between people with unilateral transtibial amputation and able-bodied. One potential reason why this study showed no differences in metabolic cost between groups is the sample of people with amputation were young and fit service men who underwent amputation due to trauma. The sample studied is not representative of typical people with lower limb amputation who are studied, both in age and fitness. Thus, while highly-active and fit people with lower limb amputation might not exhibit an elevated cost of transport in walking, this is the exception rather than the rule.

There are many variables that could potentially explain the greater metabolic energy expenditure for people with lower limb amputation, one such being muscle activity. Muscle activation accounts for the metabolic cost of locomotion, and if there is increased muscle activity and co-contraction, then there will be higher energy expenditure. People with transtibial amputation have higher quadriceps muscle activity on the intact side during braking (Fey et al., 2010) and because of the quadriceps' relatively large muscle volume, it is more energetically costly. Aside from the intact side, people with amputation demonstrate increased co-contraction of prosthetic side thigh muscles (Fey et al., 2010; Isakov et al., 2000; Seyedali et al., 2012) and shank residual limb muscles (Seyedali et al., 2012) during the first half of stance. These differences in muscle activity potentially account for the greater metabolic cost, but there are other variables that could explain the difference.

The cost of generating work hypothesis states the mechanical work done by the muscles can account for the metabolic cost of locomotion (Donelan et al., 2002; Umberger & Martin, 2007). A simplistic model for human walking is comparing walking to two coupled pendula, with the stance leg being an inverted pendulum over the fixed foot and the swing leg like a pendulum about the hip (Kuo et al., 2005). During single support, gravitational and potential energy fluctuates equally with the inverted pendulum but during double support mechanical work is needed to re-direct the center of mass and therefore is purported to be a major determinant of metabolic energy expenditure (Kuo et al., 2005). Houdijk et al., (2009) examined the mechanical work of the step-to-step transition for people with unilateral transtibial amputation at preferred walking speed and a fixed walking speed. At the fixed speed (1.3 m/s), the metabolic energy consumption was significantly higher in people with amputation compared to controls, but at the preferred walking speed there was no difference. When the intact limb was the leading limb, negative work at the fixed walking speed was significantly higher for the people with amputation compared to the controls, and was highly correlated to higher metabolic energy consumption (Houdijk et al., 2009). The cost of generating work hypothesis may explain the increased metabolic cost for people with lower limb amputation, but it has not been used to analyze multiple stride frequencies or even a symmetrical pattern with locomotion.

A prosthesis has different mass and inertial properties than a biological limb, and those differences may contribute to the inter-limb asymmetries. Mattes et al. (2000) had people with unilateral transtibial amputation walk without an added load, with a 50% match of intact limb inertial properties and then a 100% match of inertial properties.

When intact limb inertial properties were matched, metabolic energy expenditure was 6-7% greater compared to walking without any additional load. Aside from greater metabolic energy expenditure, step length, swing time and stance time became more asymmetrical when intact limb inertial properties were matched. The results of this study show that matching mass and inertial properties alone has negative impact on metabolic energy expenditure, and the most likely reason is adding non-force generating mass. The mass of the biological limb that is lost with amputation produces force, but the mass added in this study did not. A prosthetic foot has decreased force capacity and inability to accelerate the center of mass, and adding mass to match inertial properties further hinders the prosthetic foot's capacity.

2.3.4 Effect of asymmetry on metabolic cost with able-bodied gait

Ellis et al. (2013) showed the effect of step and stride asymmetry in their study that constrained able-bodied subjects to walk with varying levels of stride asymmetry. As the amount of asymmetry increased, metabolic power and positive mechanical power production increased directly. The lowest net metabolic power was with the preferred stride characteristics which happened to be symmetrical. The positive mechanical power values showed a similar relationship as metabolic power, with increasing power as stride asymmetry increased. The effect of inter-limb asymmetry on metabolic cost has not been shown as clearly for people with lower limb amputation and other populations.

2.3.5 Gait training

A common goal of gait training in rehabilitation is to improve inter-limb symmetry. Restoring symmetry is the goal for various ailments afflicting people, from a young athlete with an anterior cruciate ligament reconstruction or an older person who experienced a cerebral vascular accident (stroke). The effect of improving symmetry has been investigated in many populations and with different goal parameters (e.g., stride time, stride length, ground reaction forces), yet there have been only been a few studies interested in people with lower limb amputation walking symmetrically (Davis et al., 2004, Dingwell et al., 1996; Zmitrewicz et al., 2007).

Two experimental studies (Davis et al., 2004; Dingwell et al., 1996) and one computer simulation study (Zmitrewicz et al., 2007) have constrained people with lower limb amputation to walk with inter-limb temporal symmetry. Both experimental studies provided real time visual feedback about stance and swing percentage of the stride cycle for each limb, as well as the amount of push off force in the vertical and anterior-posterior directions. Dingwell et al. (1996) compared the prosthetic and intact limbs of 6 people with unilateral transtibial amputation who received real time visual feedback while walking on a force treadmill. The subjects received various forms of feedback (e.g., push off force, stance-swing percentage) and then walked without feedback. The subjects had significant improvements in symmetry after training. These results showed people with lower limb amputation are able to improve stride asymmetry, but the effect on metabolic energy expenditure was not measured.

Davis et al. (2004) found lesser metabolic cost after training for push off force symmetry, but not after stance-swing percentage of stride training. The subjects had a mix of lower limb amputations, between above-knee (3) and below-knee (8), as well as different causes of amputation, traumatic (8, 3 above-knee and 5 below-knee) and dysvascular (3 below-knee). Even though this was a promising finding, general conclusions about metabolic cost and gait asymmetry cannot be made because of the varied subject sample.

In a modeling study, Zmitrewicz et al. (2007) used a computer modeling and simulation approach to understand the contribution of individual muscles and a prosthetic foot to symmetrical walking. They used a musculoskeletal model that had lower leg muscles removed from one side and an elastic storage and return (ESAR) prosthetic foot instead of a biological foot and ankle. The intent of the model was to mimic a person with a unilateral lower transtibial amputation by accounting for the available force-producing structures. The ESAR foot was not able to contribute to forward trunk progression as much as a biological limb. The model predicted that the intact limb's gastrocnemius and soleus needed to increase energy contribution, as well as each limb's iliopsoas, to maintain forward trunk progression. The modeling study provided insight into potential compensations that are necessary to achieve symmetrical gait for a person with a unilateral transtibial amputation, but this has not been verified experimentally. Therefore, the difference in metabolic cost between symmetrical and asymmetrical stride patterns is not fully known for people with unilateral lower limb amputations.

Rehabilitation programs for people after a cerebral vascular accident are designed to improve functional mobility by increasing utilization of the hemiparetic lower extremity. Awad et al. (2015) had people with chronic hemiparesis (>6 months since stroke) perform 12 weeks of walking rehabilitation with 3 sessions per week. There were

3 groups, one group trained with a self-paced walk, another group did a walk as fast as they could maintain for 4 minutes, and the final group trained to walk as fast they could with functional electrical stimulation. They found that people who could walk faster and more symmetrically at the end of the training had the greatest improvement in metabolic energy expenditure. People that either improved symmetry or could walk faster did not lead to as great of an improvement as the combination of the two.

After a cerebral vascular accident there are many gait asymmetries, and what parameter a training program targets will be the one that improves. Reisman et al. (2013) utilized a split-belt for 12 training sessions to reduce step length asymmetry. Temporal variables such as stance time were not targeted, and after training there was decreased stride length asymmetry but no improvements in stance time asymmetry. In a case series of two people post-stroke, they received 18 sessions over 6 weeks of gait training with visual and proprioceptive feedback in an immersive virtual environment with dual belt treadmill (Lewek et al., 2012). Both subjects improved gait speed, but they received different forms of feedback based on their respective asymmetry. The person who received step-length feedback had decreased step length asymmetry at the end of training but did not improve stance time asymmetry. The other subject received stance time feedback and improved symmetry by the end of the sessions.

Real time feedback has been used in other populations that have an intact neurological system, such as people post total hip arthroplasty. White and Lifeso (2005) had people at least 2 months after hip surgery walk for 15 minutes on a treadmill, 3 times a week for 8 weeks, either with or without feedback. The feedback group received feedback about step-to-step ground reaction forces. After 24 sessions, the loading rate and impulse equalized for the feedback group, but the loading rate also equalized for the non-feedback group. In the case of this study, the prolonged walking on treadmill alone improved symmetry with one parameter.

2.4 Gait Stability

2.4.1 Falls-People with lower limb amputation

People with lower limb amputation of all levels have an increased incidence of falls, more commonly for people with transfemoral amputation than transtibial amputation (Gauthier-Gagnon et al., 1999; Kulkarni et al., 1996; Miller et al., 2001(a)). Due to an increased incidence of falls, there is an increased fear of falling (Miller et al., 2001(a); Kulkarni et al., 1996), that may contribute to decreased mobility. Even in young people with lower limb amputation, both transtibial and transfemoral, falls occurred in 87.5% of a sample within the first 6 months of amputation (Felcher et al., 2015). After the first 6 months, 50% of people with lower limb amputation fall at least once per year (Miller et al., 2001(a); Miller et al., 2001(b)). As a result of falling, 40.4% resulted in an injury and 19.3% of those injuries resulted in medical attention (Miller et al., 2001(a); Miller et al., 2001(b)). In the case of people with amputation due to vascular causes, which is more common than traumatic causes, a fall could result in a worse medical outcome (Seth & Lamberg, 2017). The increased incidence and fear of falling has an effect on willingness to be physically active and overall quality of life. With decreased mobility and overall physical activity, people are at greater risk for other pathologies, such as heart disease and diabetes (Booth et al., 2012). Preventing falls for people with lower limb amputation should be one of the primary goals with rehabilitation. In order to prevent falls, gait stability needs to be assessed for people with lower limb amputation wihile walking and when perturbed.

2.4.2 Global stability

Global stability can be defined as a person's ability to resist external perturbations (e.g., trips and slips) (Dingwell et al., 2000). In the case of gait, a person can remain upright and continue walking, or they fall over when perturbed. Remaining upright and continuing to walk can be described as the attractor state in a dynamical system perspective, and the system remains stable if it remains directed towards the attractor (Kaplan & Glass, 1995; Strogatz, 1994). If a person remains upright and continues walking after being perturbed, then the gait pattern is stable.

2.4.3 Margin of stability

During gait, the center of mass and base of support are continuously moving, and where the center of mass is relative to the base of support can determine the stability of a gait pattern. The center of mass position-velocity limits relating to the center of mass staying within the base of support during stable standing had been established earlier (Pai & Patton, 1997). Hof et al. (2005) later developed a measure that relates center of mass motion to the base of support during walking based on an inverted pendulum model. The instantaneous velocity of the center of mass is also taken into account, and when combined with the position at that instant, the extrapolated center of mass (xCoM) is determined. The pendulum's eigen frequency is accounted for by scaling the xCoM by the length of the segment (l) and gravity (g). The equation for the extrapolated center of mass according to Hak et al. (2012):

$$\boldsymbol{xCoM = P_{CoM} + v_{CoM} \times \sqrt{l/g}}$$

The P_{CoM} is the instantaneous position of the center of mass and the V_{CoM} is the instantaneous velocity of the center of mass. The margin of stability (MoS) refers to the distance between the xCoM and the base of support (BoS) (i.e., border of the foot) (Figure 3) (Hof et al., 2005; Hof et al., 2007; Hak et al., 2012), and is represented by this equation:

$$MoS = BoS - xCoM$$

The two directions that the margins of stability are typically calculated are the backwards and medial-lateral directions (Hak et al., 2012). The backwards margin of stability is relevant because it relates to a person's ability to avoid falling forward and taking recovery steps, as well maintaining forward progression of the center of mass. The backwards margin of stability is typically calculated at terminal stance and initial contact when a fall backwards or not progressing forward is most likely to occur. The medial-lateral margin of stability is relevant because it represents a person's ability to resist a fall off to the side. The medial-lateral margin of stability is calculated throughout stance phase, with the timing during the gait cycle and magnitude of the minimum value being of greatest interest.

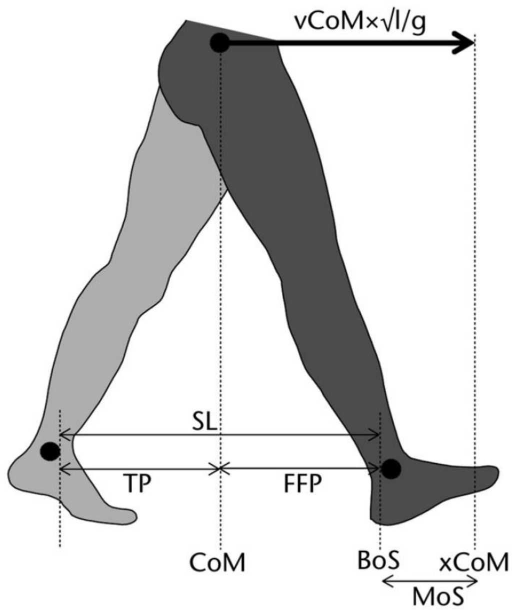

Figure 2.3: Backwards margin of stability representation. The figure from Hak et al. (2014) represents the concept of backwards margin of stability (MoS) as the extrapolated center of mass (xCoM) position relative to the base of support (BoS). The extrapolated center of mass is determined from the center of mass position plus the velocity of the center of mass (vCoM) times the square root of leg length divided by gravity ($\sqrt{l/g}$). SL = step length, TP = trunk progression, FFP = forward foot placement

2.4.4 Margin of stability: Able-bodied

Margin of stability has been quantified for overground and treadmill walking without perturbation, but more commonly has been done with a perturbation. A perturbation while walking is done to examine the stability of walking with various environmental conditions, and determine how resilient the system is in avoiding a fall. When healthy subjects walk on a treadmill and experience random medial-lateral perturbations, they do not change walking speed, but take shorter, faster, and wider steps. As a result, they increase the backwards and medial-lateral margin of stability in response to these perturbations (Hak et al., 2012). The authors proposed that changing the step length, rate and width are strategies utilized by healthy people to decrease the risk of falling. In a follow-up study by Hak et al. (2013), they manipulated stride length, stride frequency and walking speed independently to see the effects on margin of stability for healthy subjects. Medial-lateral margin of stability improved with increased stride frequency. Also, backwards margin of stability was inversely related to step length, and directly related to the walking speed. In other words, as step length decreased and walking speed increased, the backwards margin of stability increased. They concluded that focusing gait training on different stepping strategies may enhance stability and decrease the risk of falls. McAndrew Young et al. (2012) looked at backwards and medial-lateral margin of stability with healthy subjects who underwent platform and visual perturbations. The subjects had larger mean medial-lateral margin of stability in the perturbed conditions compared to un-perturbed. The authors noted that understanding how people control stability may be more related to how they changed margin of stability across steps by altering foot placement rather than the mean margin of stability. As people adapt to a task, stability may change and the ability of the system to resist a fall may increase.

2.4.5 Margin of stability: People with lower limb amputation

Margin of stability has been used to evaluate global stability of people with unilateral transtibial and transfemoral amputation. It may be an especially relevant measurement of stability for this population because a prosthetic foot produces less push off power than a biological limb, and therefore there is a decreased ability to accelerate the center of mass (Neptune et al., 2001). Hof et al. (2007) showed that people with transfemoral amputation utilized a larger step width and therefore had a larger medial-lateral margin of stability with the prosthetic side compared to the intact side and the controls across multiple speeds. Step width did decrease on the prosthetic side with increasing speed and therefore the margin of stability decreased. Also across all speeds, the intact side more closely resembled the able-bodied control limbs than the prosthetic side.

Most of the research that has been done on the margin of stability for people with lower limb amputation has been with different perturbations while walking. The reason to perturb a person while walking is to test the global stability of the system and find how much of a perturbation it can tolerate and still remain on task. In a study comparing people with unilateral transtibial amputation to able-bodied while walking on a treadmill with medial-lateral perturbation and without, the people with amputation walked slower, with a lower step frequency and wider steps in the unperturbed condition. This resulted in a larger medial-lateral margin of stability but a smaller backwards margin of stability. During the perturbation trials, the people with amputation increased medial-lateral and backwards margin of stability by decreasing step length and increasing step width, respectively (Hak et al., 2013). In a follow-up study of people with unilateral transtibial amputation, Hak et al. (2014) investigated backwards margin of stability and step length between limbs. The intact side had a shorter step length and therefore a larger backwards margin of stability compared to the prosthetic side. They concluded that inter-limb asymmetries may be a functional consequence to improve stability and deal with decreased prosthetic side push-off capacity.

The mean value of the margin of stability does not represent the progression or variability of stability, and therefore it does not fully represent progression of a task.

Gates et al. (2013) found that people with unilateral transtibial amputation had higher variability of margin of stability when walking over a loose rock surface, indicating larger step-to-step corrective responses that led to similar results as able-bodied controls doing the same task. The prosthetic side had decreased margin of stability compared to the intact side for the task. Beltran et al. (2014) compared people with unilateral transtibial amputation versus able-bodied when walking on a treadmill while experiencing medial-lateral platform and visual perturbations. The people with unilateral transtibial amputation exhibited significantly greater mean and variability of medial-lateral margin of stability compared to the able-bodied. The two groups responded in a similar way with unperturbed and visually perturbed walking, but people with amputation were most affected by the platform perturbations.

2.4.6 Effect of asymmetry on able-bodied gait stability

The effect of inter-limb asymmetry on stability has been demonstrated with people with amputation in regards to global stability (Hak et al., 2013; Hak et al., 2014). A major limitation of those studies was not determining the amount of global stability for people with the lower limb amputation when walking symmetrically. The effect of inter-limb asymmetry on global stability has not been shown with able-bodied people either, but there has been recent work on the effect of asymmetry on local stability. Local stability is the human's capacity to resist very small perturbations that occur with tasks such as walking (Kang & Dingwell, 2008(a); Kang & Dingwell, 2008(b)). Ducharme & van Emmerik (2016) showed that anterior-posterior and medial-lateral local dynamic stability, as measured by the maximal finite-time Lyapunov exponent, decreased with increasing gait asymmetry. Interestingly, after repeated trials, vertical and medial-lateral local stability was regained but decreased local stability persisted in the anterior-posterior direction. (Ducharme & van Emmerik, 2016). These results are promising for future investigation into global gait stability with asymmetry.

CHAPTER 3

PROPOSED METHODS

The principle objective of this dissertation is to better understand how people with unilateral below-knee amputation regulate their locomotion, with a specific focus on stride asymmetries, metabolic cost and gait stability. People with unilateral amputations generally have prosthetic and intact side asymmetries in temporal-spatial (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997), kinematic (Sanderson & Martin, 1997), and kinetic (Sadeghi et al., 2001; Sanderson & Martin, 1997; Silverman et al., 2008; Winter & Sienko, 1988) stride measures, while people without amputation generally do not (Hamill et al., 1984). For people with unilateral lower limb amputation, the impacts of inter-limb asymmetry on metabolic cost and stability have not been established in the literature. Few studies have had people with lower limb amputation walk with symmetrical temporal stride characteristics using real time visual feedback (Dingwell et al., 1996; Davis et al., 2004), with assessing metabolic cost being the focus of only one study (Davis et al., 2004), and none assessing gait stability. To better understand the effects of temporal asymmetry on metabolic cost and gait stability, subjects will be constrained to walk with symmetrical stance times and varying degrees of asymmetry, while metabolic cost and global stability are measured.

3.1. Study 1- Stance Symmetry and Metabolic Cost of Locomotion in People with Unilateral Transtibial Amputation

3.1.1 General Introduction

The focus of study one will be to determine the effects of inter-limb stance time asymmetry on metabolic energy expenditure in people with unilateral transtibial amputation and those without. The two subject populations will walk at their preferred speed with preferred stride characteristics as a reference and then will be constrained to walk with symmetric stance times and varying degrees of asymmetry using real time visual feedback. The aim of this study is to compare metabolic energy expenditure for people with unilateral transtibial amputation versus those without, as well as the differences between preferred and constrained asymmetry conditions within each subject. The results of this study will show how metabolic energy expenditure is affected by stance time asymmetry for people with and without unilateral transtibial amputation. I hypothesize that metabolic cost versus inter-limb asymmetry will demonstrate a U-shaped curve with the lowest metabolic cost occurring with preferred stride characteristics for both groups.

3.1.2 Participants

The study will consist of 20 subjects, 10 subjects with a unilateral below-knee amputation and 10 able-bodied controls, as determined by a sample size estimation for a global effects MANOVA with $\alpha = 0.05$ using G*Power 3.1 (Faul et al., 2009) (Table 1). The reason for amputation can be due to trauma, cancer, or congenital defect, and the person must be designated at a K3 or K4 level (i.e., the person has the ability or potential for ambulation with variable cadence). The subjects will be matched for sex, age, and BMI as best as possible. All subjects will be between the ages of 18-50 and free of other factors (aside from the amputation) that limits walking ability (e.g., neurological and cardiovascular disorders). The subjects with amputation will be at least 1 year post-amputation. Subjects who have had a musculoskeletal injury or surgery that effects walking in the previous 12 months, will be excluded from this study. All subjects will be asked for fall history within the last 2 years.

Table 3.1: Sample size estimation.

Study	Dependent Variable	Effect Size	Sample Size Estimation
Dingwell 1996	Symmetry index % stance time	2.550	8
Ellis 2013	Metabolic cost	4.417	6
Davis 2004	Metabolic cost	0.573	26
Hak 2013	Backward MoS	1.264	14
Hak 2013	Medial-lateral MoS	1.621	12
Hak 2013	Step width	1.550	12

Sample size estimation based on studies with similar independent and dependent variables using G*Power 3.1 for a global effects MANOVA with $\alpha = 0.05$.

3.1.3 Protocol

Data collection will occur over two days (Figures 3.1 and 3.2) so subjects can receive familiarization with real time visual feedback for symmetry and varying levels of asymmetry.

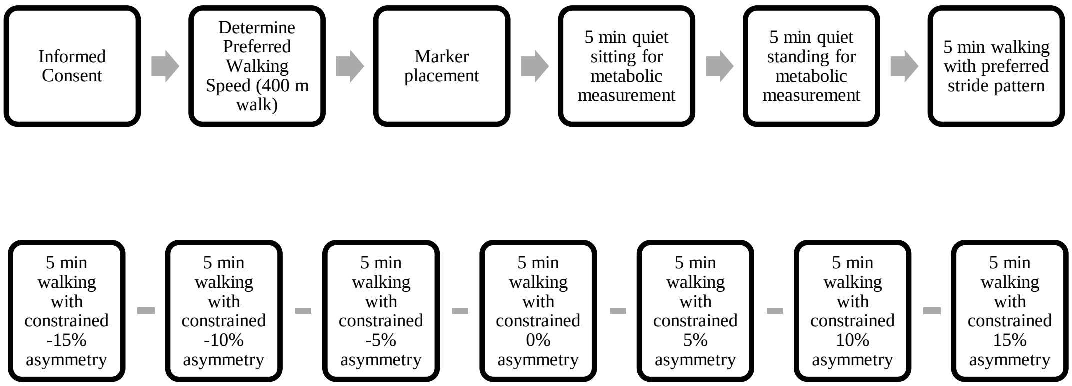

Figure 3.1: Protocol for Day 1. The protocol for data collection on day one. All walking trials will be in randomized order except for preferred stride pattern (bottom row). Subjects with amputation will not perform the -15% condition. 3 minute rest periods between conditions not pictured.

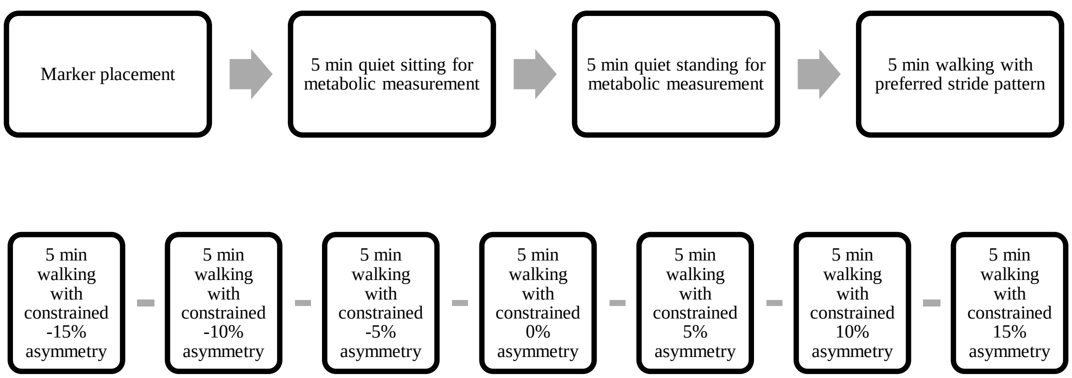

Figure 3.2: Protocol for Day 2. The protocol for data collection on day two. All walking trials will be in randomized order except for preferred stride pattern (bottom row). Subjects with amputation will not perform the -15% condition. 3 minute rest periods between conditions not pictured.

The subjects will be doing a familiarization day in which they will explore the asymmetry space without metabolic cost measurement so that they can focus on learning the different asymmetry patterns. On both days, the subjects will walk with their preferred stride characteristics, then be constrained to walk symmetrically (0%), followed by randomly order stance time asymmetry at -15%, -10%, -5%, 5%, 10%, and 15% conditions using real time visual feedback. The real time visual feedback will be a graphical display of a two stride stance time symmetry index. Positive values indicate greater stance time on the intact limb for people with lower limb amputation, and the dominant limb for able-bodied subjects. Negative values indicate greater stance time on the prosthetic limb and non-dominant side, respectively, and will be limited to -10% because of potential demands of time for the subjects and avoiding effects of fatigue. To further avoid the effects of fatigue, subjects will be given 3 minutes of seated rest after each walking trial (not pictured in figure). The subject's pain, level of fatigue and perceived exertion will be assessed at the end of each condition. To assess pain, subjects will be asked to report pain level from 0-10, with 0 being no pain and 10 being extreme pain. To assess fatigue, subjects will mark a 10 centimeter visual analog scale with 0 being no fatigue and 10 being extremely exhausted. To assess perceived exertion, subjects will rate between 1-10, with 1 being at rest and 10 being extremely difficult.

3.1.4 Metabolic Energy Expenditure and Cost of Transport

Metabolic energy expenditure will be determined from pulmonary gas exchange via open-circuit spirometry (Parvo Medics, Sandy, UT). The gross rate of metabolic energy expenditure will be estimated from the approach developed by Brockway (1987) that is based on the amount of oxygen consumed and the amount of carbon dioxide produced. The equation for energy expenditure developed by Brockway (1987) is:

$$Energy\ Expenditure\ (kJ) = 16.58\ O_2 + 4.51\ CO_2 \quad \text{(Eqn. 1)}$$

O_2 and CO_2 are the volumes of oxygen and carbon dioxide involved in respiratory exchange. The breath-by-breath relative rate of oxygen ($\dot{V}O_2$) (ml•kg^{-1}•min^{-1}) consumption and relative rate of carbon dioxide ($\dot{V}CO_2$) (ml/kg/min) production will be averaged every 5 seconds for 5 minutes, with the last 2 minutes being averaged if steady state is attained (Ellis et al., 2013). Steady state will be defined as when the variability in $\dot{V}O_2$ is <2.0 mL/kg/min (Taylor et al., 1955). If steady state is not attained by the third minute, an additional minute will be added to the trial. Each trial will be 5 minutes in length unless steady state is not achieved, and after each walking trial, subjects will rest for 3 minutes. If subjects cannot achieve steady state by the fourth minute, he or she will rest and move on to the next condition. Subjects will be given 5 minutes of quiet sitting after initially donning the metabolic equipment to become accustomed to the set-up and then resting $\dot{V}O_2$ will be collected during 5 minutes of quiet standing before the walking trials. Net metabolic energy expenditure will be derived by subtracting the energy expenditure during quiet standing from the gross energy expenditure during the walking trials.

Cost of transport is the amount of energy expended per unit distance traveled (Ralston, 1958). Net cost of transport will be calculated by dividing the rate of metabolic energy expenditure by walking speed ($m \cdot s^{-1}$) and body mass (kg) (Ralston, 1958). Because the measure takes into account the speed of each subject, it normalizes data for subjects with different preferred walking speeds. This is especially important for people with lower limb amputation who typically have a slower preferred walking speed compared with able-bodied (Skinner & Effeny, 1985). The net cost of transport will be calculated for each walking condition for each subject.

3.1.5 Preferred Walking Speed

Preferred walking speed will be determined with an overground 400 meter walk test. Subjects will complete twenty 20 meter lengths consecutively after being instructed to walk at a "comfortable walking speed" and a six meter segment of each length will be timed. Preferred overground walking speed instead of preferred treadmill walking speed will be used as the treadmill speed to avoid the potential for higher oxygen cost with a treadmill-determined preferred walking speed (Dal et al. 2010).

3.1.6 Stance Asymmetry

Stance time will be determined from insole foot switches (B&L Engineering, Santa Ana, CA) and a custom MATLAB (Math Works, Natick, MA) program. The amount of asymmetry between limb stance times will be calculated using an asymmetry index (Dingwell et al. 1996):

$$Asymmetry_{AMP} = \frac{Intact\ stance\ time - Prosthetic\ stance\ time}{Intact\ stance\ time + Prosthetic\ stance\ time} \times 100\% \quad \text{(Eqn. 2)}$$

$$Asymmetry_{CONTROL} = \frac{Dominant\ stance\ time - nondominate\ stance\ time}{Dominate\ stance\ time + nondominant\ stance\ time} \times 100\% \quad \text{(Eqn. 3)}$$

$Asymmetry_{AMP}$ is the asymmetry index for the subjects with an amputation, and $Asymmetry_{CONTROL}$ is the asymmetry index for the able-bodied controls. Equation 1 will be used to calculate the amount of stance time asymmetry for people with amputation, and equation 2 will be used to calculate the same metric for able-bodied subjects. The subjects will walk on a treadmill with preferred stride characteristics and the stance asymmetry in the fifth and final minute will be considered the preferred stance time pattern. After the preferred trial, a graphical display of a two-stride moving average of the symmetry index will be displayed on a screen in front of the treadmill. The subjects will be instructed to attain symmetry or various levels of asymmetry through the real time visual feedback display (see protocol). The subjects will experience the different conditions on day 1 without metabolic energy expenditure collection.

3.1.7 Statistical Analyses

The overall effects of stance time asymmetry on cost of transport between the two groups will be tested with a 2 (group) x 6 (asymmetry condition) MANOVA. A MANOVA will be used instead of multiple ANOVAs to analyze all possible interactions between groups and conditions. The false discovery rate procedure (Benjamini &

Hochberg, 1995) will be used for post-hoc multiple comparison testing in the event of significant main effects of asymmetry. Polynomial regression analysis will be performed to find the statistical minimum net cost of transport for each group, and polynomial contrast analysis (Keppel, 1991) will be performed to determine the mathematical relationship of net cost of transport to amount of asymmetry within each group. The net cost of transport at the preferred stance time asymmetry for each group will be compared with a paired t-test. Alpha level will be set at 0.05 for all statistical tests. Statistical analyses will be performed using R-Studio version 3.0.2 (R-Studio Inc., Boston, MA).

3.2 Study 2 – Stance Symmetry and Global Stability of Locomotion in People with Unilateral Transtibial Amputation

3.2.1 General Introduction

The focus of study two will be to determine the effect of inter-limb stance time asymmetry on global gait stability. The two subject populations will walk with preferred stride characteristics as a reference and then will be constrained to walk with symmetric stance times and varying degrees of asymmetry using real time visual feedback. The aim of this study is to compare gait stability for people with unilateral transtibial amputation versus those without, as well as the differences between preferred and constrained asymmetry conditions within each subject. The results of this study will show how gait stability is affected by stance time asymmetry for people with and without unilateral transtibial amputation. I hypothesize that gait stability versus inter-limb asymmetry will demonstrate an inverted U-shaped curve with the greatest stability occurring at the preferred stride characteristics for both groups.

3.2.2 Participants

Study 2 will be using the same subjects as study 1.The study will consist of 20 subjects, 10 subjects with a unilateral below-knee amputation and 10 able-bodied controls, as determined by a power analysis based on similar studies (Table 1). The reason for amputation can be due to trauma, cancer, or congenital defect, and the person must be designated at a K3 or K4 level (i.e., the person has the ability or potential for ambulation with variable cadence). The subjects will be matched for sex, age, and BMI as best as possible. All subjects will be between the ages of 18-50 and free of other factors (aside from the amputation) that limits walking ability (e.g., neurological and cardiovascular disorders). The subjects with amputation will be at least 1 year post-amputation. Subjects who have had a musculoskeletal injury or surgery that effects walking in the previous 12 months, will be excluded from this study. All subjects will be asked for fall history within the last 2 years.

3.2.3 Protocol

The protocol utilized in study one will be the same for study two (Figures 3.1 and

3.2.4 Stability Variables

The stability variables of interest are step length variability, step width variability, step time variability, medial-lateral margin of stability, and backwards margin of stability. Step length, width and time variability will be determined from the standard deviation of all steps in the final two minutes of each five minute trial. Step length, step time and step width represent the end kinematic result (i.e., foot placement) for the entire lower extremity movement. The amount of variability in step length, step time and step width represent the kinematic consistency, and with increased variability there may be a higher probability of a fall (Bruijn et al., 2013). The medial-lateral and backwards margin of stability represent control of the whole body center of mass during gait based on inverted pendulum dynamics (Hof, 2007). The margin of stability is based on extrapolation of the center of mass position relative to the base of support and may indicate when the body needs to adapt its motion away from inverted pendulum-like dynamics to avoid a fall (Hof, 2007; Bruijn et al., 2013).

3.2.5 Kinematic Model

Kinematics will be collected with a full body marker set at a rate of 240 Hz, and then processed using Qualisys Track Manager software (QTM, Göteborg, Sweden). The kinematics will be collected at the same time as metabolic energy expenditure (see Study 1). The kinematic model will consist of 12 segments: 2 feet, 2 shanks, 2 thighs, 2 upper arms, 2 forearm plus hands, pelvis and head-trunk segments. Markers will be placed over the following landmarks: head, C7 and T12 spinous processes, sternal notch, xiphoid process, sacrum, bilateral acromium processes, lateral humeral epicondyles, radial styloids, anterior superior iliac spines, iliac crests, posterior superior iliac spines, greater trochanters, lateral femoral epicondyles, medial femoral epicondyles, lateral malleoli, medial malleoli, fifth metatarsal heads, first metatarsal heads, tips of second toes. Marker clusters will be placed on bilateral heels, shanks and thighs. The kinematic model will be used to calculate the center of mass for each subject.

3.2.6 Calculating Margin of Stability

Margin of stability will be calculated with kinematic marker data, similar to Hak et al. (2012), which is an adaptation of the original method from Hof et al. (2005). Hof et al. (2005) utilized a force plate to determine center of mass kinematics (position and velocity) relative to the base of support (center of pressure). Hak et al. (2012) utilized pelvis markers to calculate center of mass kinematics and foot markers to determine base of support location. The center of mass position and velocity throughout the stance phase for each foot will be determined in Visual 3D (Germantown, MD) and used to calculate the extrapolated center of mass. The equation for the extrapolated center of mass according to Hak et al. (2012) is:

$$\boldsymbol{xCoM = P_{CoM} + v_{CoM} \times \sqrt{l/g}}$$

The P_{CoM} is the instantaneous position of the center of mass and the V_{CoM} is the instantaneous velocity of the center of mass. The velocity will be scaled by the pendulum's eigenfrequency (i.e., $\sqrt{(\frac{gravity}{leg\ length})}$). The base of support will be determined from the lateral marker on the heel cluster for the backwards margin of stability, and the 5th metatarsal marker for the medial-lateral base of support. The general equation for calculating margin of stability (Hof et al., 2005; Hof et al., 2007; Hak et al., 2012) is:

$$MoS = BoS - xCoM$$

The extrapolated center of mass relative (xCoM) to the base of support (BoS) in the medial-lateral and backwards directions (i.e., margin of stability) will be calculated throughout stance phase for each leg.

3.2.7 Stance Symmetry and Asymmetry

Stance time will be determined from insole foot switches (B&L Engineering, Santa Ana, CA) and a custom MATLAB (Math Works, Natick, MA) program. The amount of asymmetry between limb stance times will be calculated using an asymmetry index (Dingwell et al. 1996):

$$Asymmetry_{AMP} = \frac{Intact\ stance\ time - Prosthetic\ stance\ time}{Intact\ stance\ time + Prosthetic\ stance\ time} \times 100\% \quad \text{(Eqn. 2)}$$

$$Asymmetry_{CONTROL} = \frac{Dominant\ stance\ time - nondominate\ stance\ time}{Dominate\ stance\ time + nondominant\ stance\ time} \times 100\% \quad \text{(Eqn. 3)}$$

$Asymmetry_{AMP}$ is the asymmetry index for the subjects with an amputation, and $Asymmetry_{CONTROL}$ is the asymmetry index for the able-bodied controls. Equation 1 will be used to calculate the amount of stance time asymmetry for people with amputation, and equation 2 will be used to calculate the same metric for able-bodied subjects. The subjects will walk on a treadmill with preferred stride characteristics and the stance asymmetry in the fifth and final minute will be considered the preferred stance time pattern. After the preferred trial, a graphical display of a two-stride moving average of the symmetry index will be displayed on a screen in front of the treadmill. The subjects will be instructed to attain symmetry or various levels of asymmetry through the real time visual feedback display (see protocol). The subjects will experience the different conditions on day 1 with kinematic marker collection.

3.2.8 Statistical Analyses

The overall effects of stance time asymmetry on gait stability between the two groups will be tested with a 2 (group) x 6 (asymmetry condition) MANOVA. Gait stability measures include backward margin of stability at heel strike, minimum medial-lateral margin of stability during stance, step width and step width variability. The false discovery rate procedure (Benjamini & Hochberg, 1995) will be used for post-hoc multiple comparison testing in the event of significant main effects of asymmetry. Polynomial regression analysis will be performed to find the statistical maximum margin of stability for each group, and polynomial contrast analysis (Keppel, 1991) will be performed to determine the mathematical relationship of margin of stability to amount of asymmetry within each group. The backwards margin of stability at heel strike, minimum medial-lateral margin of stability during stance, step width and step width variability at the preferred stance time asymmetry will be compared between groups with a paired t-test. Alpha level will be set at 0.05 for all statistical tests. Statistical analyses will be performed using R-Studio version 3.0.2 (R-Studio Inc., Boston, MA).

CHAPTER 4

AMMENDMENTS TO THE PROPOSED EXPERIMENTS

This chapter describes the changes made between the proposed studies and the subsequent chapters. The studies have maintained nearly all of the originally proposed outlines. For both studies, the subject age range was changed from 18-50 years old to 16-50 years old due to recruitment issues. People between 16-17 years old demonstrate similar gait mechanics compared with people who are 18-50 years old, therefore the change in age, should have not effected the results of these studies. Also due to recruitment issues, 2 subjects participated in this study at a second site (Quinnipiac University (North Haven, CT)). Every effort was made to minimize differences between collection sites.

For study 1, metabolic energy expenditure was determined from the final minute of each condition to ensure that the subjects had attained steady state. Most subjects achieved steady state by the third minute of each condition, but in the case of the more extreme asymmetry conditions, steady state was attained in the middle of the fourth minute.

For study 2, I had initially hypothesized that all stability metrics would exhibit an inverted U-shape for the gait stability-asymmetry relationship, with the greatest stability occurring with the preferred condition. After further discussions, I realized that variability measures should be hypothesized to have a U-shaped relationship, with the least variability during the preferred conditions, because greater variability has been correlated to greater fall risk, and when subjects are walking with preferred patterns, fall risk should be low. I originally proposed that I would calculate the stability measures for the final 2 minutes of walking, but instead I calculated the stability measures for 20 strides during the last minute of each collection, when the subjects were walking at steady state metabolically. I initially proposed I would do a 2 (group) x 6 (condition) MANOVA for each study, but instead I performed a one-way ANOVA for study 1 and multiple two-way ANOVAs to compare limbs for study 2 across conditions. Also, once I calculated the asymmetries that corresponded to the optima of each stability metric for each subject, I performed an ANOVA for each stability measure to compare limbs.

CHAPTER 5

STANCE SYMMETRY AND METABOLIC COST OF LOCOMOTION IN PEOPLE WITH UNILATERAL TRANSTIBIAL AMPUTATION

5.1 Abstract

It is generally accepted that metabolic energy expenditure is one of the key factors that influences the selection of able-bodied gait patterns, but it is unclear how energy expenditure is prioritized relative to other factors (e.g., stability, smoothness) during walking in people with lower limb amputation. People with lower limb amputation generally have greater metabolic energy expenditure during walking compared with able-bodied individuals. People with unilateral amputation consistently demonstrate inter-limb asymmetries, most visibly, spending more time on the intact limb compared with the prosthetic limb, while able-bodied individuals, generally, walk with symmetrical stance timing. The purpose of this study was to determine the effects of stance symmetry and asymmetry on the metabolic cost of transport. We hypothesized that for preferred gait patterns the subjects with unilateral transtibial amputation would exhibit greater stance time on the intact side compared with the prosthetic side, while able-bodied subjects would exhibit symmetrical stance times. Further, we hypothesized that the cost of transport versus inter-limb asymmetry would demonstrate a U-shaped curve for both groups, and the cost of transport would be least at preferred stride characteristics for both groups. Cost of transport was determined for 7 subjects with unilateral transtibial amputation and 7 able-bodied controls while walking with preferred and non-preferred (± 15% in 5% increments of relative stance time between limbs) stance time conditions at preferred speed on a treadmill. Subjects with amputation had a significantly greater

stance time asymmetry (4.34 ± 1.09%) compared with able-bodied subjects (0.94 ± 2.44%) during the preferred walking condition with a very large effect size ($p = 0.008$, $d = 1.93$). A quadratic trend best explained the relationship between cost of transport and stance time asymmetry for both groups ($p < 0.001$). The asymmetries corresponding to minimum-cost of transport were not significantly different than the preferred asymmetries for both groups. If asymmetrical patterns naturally emerge in people with many years of prosthesis use, perhaps some degree of gait asymmetry should be expected and should be a goal for rehabilitation and devices. Given the sample size and the focus on only one potentially important factor, metabolic cost, our results should be interpreted cautiously. Nevertheless, they raise the possibility that asymmetrical patterns may be the best result after some injuries and do not represent a problem that should be fixed.

5.2. Introduction

It is generally accepted that metabolic energy expenditure is one of the key factors that influences the selection of able-bodied locomotor patterns, along with other likely factors such as stability, smoothness and joint loading. It is unclear how energy expenditure is prioritized relative to other factors during walking in people with lower limb amputation. People with lower limb amputation generally have greater metabolic energy expenditure during walking (Waters & Mulroy, 1999; Waters et al., 1976) compared with able-bodied individuals. Greater metabolic energy expenditure while walking can negatively impact function and quality of life (Pell et al., 1993). An objective of gait research should be to understand why metabolic energy expenditure is usually greater during walking in people with lower limb amputation, which will allow interventions to be created that can be tailored to reduce energy expenditure.

People with unilateral amputation commonly demonstrate inter-limb asymmetry when walking, while able-bodied individuals, on average, walk nearly symmetrically. People with unilateral amputations typically have asymmetries between the prosthetic and intact sides for temporal-spatial (i.e., stride time and length) (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997), kinematic (Sanderson & Martin, 1997), and kinetic (Sadeghi et al., 2001; Sanderson & Martin, 1997; Silverman et al., 2008; Winter & Sienko, 1988) stride measures. A consistent finding is that people with unilateral amputations spend more time on the intact side compared with the prosthetic side during stance. While there are some exceptions in the literature (e.g., Gunderson et al., 1989), able-bodied people typically demonstrate nearly symmetrical inter-limb stride kinematics (Forczek & Staszkiewicz, 2012; Hannah et al., 1984) and kinetics (Eng &

Winter, 1995; Hamill et al., 1984; Seeley et al., 2008) for preferred walking conditions. When inter-limb stride differences are reported for able-bodied people they are not always statistically significant, nor as bilaterally consistent as the asymmetries people with unilateral amputation exhibit. The connections between gait asymmetry in people with unilateral lower limb amputation and metabolic cost are unclear. Since energy expenditure is an important criterion for self-selected gait patterns, people with lower limb amputation may be minimizing metabolic cost by using an asymmetrical gait pattern. Conversely, it could be that promoting symmetric gait could reduce metabolic energy expenditure for people with lower limb amputation. Understanding these issues is important for effective rehabilitation strategies.

Restoring inter-limb symmetry is often a clinical goal with rehabilitation and assistive devices (e.g., lower limb exoskeletons). People walk with asymmetrical characteristics (e.g., antalgic pattern, or "a limp") after an acute musculoskeletal injury (e.g., ankle sprain) (Punt et al., 2015) and surgery (e.g., amputation, total joint arthroplasty) (Sanderson & Martin, 1997; Alnahdi et al., 2011). In the case of less severe injuries such as a sprain, symmetry is restored with time and rehabilitation; however, a return to gait symmetry may not be a realistic goal for more severe injuries or surgeries. People with lower limb amputation have altered morphology and usually must rely on a passive (i.e., no powered actuators) prosthesis in place of the missing anatomy. Depending on the cause of the amputation, there may be comorbidities affecting overall health, especially with people who have an amputation due to vascular causes such as diabetes (Roberts et al., 2006). No matter the reason for amputation, there is altered proprioception (Liao & Skinner, 1995) and muscle function (Huang & Ferris, 2012) in the residual limb. The sensory feedback from an intact foot and ankle is lost, and muscles that were used to generate most of the ground reaction force in late stance (Anderson & Pandy, 2003) have been removed or are wrapped around the distal end of the residual limb. The person will adapt their gait pattern due to the altered anatomy and reliance on a prosthesis. An asymmetrical gait pattern may be effective, given the asymmetric anatomy and device constraints. It may be that an asymmetrical gait is also optimal for metabolic energy expenditure for people with unilateral lower limb amputation, but this has not been clearly established in the literature.

Metabolic energy expenditure increases directly with the amount of asymmetry when able-bodied individuals walk with varying amounts of stride asymmetry (Ellis et al., 2013). Surprisingly, few studies (Dingwell et al., 1996; Davis et al., 2004) have trained people with unilateral lower limb amputation to walk with symmetrical stride characteristics in a research setting. In one study (Dingwell et al., 1996), people with lower limb amputation were found to improve stride (i.e., stance plus swing on one side) time and push-off force symmetry with real time visual feedback training, but metabolic energy expenditure was not measured. In another real time visual feedback study (Davis et al., 2004) in a small, heterogeneous sample (i.e., cause of amputation and amputation level), metabolic energy expenditure while walking was found to be reduced after training push-off force symmetry, but not after training stride time symmetry. It is difficult to draw firm conclusions based on existing data and more research is needed with a homogenous sample.

People with an amputation due to trauma (e.g., blast injury, car accident) generally have a lower metabolic cost of walking (Waters et al., 1976) and less stride asymmetry (Sanderson & Martin, 1997) compared with people who have lost a limb from vascular causes, while still typically being greater than able-bodied individuals (Sanderson & Martin, 1997). Also, it has been shown that preferred walking speed is greater for people with amputation due to trauma compared with people with amputation due to vascular causes, while still being slower than able-bodied individuals (Waters et al., 1976). The majority of amputations are related to vascular diseases (Zieglar-Graham et al., 2008) but because of other associated comorbidities (e.g., impaired sensation, osteoarthritis), the causes of asymmetrical gait in this population is harder to decipher due to other potential gait impairments. With the exception of one study in highly-functioning military personnel where metabolic cost and preferred speeds were equivalent to able-bodied subjects (Esposito et al., 2014), healthy young adults with unilateral transtibial amputation from non-vascular causes typically exhibit elevated cost of walking and asymmetrical gait, while generally being free from comorbidities. As such, this is an ideal population to start with, before moving on to study the larger population with amputations resulting from diabetes and related disorders.

Insights about the adaptations that are made to walk effectively with a prosthesis can be gathered by having people with unilateral transtibial amputation walk with varying degrees of stance time asymmetry, including a symmetrical condition, while determining the metabolic cost of transport (Ralston, 1958). Cost of transport, where metabolic cost is expressed per unit distance (i.e., $J \cdot kg^{-1} \cdot m^{-1}$), allows for a comparison between people with amputation and able-bodied individuals because of differences in preferred walking speed between these groups. The purpose of this study was to determine the effects of stance symmetry and asymmetry on the metabolic cost of transport. Based on previous literature regarding stride symmetry in people with and without amputation, we hypothesized that for preferred gait patterns the subjects with unilateral transtibial amputation would exhibit greater stance time on the intact side compared with the prosthetic side, while able-bodied subjects would exhibit symmetrical stance times. Further, we hypothesized that the cost of transport versus inter-limb asymmetry would demonstrate a U-shaped curve for both groups, and the cost of transport would be least at preferred stride characteristics for both groups. A direct consequence of these hypotheses was that subjects with unilateral transtibial amputation were predicted to have an elevated cost of transport when required to walk symmetrically, compared with the cost of transport for their preferred, asymmetrical gait pattern. Thus, we predicted that people with unilateral lower limb amputation walk asymmetrically, at least in part, to reduce the cost of walking.

5.3. Methods

5.3.1 Participants

Seven participants with unilateral transtibial amputation and seven able-bodied subjects participated in this study (Table 1). The subjects with unilateral transtibial amputation were between 16-48 years old, rated a Medicare activity classification of K3 or K4, had the amputation more than one year ago due to non-vascular causes (e.g., trauma, cancer, congenital), and use a passive prosthesis. Further details about the subjects with amputation are provided in Table 2. People with an activity level rating of K3 or K4 are prescribed an energy storage with elastic return prosthetic foot and ankle because they are active and can walk with variable cadences. Participants were excluded from the study if they had any condition, other than amputation, that affected their ability to walk (e.g., chronic pain, neurological or cardiovascular disorders), if they had lower limb surgery in the last year, were not between 16-50 years old and were rated at a K0, K1, or K2 activity level. The able-bodied subjects were age, sex, height and mass matched as closely as possible. This study was approved by the University of Massachusetts and Quinnipiac University Institutional Review Boards. All subjects read and signed an informed consent document prior to participation.

Table 5.1: Subject characteristics

Group	Females/ males (#)	Age (yrs)	Height (m)	Mass (kg)	Side: amp or dom	Years since amp
AMP	2/5	36.6 ± 12.5	1.80 ± 0.08	83.9 ± 18.9	5 right/ 2 left	16.5 ± 11.7
CNTL	2/5	28.7 ± 5.4	1.63 ± 0.37	85.4 ± 20.4	7 right/ 0 left	-
***p*-value**	-	0.194	0.334	0.585	-	-
Effect size	**-**	**0.883**	**0.756**	**0.076**	**-**	**-**

Characteristics of the subjects with amputation (AMP) and able-bodied subjects (CNTL). Values are mean ± 1 SD. AMP = people with amputation, amp = amputation, dom = dominant.

Table 5.2: Subjects with amputation characteristics

Subject	Amputation cause	Years since amputation	Prosthesis ankle	Suspension type
S01	Congenital	28	Ossur Vari-Flex	End-bearing
S02	Congenital	24	OssurVari-Flex	End-bearing
S03	Trauma	4.4	Ossur Pro-Flex	Pin
S04	Trauma	3	Ottobock Sprinter	Suction
S05	Trauma	25	Ossur Cheetah Xplore	Suction
S06	Trauma	2	Freedom Innovations Kinterra	Pin
S07	Cancer	29	Ossur Vari-Flex	Suction

5.3.2 Protocol

The subjects attended two sessions, 12 subjects (5 with amputation and 7 able-bodied) participated at the Biomechanics Laboratory at the University of Massachusetts Amherst (Amherst, MA) and 2 subjects with amputation participated at the Motion Analysis Laboratory at Quinnipiac University (North Haven, CT). During these sessions, the subjects walked on a treadmill (Treadmetrix, Park City, UT at UMass, and Woodway, Waukesha, WI at Quinnipiac) at their preferred overground walking speed while receiving real time visual feedback about inter-limb stance time asymmetry. In the first session, preferred overground walking speed was determined, followed by training with the real-time visual feedback conditions without metabolic measurement. In the second session, the real-time visual feedback conditions were repeated on the treadmill while metabolic data were collected. Each walking trial was five minutes long. The asymmetry feedback conditions were -15% to 15% in 5% increments, with 0% representing symmetric stance time between limbs. Positive values indicated greater stance time on the intact limb for subjects with lower limb amputation, and the dominant limb for able-bodied subjects. Negative values indicated greater stance time on the prosthetic limb and non-dominant limb, respectively. Subjects with an amputation did not perform the -15% condition because this extreme condition was not attainable during pilot testing. To avoid the effects of fatigue, subjects were given five minutes of seated rest after each walking trial. Subjects reported their perceived exertion on a scale from 1-10 (i.e., 1 was resting and 10 was extremely difficult) during each condition.

5.3.3 Stance time asymmetry

Stance time was determined from insole foot switches (B&L Engineering, Santa Ana, CA) and a custom MATLAB (Math Works, Natick, MA) program. The amount of asymmetry between limb stance times was calculated using an asymmetry index (Dingwell et al. 1996):

$$Asymmetry_A = \frac{Intact\ stance\ time - Prosthetic\ stance\ time}{Intact\ stance\ time + Prosthetic\ stance\ time} \times 100\% \quad \text{(Eqn. 1)}$$

$$Asymmetry_C = \frac{Dominant\ stance\ time - nondominate\ stance\ time}{Dominate\ stance\ time + nondominant\ stance\ time} \times 100\% \quad \text{(Eqn. 2)}$$

Asymmetry$_A$ is the asymmetry index for the subjects with an amputation, and *Asymmetry$_C$* is the asymmetry index for the able-body subjects. The real-time visual feedback was provided via a graphical display of a two-stride moving average of the stance time symmetry index. During pilot testing, we found that a two-stride moving average permitted subjects to make consistent adaptations to meet the asymmetry goal without having differences from stride-to-stride displayed that were too large (i.e., no averaging) or too small (i.e., three to four stride average).

5.3.4 Preferred walking speed

Preferred walking speed was determined with an overground 400 meter walk that consisted of twenty consecutive 20-meter lengths. A six-meter segment of each length was timed with photogates. The subjects were instructed to walk at a "comfortable walking speed." A 400 meter test was used rather than a shorter test because each individual treadmill trial was five minutes long and the length of a walking test may affect preferred walking speed determination. Overground speed was used because it matches habitual speed more closely (Malatesta et al., 2017).

5.3.5 Cost of transport

Metabolic energy expenditure was determined from pulmonary gas exchange via open-circuit spirometry (Parvo Medics, Sandy, UT). The gross rate of metabolic energy expenditure was estimated from the approach developed by Brockway (1987) that is based on the amount of oxygen consumed and the amount of carbon dioxide produced. The breath-by-breath relative rate of oxygen ($\dot{V}O_2$) ($ml \cdot kg^{-1} \cdot min^{-1}$) consumption and relative rate of carbon dioxide ($\dot{V}CO_2$) ($ml \cdot kg^{-1} \cdot min^{-1}$) production was averaged every five seconds for the five-minute trials, with data from the last minute being averaged after steady state was attained (Ellis et al., 2013). Steady state was defined as the variability in $\dot{V}O_2$ being <2.0 ml·kg^{-1}·min^{-1} (Taylor et al., 1955). Subjects sat quietly for five minutes after donning the metabolic equipment to become accustomed to the set-up. After the five minutes of sitting, quiet standing pulmonary gases were collected for five minutes to determine the metabolic cost of standing. Net metabolic energy expenditure during walking was derived by subtracting the energy expenditure during quiet standing from the gross energy expenditure during the walking trials. Net cost of transport relative to body size was calculated by dividing the rate of metabolic energy expenditure by walking speed (m·s^{-1}) and body mass (kg) (Ralston, 1958).

5.3.6 Statistical analysis

Preferred stance time asymmetry was compared between groups with an unpaired t-test. The relationship between stance time asymmetry and cost of transport was analyzed with a one-way ANOVA. Orthogonal polynomial contrast analyses (Keppel, 1991) were performed to determine the mathematical trends describing net cost of transport versus the amount of asymmetry for each group. The highest-order statistically significant trend (e.g., linear, quadratic, cubic) was then used to estimate the degree of asymmetry corresponding to minimum metabolic cost within each group. A goodness of fit between the experimental values and trend line was determined with an r-squared value. The preferred asymmetry and predicted minimum cost asymmetry within each group was compared with a paired t-test. We also calculated effect sizes (Cohen, 1988) and defined the size of the effects based on the expanded ranges defined by Sawilowsky (2009), with: d = 0.1 being a very small, d = 0.2 a being small, d = 0.5 being a medium, d

= 0.8 being a large, d = 1.2 being a very large, and d = 2.0 being a huge effect size. The relationship between stance time asymmetry and rating of perceived exertion was analyzed with a 2 (group) x 6 (asymmetry condition) MANOVA. Statistical analyses were performed using R-Studio version 3.2.2 (R-Studio Inc., Boston, MA).

5.4 Results

Subjects with amputation had a significantly greater stance time asymmetry (4.34 ± 1.09%) compared with able-bodied subjects (0.94 ± 2.44%) during the preferred walking condition with a very large effect size ($p = 0.008$, $d = 1.93$) (Figure 5.1, Table 5.1). This finding indicates that people with unilateral transtibial amputation spend more time on the intact side than the prosthetic side, and the inter-limb difference is greater in people with amputation than able-bodied subjects. A quadratic trend best explained the relationship between cost of transport and stance time asymmetry for both groups ($R^2_{amputee} = 0.837$, $R^2_{control} = 0.964$) (Figure 5.1). The predicted minimum-cost asymmetry (3.23 ± 2.90%) and the preferred asymmetry (4.34 ± 1.09%) for subjects with amputation were not significantly different, with a medium effect size ($p = 0.365$, $d = 0.557$). The predicted minimum-cost asymmetry (1.81 ± 2.18%) and the preferred asymmetry (0.94 ± 2.44%) for able-bodied subjects was not significantly different, with a small effect size ($p = 0.513$, $d = 0.378$). The asymmetry predicted to yield minimum cost for subjects with amputation (3.23 ± 2.90%) and able-bodied subjects (1.81 ± 2.18%) was not significantly different, with a medium effect size ($p = 0.323$, $d = 0.556$).

There was a significant main effect of group ($p = 0.047$) for the cost of transport-asymmetry relationship. There was not a significant main effect of group ($p = 0.192$) for the rating of perceived exertion-asymmetry relationship. A quadratic trend best explained the relationship between rating of perceived exertion and stance time asymmetry for both groups ($R^2_{amputee} = 0.969$, $R^2_{control} = 0.889$) (Figure 5.2).

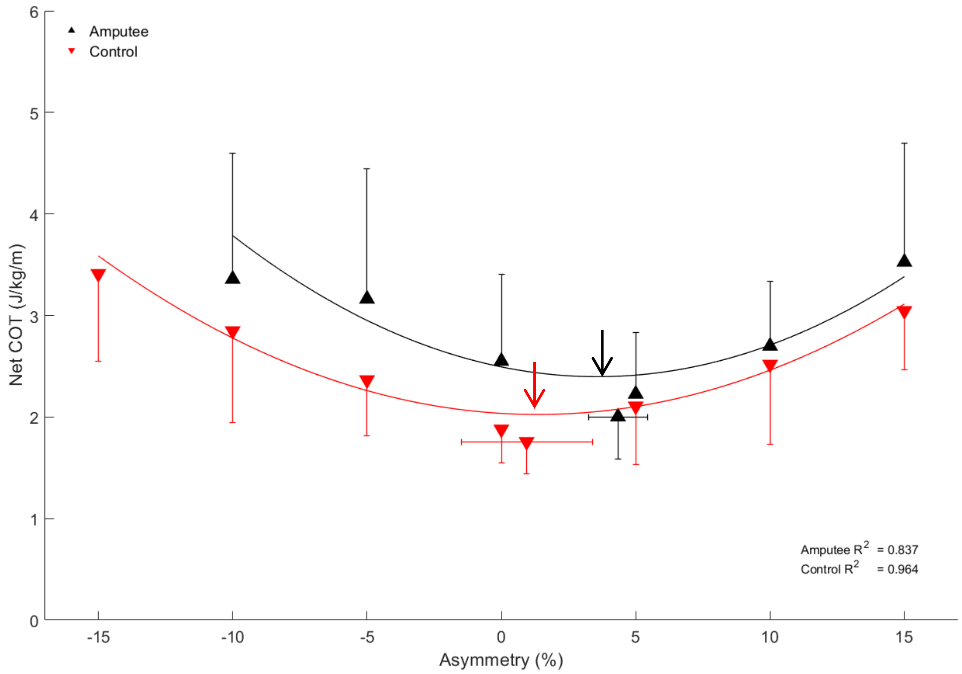

Figure 5.1: Net Cost of Transport: Net cost of transport for people with (black) and without (red) amputation across real time visual feedback conditions (vertical error bars + 1SD), and when walking with preferred patterns (horizontal error bars +/- 1 SD percent asymmetry). Quadratic trend lines for people with (black) and without (red) amputation across asymmetry conditions. Predicted asymmetry yielded by the minimum net cost of transport with the downward facing arrows. Preferred and predicted stance time asymmetry was greater (significantly greater for preferred) for people with amputation.

Table 5.3: Preferred and predicted asymmetries based on minimum-cost of transport

Group	Pref Speed ($m \cdot s^{-1}$)	Pref Asymmetry (%)	Pred Asymmetry (%)
AMP	1.13 ± 0.22	4.34 ± 1.09	3.23 ± 2.90
CNTL	1.42 ± 0.12	0.94 ± 2.44	1.81 ± 2.18
***p*-value**	0.021	0.008	0.323
d	1.71	1.93	0.556

Preferred (Pref) walking speed, preferred asymmetry and predicted (Pred) asymmetry of the people with amputation (AMP) and able-bodied subjects (CNTL). Values are mean ± 1 SD.

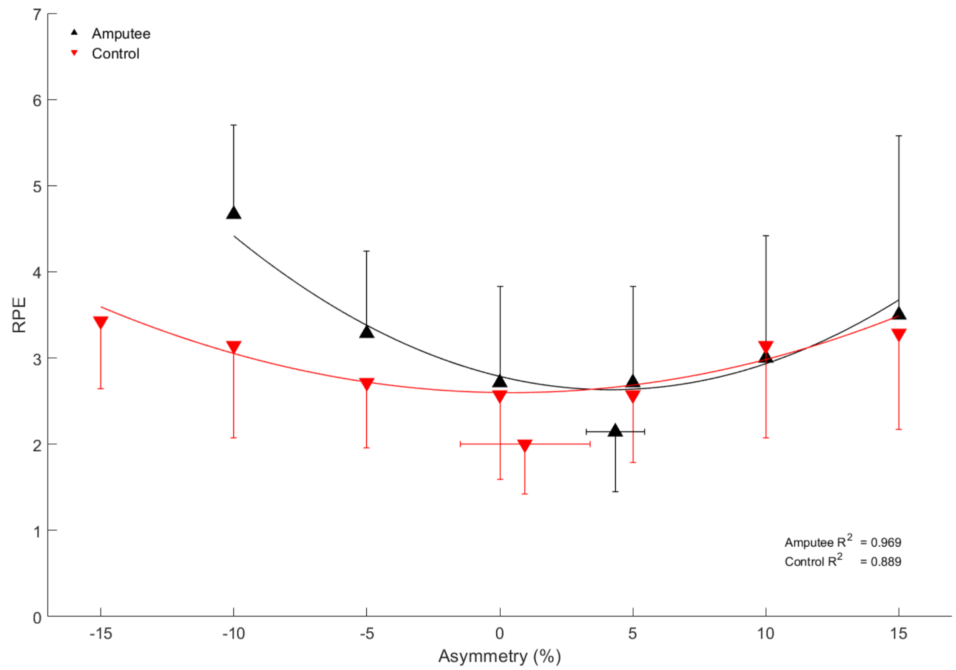

Figure 5.2: Rating of Perceived Exertion. Rating of perceived exertion for people with (black) and without (red) amputation across real time visual feedback conditions (vertical error bars + 1SD), and when walking with preferred patterns (horizontal error bars +/- 1 SD percent asymmetry). Quadratic trend lines for people with (black) and without (red) amputation across asymmetry conditions.

5.5 Discussion

The purpose of this study was to determine the effects of gait asymmetry on the metabolic cost of transport in people with and without unilateral lower limb amputation. Our hypotheses about stance time asymmetry, the cost of transport across asymmetry conditions, and the asymmetry conditions corresponding to the lowest cost of transport between groups were generally supported. Subjects with amputation had greater stance time asymmetry (i.e., more time on intact compared with prosthetic side) compared with able-bodied subjects. A quadratic, U-shaped, trend best explained the relationship between cost of transport and stance time asymmetry for both groups. Also, for both groups, the asymmetry predicted to yield the minimum cost of transport was not significantly different from preferred asymmetry. However, this latter result should be viewed cautiously, as this study may not have been adequately powered to detect such differences due to the small sample size. It is also the case that the predicted minimum-cost asymmetry for people with amputation was not significantly greater than in the able-bodied subjects, as had been the case for preferred asymmetry, though there was a moderate effect size for the minimum-cost asymmetry comparison.

Similar to previous literature, subjects with unilateral amputation chose to walk with more time on the intact limb compared with prosthetic limb (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997), and able-bodied subjects preferred more time on the dominant limb versus non-dominant limb (Vanden-Abeele, 1980), though the degree of asymmetry was less than 1% for the able-bodied subjects. The stance time asymmetries that yielded the minimum cost of transport predict greater stance time asymmetry for subjects with amputation, which agrees with the preferred asymmetries for our subjects and with previous literature.

Previous studies have consistently found greater time spent on the intact limb compared with the prosthetic limb (Skinner & Effeney, 1985; Sanderson & Martin, 1997) but in the case of able-bodied individuals, there is not a consistent trend of more time on one limb compared with the other (e.g., dominant versus non-dominant). Laterality (i.e., limb dominance) has been shown to have a significant effect on biomechanics in one study (Vanden-Abeele, 1980), but in another study, inter-limb asymmetry was found but could not be accounted for by laterality (Gunderson et al., 1989). The effect of laterality on preferred patterns with people after amputation has not been investigated recently, and laterality may stay the same or change after accommodating to a prosthesis. One study in people with amputation found that people with a left leg amputation recovered more quickly than people with a right leg amputation (Kerstein et al., 1977), indicating a potential difference in the role of right and left limbs, but the study did not indicate which limb was dominant prior to amputation. People with unilateral amputation may choose asymmetrical gait patterns because of altered anatomy and using a prosthesis, while able-bodied individuals choose near symmetrical gait patterns because of near symmetrical anatomy between limbs.

Similar to the findings of Ellis et al. (2013), there was a significant quadratic trend, with the minimum cost of transport near the preferred asymmetry (near symmetry) for able-bodied subjects. Cost of transport was lowest for our subjects with amputation when walking with asymmetrical stance timing (Figure 5.1). Since there are no other studies that have had people walk with varying degrees of inter-limb asymmetry while measuring cost of transport, there are no direct comparisons. One similar comparison that can be made is the relationship between cost of transport and walking speed. In the relationship between cost of transport and walking speed, people with amputation (Genin at al., 2008; Herr & Grabowski, 2012) and able-bodied individuals (Ralston, 1958) demonstrate a similar U-shaped trend, with greater cost of transport when walking with non-preferred walking speeds.

The process of predicting asymmetries from minimum-cost of transport is not perfect, and there are some inconclusive results (e.g., non-significant p-values with medium effect sizes). However, the lowest cost of transport experimental feedback condition was at the +5% condition for subjects with amputation, which is closest to the preferred cost of transport experimental value. The lowest cost of transport experimental feedback condition was at the symmetrical (i.e., 0%) condition for able-bodied subjects, which is closest to the preferred cost of transport experimental value. Subjects with amputation had a 49% increase in cost of transport from the 5% to -10% conditions, with 54% of that increase occurring from the 0 to -5% conditions, and 58% increase from 5 to 15% conditions, with 64% of that increase occurring from the 10 to 15% conditions. Able-bodied subjects had a 82% increase in cost of transport from the 0 to -15% conditions, with 37% of that increase occurring from the -10 to -15% conditions, and 62% increase from 0 to 15% conditions, with near equal increments in cost per 5% increase in asymmetry. One study found ~20% increase in cost of transport when increasing and decreasing speed by 0.5 $m \cdot s^{-1}$ away from preferred speed (Herr & Grabowski, 2012). The extremes of stance time asymmetry away from near-preferred experimental conditions were energetically challenging for subjects with and without amputation, which is potentially a reason why preferred patterns are not that asymmetrical for either group.

The subjects with amputation subjectively reported that the negative (i.e., more time on prosthetic limb) conditions were harder because they felt very different from usual walking. The passive energy storage and return prosthesis may be a limiting factor (Zmitrewicz et al., 2006) that could be improved with active assistance (Herr & Grabowski, 2012), but using a powered prosthesis does not always reduce metabolic energy expenditure (Quesada et al., 2016). Spending more time on the prosthesis may not feel as stable and therefore to improve stability, compensations are made that consume more metabolic energy.

Subjects with amputation perceived that spending more time on the prosthetic side was harder than more time on the intact side while able-bodied subjects perceived spending more time on either limb the same (Figure 5.2). The subjects with amputation informally reported that the conditions with more time on the prosthetic limb compared with intact limb were difficult, and the rating of perceived exertion agrees with those statements. Rating of perceived exertion is a subjective measure and because people with amputation have adapted to spend more time on the intact limb, walking with more time on the prosthetic limb may be perceived as harder because they are not as accustomed to it. To the best of the author's knowledge, there is no previous literature about the effect of asymmetry on the rating of perceived exertion in people with and without lower limb amputation.

A previous study (Esposito et al., 2014) found that people with a unilateral transtibial amputation who were still in the military, did not have a statistically different metabolic cost compared with able-bodied subjects when walking with preferred characteristics. Our results for the preferred walking conditions support that finding (Figure 1). Even though our population was not in the military, it was a group of active people who had an amputation from non-vascular causes. It is not surprising that people who are relatively active and use a high-level (i.e., energy storage and return) passive prosthesis demonstrate small differences in walking cost of transport compared with able-bodied subjects. Even when there is a significant difference of metabolic energy expenditure between people with and without unilateral transtibial amputation, prosthesis-users with unilateral transtibial amputation have the closest energy expenditure to able-bodied individuals when compared to people with higher levels (e.g., transfemoral, hip disarticulation) of amputation (Waters & Mulroy, 1999). Even with similar costs of transport, people with unilateral amputation utilize greater inter-limb asymmetry.

The number of subjects in this study was a limitation. It was difficult to recruit willing subjects who met the inclusion criteria. This is not surprising considering less than 20% of lower limb amputations are due to non-vascular causes (Zieglar-Graham et al., 2008) and our age range was limited to people between 16-50 years old for this study. While the sample size was limited, the group was homogenous, representing relative active subjects rated at a K3 or K4 activity level, making it possible to directly compare the effect of amputation on the cost of transport-asymmetry relationship without confounding factors such as advanced age or comorbidities. Even with a small sample size, there were several medium effect sizes (e.g., between the preferred asymmetry and predicted minimum-cost asymmetry for subjects with amputation), which indicates there might be a meaningful difference, and supports conducting further research to help better understand how cost of transport relates to gait asymmetry in people with amputation. There was an age disparity between groups (Table 1). The age disparity should not have had a large effect on findings because significant changes with gait usually do not occur until later in life (Judge et al., 1996).

Another limitation with the data collection was the use of two different treadmills. The treadmills had different belt composition and subjective stiffness levels (i.e., Treadmetrix was stiffer than Woodway), but since subjects were walking, not running, there should not have been a large effect on metabolic energy expenditure (Smith et al., 2017), and if there were any effects, they should be minimal for within subject comparisons. Since the treadmills could not determine force and timing for individual strides, insole footswitches were used to determine stance timing for the real time visual feedback. The insoles were different than usual shoe insoles and were connected to a computer via a box worn by the subjects at the mid-back level. Subjects subjectively reported that the insoles and box did not alter their movement, and additionally, subjects spent over 30 minutes walking with the set-up on day 1, allowing for accommodation to the system.

A common objective of rehabilitation is to restore inter-limb symmetry after an injury (e.g., joint arthroplasty, amputation), yet after anatomical structures have been altered, symmetrical function may not be optimal. Subjects with amputation in our study preferred more time on the intact limb compared with the prosthetic limb, and able-bodied subjects preferred walking almost symmetrically, with slightly more time on the dominant limb compared with the non-dominant limb. In both cases, preferred asymmetry coinciding closely with the lowest cost of transport. However, minimizing cost is likely not the only factor driving the selection of gait patterns. Further investigation is needed regarding how asymmetry affects joint loading, smoothness, and stability to better understand how preferred gait patterns emerge after an injury. If asymmetrical patterns naturally emerge in people with many years of prosthesis use, perhaps some degree of gait asymmetry should be expected and should be a goal for rehabilitation and devices. Given the sample size and the focus on only one potentially important factor, metabolic cost, our results should be interpreted cautiously. Nevertheless, they raise the possibility that asymmetrical patterns may be the best result after some injuries and do not represent a problem that should be fixed.

CHAPTER 6

STANCE SYMMETRY AND STABILITY OF LOCOMOTION IN PEOPLE WITH UNILATERAL TRANSTIBIAL AMPUTATION

6.1 Abstract

A main objective of walking is to achieve a specific displacement of the body while not falling. People with lower limb amputation of all levels have an increased incidence of falls, creating an economic and psychological burden. People with a unilateral amputation walk differently than people without amputation; most notably, they walk with more time on the intact compared with the prosthetic limb. People with unilateral transtibial amputation can walk symmetrically while using a prosthesis, yet they typically choose to walk with inter-limb asymmetries, possibly to improve gait stability. The purpose of this study was to determine the effects of inter-limb asymmetry on gait stability in people with and without unilateral transtibial amputation. We hypothesized that subjects with unilateral transtibial amputation would exhibit greater stance time on the intact side compared with the prosthetic side, while able-bodied subjects would exhibit symmetrical stance times when walking with preferred patterns. We hypothesized that gait stability, when quantified with margin of stability, versus inter-limb asymmetry would demonstrate an inverted U-shaped curve with the greatest stability at the preferred stride characteristics for both groups. In the case of step width, step length and stance time variability as a measure of stability, we hypothesized that gait stability versus inter-limb asymmetry would demonstrate a U-shaped curve, with the least variability (i.e., more stable) at the preferred stride characteristics for both groups. Gait stability was calculated from the motion data for 7 subjects with unilateral transtibial

amputation and 7 able-bodied controls while walking with preferred and non-preferred stance time conditions at preferred speed on a treadmill. Subjects with amputation spent more time on the intact limb with a significantly greater stance time asymmetry (4.34 ± 1.09%) compared with able-bodied subjects (0.94 ± 2.44%) during the preferred walking condition with a very large effect size ($p = 0.008$, $d = 1.93$). Rather than finding maximum gait stability at the preferred asymmetry conditions for the margin of stability measures, all stability metrics actually exhibited minima, except for medial-lateral margin of stability and step width variability, for which linear trends were found. Several of the predicted minima for the stability metrics were not significantly different than the preferred asymmetry values; however, these results should be viewed cautiously due to potentially too little statistical power. Gait stability may be one of the factors that determine preferred gait patterns, but other measures such as metabolic energy expenditure and joint loading may influence how preferred patterns emerge. The preferred walking patterns were asymmetrical, and asymmetrical patterns were predicted for most measures, so maybe inter-limb asymmetry should not be viewed negatively when rehabilitating from an injury.

6.2 Introduction

A main objective of walking is to achieve a specific displacement of the body while not falling. Maintaining balance while walking is more challenging for people with lower limb amputation compared with able-bodied individuals. People with lower limb amputation of all levels have an increased incidence of falls (Miller et al., 2001a; Kulkarni et al., 1996). Over 87% of people fall within the first six months after an amputation (Felcher et al., 2015). A secondary injury, such as a fracture, occurs in over 40% of people with amputation (Miller at al., 2001). Falls are more than a personal burden, falls also take an economic toll. Falls resulting in hospitalization were reported to cost $25,652 on average in the six months after falling in a small sample of people with transfemoral amputation (Mundell et al., 2017). Beyond economic effects, fear of falling is common amongst people with amputation (Miller et al., 2001a; Kulkarni et al., 1996), which may lead to gait adaptations to improve stability and avoid falling.

People with a unilateral amputation walk differently than people without amputation; most notably, they walk with multiple inter-limb asymmetries (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997). People with unilateral amputation spend more time on the intact side compared with the prosthetic side, and the time difference between limbs is greater with higher (i.e., more proximal) levels of amputation (Jaegers et al., 1995). Inter-limb asymmetry is consistently observed in people with unilateral lower limb amputation. A common goal of rehabilitation and assistive devices (e.g., prostheses and exoskeletons) is to improve balance and function by reducing asymmetry. However, due to altered anatomy and reliance on a prosthesis, an asymmetrical gait may actually be a functional adaptation (Hak et al., 2014) to decrease fall risk, and may not simply be the result of prosthesis limitations such as decreased push off power (Zmitrewicz et al., 2006). People with unilateral transtibial amputation can walk with symmetrical stride and push-off characteristics when provided real time visual feedback (Dingwell et al., 1996; Davis et al., 2004). Thus, while people with unilateral amputation can walk symmetrically while using a prosthesis, they typically choose to walk with inter-limb asymmetries. A possible reason is that people with unilateral lower limb amputation may adopt asymmetrical gait characteristics to improve stability.

Gait stability, that is not falling while walking even when perturbed (Bruijn et al., 2013), has been quantified with many measures in an attempt to predict falls (Hamacher et al., 2011). Gait stability in people with lower limb amputation has been quantified while perturbed with surface perturbations (Beurskens et al., 2014; Hak et al., 2013), visual perturbations (Beurskens et al., 2014) and walking on rocky surfaces (Gates et al., 2013). No study up until this point has quantified how asymmetrical patterns, aside from preferred inter-limb asymmetry, effect gait stability in people with unilateral lower limb amputation. One recent study examined how fractality changes with inter-limb asymmetry in able-bodied individuals, finding that walking with asymmetry leads to multifractility, that is the need to perform intermittent corrections, and is different than preferred walking which is monofractal (Ducharme et al., 2018). The study utilized just one asymmetry condition that was evoked while walking on a split-belt treadmill, with one belt moving at preferred walking speed and the other belt moving at half-preferred speed. Fractality is a measure of local stability, which is the system's ability to respond to small perturbations, and requires a long series of strides (i.e., 150 strides) to quantify stability. Global stability measures (i.e., system's ability to respond to large perturbations), such as margin of stability (Hof et al., 2005), can be calculated for individual strides. Being able to quantify stability for individual strides is relevant because most bouts of gait are less than 40 strides in duration (Orendurff et al., 2008). How inter-limb asymmetry effects global stability in people with and without unilateral amputation, has not been established by previous literature

Margin of stability represents the distance between an extrapolated center of mass position (i.e., instantaneous center of mass position plus velocity) and the boundary of the base of support (Hof et al., 2005), and may indicate when the body will need to adapt its motion away from inverted pendulum-like dynamics to avoid a fall (Hof, 2007; Bruijn et al., 2013). Margin of stability is greater in people with unilateral transtibial amputation compared with able-bodied individuals when gait is perturbed (Beltran et al., 2014; Hak et al., 2013), demonstrating that people with amputation maintain a greater margin of safety than people without amputation in response to a perturbation.

Traditional measures of stability, such as step width variability (i.e., standard deviation), have been correlated with fall risk (Maki, 1997; Hausdorff et al., 2001). People with lower limb amputation have demonstrated greater variability compared with able-bodied individuals (Hak et al., 2013; Beurskens et al., 2014), potentially indicating less kinematic consistency and therefore greater fall risk. People with lower limb amputation utilize different stability patterns compared with able-bodied individuals, but why these differences occur and how they are related to preferred inter-limb asymmetry is unknown. The effects of inter-limb asymmetry on gait stability have not been evaluated in people with amputation, and may provide information about how self-selected walking patterns emerge.

Insights about the adaptations that are made to walk safely with a prosthesis can be understood by having people with unilateral transtibial amputation walk with varying degrees of stance time asymmetry, including a symmetrical condition, while quantifying gait stability. The purpose of this study was to determine the effects of inter-limb asymmetry on gait stability in people with and without unilateral transtibial amputation. Based on previous literature regarding stride symmetry, we hypothesized that subjects with unilateral transtibial amputation would exhibit greater stance time on the intact side compared with the prosthetic side, while able-bodied subjects would exhibit symmetrical stance times when walking with preferred patterns. We hypothesized that gait stability, when quantified with margin of stability, versus inter-limb asymmetry would demonstrate an inverted U-shaped curve with the greatest margin of stability at the preferred stride characteristics for both groups. In the case of variability as a measure of stability, we hypothesized that gait stability versus inter-limb asymmetry would demonstrate a U-shaped curve, with the least variability (i.e., most stable) at the preferred stride characteristics for both groups. The implication of these hypotheses is that we predicted subjects with unilateral lower limb amputation are most stable when walking with their preferred, asymmetrical gait pattern, and being required to walk symmetrically will reduce gait stability.

6.3 Methods

6.3.1 Subjects

Seven people with unilateral transtibial amputation due to non-vascular causes (e.g., trauma, cancer, congenital) that occurred over one year ago, and seven able-bodied individuals participated in this study (Table 6.1). The participants with unilateral transtibial amputation were between 16-48 years old, rated at a Medicare activity classification of K3 or K4 (i.e., able to perform variable cadences while walking), and use a passive prosthesis. People were excluded from the study if they had any condition, other than amputation, that effected their ability to walk (e.g., chronic pain, neurological or cardiovascular disorders) or had lower limb surgery in the last year. Further details about the subjects with amputation are provided in Table 6.2. The study was approved by the University of Massachusetts and Quinnipiac University Institutional Review Boards. All participants read and signed an informed consent document prior to participation.

Table 6.1: Subject characteristics

Group	Females/ males (#)	Age (years)	Height (m)	Mass (kg)	Amp or Dom	Pref Speed ($m \cdot s^{-1}$)
AMP	2/5	36.6 ± 12.5	1.80 ± 0.08	83.9 ± 18.9	5 R/2 L	1.13 ± 0.22
CNTL	2/5	28.7 ± 5.4	1.63 ± 0.37	85.4 ± 20.4	7 R/0 L	1.42 ± 0.12
***p*-value**	**-**	**0.194**	**0.334**	**0.585**	**-**	**0.021**

Characteristics of the subjects with amputation (AMP) and able-bodied subjects (CNTL). Values are mean ± 1 SD.

Table 6.2: Subjects with amputation characteristics

Subject	Amputation cause	Years since amputation	Prosthesis ankle	Suspension type
S01	Congenital	28	Ossur Vari-Flex	End-bearing
S02	Congenital	24	OssurVari-Flex	End-bearing
S03	Trauma	4.4	Ossur Pro-Flex	Pin
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S05	Trauma	25	Ossur Cheetah Xplore	Suction
S06	Trauma	2	Freedom Innovations Kinterra	Pin
S07	Cancer	29	Ossur Vari-Flex	Suction

6.3.2 Protocol

The subjects attended two sessions, 12 subjects (5 with amputation and 7 able-bodied) participated at the Biomechanics Laboratory at the University of Massachusetts Amherst (Amherst, MA) and 2 subjects with amputation participated at the Motion Analysis Laboratory at Quinnipiac University (North Haven, CT). During these sessions, the subjects walked on a treadmill at their preferred overground walking speed while receiving real time visual feedback about inter-limb stance time asymmetry. Preferred overground walking speed was determined with a 400 m walk test. A 400 m walk test was used rather than a shorter test, to best represent an individual's preferred walking speed for a longer bout of walking (Graham et al., 2008). In the first session, subjects walked on a treadmill while receiving real-time visual feedback to become familiar with the experimental protocol. In the second session, the real-time visual feedback conditions were repeated on the treadmill while motion data were collected. Each walking trial was five minutes long. The asymmetry feedback conditions were -15% to 15% in 5% increments, with 0% representing symmetric stance time between limbs. Negative values indicated greater stance time on the prosthetic limb for subjects with lower limb amputation, and indicated greater stance time on the non-dominant side for able-bodied subjects. Positive values indicated greater stance time on the intact limb, and the dominant limb, respectively. Subjects with an amputation did not perform the -15% condition because this extreme condition was not attainable during pilot testing. Subjects were given five minutes of seated rest after each walking trial to avoid the effects of fatigue.

6.3.3 Stance time asymmetry

Stance time was determined from insole foot switches (B&L Engineering, Santa Ana, CA) and a custom MATLAB (Math Works, Natick, MA) program. The amount of asymmetry between limb stance times was calculated using an asymmetry index (Dingwell et al. 1996):

$$Asymmetry_A = \frac{Intact\ stance\ time - Prosthetic\ stance\ time}{Intact\ stance\ time + Prosthetic\ stance\ time} \times 100\% \quad \text{(Eqn. 1)}$$

$$Asymmetry_C = \frac{Dominant\ stance\ time - nondominate\ stance\ time}{Dominate\ stance\ time + nondominant\ stance\ time} \times 100\% \quad \text{(Eqn. 2)}$$

$Asymmetry_A$ is the asymmetry index for the participants with an amputation, and $Asymmetry_C$ is the asymmetry index for the able-bodied participants. The real-time visual feedback was provided via a graphical display on a monitor at eye-level at the front of the treadmill. A two-stride moving average of the stance time symmetry index was displayed to the subjects. During pilot testing, we found that a two-stride moving average permitted subjects to make consistent adaptations to meet the asymmetry goal without having differences from stride-to-stride displayed that were too large (i.e., no averaging) or too small (i.e., three to four stride average).

6.3.4 Kinematic model

Marker data were collected at a rate of 240 Hz with a Qualisys system (Qualisys, Göteborg, Sweden) at the University of Massachusetts and with a Motion Analysis system (Motion Analysis, Rohnert Park, CA) at Quinnipiac University. The data was post-processed using Qualisys Track Manager and Cortex software at the two sites, respectively. The kinematic model consisted of three segments: pelvis and two feet. Markers were placed over the following landmarks: sacrum, bilateral anterior superior iliac spines, iliac crests, posterior superior iliac spines, lateral malleoli, medial malleoli, fifth metatarsal heads, first metatarsal heads, tips of second toes. Marker clusters were placed on bilateral heels.

6.3.5 Stability measures

The stability variables of interest were medial-lateral margin of stability, backwards margin of stability, and the variability of step width, step length, and stance time. Individual strides were determined using a previously described toe marker velocity method for walking on a treadmill (Zeni et al., 2008). The margin of stability is based on the extrapolated position of the center of mass relative to the base of support (Figure 1) and may indicate when the body will need to adapt its motion away from inverted pendulum-like dynamics to avoid a fall (Hof, 2007; Bruijn et al., 2013).

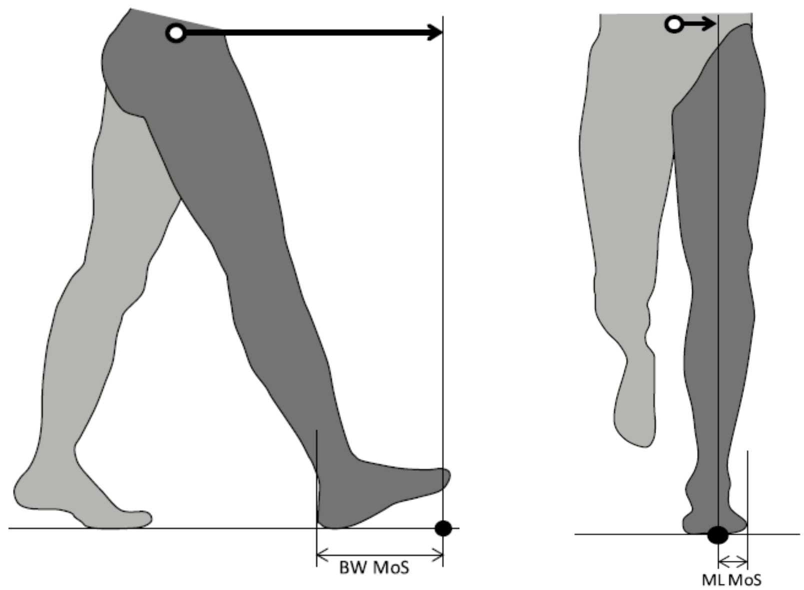

Figure 6.1: Margin of stability representation. Adapted from Hak et al. (2013) showing the relationship of center of mass position (o), velocity of the center of mass represented by arrow coming from the o, the extrapolated center of mass position at the tip of that arrow projected onto on the floor (●), and the difference between extrapolated center of mass and base of support (margin of stability) in the backwards direction (left panel) and medial-lateral direction (right panel).

Margin of stability was calculated with kinematic marker data, similar to Hak et al. (2012), which was an adaptation of the original method from Hof et al. (2005) to allow quantification in cases where individual-stride ground reaction force data were not available. Hof et al. (2005) utilized a force plate to determine center of mass kinematics (position and velocity) relative to the base of support (center of pressure). Hak et al. (2012) utilized pelvis markers to calculate center of mass kinematics and foot markers to determine base of support location. The center of mass position was determined with post-processed motion capture data, and velocity was determined with the central difference method within a custom MATLAB (Math Works, Natick, MA) program throughout the stance phase. The extrapolated center of mass was calculated within MATLAB using the following equation (Hak et al. 2012):

$$\boldsymbol{xCoM = P_{CoM} + v_{CoM} \times \sqrt{l/g}} \quad \text{(Eqn. 3)}$$

where P_{CoM} is the instantaneous position of the center of mass and V_{CoM} is the instantaneous velocity of the center of mass. The velocity was scaled by the eigenfrequency of the inverted pendulum representation of the body (i.e., $\sqrt{(\frac{leg\ lenth}{gravity})}$). The base of support was determined from the lateral marker on the heel cluster for the backwards margin of stability, and the fifth metatarsal marker for the medial-lateral base of support. The general equation for calculating margin of stability (Hof et al., 2005; Hof et al., 2007) is:

$$ML\ MoS = BoS - xCoM \text{ (Eqn. 4)}$$

$$BW\ MoS = xCOM - BoS \text{ (Eqn. 5)}$$

The extrapolated center of mass ($xCoM$) relative to the base of support (BoS) in the medial-lateral and backwards directions (i.e., margin of stability) was calculated throughout the stance phase for each leg. The margin of stability in the backwards direction was calculated by subtracting the base of support from the extrapolated center of mass position, similar to Hak et al. (2014). The minimum value of medial-lateral margin of stability during stance was determined for each stride, and the value of backwards margin of stability at heel strike was determined for each stride. The variability of step length, step width and stance time were determined from the standard deviation of 20 strides in the final minute of each five minute trial. The variability of step length, step width and stance time were also determined by the coefficient of variation to take into account the means of each measure. The standard deviations are presented in the results section and then interpreted in the discussion section, and the coefficients of variation are presented and interpreted in appendix A.

6.3.6 Statistical analysis

The overall effects of stance time asymmetry on gait stability between the two limbs for each of the two groups were tested with two-way ANOVAs for each gait stability metric. Orthogonal polynomial contrast analysis (Keppel, 1991) was performed to determine the mathematical dependence of gait stability on the amount of asymmetry for each limb. The highest-order statistically significant trend (e.g., linear, quadratic, cubic) was then used to estimate the degree of asymmetry corresponding to the minimum value for each stability metric (e.g., backwards MoS, step width variability) for each limb. The stability measures for each subject were fit with the highest-order statistically significant polynomial from the contrast analysis, and if there was a significant trend of second or higher order, we predicted the asymmetry value yielding the minimum value for each stability metric. The goodness of fit between the experimental values and trend line was determined with an r-squared value. The preferred asymmetry and the asymmetry corresponding to the predicted minimum stability values within each limb were compared with a paired t-test. We also calculated effect sizes (Cohen, 1988) and defined the size of the effects based on the expanded ranges defined by Sawilowsky (2009), with: $d = 0.1$ being a very small, $d = 0.2$ being a small, $d = 0.5$ being a medium, $d = 0.8$ being a large, $d = 1.2$ being a very large, and $d = 2.0$ being a huge effect size. After estimating the asymmetries that corresponded to optimal (i.e., minima or maxima) gait stability for each measure, an ANOVA of those predicted asymmetries was used to compare the estimated asymmetries among the four limbs (i.e., prosthetic, intact, dominant and non-dominant limbs). Alpha level was set at 0.05 for all statistical tests. Statistical analyses were performed using R-Studio version 3.2.2 (R-Studio Inc., Boston, MA).

6.4 Results

6.4.1 Preferred asymmetry

Subjects with amputation spent more time on the intact limb with a significantly greater stance time asymmetry (4.34 ± 1.09%) compared with able-bodied subjects (0.94 ± 2.44%) during the preferred walking condition with a very large effect size ($p = 0.008$, $d = 1.93$) (Table 6.2). Every subject with an amputation spent more time on the intact limb during the preferred condition. While the absolute asymmetries for able-bodied subjects where small in magnitude, the results between dominant and non-dominant limb were mixed, with some subjects spending more time on the dominant limb, and others on the non-dominant limb.

6.4.2 Medial-lateral margin of stability

There was a significant effect of limb ($p < 0.001$) for medial-lateral margin of stability. A linear trend best explained the relationship between medial-lateral margin of stability and stance time asymmetry ($R^2_{pros} = 0.067$, $R^2_{int} = 0.027$, $R^2_{dom} = 0.643$, $R^2_{ndom} = 0.899$) (Figure 6.2).

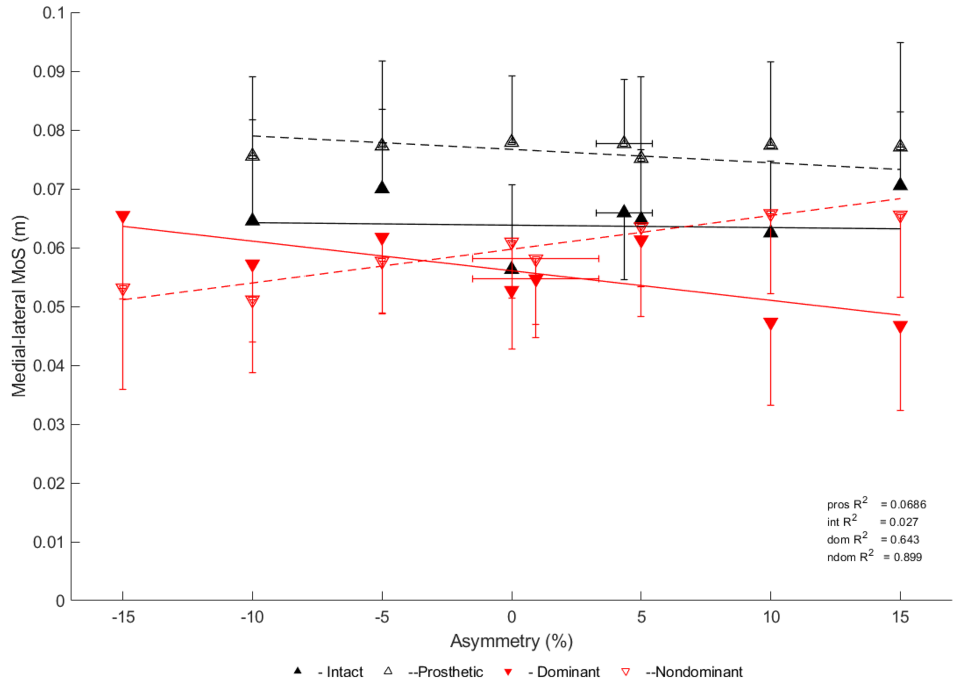

Figure 6.2: Medial-lateral margin of stability versus asymmetry. Medial-lateral margin of stability (MoS) between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Triangles that have horizontal error bars are the preferred conditions. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. A linear trend best explained the relationship between medial-lateral MoS and asymmetry.

Table 6.3: Preferred and predicted asymmetries

Group	P Asym (%)	BW MoS (m)	SL SD (m)	ST SD (s)
PROS	4.34 ± 1.09	-	4.2 ± 7.3	4.2 ± 9.3
INT	-	3.8 ± 7.8	2.5 ± 8.8	4.6 ± 5.8
DOM	0.94 ± 2.44	1.3 ± 11.1	1.4 ± 6.0	1.1 ± 5.7
NDOM	-	2.6 ± 7.6	-0.7 ± 6.7	-0.1 ± 2.2
***p*-value**	**0.008**	**0.507**	**0.732**	**0.870**

Preferred (P) asymmetry (Asym) for subjects with amputation (PROS and INT) and able-bodied subjects (DOM and NDOM). Asymmetries yielded by stability minima for backwards (BW) MoS, step length (SL) variability, and stance time (ST) variability for the prosthetic (AMP), intact (INT), dominant (DOM), and non-dominant (NDOM) limbs. Values are mean ± 1 SD. There is a dash for pros BW MoS because the quadratic fit led to a linear trend line, therefore no optima was predicted.

6.4.3 Backwards margin of stability

There was a significant effect of limb ($p < 0.001$) for backwards margin of stability. A U-shaped quadratic trend best explained the relationship between backwards margin of stability and stance time asymmetry ($R^2_{pros} = 0.817$, $R^2_{int} = 0.836$, $R^2_{dom} = 0.501$, $R^2_{ndom} = 0.816$) (Figure 6.3). The asymmetry values yielding minima for backwards margin of stability are listed in Table 6.3. The preferred asymmetry for subjects with amputation was not significantly different than the asymmetry at the minimum backwards margin of stability for the intact limb, with a small effect size ($p = 0.719$, $d = 0.354$). The preferred asymmetry for able-bodied subjects was not significantly different than the asymmetry at the minimum backwards margin of stability for the dominant limb, with a very small effect size ($p = 0.953$, $d = 0.061$) and the non-dominant limb, with a very small effect size ($p = 0.990$, $d = 0.018$). The ANOVA comparing predicted asymmetries did not have a significant effect of limb ($p = 0.507$).

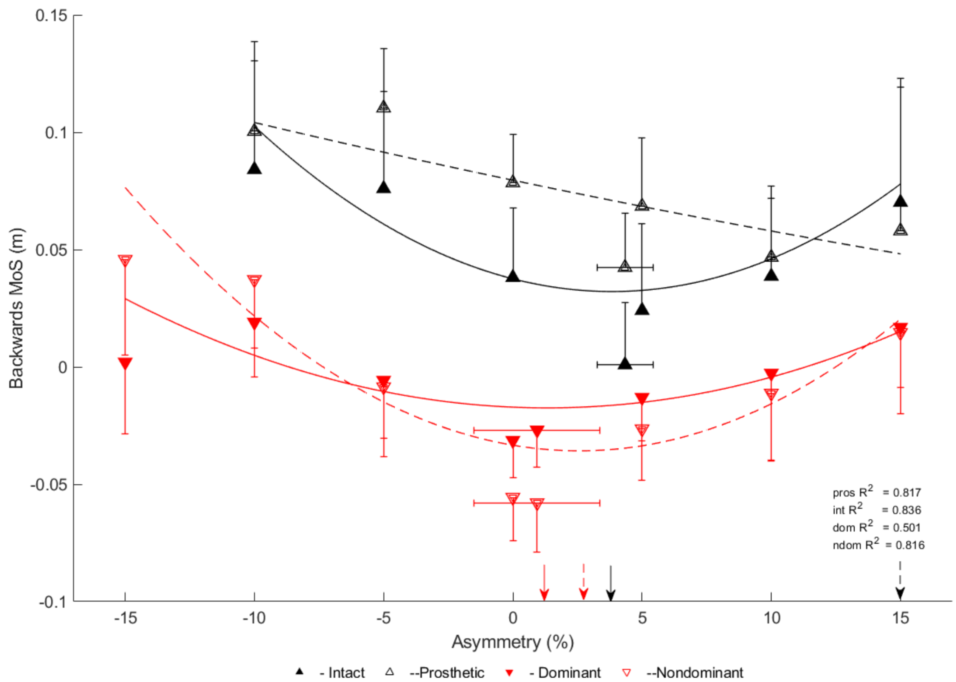

Figure 6.3: Backwards margin of stability versus asymmetry. Backwards margin of stability (MoS) between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. Downward facing arrows at the x-axis represent the predicted asymmetries corresponding to minima backwards MoS. A quadratic trend best explained the relationship between backwards MoS and asymmetry. The preferred asymmetry for subjects with amputation (upward facing triangles with horizontal error bars) was not significantly different than asymmetries corresponding to minima for backwards MoS for the prosthetic and intact limbs. The preferred asymmetry for able-bodied subjects (downward facing triangles with horizontal error bars) was not significantly different than asymmetries corresponding to minima for backwards MoS for the dominant and non-dominant limbs.

6.4.4 Step width variability

There was a significant effect of limb ($p < 0.001$) for step width variability. A linear trend best explained the relationship between step width variability and asymmetry ($R^2_{pros} = 0.248$, $R^2_{int} = 0.167$, $R^2_{dom} = 0.012$, $R^2_{ndom} = 0.511$) (Figure 6.4).

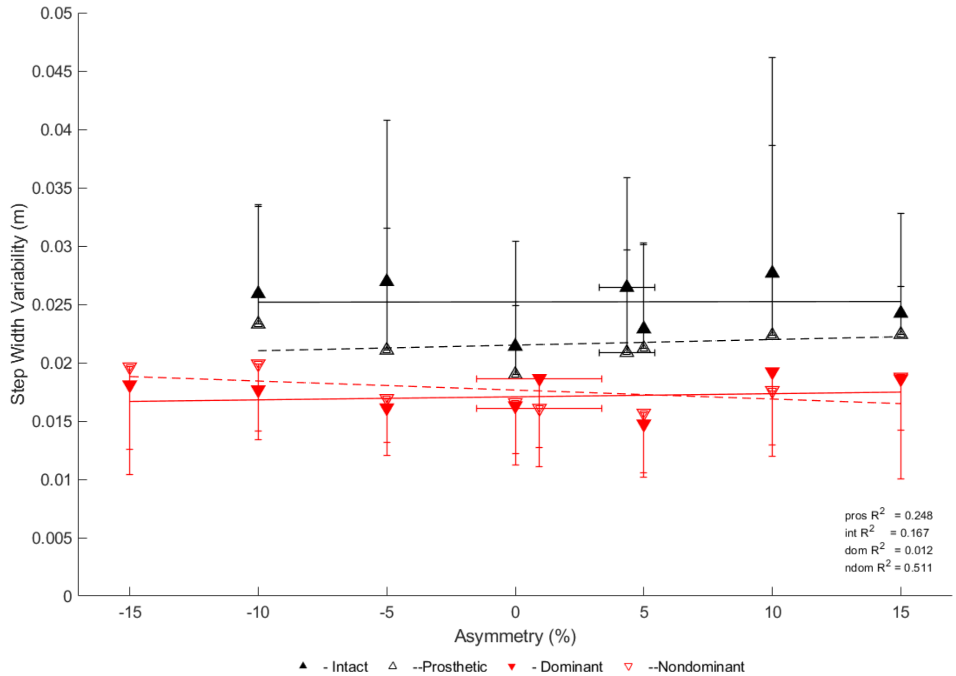

Figure 6.4: Step width variability versus asymmetry. Step width variability between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. A linear trend best explained the relationship between step width variability and asymmetry.

6.4.5 Step length variability

There was a significant effect of limb ($p = 0.002$) for step length variability. A U-shaped quadratic trend best explained the relationship between step length variability and asymmetry ($R^2_{pros} = 0.879$, $R^2_{int} = 0.925$, $R^2_{dom} = 0.667$, $R^2_{ndom} = 0.480$) (Figure 6.5). The asymmetry values yielding minima for step width variability are listed in Table 6.3. The preferred asymmetry for subjects with amputation was not significantly different than the asymmetry at the minimum step length variability for the prosthetic limb, with a very small effect size ($p = 0.8691$, $d = 0.153$) and the intact limb, with a very small effect size ($p = 0.872$, $d = 0.144$). The preferred asymmetry for able-bodied subjects was not significantly different than the asymmetry at the minimum step length variability for the dominant limb, with a medium effect size ($p = 0.615$, $d = 0.652$) and for the non-dominant limb, with a small effect size ($p = 0.682$, $d = 0.448$). The ANOVA comparing predicted asymmetries did not have a significant effect of limb ($p = 0.732$).

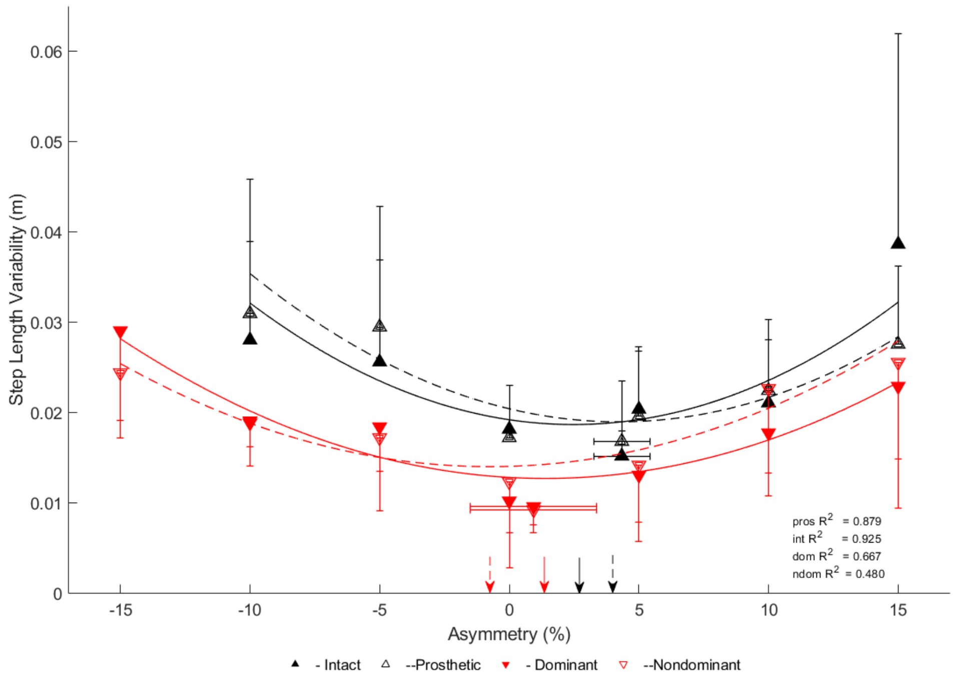

Figure 6.5: Step length variability versus asymmetry. Step length variability between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. Downward facing arrows at the x-axis represent the predicted asymmetries corresponding to minima step length variability. A cubic trend best explained the relationship between step length variability and asymmetry. The preferred asymmetry for subjects with amputation (upward facing triangles with horizontal error bars) was not significantly different than asymmetries corresponding to minima for step length variability for the prosthetic and intact limbs. The preferred asymmetry for able-bodied subjects (downward facing triangles with horizontal error bars) was not significantly different than asymmetries corresponding to minima for step length variability for the dominant and non-dominant limbs.

6.4.6 Stance time variability

There was a significant effect of limb ($p < 0.001$) for stance time variability. A U-shaped quadratic trend best explained the relationship between stance time variability and asymmetry ($R^2_{pros} = 0.974$, $R^2_{int} = 0.968$, $R^2_{dom} = 0.976$, $R^2_{ndom} = 0.943$) (Figure 6.6). The asymmetry values yielding minima for stance time variability are listed in Table 6.3. The preferred asymmetry for subjects with amputation was not significantly different than the asymmetry at the minimum stance time variability for the prosthetic limb asymmetry, with a small effect size ($p = 0.581$, $d = 0.489$) and the intact limb, with a medium effect size ($p = 0.458$, $d = 0.746$). The preferred asymmetry for able-bodied subjects was not significantly different than the asymmetry at the minimum stance time variability for the dominant limb, with a huge effect size ($p = 0.517$, $d = 2.363$) and the non-dominant limb, with a very large effect size ($p = 0.712$, $d = 1.860$). The ANOVA comparing predicted asymmetries did not have a significant effect of limb ($p = 0.870$).

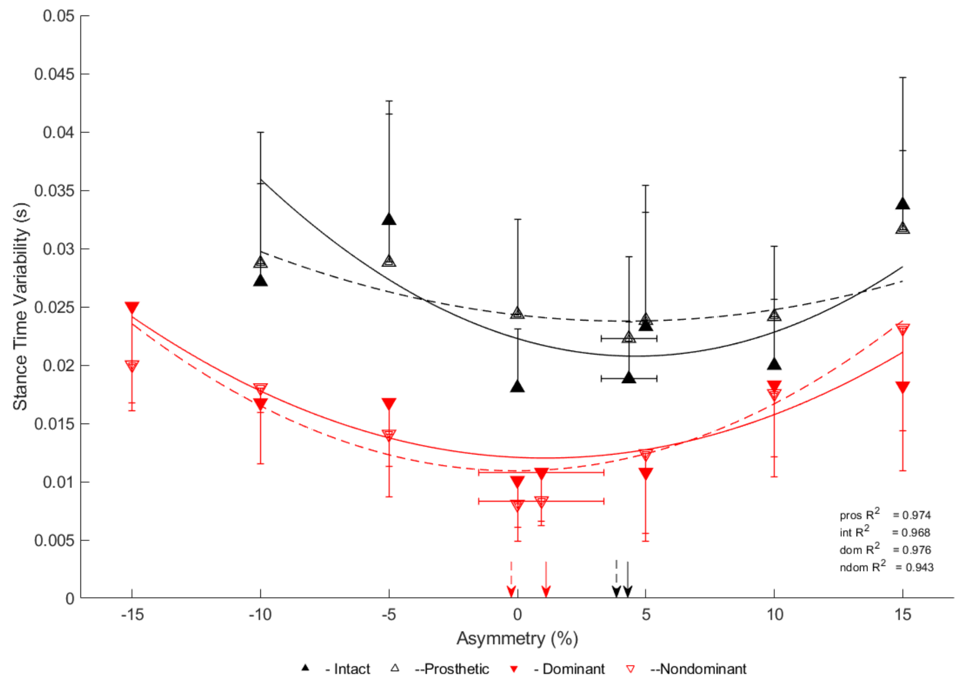

Figure 6.6: Stance time variability versus asymmetry. Stance time variability between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. Downward facing arrows at the x-axis represent the predicted asymmetries corresponding to minima stance time variability. A cubic trend best explained the relationship between stance time variability and asymmetry. The preferred asymmetry for subjects with amputation (upward facing triangles with horizontal error bars) was not significantly different than asymmetries corresponding to minima for stance variability for the prosthetic and intact limbs. The preferred asymmetry for able-bodied subjects (downward facing triangles with horizontal error bars) was not significantly different than asymmetries corresponding to minima for minima for stance variability for the dominant and non-dominant limbs.

6.5 Discussion

The purpose of this study was to determine the effect of inter-limb asymmetry on gait stability in people with and without unilateral lower limb amputation. Our hypothesis about stance time asymmetry for each group was supported, but our hypotheses about gait stability across asymmetry conditions, and the asymmetry conditions corresponding to the greatest stability between limbs were not supported for the margin of stability and step width variability measures but were supported for the step length and stance time variability measures. Subjects with amputation had greater stance time asymmetry (i.e., more time on intact limb relative to the prosthetic limb) compared with able-bodied subjects, as predicted. However, rather than finding maximum gait stability at the preferred asymmetry conditions for the margin of stability measures, all stability metrics actually exhibited minima within the experimental range, expect for medial-lateral margin of stability, for which linear trends were found. Several of the predicted minima for the stability metrics were not significantly different than the preferred asymmetry values; however, these results should be viewed cautiously. Given the small sample size, combined with the presence of some medium to very large effect sizes, it is possible this study did not have adequate statistical power to detect some significant differences.

Subjects with unilateral amputation chose to walk with more time on the intact limb compared with prosthetic limb, which agrees with previous literature (Isakov et al., 2000; Sadeghi et al., 2001; Sanderson & Martin, 1997). Able-bodied subjects preferred more time on the dominant limb versus non-dominant limb, on average (Vanden-Abeele, 1980), but the degree of asymmetry was less than 1% for the able-bodied subjects. Some able-bodied subjects preferred more time on the non-dominant limb compared with the dominant limb, therefore did not demonstrate a consistent asymmetry direction like people with amputation.

A U-shaped quadratic trend best explained the relationship of gait stability and asymmetry for all stability measures except for the medial-lateral margin of stability and step width variability. The linear trend for the medial-lateral margin of stability and step width variability may be due to a consistent step width across conditions for each limb (Appendix A). A consistent step width may regulate the margin of stability, particularly for subjects with amputation, to have set margin of safety for limb. The medial margin of stability being greater for the prosthetic limb compared with the other limbs, may be the result of a prosthesis's limitations in the medial-lateral direction. The predicted asymmetries corresponding to minima of the gait stability metrics are, with some exceptions (e.g., backwards margin of stability for the prosthetic limb), generally close approximations of the actual preferred stance time asymmetries for both groups. We originally predicted maxima of stability to occur with preferred walking for the margin of stability measures because we thought people would have the greatest resistance to perturbation, and therefore, the safest gait pattern. It may be the case that preferred walking is perceived by the individual as the gait pattern with the least likelihood of falling, and therefore a minimum margin of stability is utilized in the backwards direction. Therefore the stance time asymmetries corresponding to the minima are near the preferred asymmetries. Furthermore, if subjects walk with non-preferred inter-limb stance timing, perceived safety may decrease directly with the amount asymmetry away from preferred and subjects utilize greater margins of stability to avoid a fall. While the individual statistical comparisons of preferred and predicted asymmetry from minimum-stability must be viewed cautiously, for most variables, the magnitude of asymmetry for subjects with amputation appear greater than for the able-bodied subjects, meaning subjects with amputation might optimize stability by utilizing inter-limb asymmetry.

There are no direct comparisons between our findings and how stance time asymmetry effects gait stability in previous literature, because we are the first to examine this across preferred and non-preferred asymmetries. We cannot compare our non-preferred conditions but can compare our preferred conditions with previous literature. Our findings at the preferred condition are in agreement with previous literature that found greater medial-lateral margin of stability for subjects with unilateral transtibial amputation compared with able-bodied subjects (Gates et al., 2013; Hak et al., 2013). We found significantly greater medial-lateral margin of stability on the prosthetic limb compared with the intact limb, while another study found greater medial-lateral margin of stability on the intact limb compared with the prosthetic limb (Gates et al., 2013). Our findings at the preferred condition do not agree with previous literature for the backwards margin of stability. We found greater backwards margin of stability for subjects with amputation compared with able-bodied subjects, but another study found greater backwards margin of stability for able-bodied individuals compared with subjects with amputation (Hak et al., 2013). The difference in findings between our study and others may be due to the step length differences between groups, with greater step lengths for able-bodied subjects compared with subjects with amputation (Appendix A). Greater step length can lower the margin of stability and therefore the lower values for able-bodied subjects in our findings. Aside from step length, gait speed can affect backwards margin of stability. Backwards margin of stability in people with unilateral transtibial amputation has been shown to be lesser at slower speeds (Wedge et al., 2017), while medial-lateral margin of stability does not change with speed (Hak et al., 2012). Some studies have controlled gait speed between groups (Gates et al., 2013), while others have not (Hak at al., 2013). People with amputation usually walk slower than people without amputation, which is what we found for our subjects, and therefore can affect the backwards margin of stability. To compensate for effect of slower walking speed on backwards margin of stability, people with amputation may take shorter strides to increase the margin of stability. Gait variability has been shown to be minimized at preferred walking speed (Jordan et al., 2007). The difference in findings between our study and others could also be the result of inter-subject variability for people with amputation, due to each person having different residual limbs and prostheses.

The predicted asymmetries occurring at minima for the backwards margin of stability measure, rather than maxima, may indicate that stability is balanced with other objectives such as metabolic energy expenditure. If preferred asymmetries occurred at maximum stability, there could be a greater metabolic energy expenditure, leading to a stable yet metabolic costly gait. Previous work has theorized there is a trade-off between metabolic energy expenditure and stability depending on task goals (Monsch et al., 2012). In that study, when able-bodied subjects walked at a set speed with a more conservative, stable pattern, it led to greater metabolic cost, while walking with a more risky, less stable pattern, led to less metabolic energy expenditure. Preferred walking patterns for people with and without amputation may feel safer than walking with non-preferred patterns. Therefore when constrained to walk with non-preferred patterns, people utilize greater stability than preferred patterns by increasing the margin of safety and may also have greater metabolic energy expenditure compared with preferred. Further investigation is warranted in people with and without amputation to understand how gait stability, metabolic energy expenditure, and other factors such as joint loading and smoothness, are balanced when walking with preferred and non-preferred gait patterns.

Subjects with and without amputation had the least magnitude of step width, step length and stance time variability when walking during the preferred condition compared with the non-preferred experimental conditions (Figures 6.4-6). Similar to the backwards margin of stability findings, subjects may have felt safest (i.e., least chance of falling) when walking with preferred gait patterns and therefore demonstrated lesser variability than non-preferred patterns. Greater variability with these measures has been correlated to greater fall risk (Maki, 1997; Hausdorff et al., 2001), but the subjects in this study did not have a history of falls, so this same correlation cannot be made. Even without this correlation, there may be different stability strategies used by people with amputation compared with able-bodied individuals, and warrants further investigation in future studies.

A limitation of this study was the sample size. Even with a small sample size, subjects with amputation demonstrated more time on the intact limb than the prosthetic limb, which is in agreement with previous literature. Most of the stability measures demonstrated curvilinear trends with minima, not maxima, that corresponded to asymmetries that are near the preferred asymmetries. We cannot definitively state that subjects are selecting preferred patterns to minimize any of these stability measures because of potential statistical power issues, and possibly, people do not select patterns that would minimize these measures. However, the results overall, with predicted minima at positive asymmetry, and being greater for subjects with amputation compared able-bodied subjects, suggests people may select patterns that minimize these measures. Another limitation in this study was that 2 subjects were collected at a different site. An effort was made to ensure consistency between sites and the 2 subjects that were collected at a different site, showed the same trends as the other subjects.

The purpose of this study was to understand the effects of inter-limb asymmetry on gait stability. Medial-lateral and backwards margin of stability were quantified because they represent the control of the center of mass motion relative to foot placement, which may be critical for gait stability (Bruijn & van Dieėn, 2018). Step length, step width and stance time variabilities represent kinematic consistency, and there may be a higher probability of falls with greater variability, but this conclusion cannot be made from our findings. Gait stability may be one of the factors that determine preferred gait patterns, but other measures such metabolic energy expenditure, smoothness and joint loading may influence how preferred patterns emerge. The preferred walking patterns were asymmetrical, and asymmetrical patterns were predicted for most measures, so maybe inter-limb asymmetry should not be viewed negatively when rehabilitating from an injury.

CHAPTER 7

GENERAL DISCUSSION

7.1 Introduction

The purpose of this dissertation was to determine how metabolic energy expenditure and gait stability are affected by inter-limb gait asymmetry in people with and without unilateral transtibial amputation. People with amputation generally have greater metabolic energy expenditure compared with able-bodied individuals, as well as increased fall incidence. People with unilateral amputations typically have asymmetries between the prosthetic and intact limbs for temporal-spatial, kinematic, and kinetic stride measures, while able-bodied individuals generally demonstrate inter-limb symmetry for the same measures. One of the most consistent findings in the literature is that people with unilateral lower limb amputation spend more time on the intact limb compared with the prosthetic limb, even when prescribed a high-function, energy-storage-and-energy-return passive prosthesis. Gait asymmetries in people who use a passive prosthesis unilaterally may simply result from the altered anatomy of the residual limb and a passive prosthesis not functioning like a biological limb. Restoring symmetry is often a goal of rehabilitation and assistive devices, yet the gait differences for people with unilateral amputation relative to able-bodied walkers could in fact be optimal for metabolic energy expenditure and stability. How preferred patterns emerge after an injury is of interest because of the potential effects on rehabilitation and rehabilitative devices.

7.2 Role of cost of transport and preferred gait patterns

The aim of study 1 (chapter 5) was to understand the effects of inter-limb stance time asymmetry on net cost of transport in people with and without unilateral transtibial amputation. A goal of study 1 was to estimate the stance time asymmetry resulting in minimum net cost of transport and compare it to the preferred asymmetry in order to understand the influence of metabolic energy expenditure on preferred gait patterns. We recruited 7 relatively fit and young adults with unilateral transtibial amputation that resulted from non-vascular causes, and 7 able-bodied subjects that matched height, mass and age as best as possible. The subjects walked at their preferred overground walking speed on a treadmill while using preferred and non-preferred stance time asymmetries during 2 sessions, and metabolic energy expenditure was determined from pulmonary gas exchange during the second session. Subjects with amputation had greater stance time asymmetry (4.3% more time on intact compared with prosthetic limb, on average) compared with able-bodied subjects (<1% more time on dominant limb compared with non-dominant limb). This finding for subjects with amputation is in agreement with previous literature that has consistently shown people with amputation prefer more time on the intact compared with prosthetic limb. Able-bodied subjects spending slightly more time on the dominant compared with the non-dominant limb on average has been shown previously, but limb dominance does not consistently explain inter-limb stance timing in able-bodied subjects. For both groups, the asymmetry predicted to yield the minimum-cost of transport was not significantly different from preferred asymmetry. However, this last result should be viewed cautiously, as this study may not have been adequately powered to detect such differences due to the small sample size. Although the study may not have been adequately powered, the asymmetries predicted to yield the minimum-cost of transport for both groups were in the same direction (i.e., greater asymmetry for subjects with amputation compared with able-bodied subjects) as the preferred asymmetries. This was the first study that evaluated cost of transport in people with amputation walking with symmetrical stance timing, as well as other non-preferred asymmetrical patterns. Since cost of transport was least with preferred walking for both groups, it may play a role in how preferred patterns emerge in people with and without amputation, and thus walking asymmetrically may be optimal for people with lower limb amputation, and walking symmetrically may be optimal for able-bodied individuals.

7.3 Role of gait stability and preferred gait patterns

The aim of study 2 (chapter 6) was to determine the effects of inter-limb asymmetry on gait stability in people with and without unilateral lower limb amputation. A goal of study 2 was to estimate the stance time asymmetries corresponding to the optima for several measures of gait stability and compare them to the preferred asymmetry in order to understand the influence of gait stability on preferred gait patterns. It was hypothesized that subjects would be most stable at preferred stance time asymmetry. The same subjects from study 1 performed the same conditions as study 1 while motion capture was used to determine the movement of the pelvis and both feet. The motion data was used to quantify gait stability, represented by the medial-lateral and backwards margin of stability, step width variability, step length variability and stance time variability. Most of the stability metrics exhibited minima within the experimental range, expect for medial-lateral margin of stability and step width variability, for which linear trends were found. These results indicate that during preferred conditions, subjects may minimize stability while walking with preferred inter-limb stance timing, and therefore many of the stability metrics had their lowest values near the preferred conditions. It may be that the gait changes associated with increasing stability when walking with non-preferred asymmetry lead to greater metabolic cost, making those gait patterns undesirable unless they are necessary to prevent a fall. Several of the predicted minima for the stability metrics were not significantly different than the preferred asymmetry values; however, these results should be viewed cautiously. Given the small sample size, combined with the presence of some medium to very large effect sizes, it is possible this study did not have adequate statistical power to detect some significant differences.

7.4 Role of cost of transport and gait stability with preferred gait patterns

It is generally accepted that metabolic energy expenditure (i.e., cost or effort) and not falling while moving forward (i.e., maintaining stability) are two main performance criteria for walking that lead to self-selected locomotor patterns. It is unclear how metabolic energy expenditure and gait stability are prioritized relative other factors such as smoothness and joint loading when walking in people with unilateral lower limb amputation. Subjects with amputation preferred more time on the intact limb compared with the prosthetic limb, while able-bodied subjects had nearly symmetric stance times (slightly more time on the dominant limb compared with the non-dominant limb). The asymmetries predicted to optimize cost of transport and gait stability were generally not significantly different than the preferred asymmetries for both groups, but this should be viewed cautiously because of limited sample size and medium to large effect sizes for some comparisons. It is possible these studies did not have adequate statistical power to detect some significant differences. However, the results overall, with predicted minima at positive asymmetry, and being greater for subjects with amputation compared to able-bodied subjects, suggest people may select patterns that minimize these metabolic cost and gait stability. The initial findings from both studies indicate that cost of transport and gait stability may play a role with how preferred patterns emerge after unilateral transtibial amputation. Gait stability may be able to be minimized, except in the medial-direction, to allow for lesser metabolic energy expenditure, while medial-lateral stability remains elevated in people with amputation because of a higher likelihood of a lateral fall due to prosthesis limitation. Preferred gait patterns may also be influenced by other factors such as smoothness and joint loading. These are the first studies to examine the effect of inter-limb gait asymmetry on metabolic cost and gait stability in people with amputation. Even though we need to be cautious about some of the interpretations, these findings warrant further investigation into how preferred patterns emerge in people with amputation. Understanding why preferred patterns are asymmetrical in people with unilateral transtibial amputation may provide insights for rehabilitation and assistive device design, and also show that an asymmetric gait may be the best result after some injuries and do not represent a problem that should be fixed.

7.5 Future directions

The subjects with amputation in these studies represent the minority of people with amputation. They were younger, more active and had an amputation from non-vascular causes. Most amputations occur because of vascular issues (e.g., diabetes) in older people. The subjects also had a unilateral transtibial amputation, which is the most common level of amputation, but it does not account for transfemoral amputations, which are the next most common level, and people with bilateral lower limb amputations. Future studies should aim to more generally understand how people with amputation determine preferred gait characteristics. Comparisons need to be made of younger and older groups, non-vascular amputation versus vascular amputation, and between different levels of amputation. Even though there are greater mobility challenges for people with vascular amputations, there is a greater potential public health impact. Small changes in rehabilitation and devices could lead to greater mobility, better management of other comorbidities (e.g., obesity) and could improve quality of life. This same paradigm of understanding the effect of gait asymmetry on metabolic energy expenditure and gait stability could be applied to other populations such as total joint arthroplasty and people with stroke. Other factors that influence how preferred patterns emerge, such as joint loading and smoothness, should be included in future studies alongside metabolic energy expenditure and gait stability. Understanding why people move differently after an injury could lead to more efficient rehabilitation and better overall outcomes.

APPENDICES

APPENDIX A

ADDITIONAL FIGURES FOR STUDY 2

The variability of step width, step length and stance time are represented as the coefficient of variation in the next three figures. The coefficient of variation accounts for the mean of the data and can be a better representation of how variable the data are. Standard deviation is most commonly reported in the literature, but may not the best representation of data's variability. The step width, step length and stance time coefficients of variation were similar to the step width, step length, and stance time standard deviation. The prosthetic and intact limbs have closer magnitudes between limbs and also closer to the limbs for the subjects without amputation. The coefficients of variation indicate that the prosthetic and intact limbs are less variable than presented by standard deviation. The data can be interpreted as less variable, but the focus of this dissertation was to find the predicted asymmetry from the minimum of the measure. The asymmetries that correspond to the minimums for the step length and stance time coefficient of variations are similar to the asymmetries predicted from the standard deviation. Therefore, the standard deviation was presented in the main results and discussion section.

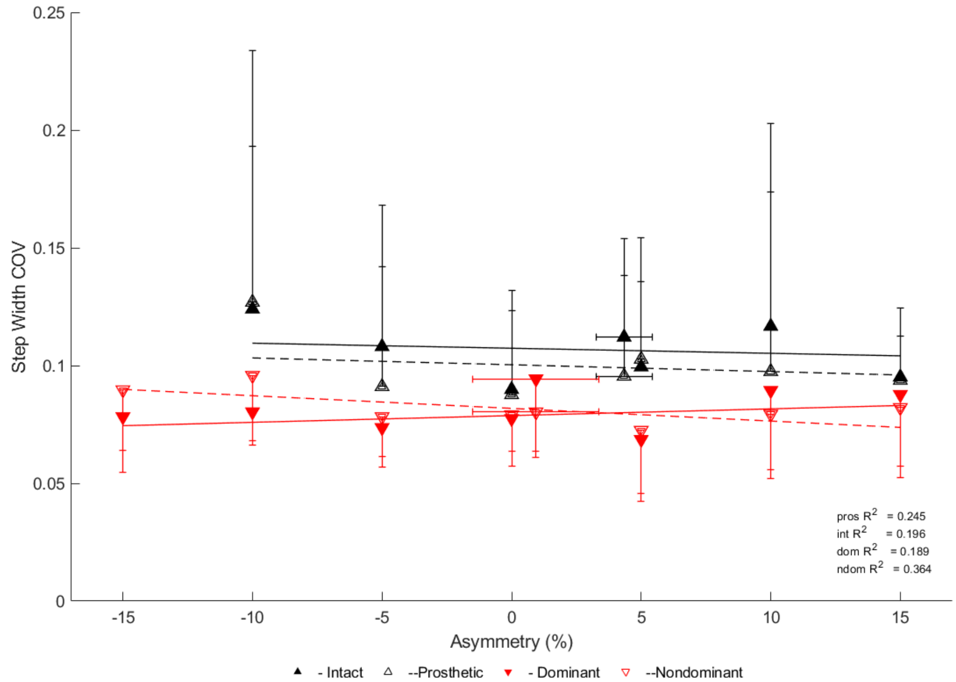

Figure A.1: Step width coefficient of variation. Step width variability, represented by coefficient of variation, between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. A linear trend best explained the relationship between step width variability and asymmetry.

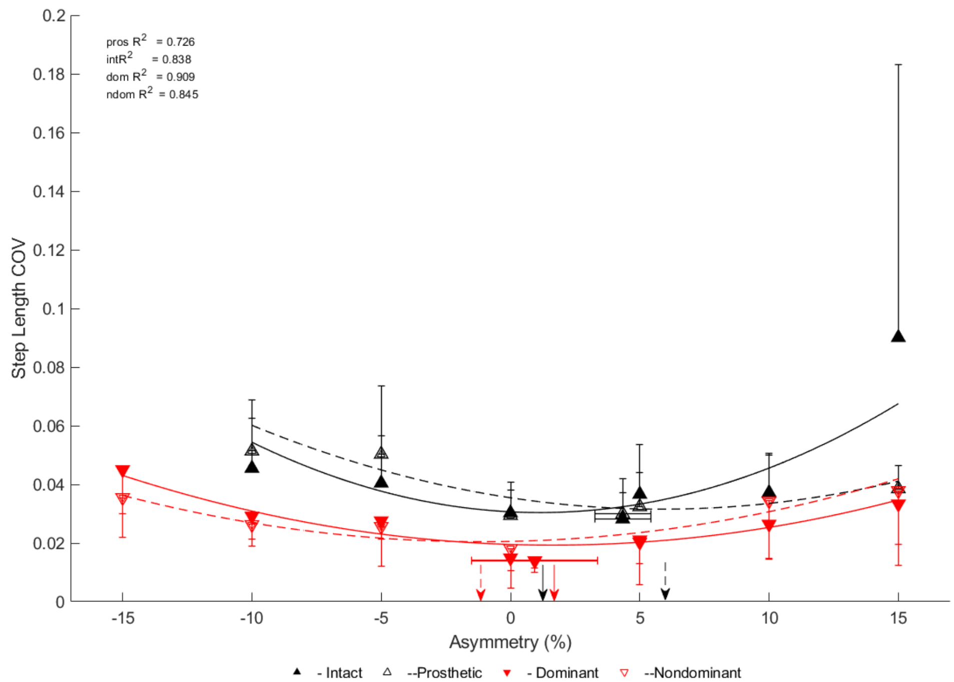

Figure A.2: Step length coefficient of variation. Step length variability, represented by coefficient of variation, between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. Downward facing arrows at the x-axis represent the predicted asymmetries corresponding to minima step length variability. A quadratic trend best explained the relationship between step length variability and asymmetry.

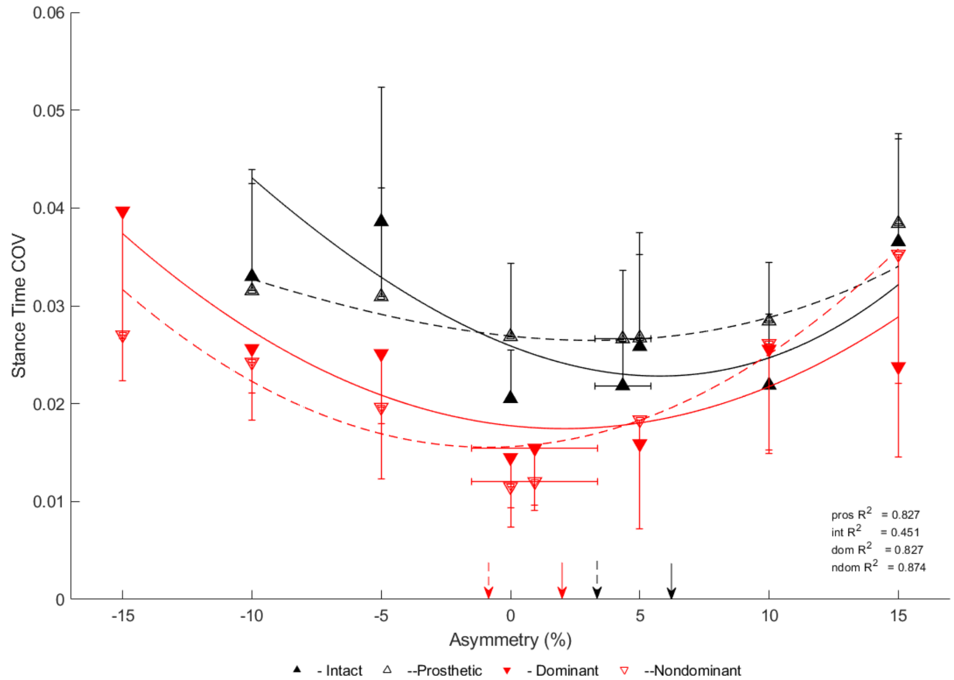

Figure A.3: Stance time coefficient of variation. Stance time variability, represented by coefficient of variation, between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. Intact and dominant limbs are represented by solid lines, prosthetic and non-dominant limbs are represented by dashed lines. Downward facing arrows at the x-axis represent the predicted asymmetries corresponding to minima stance time variability. A quadratic trend best explained the relationship between stance time variability and asymmetry.

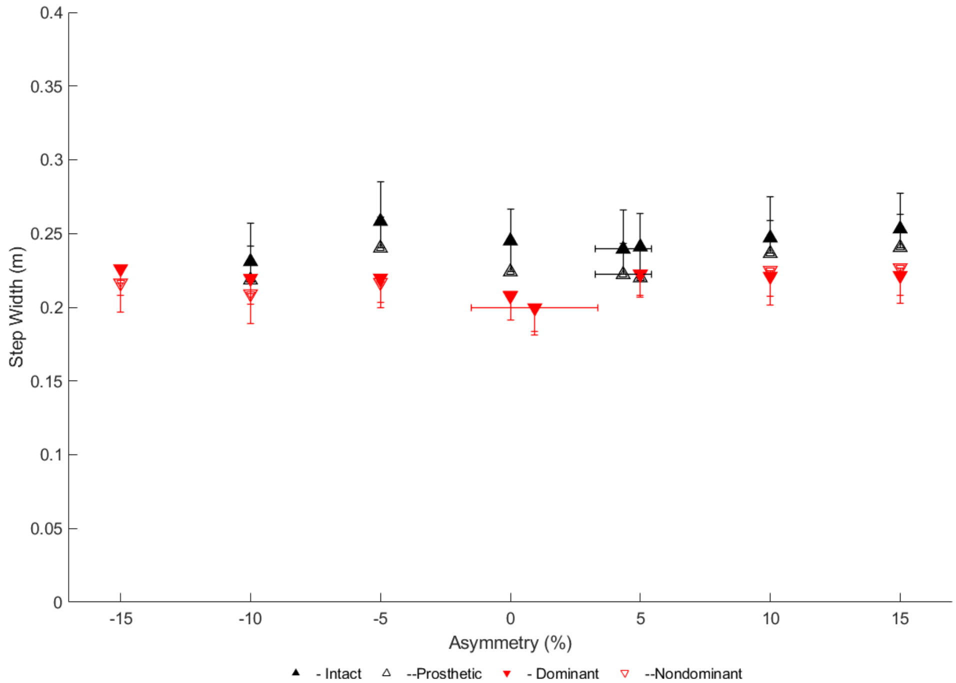

Figure A.4: Step width. Step width between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. The step width was consistent across conditions for each limb.

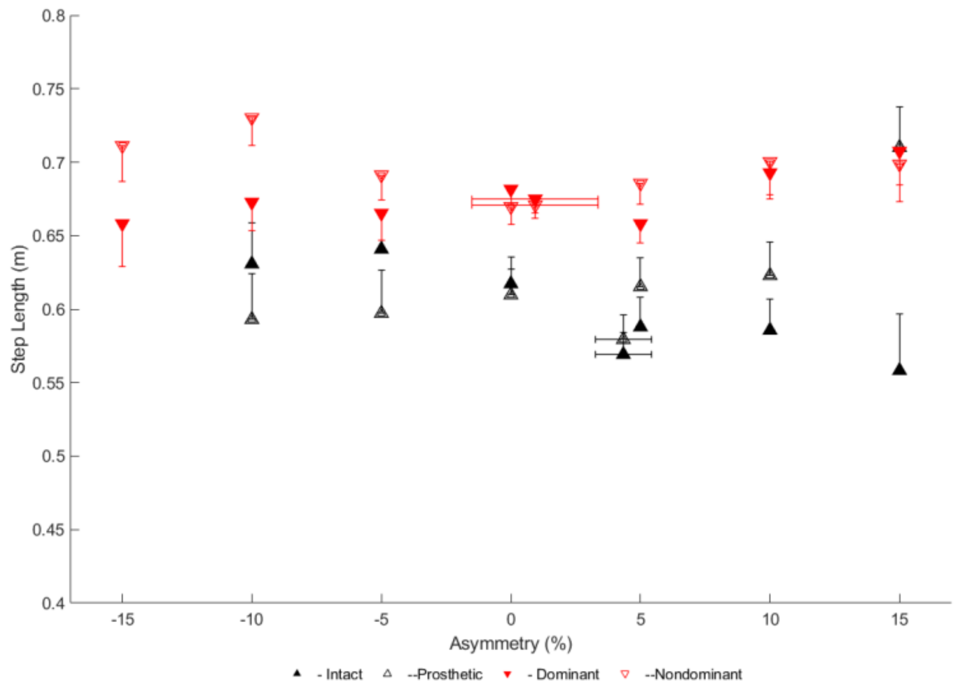

Figure A.5: Step length. Step length between subjects with amputation (black) and able-bodied subjects (red). Triangles are mean values with an error bar that is 1 standard deviation. The step length was lesser for subjects with amputation than able-bodied subjects across conditions, which may be accounted for by the slower preferred walking speed for people with amputation compared with the able-bodied subjects.

APPENDIX B

INFORMED CONSENT DOCUMENT PEOPLE WITH AMPTUTATION

Consent Form for Participation in a Research Study – Primary Participant

University of Massachusetts Amherst

Principal Investigator:	Professor Brian Umberger
Student Researcher:	Ryan D. Wedge
Study Title:	Metabolic cost and stability of locomotion in people with lower limb amputation

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1. WHAT IS THIS FORM?
This form is called a Consent Form. It will give you information about the study so you can make an informed decision about participation in this research study.

2. WHO IS ELIGIBLE TO PARTICIPATE?

Inclusion criteria

- Healthy people with a unilateral transtibial (i.e., below knee and above ankle) amputation that is more than a year old
- Rated by Medicare guidelines at a K3 or K4 level (i.e., able to walk with variable cadences)
- Between 16 and 50 years old

Exclusion criteria

- Younger than 16 years old or older than 50 years old

- Lower limb amputation within the last year
- Medicare classification of K0, K1 or K2 level (i.e. non-prosthesis user, household walker, low-level community walker, respectively)
- Chronic pain, arthritis, and other ailments that affect ability to walk, aside from amputation.
- Dysvascular disease (e.g., peripheral arterial disease, diabetes)
- Confounding medical condition that would place participant at risk (e.g., heart condition)
- Surgery in the last year or other condition that affects ability to walk

3. WHAT IS THE PURPOSE OF THIS STUDY?

You are being asked to participate in this research study to help understand the relative importance of minimizing energy (effort) and maintaining stability (staying upright) during walking in people with and without a unilateral lower limb amputation. The benefits of this experiment would be to help with rehabilitation for people with lower limb amputation and potentially influence the design of future prosthetic devices.

4. WHERE WILL THE STUDY TAKE PLACE AND HOW LONG WILL IT LAST?

The study will be conducted at the University of Massachusetts, Amherst in the Biomechanics Laboratory located in the Totman building. The study will take place over two sessions of approximately two hours per session.

5. WHAT WILL I BE ASKED TO DO?

If you agree to take part in this study, you will be asked to walk overground for 400 m and on a treadmill for approximately 1 hour on 2 different days. The 2 sessions will be 6-14 days apart. Before walking on day 1, you will have your leg lengths measured with a calibrated ruler. While walking on the treadmill, you will wear reflective markers at designated locations on the torso, arms and legs on both days. The marker locations are: top of the head with a headband, both shoulders, both elbows, both wrists, base of the neck, middle of the back, top of the chest bone, tops of both hips, front of both hips, low back, outside of both hips, outer portion of the intact knee, outer portion of the upper prosthesis aligned with outer intact knee, inner portion of the intact knee, inner portion of the upper prosthesis aligned with the inner intact knee, outer portion of the intact side ankle and outer portion of the prosthesis ankle aligned with outer intact side, inner portion of the intact side ankle and inner portion of the prosthesis ankle aligned with the inner intact side, outer portion of both shoes, inner portion of both shoes and tips of both shoes, 4 markers on a plastic plate placed on both thighs and the intact side lower leg, 4 markers placed on the outer portion of the prosthesis socket, and 3 markers on a plastic plate placed on the back of both shoes. The reflective markers help capture the motion of your body segments using high-speed cameras. The markers are secured in place through the use of medical adhesives and athletic tape. In addition to the markers, you will wear a thin, low-profile, device inside both of your shoes (like an insole) that will be used to provide real time feedback of your walking. On the second day, you will also wear head gear that has a mouth piece and tubing attached to it. The oxygen you breathe in and the carbon dioxide you breathe out will be collected from the mouth piece and used to determine the amount of energy you are expending. To determine how much energy you expend while resting, you will wear the headgear with the mouthpiece and tubing during 5 minutes of quiet sitting and 5 minutes of quiet standing. After the sitting and standing periods, you will begin the walking trials. When on the treadmill, you will be asked to walk the way you prefer and with non-preferred walking patterns. To perform the non-preferred walking patterns, you will receive real time visual feedback about the timing of your feet hitting the ground and asked to match your walking to a target on the screen. All of the non-preferred walking patterns are slightly different timing patterns compared with how you normally walk, similar to what you do when walking over uneven ground. We expect that you should be able to walk with all of the timing patterns, but any of the conditions can be skipped if you do not feel that you can do them. The data collected will not identify you personally. The video footage only tracks the motion of the markers on your body and does not record images of you. Photographs will be taken of the marker placement on your body, however they will be neck down and will not include your face. Each walking condition will be 5 minutes long followed by 5 minutes of seated rest. You will be asked to walk for approximately 35 minutes in total: Preferred walking plus 6 non-preferred conditions at 5 minutes each, with 5 minute seated rest after each condition. Between the 2 test days, you will be asked to wear an activity monitor (similar to a pedometer) for 3 weekdays and 1 weekend day over your dominant leg that is attached to belt worn around your waist. You will need to wear the monitor each day during waking hours. The activity monitor is small and should not obstruct movement or clothing throughout the day. In addition to the monitor, we will ask you to keep a log of when you put the monitor on and when you take it off each day.

6. WHAT ARE MY BENEFITS OF BEING IN THIS STUDY?

You may not directly benefit from this research; however, we hope that your participation in the study will help in the development of new rehabilitation procedures and future designs of prosthetic devices that will improve the quality of life for people with lower limb amputation.

7. WHAT ARE MY RISKS OF BEING IN THIS STUDY?

Any study involving physical activity involves some degree of risk, but we believe that the risks associated with this experiment are minimal. You will only be asked to perform movements that are part of normal, everyday life. The non-preferred walking patterns are not substantially different than your preferred walking patterns as they only represent modest differences in the timing of movements between your two legs, such as you might use when walking over uneven ground. If you would like to stop walking during a trial, you can grab the handrail located at the front of the treadmill and step off the treadmill belt. You will be required to stand and walk during the experiment, but breaks will be given between trials, during which you will be allowed to sit down. The activity monitor being worn between sessions is small and should not obstruct or alter movement throughout the day.

While we believe the risks associated with this research study are minimal, a possible inconvenience may be the time it takes to complete the study. Another possible risk of the study is the potential for skin irritation due to the adhesive used to place the markers on the body. While the intensity of the walking tasks will be low and adequate rest between trials will be provided, another possible risk is moderate fatigue after completing the sessions. There is a minimal risk for a breach of confidentiality. We keep this risk low by storing the information and data you are providing in a secure location. Also, the video system used to record the motion of your body does not capture personally identifiable features. The video footage only tracks motion of the markers on the body and does not record images that could reveal your identity.

8. WILL I BE COMPENSATED FOR MY TIME SPENT?

You will be provided monetary compensation of $20.00 total per session, for your participation in the study which will take approximately two hours per session for two sessions. If you are uncomfortable for any reason and decide to withdraw from the study after the session has begun, you will be paid at a rate of $10/hour, rounded to the nearest dollar.

9. HOW WILL MY PERSONAL INFORMATION BE PROTECTED?

The following procedures will be used to protect the confidentiality of your study records. The researchers will keep all study records (including any codes linked to your data) in a locking file cabinet in the Biomechanics Laboratory. Research records will be labeled with a code. Informed consent documents and a master key that links names and codes will be maintained in a separate and secure location. All electronic files (e.g., database, spreadsheet, etc.) containing identifiable information will be password protected. Any computer hosting such files will also have password protection to prevent access by unauthorized users. Only the members of the research staff will have access to the passwords. Upon conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations without your expressed written consent.

10. WHAT IF I HAVE QUESTIONS?

Take as long as you like before you make a decision. We will be happy to answer any question you have about this study. If you have further questions about this project or if you have a research-related problem, you may contact the principal investigator, Professor Brian Umberger at the University of Massachusetts Amherst Biomechanics Laboratory (413) 545-1436 or the student researcher Ryan Wedge at (860) 581-0055. If you have any questions concerning your rights as a research subject, you may contact the University of Massachusetts, Amherst, Human Research Protection Office (HRPO) at (413) 545-3428 or humansubjects@ora.umass.edu.

11. CAN I STOP BEING IN THE STUDY?

You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. There are no penalties or consequences of any kind if you decide that you do not want to participate.

12. WHAT IF I AM INJURED?

The University of Massachusetts does not have a program for compensating subjects for injury or complications related to human subject research, but the study personnel will assist you in getting treatment.

13. VIDEO AND PHOTOGRAPHY CONSENT

I give permission to be photographed and/or videotaped during the study, with the understanding that my identity will be decoupled from data, meaning that my face and any identifiable markings will be blurred. Audio will not be recorded if videotaped during the study.

□ Agree

□ Do not agree

14. OPTIONAL CONSENT FOR USE OF PARTICIPANT INFORMATION

□ Check here to give permission to be contacted for potential participation in future studies. Your contact information (e-mail and/or phone number) will be kept in either a locked cabinet or encrypted computer file accessible only to the study personnel.

15. SUBJECT STATEMENT OF VOLUNTARY CONSENT

I have read this form and decided that I will participate in the project described above. The general purposes and particulars of the study as well as possible hazards and inconveniences have been explained to my satisfaction. I understand that I can withdraw at any time.

________________________	____________________	__________
Participant Signature:	Print Name:	Date:

By signing below I indicate that the participant has read and, to the best of my knowledge, understands the details contained in this document and has been given a copy.

_________________________	____________________	__________
Signature of Person Obtaining Consent	Print Name:	Date:

APPENDIX C

INFORMED CONSENT DOCUMENT ABLE-BODIED INDIVIDUALS

Consent Form for Participation in a Research Study – Primary Participant

University of Massachusetts Amherst

Principal Investigator:	Professor Brian Umberger
Student Researcher:	Ryan D. Wedge
Study Title:	Metabolic cost and stability of locomotion in people with lower limb amputation

---

1. WHAT IS THIS FORM?

This form is called a Consent Form. It will give you information about the study so you can make an informed decision about participation in this research study.

2. WHO IS ELIGIBLE TO PARTICIPATE?

Inclusion criteria

- Healthy people without amputation
- Between 16 and 50 years old

Exclusion criteria

- Younger than 16 years old or older than 50 years old
- Chronic pain, arthritis, and other ailments that affect ability to walk
- Dysvascular disease (e.g., peripheral arterial disease, diabetes)
- Confounding medical condition that would place participant at risk (e.g., heart condition)
- Surgery in the last year or other condition that affects ability to walk

3. WHAT IS THE PURPOSE OF THIS STUDY?

You are being asked to participate in this research study to help understand the relative importance of minimizing energy (effort) and maintaining stability (staying upright) during walking in people with and without a unilateral lower limb amputation. The benefits of this experiment would be to help with rehabilitation for people with lower limb amputation and potentially influence the design of future prosthetic devices.

4. WHERE WILL THE STUDY TAKE PLACE AND HOW LONG WILL IT LAST?

The study will be conducted at the University of Massachusetts, Amherst in the Biomechanics Laboratory located in the Totman building. The study will take place over two sessions of approximately two hours per session.

5. WHAT WILL I BE ASKED TO DO?

If you agree to take part in this study, you will be asked to walk overground for 400 m and on a treadmill for approximately 1 hour on 2 different days. The 2 sessions will be 6-14 days apart. Before walking on day 1, you will have your leg lengths measured with a calibrated ruler. While walking on the treadmill, you will wear reflective markers at designated locations on the torso, arms and legs on both days. While walking on the treadmill, you will wear reflective markers at designated locations on the torso, arms and legs on both days. The marker locations are: top of the head with a headband, both shoulders, both elbows, both wrists, base of the neck, middle of the back, top of the chest bone, tops of both hips, front of both hips, low back, outside of both hips, outer portion of the both knees, inner portion of both knees, outer portion of both ankles, inner portion of both ankles, outer portion of both shoes, inner portion of both shoes and tips of both shoes, 4 markers on a plastic plate placed on both thighs and lower legs, and 3 markers on a plastic plate placed on the back of both shoes. The reflective markers help capture the motion of your body segments using high-speed cameras. The markers are secured in place through the use of medical adhesives and athletic tape. In addition to the markers, you will wear a thin, low-profile, device inside both of your shoes (like an insole) that will be used to provide real time feedback of your walking. On the second day, you will also wear head gear that has a mouth piece and tubing attached to it. The oxygen you breathe in and the carbon dioxide you breathe out will be collected from the mouth piece and used to determine the amount of energy you are expending. To determine how much energy you expend while resting, you will wear the headgear with the mouthpiece and tubing during 5 minutes of quiet sitting and 5 minutes of quiet standing. After the sitting and standing periods, you will begin the walking trials. When on the treadmill, you will be asked to walk the way you prefer and with non-preferred walking patterns. To perform the non-preferred walking patterns, you will receive real time visual feedback about the timing of your feet hitting the ground and asked to match your walking to a target on the screen. All of the non-preferred walking patterns are slightly different timing patterns compared with how you normally walk, similar to what you do when walking over uneven ground. We expect that you should be able to walk with all of the timing patterns, but any of the conditions can be skipped if you do not feel that you can do them. The data collected will not identify you personally. The video footage only tracks the motion of the markers on your body and does not record images of you. Photographs will be taken of the marker placement on your body, however they will be neck down and will not include your face. Each walking condition will be 5 minutes long followed by 5 minutes of seated rest. You will be asked to walk for approximately 40 minutes in total: Preferred walking plus 7 non-preferred conditions at 5 minutes each, with 5 minute seated rest after each condition. Between the 2 test days, you will be asked to wear an activity monitor (similar to a pedometer) for 3 weekdays and 1 weekend day over your dominant leg that is attached to belt worn around your waist. You will need to wear the monitor each day during waking hours. The activity monitor is small and should not obstruct movement or clothing throughout the day. In addition to the monitor, we will ask you to keep a log of when you put the monitor on and when you take it off each day.

6. WHAT ARE MY BENEFITS OF BEING IN THIS STUDY?

You may not directly benefit from this research; however, we hope that your participation in the study will help in the development of new rehabilitation procedures and future designs of prosthetic devices that will improve the quality of life for people with lower limb amputation.

7. WHAT ARE MY RISKS OF BEING IN THIS STUDY?

Any study involving physical activity involves some degree of risk, but we believe that the risks associated with this experiment are minimal. You will only be asked to perform movements that are part of normal, everyday life. The non-preferred walking patterns are not substantially different than your preferred walking patterns as they only represent modest differences in the timing of movements between your two legs, such as you might use when walking over uneven ground. If you would like to stop walking during a trial, you can grab the handrail located at the front of the treadmill and step off the treadmill belt. You will be required to stand and walk during the experiment, but breaks will be given between trials, during which you will be allowed to sit down. The activity monitor being worn between sessions is small and should not obstruct or alter movement throughout the day.

While we believe the risks associated with this research study are minimal, a possible inconvenience may be the time it takes to complete the study. Another possible risk of the study is the potential for skin irritation due to the adhesive used to place the markers on the body. While the intensity of the walking tasks will be low and adequate rest between trials will be provided, another possible risk is moderate fatigue after completing the sessions. There is a minimal risk for a breach of confidentiality. We keep this risk low by storing the information and data you are providing in a secure location. Also, the video system used to record the motion of your body does not capture personally identifiable features. The video footage only tracks motion of the markers on the body and does not record images that could reveal your identity.

8. WILL I BE COMPENSATED FOR MY TIME SPENT?

You will be provided monetary compensation of $20.00 total per session, for your participation in the study which will take approximately two hours per session for two sessions. If you are uncomfortable for any reason and decide to withdraw from the study after the session has begun, you will be paid at a rate of $10/hour, rounded to the nearest dollar.

9. HOW WILL MY PERSONAL INFORMATION BE PROTECTED?

The following procedures will be used to protect the confidentiality of your study records. The researchers will keep all study records (including any codes linked to your data) in a locking file cabinet in the Biomechanics Laboratory. Research records will be labeled with a code. Informed consent documents and a master key that links names and codes will be maintained in a separate and secure location. All electronic files (e.g., database, spreadsheet, etc.) containing identifiable information will be password protected. Any computer hosting such files will also have password protection to prevent access by unauthorized users. Only the members of the research staff will have access to the passwords. Upon conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations without your expressed written consent.

10. WHAT IF I HAVE QUESTIONS?

Take as long as you like before you make a decision. We will be happy to answer any question you have about this study. If you have further questions about this project or if you have a research-related problem, you may contact the principal investigator, Professor Brian Umberger at the University of Massachusetts Amherst Biomechanics Laboratory (413) 545-1436 or the student researcher Ryan Wedge at (860) 581-0055. If you have any questions concerning your rights as a research subject, you may contact the University of Massachusetts, Amherst, Human Research Protection Office (HRPO) at (413) 545-3428 or humansubjects@ora.umass.edu.

11. CAN I STOP BEING IN THE STUDY?

You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. There are no penalties or consequences of any kind if you decide that you do not want to participate.

12. WHAT IF I AM INJURED?

The University of Massachusetts does not have a program for compensating subjects for injury or complications related to human subject research, but the study personnel will assist you in getting treatment.

13. VIDEO AND PHOTOGRAPHY CONSENT

I give permission to be photographed and/or videotaped during the study, with the understanding that my identity will be decoupled from data, meaning that my face and any identifiable markings will be blurred. Audio will not be recorded if videotaped during the study.

□ Agree

□ Do not agree

14. OPTIONAL CONSENT FOR USE OF PARTICIPANT INFORMATION

□ Check here to give permission to be contacted for potential participation in future studies. Your contact information (e-mail and/or phone number) will be kept in either a locked cabinet or encrypted computer file accessible only to the study personnel.

15. SUBJECT STATEMENT OF VOLUNTARY CONSENT

I have read this form and decided that I will participate in the project described above. The general purposes and particulars of the study as well as possible hazards and inconveniences have been explained to my satisfaction. I understand that I can withdraw at any time.

________________________	____________________	__________
Participant Signature:	Print Name:	Date:

By signing below I indicate that the participant has read and, to the best of my knowledge, understands the details contained in this document and has been given a copy.

_________________________	____________________	__________
Signature of Person	Print Name:	Date:
Obtaining Consent		

APPENDIX D

ASSENT DOCUMENT

Assent Form for 16-17 Year Olds

Project Title: Metabolic cost and stability of locomotion in people with lower limb amputation
Principle Investigators: Brian Umberger and Ryan Wedge

What is a research study?
A research study is a way to find out new information about something. You do not need to be in a research study if you do not want to.

Why are you being asked to be part of this research study?
You are being asked to take part in this research study because we are trying to understand more about how people with amputation walk. We are inviting you to be in this study because people at 16 years and older, walk in a similar way. About 20 participants will be in this study.

If you join the study what will you be asked to do?
If you agree to join this study, we will have you come to the lab for 2 sessions so you can walk overground and on a treadmill. The first session will be approximately 90 minutes and the second session will be approximately 120 minutes. During both sessions, you will be wearing reflective dots, like the ones used to make video games, on your trunk, arms and legs so we find out how your body moves when walking. You will also be wearing thin inserts for your shoes so we know the time it takes for each step you take. During the second session, we will be collecting the air you breathe in and out with a mouthpiece, so we can determine how much energy (e.g., calories) you are using. In between the sessions, you will wear a small activity tracker each day when awake, so we can measure how active you are over one week.

How will being in this study affect me?
You may get a little tired and sore from walking after each session, but you will be given rest between each walking trial to avoid these effects. The markers are attached with tape and may irritate your skin. The data we get from this study will be confidential. We will never tell anyone your name or that you were part of this study.

This study might find out things that will help other people someday. We will use our data to write up our results in research papers and share what we learn with other people who study walking in people with amputation.

Do your parents know about this study?
This study was explained to your parents and they said that we could ask you if you want to be in it. You can talk this over with them before you decide. If you want to be in the study, your parents will need to sign a form too.

Who will see the information collected about you?

- The information collected about you during this study will be kept safely locked up. Nobody will know it except the people doing the research.
- The study information about you will not be given to your parents. The researches will not tell your friends.

What do you get for being in the study?
You will get $20 for each session (total of $40 for the 2 sessions).

Do you have to be in the study?
You do not have to be in the study. No one will be upset if you don't want to do this study. If you don't want to be in this study, you just have to tell us. It's up to you. You can also take more time to think about being in the study.

What if you have any questions?
You can ask any questions that you may have about the study. If you have a question later that you didn't think of now, you can call Ryan Wedge at (860)-581-0055 or Brian Umberger at (413)-545-1436.

You can also take more time to think about being in the study and also talk some more with your parents about being in the study.

If you have any concerns about your rights as a research subject, you may contact the University of Massachusetts Amherst Human Research Protection Office (HRPO) at (413)-545-3428.

Other information about the study:
If you decide to be in the study, please write your name below.

You can change your mind and stop being part of it at any time. All you have to do is tell the person in charge. It's okay.

You will be given a copy of this paper to keep.

If you want to be in this study, please sign your name below.

Signature____
Date_____________________

Participant Name____
Date_____________________

Name of Person obtaining consent_________________________
Date_____________________

APPENDIX E

PARENT PERMISSION FORM-PEOPLE WITH AMPUTATION

University of Massachusetts Amherst

PARENT PERMISSION FOR MINOR TO PARTICIPATE IN RESEARCH

METABOLIC COST AND STABILITY OF LOCOMOTION IN PEOPLE WITH LOWER LIMB AMPUTATION

Professor Brian Umberger PhD (principal investigator) and Ryan Wedge MPT (student researcher) from the Department of Kinesiology at the University of Massachusetts Amherst (UMass Amherst) are conducting a research study.

Your child was selected as a possible participant in this study because we are trying to understand more about how people with amputation walk. We are inviting your child to be in this study because people at 16 years and older, walk in a similar way. Your child's participation in this research study is voluntary.

Why is this study being done?

Your child is being asked to participate in this research study to help understand the relative importance of minimizing energy (effort) and maintaining stability (staying upright) during walking in people with and without a one-sided below knee amputation. The benefits of this experiment would be to help with rehabilitation for people with lower limb amputation and potentially influence the design of future prosthetic devices.

What will happen if my child takes part in this research study?

If you agree to allow your child to participate in this study, we would ask him/her to:

- Walk overground for 400 m
- Walk on a treadmill for approximately 1 hour on 2 different days
- Have your leg lengths measured with a calibrated ruler
- While walking on the treadmill, you will wear reflective markers at designated locations on the torso, arms and legs on both days. The reflective markers help capture the motion of your body segments using high-speed cameras. The markers are secured in place through the use of medical adhesives and athletic tape. The marker locations are:
  - Top of the head with a headband
  - Both shoulders
  - Both elbows
  - Both wrists
  - Base of the neck
  - Middle of the back
  - Top of the chest bone
  - Tops of both hips
  - Front of both hips
  - Low back
  - Outside of both hips
  - Outer portion of the intact knee
  - Outer portion of the upper prosthesis aligned with outer intact knee
  - Inner portion of the intact knee
  - Inner portion of the upper prosthesis aligned with the inner intact knee
  - Outer portion of the intact side ankle
  - Outer portion of the prosthesis ankle aligned with outer intact side
  - Inner portion of the intact side ankle
  - Inner portion of the prosthesis ankle aligned with the inner intact side
  - Outer portion of both shoes
  - Inner portion of both shoes
  - Tips of both shoes
  - 4 markers on a plastic plate placed on both thighs
  - 4 markers on a plastic plate placed on the intact side lower leg
  - 4 markers placed on the outer portion of the prosthesis socket
  - 3 markers on a plastic plate placed on the back of both shoes

- In addition to the markers, you will wear a thin, low-profile, device inside both of your shoes (like an insole) that will be used to provide real time feedback of your walking.
- On the second day, you will also wear head gear that has a mouth piece and tubing attached to it. The oxygen you breathe in and the carbon dioxide you breathe out will be collected from the mouth piece and used to determine the amount of energy you are expending.

- To determine how much energy you expend while resting, you will wear the headgear with the mouthpiece and tubing during 5 minutes of quiet sitting and 5 minutes of quiet standing. After the sitting and standing periods, you will begin the walking trials.
- When on the treadmill, you will be asked to walk the way you prefer and with non-preferred walking patterns. To perform the non-preferred walking patterns, you will receive real time visual feedback about the timing of your feet hitting the ground and asked to match your walking to a target on the screen. All of the non-preferred walking patterns are slightly different timing patterns compared with how you normally walk, similar to what you do when walking over uneven ground. We expect that you should be able to walk with all of the timing patterns, but any of the conditions can be skipped if you do not feel that you can do them.
- The data collected will not identify you personally. The video footage only tracks the motion of the markers on your body and does not record images of you.
- Photographs will be taken of the marker placement on your body, however they will be neck down and will not include your face.
- Each walking condition will be 5 minutes long followed by 5 minutes of seated rest. You will be asked to walk for approximately 35 minutes in total: Preferred walking plus 6 non-preferred conditions at 5 minutes each, with 5 minute seated rest after each condition.
- Between the 2 test days, you will be asked to wear an activity monitor (similar to a pedometer) for 3 weekdays and 1 weekend day over your dominant leg that is attached to a belt worn around your waist. You will need to wear the monitor each day during waking hours. The activity monitor is small and should not obstruct movement or clothing throughout the day.
- In addition to the monitor, we will ask you to keep a log of when you put the monitor on and when you take it off each day.

How long will my child be in the research study?

Participation will take a total of about 4 hours over the course of 2 sessions of approximately 2 hours per session. The sessions will be 6-14 days apart.

Are there any potential risks or discomforts that my child might experience from participating in this study?

Any study involving physical activity involves some degree of risk, but we believe that the risks associated with this experiment are minimal. Your child will only be asked to perform movements that are part of normal, everyday life. The non-preferred walking patterns are not substantially different than preferred walking patterns as they only represent modest differences in the timing of movements between your two legs, such as when walking over uneven ground. If your child would like to stop walking during a trial, they can grab the handrail located in the front of the treadmill and step off the treadmill belt. Your child will be required to stand and walk during the experiment, but breaks will be given between trials, during which they will be allowed to sit down. The activity monitor being worn between sessions is small and should not obstruct or alter movement throughout the day.

While we believe the risks associated with this research study are minimal, a possible inconvenience may be the time it takes to complete the study. Another possible risk of the study is the potential for skin irritation due to the adhesive used to place the markers on the body. While the intensity of the walking tasks will be low and adequate rest between trials will be provided, another possible risk is moderate fatigue after completing the sessions. There is a minimal risk for a breach of confidentiality. We keep this risk low by storing the information and data you are providing in a secure location. Also, the video system used to record the motion of your child's body does not capture personally identifiable features. The video footage only tracks motion of the markers on the body and does not record images that could reveal their identity.

Will my child receive compensation for participating?

Your child will receive monetary compensation of $20.00 total per session for two sessions. If your child is uncomfortable for any reason and decides to withdraw from the study after the session has begun, they will be paid at a rate of $10/hour, rounded to the nearest dollar.

How will information about my child's participation be kept confidential?

Any information that is obtained in connection with this study and that can identify your child will remain confidential. It will be disclosed only with your permission or as required by law. Confidentiality will be maintained by means of keeping all study records (including any codes linked to your data) in a locking file cabinet in the Biomechanics Laboratory. Research records will be labeled with a code. Parental consent and minor assent documents and a master key that links names and codes will be maintained in a separate and secure location. All electronic files (e.g., database, spreadsheet, etc.) containing identifiable information will be password protected. Any computer hosting such files will also have password protection to prevent access by unauthorized users. Only the members of the research staff will have access to the passwords.

Upon conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations without your expressed written consent.

What are my and my child's rights if he or she takes part in this study?

- You can choose whether or not you want your child to be in this study, and you may withdraw your permission and discontinue your child's participation at any time.
- Whatever decision you make, there will be no penalty to you or your child, and no loss of benefits to which you or your child were otherwise entitled.
- Your child may refuse to answer any questions that he/she does not want to answer and still remain in the study.

Who can I contact if I have questions about this study?

- **The research team:**
  If you have any questions, comments or concerns about the research, you can talk to the one of the researchers. Please contact the principal investigator, Professor Brian Umberger at the University of Massachusetts Amherst Biomechanics Laboratory (413) 545-1436 or the student researcher Ryan Wedge at (860) 581-0055.

- **UMass Amherst Human Research Protection Office (HRPO):**

If you have questions about your child's rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, please call the HRPO at (413) 545-3428 or email humansubjects@ora.umass.edu

You will be given a copy of this information to keep for your records.

SIGNATURE OF PARENT OR LEGAL GUARDIAN

Name of Child

Name of Parent or Legal Guardian

Signature of Parent or Legal Guardian

Date

SIGNATURE OF PERSON OBTAINING CONSENT

Name of Person Obtaining Consent

Contact Number

Signature of Person Obtaining Consent

Date

APPENDIX F

PARENT PERMISSION FORM-ABLE-BODIED INDIVIDUALS

University of Massachusetts Amherst

PARENT PERMISSION FOR MINOR TO PARTICIPATE IN RESEARCH

METABOLIC COST AND STABILITY OF LOCOMOTION IN PEOPLE WITH LOWER LIMB AMPUTATION

Professor Brian Umberger PhD (principal investigator) and Ryan Wedge MPT (student researcher) from the Department of Kinesiology at the University of Massachusetts Amherst (UMass Amherst) are conducting a research study.

Your child was selected as a possible participant in this study because we are trying to understand more about how people with amputation walk. We are inviting your child to be in this study because people at 16 years and older, walk in a similar way. Your child's participation in this research study is voluntary.

Why is this study being done?

Your child is being asked to participate in this research study to help understand the relative importance of minimizing energy (effort) and maintaining stability (staying upright) during walking in people with and without a one-sided below knee amputation. The benefits of this experiment would be to help with rehabilitation for people with lower limb amputation and potentially influence the design of future prosthetic devices.

What will happen if my child takes part in this research study?

If you agree to allow your child to participate in this study, we would ask him/her to:

- Walk overground for 400 m
- Walk on a treadmill for approximately 1 hour on 2 different days
- Have your leg lengths measured with a calibrated ruler
- While walking on the treadmill, you will wear reflective markers at designated locations on the torso, arms and legs on both days. The reflective markers help capture the motion of your body segments using high-speed cameras. The markers are secured in place through the use of medical adhesives and athletic tape. The marker locations are:
    - Top of the head with a headband
    - Both shoulders
    - Both elbows
    - Both wrists
    - Base of the neck
    - Middle of the back
    - Top of the chest bone
    - Tops of both hips
    - Front of both hips
    - Low back
    - Outside of both hips
    - Outer portion of the intact knee
    - Outer portion of the upper prosthesis aligned with outer intact knee
    - Inner portion of the intact knee
    - Inner portion of the upper prosthesis aligned with the inner intact knee
    - Outer portion of the intact side ankle
    - Outer portion of the prosthesis ankle aligned with outer intact side
    - Inner portion of the intact side ankle
    - Inner portion of the prosthesis ankle aligned with the inner intact side
    - Outer portion of both shoes
    - Inner portion of both shoes
    - Tips of both shoes
    - 4 markers on a plastic plate placed on both thighs
    - 4 markers on a plastic plate placed on both lower legs
    - 3 markers on a plastic plate placed on the back of both shoes

- In addition to the markers, you will wear a thin, low-profile, device inside both of your shoes (like an insole) that will be used to provide real time feedback of your walking.
- On the second day, you will also wear head gear that has a mouth piece and tubing attached to it. The oxygen you breathe in and the carbon dioxide you breathe out will be collected from the mouth piece and used to determine the amount of energy you are expending.

- To determine how much energy you expend while resting, you will wear the headgear with the mouthpiece and tubing during 5 minutes of quiet sitting and 5 minutes of quiet standing. After the sitting and standing periods, you will begin the walking trials.
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- Each walking condition will be 5 minutes long followed by 5 minutes of seated rest. You will be asked to walk for approximately 35 minutes in total: Preferred walking plus 6 non-preferred conditions at 5 minutes each, with 5 minute seated rest after each condition.
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- In addition to the monitor, we will ask you to keep a log of when you put the monitor on and when you take it off each day.

How long will my child be in the research study?

Participation will take a total of about 4 hours over the course of 2 sessions of approximately 2 hours per session. The sessions will be 6-14 days apart.

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Will my child receive compensation for participating?

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How will information about my child's participation be kept confidential?

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Upon conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations without your expressed written consent.

What are my and my child's rights if he or she takes part in this study?

- You can choose whether or not you want your child to be in this study, and you may withdraw your permission and discontinue your child's participation at any time.
- Whatever decision you make, there will be no penalty to you or your child, and no loss of benefits to which you or your child were otherwise entitled.
- Your child may refuse to answer any questions that he/she does not want to answer and still remain in the study.

Who can I contact if I have questions about this study?

- **The research team:**
  If you have any questions, comments or concerns about the research, you can talk to the one of the researchers. Please contact the principal investigator, Professor Brian Umberger at the University of Massachusetts Amherst Biomechanics Laboratory (413) 545-1436 or the student researcher Ryan Wedge at (860) 581-0055.

- **UMass Amherst Human Research Protection Office (HRPO):**

If you have questions about your child's rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, please call the HRPO at (413) 545-3428 or email humansubjects@ora.umass.edu

You will be given a copy of this information to keep for your records.

SIGNATURE OF PARENT OR LEGAL GUARDIAN

Name of Child

Name of Parent or Legal Guardian

Signature of Parent or Legal Guardian

Date

SIGNATURE OF PERSON OBTAINING CONSENT

Name of Person Obtaining Consent

Contact Number

Signature of Person Obtaining Consent

Date

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