ABSTRACT

Title of Dissertation: LOWER LIMB ASYMMETRY AND LOADING IN INDIVIDUALS WITH UNILATERAL TRANSFEMORAL AMPUTATIONS WITH A LIFETIME OF OSSEOINTEGRATED PROSTHESIS USE

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Individuals with transfemoral amputation commonly develop chronic health problems due to decreased physical activity as a result of the missing musculature and tissue on the amputated side, and the poor imitation of the intact limb provided by the prosthesis. In addition, the indirect and semi-rigid connection of the socket to the body may increase interlimb asymmetries, as well as lead to pain and discomfort on the residual limb. Recent innovations have introduced a bone-anchored or osseointegrated (OI) implant which connects the prosthesis to the skeleton, and removes most of the socket related pain and discomfort complaints, as well as providing a rigid connection which may reduce the interlimb asymmetries. However, the direct bone and prosthesis connection may also introduce longitudinal bone health concerns due to the repetitive loads during walking. This dissertation investigated the effect of walking speed on the loads placed on the lower limbs of 11 individuals who use an OI prosthesis at 3 different anatomical levels, including the whole limb through interlimb ground reaction force, the joints through interlimb joint kinematics and kinetics, and finally the residual limb

bone through implant input forces, finite element analysis of bone strain, and the probability of bone injury with a simulated lifetime of use.

In study 1, the interlimb ground reaction force asymmetries were found to be moderate to large at all walking speeds, and to have a general increase as individuals walked faster, indicating there is an intact limb reliance strategy which may be used to compensate for the limitations of the amputated limb. Similarly, in study 2, the interlimb joint kinematics and kinetics were found to have moderate to large asymmetries at each joint level, with a general increase in asymmetry at faster walking, with this increase largely due to limitations within the prothesis. In study 3, the abutment force decreased in magnitude with walking speed, but the peak strain on the bone, and the probability of injury was greater for the preferred speed and fast speed walking when compared to slow speed walking. However, the overall probability of injury was low for all speeds, indicating the ability of the bone to repair and adapt with sustained loading likely provides effective protection over a lifetime of simulated OI prothesis use. The findings of this dissertation suggest that the more rigid connection afforded by the OI implant cannot fully remove the interlimb asymmetries which occur as a result of the poor imitation of the intact limb provided by the prosthesis and prosthesis components, but that there is minimal risk to the bone due to a lifetime of sustained walking with an OI prosthesis as a result the inherent ability of the bone to repair and adapt to variable loads over time. Therefore, while an OI prosthesis may not fully mitigate the interlimb asymmetries which occur as a result of the prosthesis limitations, individuals who use an OI prosthesis may feel confident that there is minimal longitudinal risk to the bone as a result of walking over their lifetime.

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by

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LIST OF ABBREVIATIONS

OI	osseointegrated
FEA	finite element analysis
SACH	Solid Ankle, Cushion Heel
ESAR	energy storage and return
FEM	finite element model
AP	anterior-posterior
ML	medial-lateral

CHAPTER 1: INTRODUCTION

1.1. Background

Physical activity and mobility are critical for living a healthy and high-quality life. However, individuals with lower extremity amputation typically report decreased activity time, including a steps per day count that is between 1500 and 5500 (Bussmann et al., 2004; Wong et al., 2021), a number that is drastically lower than the recommended 10,000 steps. These individuals also report a general dissatisfaction with their quality of life due to their lack of mobility (Pepin et al., 2019; Wurdeman et al., 2017). The decreased activity, mobility, and quality of life are generally believed to be the result of the missing tissue and limb, as well as the poor to moderate imitation of the intact limb generated by using a prosthesis, socket, and associated componentry (Goldfarb, 2013). This dissertation plans to investigate a new and innovative prosthesis fixation method which uses an osseointegrated (OI) or bone anchored implant to attach the prosthesis to the residual limb. Fixing the prothesis to the residual limb with an OI implant is expected to result in functional performance improvements, but also may cause high loads to be transferred to the residual limb bone which may lead to injuries with a lifetime of use. This research is critical for clinicians and medical staff to understand the influence of a skeletally fixed prosthesis on body mechanics, as well as for the individual with lower extremity amputation, as the direct skeletal fixation may afford better function and the chance for improved physical activity and long-term

health.

1.1.1. Lower extremity amputation and long-term health

Individuals with lower extremity amputation typically have decreased daily physical activity rates and function when compared to their healthy adult peers (Bussmann et al., 2004; Pepin et al., 2019), and commonly suffer from acute and chronic health problems, including cardiovascular disease and obesity (Naschitz & Lenger, 2008b; Saris et al., 2003; Singh et al., 2007), high osteoarthritis rates in the knee limb (Gailey et al., 2008; Norvell et al., 2005; Struyf et al., 2009), and chronic low back pain (Gailey et al., 2008; Hammarlund et al., 2011; Highsmith et al., 2019; Stam et al., 2004). The decrease in physical activity and increase in common health problems is largely believed to be the result of the missing musculature and tissue, as well as due to the poor imitation of the intact limb provided by using a prosthesis (Goldfarb, 2013).

One common prosthesis related complaint by individuals with lower extremity amputation is with their prosthesis fixation method. In general, most individuals with a lower limb amputation use a socket-based fixation method, and, despite the many advancements in socket technology, many individuals experience problems with the fit and comfort of their socket. In particular, individuals who use a socket-based prosthesis report skin problems (K. Hagberg & Brånemark, 2001; Lyon et al., 2000), residual limb volume changes throughout the day (Sanders et al., 2018), and difficulty donning and doffing their socket in a consistent manner (K. Hagberg & Brånemark, 2001), all of which may make it difficult for them to use their prosthesis for long periods of time

comfortably. The problems related to socket fit also extend to the individual's biomechanics, often resulting in movement asymmetries between the limbs (Winiarski et al., 2021), compensatory actions on the amputated side (Gailey et al., 2008; Morgenroth et al., 2010; Wasser et al., 2020), and increased reliance on the intact limb for motion generation (Schaarschmidt et al., 2012; Sibley et al., 2021). The asymmetries between the limbs, and compensatory behaviors by the both limbs are expected to contribute significantly to the decreased mobility, and whether prothesis or socket technology can mitigate the interlimb asymmetries, increased reliance on the intact limb, and compensatory behaviors is unclear. However, recent advancements in bone anchored or osseointegrated (OI) prostheses (Fig. 1) may present a potential solution to the comfort and fit issues, as well as the function decrements individuals with lower extremity amputation experience.

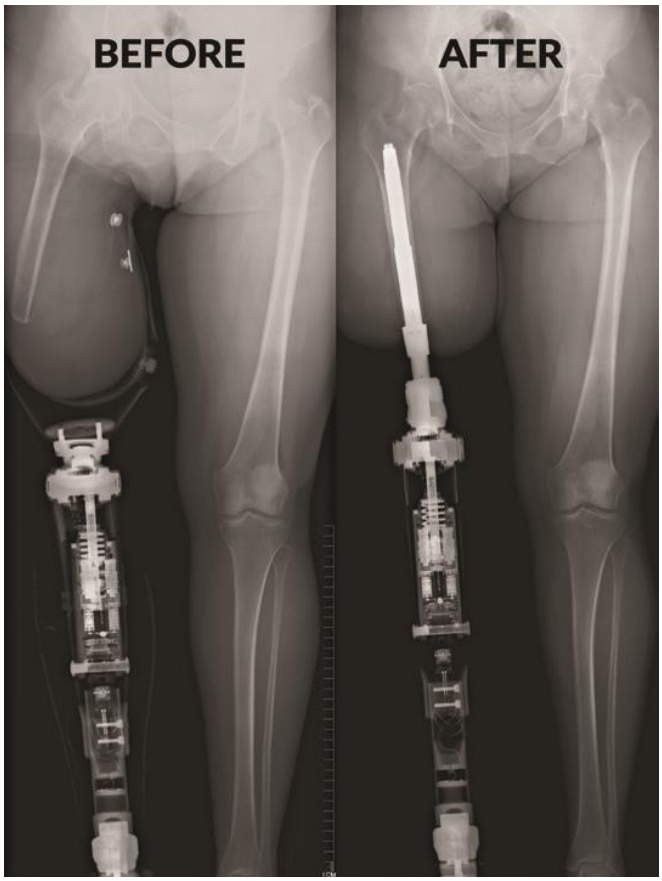

Figure 1. X-ray images of an individual who uses a socket-based prosthesis (left) and an osseointegrated prosthesis (right). Note the differences in anatomical positioning of the femur, as well as the pelvis. Image taken from Thomson et al (2019).

1.1.2. <u>An innovative solution for prosthesis fixation</u>

Recent medical innovations

have made the rigid OI prosthesis a viable option. This technology involves the use of a titanium implant which is fixed in the femoral medullary canal (Fig. 1). The implant then extends out from the bone, and through the soft tissue and skin of the residual limb. The prosthetic system is attached to the abutment or end of the titanium implant, directly connecting the prosthesis and skeletal system. The direct connection between the skeleton and prosthesis removes many, if not all, of the socket fit and comfort issues, and ostensibly results in increased function and performance during movement (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013).

Specifically, the direct fixation afforded with an OI prosthesis is associated with increased function across three categories, self-evaluated (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013) and clinical performance (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), residual limb physiology (Clemente et al., 2017; Häggström et al., 2013; Ranker et al., 2021), and basic kinematic performance (K Hagberg et al., 2005; Tranberg, Zugner, et al., 2011). The overall result of the increased function and performance is that individuals who use an OI prosthesis are expected to have increased physical activity and mobility, long-term health, and quality of life.

1.1.3. Limited research investigating how an OI prosthesis and walking speed affects the individual's biomechanics

However, while the functional improvements are promising, there is limited research investigating the kinematics and kinetics of individuals who use an OI prosthesis. The attraction of many individuals to the OI prosthesis is the claim of

improved function and performance, but whether the use of an OI prosthesis addresses not only the socket complaints, but also the existing interlimb asymmetries in kinetics and kinematics found in individuals who use a socket-based prosthesis is essentially uninvestigated. In addition, using an OI prosthesis may present a unique problem due to the direct connection between the residual limb bone, and prosthesis. In healthy adults, during impacts with the ground, shock attenuation is largely done by the muscle and the soft tissue of the limb (J. M. Wakeling & Nigg, 2001; James M. Wakeling et al., 2002). Similarly, when using a socket-based prosthesis, the impact with the ground is expected to be attenuated by the socket and the soft tissue of the residual limb. However, this soft tissue attenuation is likely not available for individuals who use an OI prosthesis due to the direct connection between the bone, OI implant, and prosthesis. Instead, when using an OI prosthesis, the impact with the ground is expected to be transferred into the bone with minimal attenuation, potentially resulting in high magnitude impact forces which are placed on the OI implant abutment and bone of the residual limb. The direct transfer of force may lead to several health concerns, including bone fractures around the implant (J. S. Hoellwarth et al., 2020; Jason Shih Hoellwarth & Rozbruch, 2022), or cumulative tissue trauma injuries such as stress fractures, a common injury which develops as a result of sustained, repetitive impacts (Bennell et al., 1996).

In order to establish if there is a risk for traumatic injuries such as bone fracture, or cumulative tissue trauma injuries such as stress fractures, the forces at the abutment have been investigated. A few studies have characterized the forces at the abutment

during walking at a self-selected speed (L. Frossard et al., 2013, 2021a; L. A. Frossard, 2010; Lee et al., 2007; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P. K. Tomaszewski et al., 2010), finding that these forces are not abnormally high. However, in order to truly understand whether the abutment forces are dangerous to the bone, the stress and strain experienced by the bone due to the abutment forces must be investigated. Several studies have investigated the bone stress and strain using finite element analysis (Newcombe et al., 2013; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P K Tomaszewski et al., 2010; Xu et al., 2006) during walking, generally concluding that the stress and strain on the bone is not beyond that of the yield strength of bone, and is likely sustainable. However, all of the studies investigating force placed on the residual limb at the abutment and the bone stress and strain have limited their analysis to a single time point while the individual walked at a single, self-selected speed, reducing the validity of their conclusions in a few ways. First, establishing that the stress and strain from a single stance phase a single point in time does not truly determine the risk for bone injuries over a lifetime of walking. Specific mathematical models such as probabilistic modeling or longitudinal studies could investigate this risk. Probabilistic models have several benefits over that of longitudinal studies, including the ability to isolate a specific effect such as walking speed on the long-term health outcomes, and not requiring many years of data collections and participant involvement. Second, it is unlikely that people walk only at their preferred walking speed throughout the day. Specific tasks may require individuals to walk faster or slower. For example, crossing the street may require a faster walking speed than

strolling with a friend or child. Walking speed has been found to affect both the magnitude and asymmetry of several biomechanical variables, including the ground reaction force (Lee Nolan et al., 2003), joint kinetics (Bonnet et al., 2014) and joint kinematics (Frigo & Tesio, 1986; Kobayashi et al., 2022) of individuals with transfemoral amputation who use a socket-based prosthesis, but the effect of walking speed has not been quantified in individuals who use an OI prosthesis. Investigating only preferred walking speed is particularly egregious for individuals with an OI prosthesis, as the increase in walking speed is expected to result in increased ground reaction force on the amputated side (Lee Nolan et al., 2003). The increased ground reaction force on the amputated side is then expected to result in greater loads on the abutment of the OI implant, and potentially higher risks for cumulative tissue or traumatic injury. In addition, despite the claims of improved function and performance with an OI prosthesis and the evidence for walking speed exacerbating interlimb asymmetries in individuals who use a socket-based prosthesis, it is largely unknown how the interlimb mechanics of individuals with an OI prosthesis change with walking speed. Therefore, in order to understand not only the safety of using an OI prosthesis over a lifetime, but also to establish the interlimb mechanics of individuals who use an OI prosthesis at different walking speeds, it is necessary to investigate the interlimb kinematics, kinetics, and residual limb loading while individuals who use an OI prosthesis walk at different speeds.

1.2. Knowledge Gap and Problem Statement

Individuals with transfemoral amputation who use a socket-based prosthesis have interlimb asymmetries, largely believed to be due to the poor imitation of the intact limb provided by the prosthesis. One component of the prosthesis, the socket, is a large source of complaints for individuals with a transfemoral amputation. The innovative OI implant largely reduces many of these socket-related complaints, including the skin irritation, relative motion of the socket, and discomfort. While the OI prosthesis ostensibly provides individuals with transfemoral amputation improved clinical test performance and quality of life (Al Muderis et al., 2017; Clemente et al., 2017; K Hagberg et al., 2005; Häggström et al., 2013; Leijendekkers et al., 2019a; Tranberg, Zugner, et al., 2011; Van De Meent et al., 2013), it also introduces a unique risk to the residual limb bone health due to the transfer of high magnitude forces from the ground reaction force to the implant abutment and bone. Studies characterizing the force at the abutment and the corresponding stress and strain on the bone have found that the stress is not beyond the yield strength of bone (Robinson et al., 2020; P. K. Tomaszewski et al., 2010; Xu & Robinson, 2008) and that the forces are similar across activities of daily living (Lee et al., 2007). However, these studies include limitations such as only investigating a single time point, which is difficult to extrapolate to the long-term health and injury consequences, and only studying single speed walking or a few activities of daily living.

Walking speed has been found to affect the magnitude of, and interlimb asymmetry of the ground reaction force (Lee Nolan et al., 2003), joint kinetics (Bonnet

et al., 2014) and joint kinematics (Frigo & Tesio, 1986; Kobayashi et al., 2022) of individuals with transfemoral amputation who use a socket-based prosthesis, but the effect of walking speed is largely unstudied in individuals who use an OI prosthesis. This is a large oversight, as increasing the walking speed is expected to increase the ground reaction force, and therefore also increase the abutment forces and stress and strain on the bone, potentially increasing the risk for a traumatic or cumulative tissue injury with sustained walking. In addition, despite the claims that using an OI prosthesis improves performance, the interlimb asymmetries found in individuals who use a socket-based prosthesis are generally uninvestigated when using an OI prosthesis, and the effect of walking speed on these asymmetries is unknown in this population. The knowledge gaps surrounding the effect of walking speed on interlimb kinematics, kinetics, and residual limb loading must be investigated to ensure the long-term health of individuals who use an OI prosthesis while maintaining the increased function and quality of life afforded by the OI implant.

Therefore, to address these knowledge gaps, three studies are presented in this dissertation. The first Specific Aim investigated the influence of walking speed on the interlimb GRF asymmetry in order to establish whether individuals with an OI prosthesis use an intact limb reliance strategy. The second Specific Aim investigated the knowledge gap surrounding the influence of walking speed on the interlimb joint kinematic and kinetic asymmetries in order to establish whether the rigid connection between the prosthesis and the body may reduce the limitations previously documented in the amputated limb. And finally, the third Specific Aim investigated the knowledge

gap surrounding the influence of walking speed on the longitudinal bone health with a lifetime of OI prosthesis use.

1.3. Specific Aims and Hypotheses

To address the knowledge gaps discussed above, this dissertation aims to investigate the loading on the both limbs of individuals who use an OI prosthesis at three different anatomical levels (limb, joint, residual limb bone) while walking at multiple speeds to determine (1) how using an OI prosthesis influences the interlimb whole limb and joint kinematics and kinetics during walking at different speeds (Specific Aims 1 and 2), and (2) whether using an OI prosthesis over a lifetime may result in cumulative injury risk to the bone surrounding the implant due to repetitive loads transferred through the direct skeletal fixation and into the bone (Specific Aim 3). To address this purpose, the following specific aims and objectives will be investigated:

1.3.1. Specific Aim 1

Aim 1.1: Investigate differences between the ground reaction forces on the intact and amputated limb in individuals with a transfemoral amputation who use an OI prosthesis while walking at three different speeds to determine how using an OI implant influences the intact limb reliance.

1.3.1.1. Hypothesis justification

1.3.1.1.1. Aim 1.1: Interlimb ground reaction force asymmetries during walking at 3 different speeds with an OI prosthesis

Individuals who use a socket-based prosthesis generally rely on their intact limb at all speeds for motion generation, as their prosthesis is a poor imitation for the missing musculature and tissue (Kobayashi et al., 2022; Lee Nolan et al., 2003) and the semi-rigid fixation created by the socket causes significant losses in efficiency and energy. This intact limb reliance results in asymmetries at the whole limb level, with ground reaction force asymmetry increasing as walking speed increases (Kobayashi et al., 2022). However, the more anatomical and rigid fixation created by the OI implant largely results in improved clinical test performance and quality of life (Al Muderis et al., 2017; Clemente et al., 2017; K Hagberg et al., 2005; Häggström et al., 2013; Leijendekkers et al., 2019a; Tranberg, Zugner, et al., 2011; Van De Meent et al., 2013), with individuals who use an OI prosthesis walking faster and farther than their socket-based peers (Van De Meent et al., 2013). It is largely expected that the rigid attachment to the skeletal system that occurs with the OI prosthesis will result in decreased asymmetry between the limbs, and therefore decreased intact limb reliance, with fewer compensatory behaviors required during locomotion. However, whether the walking speed has a similar effect on the ground reaction force asymmetry between the limbs such as occurs with socket-based prosthesis is largely unknown in individuals who use an OI prosthesis.

1.3.1.2. Hypothesis for Specific Aim 1

Hypothesis 1.1: We hypothesize that the interlimb ground reaction force will not be asymmetric during the slower than preferred and preferred walking speed as a result of the improved function and rigid attachment afforded by the OI prosthesis, but that the force will become asymmetric at the faster than preferred walking speed as a result of the increased reliance on the intact limb for motion generation.

1.3.2. Specific Aim 2

Aim 2.1: Investigate the differences in the joint kinematics in the intact and amputated limb of individuals with a transfemoral amputation who use an OI prosthesis while walking at three different speeds to determine whether an OI prosthesis influences the kinematic strategies used for locomotion.

Aim 2.2: Investigate the differences in the joint kinetics between the intact and amputated limbs in individuals with a transfemoral amputation who use an OI prosthesis while walking at three different speeds to determine whether an OI prosthesis influences the kinetic strategies used for locomotion.

1.3.2.1. Hypothesis justification

1.3.2.1.1. Aim 2.1: Interlimb joint kinematic asymmetries during walking at 3 speeds with an OI prosthesis and Aim 2.2: Interlimb joint kinetic asymmetries during walking at 3 speeds with an OI prosthesis

Individuals with a socket-based prosthesis generally have large asymmetries in kinematics (M. Finco et al., 2022; Kaufman et al., 2012; Winiarski et al., 2021) and kinetics (Harandi et al., 2020; Kobayashi et al., 2020; Seroussi et al., 1996) at the ankle,

knee, and hip, largely believed to be due the missing tissue, poor imitation of the intact limb provided by the prosthesis, and compensation strategies used to make up for the energy lost by the semi-rigid connection to the body by the socket and the lack of propulsion on the amputated side (Pinhey et al., 2022). These asymmetries and the prosthesis' inability provide propulsive work are largely exacerbated when the individual is required to walk at a faster speed, as the individual begins to rely on the intact limb even further (Pinhey et al., 2022), leading to greater interlimb differences.

It is unclear whether the joint kinematic and kinetic asymmetries exist when using an OI prosthesis due to the limited research on this population. Despite this limited research, the claim for undergoing the OI surgery is that it improves the function and performance, with this claim corroborated by clinical performance tests and surveys (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013). The underlying thought is that, because the OI implant provides a more rigid attachment between the body and the prosthesis when compared to a socket, there is improved performance which should lead to reductions in the compensation strategies used by individuals who have a socket-based prosthesis. Using an OI prosthesis, is therefore largely expected to reduce some of the compensation strategies required when using a socket-based prosthesis simply due to the better fixation between the body and the prosthesis.

In addition, during and after the OI surgery, there are several anatomical differences between individuals who use a socket-based prosthesis and those use undergo the OI surgery. First, during the OI surgery and rehab, muscles are re-attached

to the end of the residual bone, and the individual goes through a rehabilitation and physical therapy process which re-trains them to use the residual limb muscles (Kerstin Hagberg & Brånemark, 2009). This re-training process is expected to result in better muscle activation around the hip, which may also the intact limb reliance found in individuals who have a socket-based prosthesis. Second, after OI surgery, the femur is largely back to a more natural anatomical position in relationship to the skeleton and prosthesis componentry (Thomson et al., 2019). The more accurate anatomical positioning of the skeleton, in combination with the rigid prosthesis attachment and the increased use of the muscles around the hip, is expected to result in improved mechanics on the amputated side. Research investigating the hip and pelvis with an OI prosthesis has corroborated this, as previous research indicates that the hip range of motion (K Hagberg et al., 2005; Tranberg, Zügner, et al., 2011) and the pelvis angle during walking (Tranberg, Zugner, et al., 2011) are improved with an OI prosthesis when compared to those who use a socket-based prosthesis.

This initial data suggests that, in individuals who use an OI prosthesis, the interlimb kinematics and kinetics may have reductions in the asymmetries when walking. However, the effect of walking speed may still result in asymmetries at faster walking speeds. The limitations provided by the prosthesis during late stance on the amputated side require compensatory strategies in individuals with a socket-based prosthesis which may not be fully mitigated at faster walking speeds by the rigid connection afforded by the OI implant. Therefore, it is likely that there is still some intact limb reliance that occurs at faster walking speeds, but this may not occur at

slower and preferred walking speeds. If there is intact limb reliance at faster walking speeds, then this likely results in interlimb asymmetries in joint kinetics and kinematics.

1.3.2.2. Hypotheses for Specific Aim 2

Hypothesis 2.1: We hypothesize that the joint angles will not be asymmetric while walking at the slow and preferred speed as a result of the improved function afforded by the OI prosthesis due to the rigid attachment, muscle re-attachment, rehabilitation and training and more natural anatomical positioning at the hip, but that the joint angles will become asymmetric at the faster walking speed as individuals transition to an intact limb reliance strategy due to the limitations of the amputated limb and prosthesis.

Hypothesis 2.2: We hypothesize that the joint moments will not be asymmetric while walking at the slow and preferred speed as a result of the improved function afforded by the OI prosthesis due to the rigid attachment, muscle re-attachment, rehabilitation and training and more natural anatomical positioning at the hip, but that the joint moments will become asymmetric at the faster walking speed as individuals transition to an intact limb reliance strategy due to the limitations of the amputated limb and prosthesis.

1.3.3. Specific Aim 3

Aim 3.1: Investigate the abutment force during walking at different speeds in individuals with an OI prosthesis over a lifetime of walking to determine how walking at different speeds may influence the force which is transferred to the bone via the OI implant.

Aim 3.2: Investigate the strain on the bone at three locations of interest, including the bone diaphysis, the bone-implant interface, and the femoral neck, during walking at different speeds in individuals with an OI prosthesis over a lifetime of walking to determine the risk for bone-OI implant degeneration over time.

Aim 3.3: Investigate the probability of bone failure from cumulative loading on the residual limb bone in individuals with an OI prosthesis over a lifetime of walking to determine the risk for bone-OI implant degeneration over time.

1.3.3.1. Hypothesis justification

1.3.3.1.1. Aim 3.1: Abutment kinetics of an OI prosthesis during walking at 3 different speeds

It is believed that using an OI prosthesis will decrease the reliance on the intact limb during walking seen in individuals who use a socket-based prosthesis (Kobayashi et al., 2022; Lee Nolan et al., 2003), resulting in higher ground reaction forces placed on the amputated limb during impact with the ground. In addition, due to the prosthesis material properties and design, minimal damping of the ground reaction force is expected as the force is transferred from the prosthesis to the bone, resulting in high magnitude forces placed on the bone. Previous research with individuals with transfemoral amputation has established that the force placed on the limbs is correlated with walking speed, as when walking speed increases, so does the force generated during the impact with the ground (Lee Nolan et al., 2003). Due to the minimal damping and the increase in ground reaction force with walking speed, it is largely expected that the force on the abutment may increase when individuals who use an OI prosthesis

walk faster, perhaps leading to higher risks for traumatic or cumulative tissue injuries. However, whether the abutment forces increase with walking speed has not been investigated, despite the clear connection between walking speed and ground reaction force, and ground reaction force and abutment force.

1.3.3.1.2. Aim 3.2: Bone strain during walking at 3 different speeds with an OI prosthesis

Previous research with finite element analysis of the femur and OI implant during self-selected, single speed walking has established that the bone strain from the peak force generated during walking should not lead to a traumatic bone injury around the OI implant (Newcombe et al., 2013; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P K Tomaszewski et al., 2010; Xu et al., 2006). However, these investigations have investigated the stress and strain on the bone with preferred speed walking. This is not realistic for what occurs throughout the day, as individuals likely walk faster or slower as required by their environment and the task. For example, individuals may be required to walk faster to cross a street and avoid being hit by a car or walk slower to take a stroll with a friend. As discussed in the justification for Aim 1.1, there has been a previously established relationship between force and walking speed, with the ground reaction and abutment forces largely expected to increase with walking speed (Kobayashi et al., 2022; Lee Nolan et al., 2003), potentially resulting in increased stress or strain placed on the bone and implant. It is therefore important to determine the effect of walking speed on the bone stress and strain in order to determine if the risk for a traumatic injury is still low when walking at speeds other than the preferred speed.

Using finite element analysis (FEA) allows investigations of peak stress and strain on the bone, as well as their distribution across the bone, without requiring invasive sensors or methods such as strain gauges. FEA also can indicate the risk for a traumatic injury at an instantaneous time point, while isolating the effect of a single factor such as walking speed on the stress and strain.

1.3.3.1.3. Aim 3.3: Probability of bone failure with a lifetime of OI prosthesis use

As discussed in the justification for Aim 1.2, previous research has established that the risk for a traumatic bone injury as a result of preferred speed walking is low (Newcombe et al., 2013; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P K Tomaszewski et al., 2010; Xu et al., 2006). However, the effect of repetitive loading and the accumulated damage to the bone from walking over a given period of time has not been investigated. There is a delicate balance between the damage, repair, and adaptation systems of the bone, with material added or removed from the bone depending on the loading distribution patterns (S. C. Cowin, 1986; Wolff, 1892). If the damage and repair cycles become mismatched, with more damage accumulating than can be efficiently repaired, bone injuries may develop similar to those which occur with endurance athletes. The development of these injuries is largely related to the stress and strain on the bone, with high or abnormal stress and strain increasing the risk for injury with repetitive exposure. As discussed in Aim 1.1 and Aim 1.2, walking at faster or slower than the preferred walking speed may result in increased or abnormal loading to the bone. If the abnormal loading occurs repetitively, this may result in accumulated damage to the bone that cannot be repaired effectively, leading to bone injuries over a

given period of time. Whether the accumulation of damage from a lifetime of walking may outpace the repair capability of the bone has not been investigated, and whether the risk for injuries is higher when individuals with an OI prosthesis spend more time walking faster or slower than their preferred speed is unknown, despite the potential for abnormal input forces, and peak strains when walking at faster or slower speeds resulting in increased injury risk.

Probabilistic models of repetitive loading of the bone have been used in other populations such as endurance runners to predict the probability of developing a stress fracture (B. W. Edwards et al., 2010b). Probabilistic models are an effective analysis tool, as they can extrapolate the data collected during a single time point to the accumulated effect of the variable of interest over many years, and allow the analysis of failure probability as a result of an isolated factor such as walking speed. The probability of failure as a result of several individual locomotion patterns can also be incorporated into the overall probabilistic model, allowing investigations of whether the combination of time spent performing different locomotor actions can result in increased failure probability. Using the strain from Aim 1.2 for each walking speed, and varying the proportion of time spent at each walking speed, probabilistic models of bone damage, repair, and adaptation can investigate the probability of bone failure after a simulated lifetime of OI prosthesis use.

1.3.3.2. Hypotheses for Specific Aim 3

Hypothesis 3.1: We hypothesize that (1) the forces at the abutment will increase with walking speed, as ground reaction force increases as individuals walking faster

and there will be minimal damping of the ground reaction force by the prosthesis,

Hypothesis 3.2: We hypothesize that the peak strain on the bone during a single stance phase will increase with walking speed as the magnitude of the input forces increase with walking speed, but that the strain pattern across the bone will be similar on the diaphysis, internal boundary between the bone and implant, and the femoral neck due to the abutment force being directed almost completely in the axial direction

Hypothesis 3.3: We hypothesize that the probability of bone injury will be low over the individual's lifetime due to the inherent strength and remodeling of the bone with loading, but that increasing the proportion of time spent walking at faster than the preferred speed will result in increased probability of bone failure due to the increased peak stress and strain on the bone at faster walking speeds.

1.4. Organization of this Dissertation

Following this introduction chapter, Chapter 2 will contain a literature review synthesizing the current state of the literature surrounding first the interlimb asymmetries in the kinematics and kinetics, and then the residual limb loading when individuals with either a socket-based prosthesis or an OI prosthesis walk at their preferred speed. Following the discussion about walking at preferred speed, the literature review will discuss the factors which may contribute to interlimb asymmetries, such as the choice of the prosthetic foot and knee, before covering the influence of walking speed on the kinematics, kinetics, and residual limb loading in individuals who use a socket-based prosthesis. Following the literature review,

Chapters 3 through 6 will address each Specific Aim. Chapter 3 will discuss the results of this dissertation with regard to walking speed and interlimb GRF differences (Specific Aim 1), while Chapter 4 will discuss the relationship between walking speed and interlimb kinematic (Specific Aim 2.1) and kinetic (Specific Aim 2.2) differences at the joint level. Finally, Chapters 5 and 6 will cover the results of this dissertation with regard to the influence of walking speed on abutment forces (Specific Aim 3.1), bone strain (Specific Aim 3.2), and probability of bone failure with a simulated lifetime of OI prosthesis use (Specific Aim 3.3). The last chapter, Chapter 7, summarizes the findings of the four studies and their respective Specific Aims, before presenting noteworthy findings from this dissertation, limitations in the application of the results, and future work that needs to be conducted to expand on this dissertation.

2. CHAPTER 2: REVIEW OF LITERATURE

Individuals with unilateral lower extremity amputation commonly develop health problems (Gailey et al., 2008; Hammarlund et al., 2011; Highsmith et al., 2019; Naschitz & Lenger, 2008a; Norvell et al., 2005; Saris et al., 2003; Stam et al., 2004; Struyf et al., 2009) due to their physical activity limitations and the missing tissue and musculature on the amputated side (Bussmann et al., 2004; Pepin et al., 2019). These health problems and physical activity limitations may be related to the poor imitation of the intact limb provided by the use of a socket and prosthetic componentry (Pinhey et al., 2022). In general, the use of the socket fixation method is related to problems associated with comfort, skin problems (K. Hagberg & Brånemark, 2001; Lyon et al., 2000), residual limb volume changes throughout the day (Sanders et al., 2018), and difficulty donning and doffing their socket in a consistent manner (K. Hagberg & Brånemark, 2001). One innovative solution that removes the socket completely is the use of a bone anchored or osseointegrated (OI) implant which fixes the individual's prosthesis directly to their skeletal system, providing a rigid fixation which theoretically improves their physical function (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013) and quality of life (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013). The function and quality of life improves have been established with clinical tests such as the Timed Up and Go, and the 6 Minute Walk Test (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), but the biomechanical changes which occur with an OI

prosthesis are essentially uninvestigated, minus a few studies that have established joint moments and angles during self-selected walking or a few activities of daily living such as stair ascent and descent.

Individuals with transfemoral amputation who use a socket-based prosthesis, when compared to healthy adults, generally walk slower and walk less throughout the course of the day, commonly only taking between approximately 1500 and 5500 steps (Wong et al., 2021), a number which is much lower than the recommended 10,000 steps each day for a healthy lifestyle. In comparison, the use of an OI prosthesis is expected to allow the individual to walk farther and faster (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), potentially resulting in health improvements simply by making walking a more achievable task. It is unlikely that individuals will walk at a single speed throughout the day, as walking at variable speed is a common requirement for specific tasks. For example, walking across the street may require an individual to walk faster to avoid a car or strolling through a park with a friend or child may require a slower walking speed. Walking at variable speed is largely unstudied in individuals with transfemoral amputation, and especially in those with an OI prosthesis, despite the clear connection between walking speed and impact forces. This is particularly egregious for individuals who use an OI prosthesis, as there is minimal damping between the prosthesis and the bone, resulting in the transfer of forces directly to the bone with each step. The risk for the transfer of high magnitude forces to the bone is the underlying logic behind the recommendation that it is not safe for individuals who use an OI prosthesis to run or do high-impact activities. Therefore,

before investigating higher locomotion speeds such as running, it is important to understand the effect of walking speed on the biomechanics and the long-term health of individuals who use an OI prosthesis. This literature review is focused on establishing potential explanations for the interlimb loading asymmetries found in individuals with transfemoral amputation, and how walking speed and using an OI prosthesis may confound the interlimb asymmetries. This chapter will focus first on introducing the interlimb loading asymmetries in kinetics and kinematics at the whole limb, joint, and bone level for individuals with a transfemoral amputation during preferred speed walking. The potential mechanisms underlying these asymmetries with then be discussed. The chapter will conclude with a brief discussion of the effect of walking speed on the interlimb asymmetries, before concluding with a summary.

Due to the limited knowledge surrounding the biomechanical strategies used by individuals who have an OI prosthesis, much of this literature review is focused on individuals who use a socket-based prosthesis. When appropriate literature is available for investigations with OI prostheses, these studies will be referenced. However, the current literature surrounding individuals with unilateral transfemoral amputation is predominantly focused on socket-based prostheses, and, while this information is not directly applicable due to the improved function afforded by the OI implant, the knowledge about individuals who use a socket-based prosthesis will provide some foundational information for how amputation may influence the biomechanical strategies used during walking.

2.1. Interlimb loading asymmetries during walking in individuals with transfemoral amputation

Individuals with transfemoral amputation typically rely on their intact limb to compensate for the inability of the prosthesis to produce propulsive work (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022). This intact limb reliance results in interlimb loading asymmetries at three anatomical levels, the ground reaction force (GRF) at the whole limb level, the kinetics and kinematics at the joint level, and finally the loading placed on the bone at the skeletal level. The following will introduce the specific interlimb asymmetries at the preferred walking speed in individuals with a transfemoral amputation, with most research studying those who use a socket-based prosthesis, unless otherwise noted.

2.1.1. Interlimb asymmetries in kinematics during preferred speed walking

Individuals with transfemoral amputation generally walk slower than their healthy adult peers (Carse et al., 2020a), but may approach a preferred walking speed that is similar to healthy adults when they are highly functional (Jarvis et al., 2017). Many individuals also rely on their intact limb to generate their forward motion (Pinhey et al., 2022), creating an uneven sharing of the work between the limbs which results in kinematic asymmetries. In particular, individuals with transfemoral amputation have asymmetric step lengths and step times (Carse et al., 2020a; M. Finco et al., 2022), with longer step lengths and shorter stance times on the amputated side (M. Finco et al., 2022), with normalized step length asymmetries which are on the order of 66.4 to

98.5% and stance time asymmetries between 58.6 and 98.4%. In this situation, 100% represents perfect symmetry and 0% representing perfect asymmetry (M. Finco et al., 2022). This indicates that individuals with transfemoral amputation, especially those that are not highly functional, may have highly asymmetric temporal and spatial mechanics between the limbs.

The asymmetries in the stance characteristics are extended to the joint level, with asymmetric joint angles, and ranges of motion in the sagittal plane during gait (M. Finco et al., 2022; Kaufman et al., 2012; Winiarski et al., 2021). The greatest asymmetries are generally found at the ankle, with individuals with transfemoral amputation having large asymmetries in the ankle range of motion and peak joint angles (Kaufman et al., 2012; Winiarski et al., 2021). The normalized asymmetry at the ankle ranges between 53.2 to 83.2% at the ankle, with an average of 68.2%, with 100% again representing perfect symmetry. At the knee level, the asymmetry is slightly reduced when compared to the ankle level, with a normalized asymmetry value ranging between 70.5 to 98.2%, and averaging to 86.0% (M. Finco et al., 2022). While there is a reduction in joint asymmetry at the knee compared to the ankle, individuals still have decreased joint angle and range of motion during the stance phase (Kaufman et al., 2012; Winiarski et al., 2021). At the hip, the asymmetry is slightly greater than at the knee, but still smaller than at the ankle. The normalized asymmetry index ranges between 55.0 and 91.9%, with an average index of 73.3% (M. Finco et al., 2022). However, some studies indicate that there can be symmetric joint angle peaks and range of motion at the hip level (Kaufman et al., 2012; Winiarski et al., 2021), indicating that

the hip asymmetry may be individual or function level dependent. In summary, there are kinematic asymmetries which occur in individuals with transfemoral amputation, with longer step lengths and shorter stance times on the amputated side, and large asymmetries at the ankle level and more moderate asymmetries at the knee and hip level in regard to joint range of motion and peak angles. However, whether the interlimb kinematics are still asymmetric when using an OI prosthesis is largely unknown, despite the claims of increased performance and function

2.1.2. Interlimb asymmetries in kinetics during preferred speed walking

Similarly to the walking kinematics, walking kinetics are generally investigated at multiple levels of the limb, including the whole limb, and joints. Changes at any of these levels expected to lead to differences in motion. At the whole joint level, many individuals rely on their intact limb to generate the required work during walking (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022). Specifically, individuals with transfemoral amputation generate less whole limb collision, midstance, and push-off work and impulse on the amputated side when compared to the intact side (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022). In addition to the asymmetries in propulsive work, there is some evidence that the amputated limb has a lower GRF when compared to the intact limb (Carse et al., 2020b; Castro et al., 2014; Kobayashi et al., 2022; Schmid-Zalaudek et al., 2022). However, other research indicates the GRF may be similar between the limbs at the preferred speed (Lee Nolan et al., 2003; Schaarschmidt et al., 2012; Winiarski et al., 2021).

At the joint level, there are contradictory results regarding the asymmetries in

the joint moments when using a socket-based prosthesis. Some research indicates that individuals with transfemoral amputation have asymmetric joint moments at the knee, but not necessarily at the hip and ankle (Kaufman et al., 2012). However, other research indicates there may be differences in the ankle moments in late stance (Harandi et al., 2020; Kobayashi et al., 2020; Seroussi et al., 1996), the hip moments in early and mid to late stance (Harandi et al., 2020; Kobayashi et al., 2020; Seroussi et al., 1996), and the knee moments during early and midstance (Harandi et al., 2020; Seroussi et al., 1996). These joint moment asymmetries are likely the result of increased plantarflexor moments in late stance by the intact limb, increased hip extensor moments by the intact limb during early stance, and increased hip flexion moments by the amputated limb during late stance (Harandi et al., 2020; Kobayashi et al., 2020; Seroussi et al., 1996). At the knee, the asymmetry during early and midstance is the result of a decreased extensor moment on the amputated side (Harandi et al., 2020; Seroussi et al., 1996).

Whether these asymmetries are extended to individuals who use an osseointegrated prosthesis is largely unstudied. A recent case study by Davis-Wilson et al. (2023) indicates that the asymmetries at the knee and hip may decrease when comparing individuals before and after osseointegration surgery, but that symmetry is not achieved at the knee and hip (Davis-Wilson et al., 2022), indicating that other factors may contribute to the asymmetry outside of prosthesis fixation.

In summary, there are asymmetries in the whole limb work, with increased propulsive, collision, and midstance work contributing to forward motion by the intact limb, increased GRF on the intact limb side, and evidence both for and against joint

moment asymmetries between the limbs during various periods of the stance phase. However, while using an OI prosthesis may reduce some of these interlimb asymmetries, as evidenced by the reductions in interlimb asymmetry at the knee and hip, these interlimb asymmetries may not be fully removed when using an OI prosthesis.

2.1.3. Residual limb bone loads during preferred speed walking

Typically, with individuals who use a socket-based prosthesis, the health of the bone and its ability to withstand repetitive loading is not a large concern. Because the residual limb bone is not attached to the prosthesis, any concern surrounding bone health focuses on the bone density loss that occurs with decreased loading. However, with the introduction of an OI prosthesis, the direct connection between the prosthesis and bone now introduces large concerns surrounding the longer-term health of the bone and its ability to withstand the repetitive loads of walking. Because of the direct connection between the prosthesis and skeletal system with an OI prosthesis, there is generally an assumption that there is better sharing of the loads between the limbs and therefore increased loads placed on the amputated limb during walking. The increased use and loads would be expected to result in higher GRF, therefore greater forces transmitted to the bone through the OI implant, potentially leading to greater concerns surrounding the long-term health of the residual limb bone with sustained used. However, due to the inherent physiological response of the bone to loading and strain, some of this concern may be mitigated. Prior to discussing the abutment and bone loads, it is important to understand the physiological response of bone to sustained

loads.

2.1.3.1. Bone physiology and how bone responds to loads

Bone has a specific response to loading and strain in that there is a fine balance between loading, damage, repair, and adaptation over time. When the load and strain on the bone increases, and this higher load occurs repetitively over a sustained period of time, microdamage can develop and accumulate on the bone. The microdamage then results in the initiation of specific physiological pathways which will lead to repair and eventual adaptation of the bone (Stephen C Cowin, 1984; Wolff, 1892). The opposite can also occur, where the load on the bone is decreased over a period of time, resulting in the removal of bone cells, essentially weakening the bone (Stephen C Cowin, 1984; Wolff, 1892).

The adaptations to the bone with changes to the sustained load are typically seen in athletes or individuals are a result of their activities. In military recruits, increases in the trabecular and cortical components of the tibia were measured after 10 weeks of training. The bone strength and bone geometry at 38 and 66% of the tibia (diaphyseal sites) were significantly higher at the end of training (Izard et al., 2016). In unilateral jump events such as pole vault or high jump, it has been documented that specific bone density and radius changes occur in the jump leg when compared to the lead leg. When comparing the influence of activity on tibia shaft cross-sectional area in twins, is has been shown that tibia area is increased, as is cortex and moment of inertia, in the active twin compared to the inactive twin. The activity also increased the bone mineral density and cortical thickness at the distal tibia, therefore indicating that

function adaptation occurs as a result of activity (Ma et al., 2009). Overall, the bone strength, cross-section, and density adaptations implies that repetitive loading will result in bone adaptations which increase its ability to withstand impacts and strain (Weatherholt & Warden, 2016). In contrast, when rats that were immobilized, the bone mineral content decreased by 64.0%, and the bone mineral density decreased by 47.0% (Yuen-Chi Lau et al., 2017). This indicates, with decreased repetitive loads or complete unloading of the bone, there will be loss of bone density, which can occur when activity is halted or loading is decreased. Therefore, increased loading on the bone not only can increase bone density, but decreased loading or immobilization in athletes and active individuals can result in detrimental adaptations to the bone.

Within individuals with lower extremity amputation who use a socket-based prosthesis, the residual limb bone is no longer directly loaded during impact with the ground. This largely results in the removal of bone cells and decreased bone density, strength, and cross-section (Sherk et al., 2008). As previously discussed, this unloading and decreased bone strength is generally not a large concern with individuals who use a socket-based prosthesis, as the bone is not expected to withstand any direct loads. Rather the socket and specific points on the residual limb are expected to act as load bearing points. However, when using an OI prosthesis, there is a direct connection between the prosthesis and skeletal system, with the implant acting as an intermediary. The implant can therefore allow the transfer of high impact forces during walking, making the bone health a large concern for the individual over their lifetime.

Initially, the decreased bone density and strength which has developed during

the time period when the individual either used a socket or did not use a prosthesis at all is a large concern prior to undergoing the OI implant procedure. However, after the OI implant procedure, extensive rehabilitation is completed to gradually increase the strength of the bone through a graded loading process (Integrum, 2015). This graded loading process activates the physiological pathways which result in the deposition of new bone cells and the gradual increase in bone density, cross-section, and strength around the OI implant (Haket et al., 2017), indicating that the bone is able to adapt and protect the bone from traumatic and cumulative injuries. Radiological imaging indicates that the bone density increases along the entire diaphysis of the femur surrounding the implant (Haket et al., 2017), but there is some evidence from finite element analysis and modeling which contradicts that finding. Rather than the entire diaphysis improving in bone density and strength, the finite element analysis and models indicate that the bone surrounding the OI implant increases in density at the proximal end of the implant, while the bone decreases in density at the distal end of the implant (P K Tomaszewski et al., 2012; Xu & Robinson, 2008). This difference between the radiological and finite element analysis results may be due to the modeling limitations, as finite element analysis does not generally include the muscle forces at the distal end of the femur. As a result, the simulated physiological loading on the bone in the models may be missing the forces which are put on the bone around the distal end, leading to simulated bone density removal which is not true in reality. However, the results of both the radiological and finite element analysis modeling indicates that the bone around the OI implant will increase the bone density and cross-sectional area

in response to loads placed on the implant during activities of daily living. While there is contradictory evidence surrounding where bone density increases surrounding the implant, the bone does still respond to impact loads with the deposition of new bone cells, providing reassurance that, with the proper rehab process and the avoidance of specific high impact activities, the long-term health of the bone may be sustained with an OI prosthesis.

2.1.3.2. OI implant and abutment kinetics during activities of daily living

The literature has previously established that the residual limb bone density will strengthen in areas of high stress or strain after the OI procedure and extensive rehab, despite the potential for the bone to have been left unloaded for many years. However, as a precaution, most individuals who undergo the OI procedure are told it is not recommended that it is safe for them to run or do high impact activities, due to concerns surrounding the forces which may be transmitted to the bone through the abutment. In addition, many individuals who use an OI prosthesis walk faster and farther than their socket-based peers, resulting in high impacts throughout the day, along with higher performance which may lead to decreased intact limb reliance and increased loading on the amputated limb and residual limb bone. The combination of the direct skeletal fixation, increased activity throughout the day, and potentially greater reliance on the amputated limb may result in greater cumulative loads placed on the residual limb bone of individuals who use an OI prosthesis. Therefore, in order to ensure the risks surrounding the long-term health of the bone while maintaining the increased performance provided by the OI prosthesis, the kinetic loads placed on the abutment

and bone must be understood.

The kinetic loads which are placed on the abutment, and therefore the bone, have been characterized during preferred speed walking, and a few activities of daily living, with the general consensus that the loads transferred to the abutment during these activities are not expected to provide a high risk for a traumatic injury. Specifically, the forces at the abutment ranged from 72.53 to 100.63% BW for the axial direction, -22.45 to 17.82% BW for the anterior-posterior axis, and 4.59 to 13.93% BW for the medial-lateral axis (L. Frossard et al., 2013; Lee et al., 2007; Thesleff et al., 2020) for walking, and ascending and descending a staircase and ramp. In addition, one study found that the forces placed on the abutment during ramp ascent and descent, stair ascent and descent, and walking in a circle were not statistically different from the loads experienced during straight line walking (Lee et al., 2007), but another found significant differences between walking and stair ascent and descent (Thesleff et al., 2020). However, the study that found significant differences did acknowledge that their statistical differences should be interpreted with caution, as many individuals used the handrail to assist during the stair ascent and descent task, perhaps influencing the results (Thesleff et al., 2020). While these initial investigations indicate that loads placed on the abutment are not abnormal for a few activities of daily life, the effect of walking speed on the abutment forces is largely unknown, despite the clear relationship between impact loads and faster walking speeds. In addition, the abutment forces are not necessarily the best metric for establishing the load placed on the bone, as there may not be a direct connection between abutment forces and bone stress. Therefore, to

understand the long-term health implications of using an OI prosthesis, it is important to understand the stress and strain on the bone that result from the abutment forces.

2.1.3.3. Residual limb bone stress and strain due to the abutment kinetics

High impact stresses are generally not a concern for healthy adults or individuals who use a socket-based prosthesis, as there is soft tissue which acts to attenuate much of the force before it reaches the skeletal system. However, due to the direct connection between the bone and prosthesis via the implant, minimal damping of the force is expected, leading to high forces which are transferred to the bone. The forces measured at the abutment, as discussed above, are not necessarily abnormal, but, because the amputated bone may not have the same relationship between input forces, bone strength, and stress, it is important to investigate the stress and strain which occurs on the bone from the impact with the ground.

Previous research has generally used finite element analysis to investigate the bone stress and strain due to the inability to access the bone for *in vivo* investigations. Finite element analysis, while generally effective in computing the stress and strain on a simulated object, has some limitations. Specifically, finite element analysis requires advanced and complex computational skills, as well as effective and realistic modeling and computer aided design skills. In addition, it is generally impossible to model a fully realistic residual limb, bone, and implant system, as there is a complex relationship between the bone, muscles, implant, and skin which is nearly impossible to accurately represent in a simulation. As a result, many simplifications are made with finite element analysis, limiting the validity of the results as representations of the real world, and

causing there to be only a few studies that have investigated this particular population with regard to the stress and strain on the femur-implant system. In the studies that have been completed, the general methods are similar, but the model specifics, such as the use of simple or complex material properties, threaded or unthreaded implant models, length of the residual limb, and bone geometry, can make it difficult to generalize across the studies. Therefore, the results of the various models and studies will be reported first as to the similarities in their results, and then specific differences will be reported.

In general, the studies agree that the peak stresses and strains on the bone occur at the proximal end of the implant, around the greater trochanter, and within the femoral neck, but that the stress or strain at these regions is not over the yield strength of bone (Robinson et al., 2020; P. K. Tomaszewski et al., 2010; Xu & Robinson, 2008). In addition, most studies have found stress along the diaphysis on the medial and lateral sides, with the stress increasing above the proximal end of the implant due to the implant acting as a stress shield for the distal part of the diaphysis (Robinson et al., 2020; P. K. Tomaszewski et al., 2010; Xu et al., 2006). One study also noted a higher risk of failure for an individual with a body mass close to the current medically accepted maximum for individuals who get the OI procedure, perhaps indicating there exists a low threshold for the safety factor when considering an individual's body mass (P. K. Tomaszewski et al., 2010).

While many studies showed agreement in the locations of peak stress and strain, and the distribution of the stress and strain on the bone, a few studies found

unique or different results. One study modeled a transplanted bone plug around the distal end of the implant, finding large compressive stresses and strains within the transplanted bone due to the approximately 1 mm bending of the implant (Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017b). This is slightly different than previous study models, as most models do not include a transplanted bone plug at the distal end of the implant. While this is likely to be a realistic result if the bone transplanted to that location or if the bone grows fully around the implant at the distal end, there is some evidence that suggests that bone density may be reduced near the distal end, perhaps resulting in implant loosening in particularly aggressive cases. A second study found that there was a 97 to 112% chance of bone failure with walking loads, approximately three times that of the intact femur, with the failure percent determined by whether the contact between the bone and implant was modeled as fully osseointegrated or only partially osseointegrated. However, it is important to note that, in the fully osseointegrated model, only a single element on the posterior side was found to fail and, for each contact case, the metric for failure was based on a simple strain based criterion that was not validated or well explained in the study (Helgason et al., 2009). While this result could be realistic, it is unlikely, as the general body of evidence suggests that the failure risk is low to moderate for walking loads.

In summary, there is general agreement that the stress and strain on the bone will have higher magnitudes around the femoral neck, greater trochanter region, and proximal end of the implant, with these stress and strain magnitudes not exceeding that of the bone's yield strength. Along the diaphysis, there is expected to be stress shielding

until the proximal end of the implant is reached, as the implant is expected to absorb much of force at the abutment due to its material properties. A few studies have found contradictory evidence, with one finding increased stress at the distal end of the implant if bone is transplanted as a plug around the implant, and a second study finding high rates of failure for the implant with walking loads. Overall, the evidence suggests that is low to moderate risk to the bone during walking, with most stress concentrated above the implant. However, the research that has been conducted up until this point has largely concentrated on single speed walking, and has not investigated the stress and strain during other activities of daily life or when individuals walk outside of their preferred speed.

2.1.4. Summary of interlimb asymmetries and loading on the bone in individuals with transfemoral amputation

Due to the missing musculature and poor imitation of the intact limb provided by the prosthesis, there exist interlimb asymmetries at the whole limb, joint, and bone level in individuals with transfemoral amputation. Specifically, at the whole limb level, there is an intact limb reliance which results in greater GRF and propulsive work on the intact limb than on the amputated limb. This greater GRF and propulsive work is believed to largely be the result of the inability of the prosthesis to plantarflex during late stance, and the compensatory strategies used at the joint level. Specifically, at the joint level, there are greater joint angles and ranges of motion at the ankle, knee and potentially the hip of the intact limb. In addition, there are specific kinetic compensation strategies used by both limbs which result in asymmetries. These

compensation strategies result in greater ankle plantarflexion moments by the intact limb and greater hip flexor moments by the amputated limb in late stance, as well as greater hip extensor moments by the intact limb during early stance. In addition, there is a greater knee extensor moment by the intact limb in early and midstance which is not seen in the amputated limb. These interlimb asymmetries are clearly evident in individuals who use a socket-based prosthesis, with potential contributions to these asymmetries as the result of the poor connection between the prosthesis and the body. The OI prosthesis, however, provides a rigid connection between the prosthesis and body that reduces many of the skin health complaints, as well as improving performance and function. However, it also introduces a unique concern surrounding the health of the residual limb bone due to the potential for the transfer of high impact forces directly into the bone. There is evidence suggesting that the bone will increase the density along the diaphysis in response to a graded rehabilitation process, thereby increasing the strength of the bone and allowing the use of a prosthesis during activities of daily life. The kinetics placed on the abutment have been established to not exceed a safe level, and the stress and strain on the bone appears to fall under the yield strength of bone during a single stance phase of walking. However, it has not been established how walking speed may affect not only the abutment forces, stress on the bone, and the long-term health of the bone, but also the interlimb kinetic and kinematics asymmetries. This is important to understand, as individuals who use an OI prosthesis generally walk farther and faster than their socket-based peers, and are expected to have functional and performance improvements which may result in better load sharing between the lower

limbs. However, prior to understanding how an OI prosthesis may change the interlimb loads, it is important to establish the underlying factors which result in these interlimb asymmetries at baseline.

2.2. Factors contributing to interlimb asymmetries

The above section established the evidence for asymmetries in both the interlimb kinematics and kinetics, before discussing long-term bone health with the use of an OI prosthesis when individuals with a transfemoral amputation walk at their preferred speed. In order to understand how to mitigate these asymmetries, the following section will discuss the potential mechanisms underlying the asymmetries.

2.2.1. Proximal to distal shift in joint moments

In individuals with transfemoral amputation, there are changes to the kinetics produced at the hip during gait for both the amputated and intact limb side. During late stance, the increase in hip flexor moment on the amputated side may be a compensation for the decreased push-off or propulsive work which can be generated at the prosthetic ankle (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022). As a result, the additional work may be generated by a proximal shift to the hip on the amputated side in late stance and the intact side during early stance, similar to the shift which occurs in older adults. This proximal shift creates additional hip flexor moments on the amputated side and additional hip extensor moment on the intact side, helping to generate the required push-off work during the late stance on the amputated side

(Kobayashi et al., 2020; Seroussi et al., 1996).

An additional explanation for the joint moment asymmetry could be due to the working range of the joint moments of the individual. Individuals with transfemoral amputation have decreased maximum joint moments at the amputated hip in both flexion and extension when compared to the intact limb (Rutkowska-Kucharska et al., 2018). The decreased peak moments and smaller working range of joint moments which can be generated during gait may result in individuals approaching their maximum joint moment during gait on the amputated side, and therefore capping the joint moments they can generate. In contrast, the intact limb has a wider joint moment working range, allowing the individual to generate moments that are not achievable on the amputated side, and potentially exacerbating any existing asymmetries which already occur. Therefore, the increased asymmetry at the hip and ankle found in some research could be due to the inability of the prosthesis to provide a push-off, the proximal to distal shift found on the amputated side as a compensation for the reduced plantarflexion, and the physical limitations of the individual to generate joint moments on the amputated side.

2.2.2. Prosthesis componentry

Prosthesis componentry is varied and offers everything from passive joint components and feet to powered or variable damping joints and energy storage and return feet. The choice of componentry likely influences the asymmetries between the limbs, and the current knowledge surrounding prosthesis components, interlimb

asymmetry, and individuals with transfemoral amputation is summarized below. Unless otherwise stated, due to the limited research on interlimb kinetics and kinematics, the referenced literature is studying individuals who use a socket-based prosthesis.

2.2.2.1. Prosthetic foot choice

There are several feet available for individuals with lower extremity amputation, with each foot providing various benefits. The choice of foot can affect the interlimb kinematic and kinetic asymmetries, with the effect foot specific. In regard to kinematics, a Solid Ankle Cushion Heel (SACH) foot and an energy storage and return (ESAR) foot show similar plantarflexion angle range of motion at push-off (Pröbsting et al., 2022). However, the use of a powered foot, increases the plantarflexion range of motion at push-off, largely due to the foot's power capabilities (Pröbsting et al., 2022). Similarly, the use of a multi-axis foot may increase the amputated side plantarflexion range of motion over that of the SACH foot, with evidence suggesting that the range of motion increased 10 degrees with the multi-axis foot (L. Nolan & Lees, 2000). Therefore, the use of a powered foot or multi-axis foot could be expected to reduce the joint angle and range of motion asymmetries seen at push-off, as well as potentially reduce some of the compensatory behaviors which result from a prosthetic foot's inability to plantarflex and produce a plantarflexion moment in late stance.

2.2.2.2. Prosthetic knee choice

Evidence suggests that using an active microprocessor or variable-damping knee may reduce some of the asymmetries at the ankle, knee, and hip found in the

kinetics but not necessarily the kinematics when walking speed is controlled (Johansson et al., 2005; Kaufman et al., 2012; Segal et al., 2006). In particular, the use of an active microprocessor knee allowed the individual to generate a slight knee flexor moment during the early to midstance phase, rather than a consistent extensor moment (Kaufman et al., 2012; Segal et al., 2006). This slight knee flexion moment is likely the result of a slight increase in the knee range of motion on the amputated side, as the active microprocessor knee could restore some of the knee flexion which occurs during the stance phase (Creylman et al., 2016). As a result of the ability of the microprocessor knee to produce a slight flexion moment, there is a reduction in the asymmetries at the knee (Kaufman et al., 2012), and possibly at the hip (Creylman et al., 2016). When an active microprocessor knee is used, slight reductions occurred in the early stance joint moment on the intact side and late stance joint moment on the amputated side (Creylman et al., 2016). Research investigating the use of a variable-damping knee also indicates that it may perform better than a passive and microprocessor knee (Johansson et al., 2005). At the hip, using a variable-damping knee or microprocessor knee resulted in lower peak extension moments at toe off when compared to the passive knee (Johansson et al., 2005). In addition, the variable-damping knee component performed better than a microprocessor knee at the ankle during early stance, as the variable-damping knee had greater plantarflexion angles (Johansson et al., 2005). In summary, the use of a microprocessor or variable-damping knee component appears to afford individuals with transfemoral amputation improved function in the joint kinetics but not necessarily in kinematics, perhaps leading to reductions in joint kinetic

asymmetries due to the amputated knee producing a flexion moment which offsets some of the hip compensatory behavior.

2.2.2.3. Prosthesis fixation

The traditional fixation method for lower extremity prostheses uses a socket which acts as a semi-rigid attachment to the residual limb and body. The effectiveness of this attachment, and therefore the use of the prosthesis, is largely influenced by suspension method (Salazar-Salgado & Rendón-Vélez, 2020), and socket type (Klotz et al., 2011; Rabuffetti et al., 2005), along with other factors such as the resulting residual limb pain with prosthesis use (Sherman, 1999). These factors are also expected to influence the kinematics and kinetics of both lower limbs, as less effective attachment of the prosthesis to the body by the socket is expected to lead to energy and work loss, as well as interlimb asymmetries.

On the amputated side, using a socket is associated with reductions in the hip range of motion in both flexion-extension, and abduction-adduction, as well as a more anteriorly tilted pelvis at foot strike (Klotz et al., 2011; Rabuffetti et al., 2005). This reduction in hip range of motion is likely due to the physical restriction created by the socket shape, as the hip range of motion is decreased when the range of motion of the amputated limb is compared between wearing and not wearing a socket (K Hagberg et al., 2005). In addition, different socket designs appear to restrict the movement of the hip extension to different degrees (Klotz et al., 2011), with the most restriction in hip flexion-extension and abduction-adduction with the ischial containment and quadrilateral socket, while the ischial ramus socket has slightly less restriction in the

hip range of motion (Klotz et al., 2011).

Along with the socket shape restricting hip kinematics, one of the largest barriers to prosthesis use is the perceived comfort of the socket, as many individuals complain about residual limb pain and skin irritation which reduces their ability to use their prosthesis (Sherman, 1999). The pain, skin irritation, and lower perceived comfort are likely associated with movement of the residual limb within the socket, as the residual limb has been found to have up to 8.6 mm of movement in the medial-lateral direction, 28.4 mm of pistoning, and 20.4 mm of movement in the anterior-posterior direction (Gale et al., 2020). This large motion within the socket not only produces pain for the individual, but is also likely to result in energy loss, which then contributes to the decreased propulsive work which can be done by the amputated limb, and the result compensation strategies that are required.

The relative motion of the residual limb is commonly controlled for by a suspension system, but minimal research has been conducted investigating how the socket suspension systems influences the relative motion of the residual limb, as well as how the suspension system contributes to the interlimb asymmetries found during gait in individuals with transfemoral amputation. However, a systematic review of residual limb displacement suggests that the vacuum assisted suspension system may result in lower relative motion when compared to a suction suspension system (Salazar-Salgado & Rendón-Vélez, 2020). In summary, the effectiveness of a socket in attaching the prosthesis to the body is likely affected by the socket shape, and the ability of the suspension system to reduce the relative motion of the residual limb within the socket,

as ineffective attachment can lead to high relative motion, significant pain within the residual limb, and other skin irritations which contribute to interlimb asymmetries.

However, while using a socket can be generally functional for the majority of individuals with a transfemoral amputation, some individuals struggle to wear a socket. As a result, these individuals are unable to use a prosthesis, and struggle with their long-term health due to their decreased physical activity. An alternative fixation method, called osseointegration (OI), uses a titanium implant which is fixed in the medullary canal of the bone. This implant then extends out of the bone, muscle, and skin for attachment with a prosthesis, providing a direct, rigid connection between the prosthesis and the skeletal system. The use of the titanium implant largely removes the pain, skin irritation, and discomfort may individuals complain about when using a socket, as well as the relative motion of the residual limb relative to the prosthesis fixation method. The removal of these factors is expected to reduce some of the energy and work losses which occur with a socket-based prosthesis, potentially leading to lower interlimb asymmetries during walking.

While the use of an OI prosthesis is largely unstudied, qualitative evidence suggests that the use of an OI prosthesis provides improved function and quality of life for individuals with transfemoral amputation (Al Muderis et al., 2017; Kerstin Hagberg et al., 2004; Leijendekkers et al., 2016, 2019b). Only a few studies have investigated kinematic or kinetic variables when using an OI prosthesis, with the results of these studies suggesting that using an OI prosthesis may influence the hip kinematics, as well as the knee and hip kinetics. In particular, when using an OI prosthesis, there was an

increase in the hip extension angle and pelvic tilt, shifting both variables such that they are more similar to that of healthy adults (K Hagberg et al., 2005; Tranberg, Zügner, et al., 2011). However, the increase in peak hip extension angle may simply be due to no longer using a socket, as the shape of the socket largely stops the movement of the thigh and restricts the extension angles at the hip (K Hagberg et al., 2005). When the knee and hip kinetics were investigated, initial evidence suggests that the use of an OI prosthesis reduces the peak knee extension moment in the intact limb and the peak hip extension moment in the intact and amputated limb, while increasing the peak knee extension moment on the amputated side, and hip abduction moment on the intact and amputated limb during walking at a self-selected speed (Davis-Wilson et al., 2023). These changes resulted in improved interlimb asymmetry at the knee and hip during walking at preferred speed (Davis-Wilson et al., 2023), but symmetry was not fully achieved, indicating either there are limitations on the amputated side even with the more rigid osseointegrated fixation or biomechanical strategies which require the individuals to rely on the intact limb.

However, while the use of an OI prosthesis sounds promising, several restrictions are put in place to ensure the safety of the user. Individuals who use an OI prosthesis are not allowed to run or play high impact sports, as the direct connection between the bone and prosthesis is expected to result in the transmission of high forces to the bone through the implant. The forces placed on the implant and bone appear to largely be safe with walking and a few other activities of daily living (Lee et al., 2007; Stenlund, Trobos, Lausmaa, Br, et al., 2017; P. K. Tomaszewski et al., 2010; Paweł

Krzysztof Tomaszewski, 2012; Xu et al., 2006), but the effect of increasing walking speed or the long term probability of bone injuries with an OI prosthesis have not been investigated. The specifics surrounding the loading placed on the bone with an OI prosthesis is discussed above in Section 1.1.3.

In summary, evidence suggests that using an OI prosthesis for low impact activities like walking a self-selected speed and other activities of daily living are safe for individuals with transfemoral amputation. In addition, using an OI prosthesis may provide function and quality of life improvements over that of a socket-based prosthesis, as individuals who use an OI prosthesis have improved hip kinematics, and hip, and knee kinetics. However, these improvements, while reducing the asymmetry, still do not result in symmetry motion between the limbs. Additional research is required to determine how walking speed influences the joint kinematics and kinetics in those with an OI prosthesis, as well as the interlimb asymmetries.

2.3. Walking speed

Walking speed has a well understood relationship with the ground reaction force such that, as the walking speed increases, so does the ground reaction force which is measured during impact. However, as is previously established, individuals with transfemoral amputations have prosthetic devices which contribute to interlimb asymmetries, with these asymmetries likely exacerbated by walking at speeds outside of their preferred speed. At all walking speeds, individuals with transfemoral amputation have been found to struggle to produce the required propulsive work on the

amputated side (Pinhey et al., 2022). The use of an OI prosthesis has been shown to improve walking speed and other clinical tests of performance. However, using an OI prosthesis comes with restrictions in approved physical activities, as individuals are told it is not recommended that they can run or do high impact activities. As a result, in order to understand what recommendations clinicians should make regarding activity and the use of an OI prosthesis, it is important to establish how walking speed influences the whole limb kinetics, joint kinematics and kinetics, and the load and stress and strain experienced by the residual limb bone at walking speeds outside of the preferred speed.

Few studies have investigated the interlimb asymmetries and bone loading at walking speeds outside of the preferred speed for individuals who use an OI prosthesis. As a result, the literature reviewed below discusses the existing knowledge surrounding walking speed and individuals who have a transfemoral amputation and use a socket-based prosthesis and provides some potential foundational understanding of how walking speed may affect the kinematics, kinetics, and bone loading of individuals who use an OI prosthesis.

2.3.1. Kinematic changes with walking speed

At the preferred speed, the individuals with transfemoral amputation walk with whole limb and joint level differences which result in greater reliance on the intact limb for motion (M. G. Finco et al., 2022; Kaufman et al., 2012; Winiarski et al., 2021). This intact limb reliance is expected to be exacerbated when the individuals are required to walk at speeds which are different than their preferred speed. For example, as speed

increases from 2.0 km/h (0.5 m/s) to 5.5 km/h (1.53 m/s), the step length, and cadence increase significantly, while the stance time, and swing time decrease significantly for both the intact and amputated limb (Kobayashi et al., 2022). However, there are differences between the intact and amputated limb for all speeds, with the intact limb step length and swing time significantly smaller than the amputated limb step length and swing time, and the intact limb stance time and cadence significantly greater than the amputated limb stance time and cadence at every walking speed (Kobayashi et al., 2022). These interlimb differences result in asymmetries between the limb for every walking speed (Kobayashi et al., 2022), with asymmetries values which are essentially constant for all walking speeds and variables, minus a more asymmetric swing and stance time at 2.0 km/h when compared to the swing and stance time at 2.5 km/h (Kobayashi et al., 2022). Walking speed also has a significant effect on the magnitude of temporal kinematic characteristics such as stance and swing time, but may only largely influence the asymmetry at slower walking speeds. Instead, the asymmetry may be relatively constant when walking at moderate and faster walking speeds, perhaps indicating that the differences in interlimb temporal kinematics may not suffer significantly with increased walking speed.

Joint kinematics in healthy adults have been shown to have magnitude changes with increasing walking speed (Fukuchi et al., 2019). However, this is largely uninvestigated in individuals with lower extremity amputation. A single study by Frigo and Tesio (1986) has investigated the changes to the joint angles with walking speed in individuals with transfemoral amputation, indicating that there are qualitative

changes at the hip, knee, and ankle with walking speed (Frigo & Tesio, 1986). The specific details are largely undiscussed in the study, outside of qualitatively acknowledging how the walking speed affects the ability of the knee to lock in extension during the late swing phase (Frigo & Tesio, 1986). A more explicit study of the joint angle changes and asymmetries in individuals with transfemoral amputation has not been conducted, despite the evidence for changes to the temporal kinematics with walking speed. Despite this lack of evidence, it is largely expected that, at faster walking speeds, the inability of the prosthesis to generate propulsive force, as well as the poor imitation of the knee by the prosthetic knee, will result in an increased reliance on the intact limb, resulting in greater range of motion for the joints on the intact limb side. While the intact limb joint angle range of motion is expected to increase with walking speed, the amputated joint angles are expected to stay largely the same or increase only slightly. This inequal change in range of motion of the joints is expected to result in increasing asymmetry between the limbs at faster walking speeds, largely due to the increased reliance on the intact limb for propulsive work.

2.3.2. Kinetic changes with walking speed

Similarly to the kinematics, at the preferred walking speed, there are joint kinetic asymmetries between the limbs. In addition, as walking speed increases, the amputated side struggles to produce the required propulsive work, with the propulsive work produced at 1.53 m/s only slightly increased when compared to the work produced at 0.55 m/s (Bonnet et al., 2014; Pinhey et al., 2022). The intact limb, however, has large increases in the propulsive work done at those two speeds, likely as

a compensation mechanism to make up for the inability of the amputated side (Bonnet et al., 2014; Pinhey et al., 2022). This asymmetric increase in propulsive work is also reflected in the ground reaction force, as the asymmetry between the limbs at the first vertical GRF peak at 0.5 m/s increases significantly when the individual is asked to walk at their fastest walking speed of approximately 1.5 m/s (Lee Nolan et al., 2003). The vertical GRF peak measured on the amputated side only increases slightly by 0.08 BW, while the vertical GRF peak on the intact side increases by up to 0.26 BW from 0.5 m/s to the maximum walking speed of the individual (Lee Nolan et al., 2003).

The asymmetries in propulsive work and GRF may be attenuated to the joint kinetics with walking speed as well. As walking speed increases, the peak flexion moment for both limbs increases has been found to increase (Bonnet et al., 2014). However, at the baseline walking speed, there exist asymmetries in the peak flexion moment produced at the hip such that the amputated limb has a greater flexion moment. Therefore, with walking speed, this asymmetry is maintained, with both limbs increase their peak flexion moment, but the intact limb always 0.10 to 0.20 Nm/kg lower than the amputated limb (Bonnet et al., 2014). This hip moment asymmetry is expected to be a compensation strategy, as discussed in Section 1.1.2 and 1.2.1, where the amputated limb produces a greater flexion moment in late stance to compensate for the decreased plantarflexion moment at the ankle. Overall, there are few studies investigating the effect of walking speed on the joint kinetics and kinematics in individuals with transfemoral amputation. However, due to the inability of the amputated limb to increase its propulsive work as walking speed increase, it is largely

expected that the existing interlimb asymmetries will be at least maintained, if not made worse by walking faster.

2.3.3. Residual bone load changes with walking speed

There have been no studies investigating either the abutment kinetics or the changes to the bone stress and strain with walking speed. However, it is largely expected that increasing the walking speed will result in greater forces placed on the amputated limb, which are transferred up the limb and into the abutment and bone. As a result, the bone stress and strain are expected to increase in magnitude, leading to increased risk for injury to the bone with sustained loading over time. Because individuals are expected to walk at different speeds throughout the day, with the speed determined by the task requirements, it is important to understand how walking speed influences the load and potential damage to the bone during a single stance phase, as well as the accumulation of the damage with sustained OI prosthesis use.

2.4. Summary

Individuals with transfemoral amputation typically have interlimb asymmetries which exist at multiple levels of the limb. In individuals who use a socket-based prosthesis, these asymmetries generally manifest as longer step lengths and shorter stance times on the amputated side, and large asymmetries at the ankle level and more moderate asymmetries at the knee and hip level in regard to joint range of motion and peak angles. These individuals also have been found to have increased propulsive and collision work, and GRF on the intact limb, as well as specific asymmetries during

early and late stance in joint kinetics. The limb and joint asymmetries are assumed to be the result of the missing musculature and tissue on the amputated side, as well as the poor imitation of the intact limb provided by the prosthesis resulting in compensatory behaviors by both the intact and amputated limb, including an intact limb reliance for propulsive work, and a proximal to distal shift in joint kinetics for both limbs. In addition, the load placed on the bone of an individual who has an OI prosthesis has not been found to exceed the yield strength of bone during a single stance phase or specific activities of daily living, providing promising initial evidence as to the safety of this device with a lifetime of use. Using an OI prosthesis has also shown some potential to reduce the asymmetries between the limbs, believed to be due to the rigid skeletal attachment which removes many of the problems associated with using a socket.

Prosthetic components are largely expected to contribute the interlimb asymmetries, as the prosthesis is a poor imitation of the intact limb. Specifically, powered and energy storage and return feet have been found to reduce the asymmetries over solid ankle, cushion heel feet, and microprocessor and variable damping knees been found to reduce the kinetic asymmetries when compared to a passive knee. However, likely one of the largest contributors to the interlimb asymmetries is the prosthesis fixation. Most individuals use a socket-based prosthesis, but experience discomfort, skin irritation, and other problems which make it difficult to wear their prosthesis for long periods of time. In addition, the socket acts as a semi-rigid, indirect connector between the prosthesis and body, allowing motion of the residual limb within

the socket which may result in potentially high energy losses. An alternative fixation using an OI implant has been introduced, and has been found to perform better than a socket when completing clinical tests and qualitative surveys. However, as is discussed above, it also introduces activity restrictions and concerns surrounding cumulative damage to the bone with repetitive walking loads. In addition, it is not well understood how the use of an OI prosthesis affects the interlimb kinematic and kinetic asymmetries found in individuals who use a socket-based prosthesis, despite the expectation that using an OI prosthesis improves the function and performance of the individual.

One significant concern surrounding the use of an OI prosthesis is the effect of faster locomotion speed. However, before running speeds can be investigated, it is important to establish how walking speed changes the kinematics, kinetics, and joint loads. No research has been conducted investigating the effect of walking speed, despite the clear understanding that walking speed increases the loads and changes the kinetics and kinematics in individuals who use a socket-based prosthesis. Understanding how walking speed influences the mechanics of individuals who use an OI prosthesis will inform not only future research, but clinical recommendations surrounding the use of the OI prosthesis. Specific unanswered questions that could help clarify the effect of walking speed on the mechanics of individuals who use an OI prosthesis are:

1. Does increasing walking speed result in greater abutment kinetics, higher stress and strain on the bone, and a higher probability of bone injury with a lifetime of OI prosthesis use?

2. Do the interlimb GRF asymmetries which exist in individuals with transfemoral amputation who use a socket-based prosthesis also exist in individuals who use an OI prosthesis and does walking speed affect the magnitude of the GRF asymmetries?
3. Do the interlimb joint kinetic and kinematic asymmetries which exist in individuals with transfemoral amputation who use a socket-based prosthesis also exist in individuals who use an OI prosthesis and does walking speed affect the magnitude of the joint kinetic and kinematic asymmetries?

3. CHAPTER 3: STUDY 1 INVESTIGATING SPECIFIC AIM 1

3.1. Introduction

Individuals with lower extremity amputation commonly develop chronic health problems such as increased risk for cardiovascular disease and obesity (Naschitz & Lenger, 2008b; Saris et al., 2003; Singh et al., 2007) as the result of decreased physical activity. Specifically, individuals with lower extremity amputation report an average daily step count of 1500-5500 steps (Bussmann et al., 2004; Pepin et al., 2019), a number that is much lower than the recommended 10,000 steps for a healthy lifestyle. This lower step count, and decreased physical activity indicate that individuals with amputation likely struggle to get enough exercise to combat their chronic health problems. In addition, the decreased step count and physical activity are further exacerbated by the poor imitation of the intact limb provided by the prosthesis, largely believed to be due to the prosthesis's inability to produce positive net work during walking (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022). This inability of the prosthesis to generate positive work results in an increased reliance on the intact limb (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022), with this reliance found to be exacerbated by walking speed (Bonnet et al., 2014; Pinhey et al., 2022). As individuals with amputation walk faster, the net increase in the ground reaction force is larger on the intact limb side (Lee Nolan et al., 2003), resulting in greater interlimb asymmetries in the ground reaction force, and potentially contributing to some of the chronic health problems such as the increased osteoarthritis in the intact limb.

Along with the poor imitation of the intact limb by the prosthesis and reliance on the intact limb, many individuals report dissatisfaction with their current prosthesis, and commonly report general discomfort when wearing their socket (Sherman, 1999). The discomfort and dissatisfaction with their socket commonly are associated with skin irritation and ulcers (K. Hagberg & Brånemark, 2001; Lyon et al., 2000), volume changes throughout the day (Sanders et al., 2018), and difficulty donning and doffing their prosthesis (K. Hagberg & Brånemark, 2001), which all act as further barriers to wearing and using their prosthesis throughout the day. The discomfort and dissatisfaction with their prosthesis may also contribute to the interlimb asymmetries in ground reaction force found during walking, as individuals may choose an intact limb reliance strategy to reduce the risk of injuring the skin or tissue of their residual limb.

One potential solution to the discomfort complaints is to remove the socket entirely and use an osseointegrated (OI) or bone-anchored prosthesis. Recent innovations in prosthesis fixation methods has introduced the OI prosthesis in the United States, resulting in a more rigid and anatomically correct connection (Ranker et al., 2021) to the skeletal system using a titanium implant which is embedded in the bone's medullary canal. Using an OI prosthesis is believed to result in improved performance due to the direct connection between the prosthesis and the skeleton, with these improvements documented by various clinical tests such as the Timed Up and Go and the Six Minute Walk Test performance (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013). Additional improvements included better hip

range of motion, improved sitting comfort, and faster walking speed when compared to when individuals used a socket (K Hagberg et al., 2005; Tranberg, Zugner, et al., 2011). However, the OI fixation method has not been systematically investigated to determine whether it improves the intact limb reliance and greater ground reaction force on the intact limb found when individuals use a socket-based prosthesis (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022), and whether walking faster results in greater intact limb reliance and loading, as has been found with the use of socket-based prosthesis (Lee Nolan et al., 2003), is unstudied in individuals with an OI prosthesis. Instead, the literature investigating the biomechanics of individuals with an OI prosthesis has focused on clinical tests or basic spatiotemporal metrics of walking at an individual's preferred speed. Investigating only an individual's preferred speed is not particularly realistic for how an individual walks throughout a day (Davis-Wilson et al., 2022; P. K. Tomaszewski et al., 2010), as different situations such as cross the street or walking casually with a friend are expected to result in variable walking speeds. Therefore, in order to understand whether the rigid and direction connection between the prosthesis and the body provided by the OI implant results in improvements to the intact limb reliance and the risk for overuse injuries in the intact limb, the influence of walking speed on the ground reaction force for both the amputated and intact limbs must be investigated.

The purpose of this study was to investigate differences between the ground reaction forces on the intact and amputated limb in individuals with a transfemoral amputation who use an OI prosthesis while walking at three different speeds to

determine how using an OI implant influences the intact limb reliance. We hypothesized that the ground reaction force on the intact and amputated limbs will be similar during the slower than preferred and preferred walking speed conditions as a result of the improved function and rigid attachment afforded by the OI prosthesis, but that the force will be different between the intact and amputated limbs during the faster than preferred walking speed as a result of the increased reliance on the intact limb for motion generation.

3.2. Methods

3.2.1. Population of interest and power analysis

Ten individuals with transfemoral amputation who use an OI prosthesis will be recruited for this study. Inclusion criteria will consist of the following. Participants will be recruited if they (1) between the ages of 18 and 70, (2) are at least 1 year post-OI surgery, (3) are cleared by their medical professional for ambulation, (4) present no functional limitations which would affect their ability to walk or complete activities of daily life unaided, and (5) have at least 6 months' experience with their definitive prosthesis. Demographic and health information, including age, body weight, height, gender, and other relevant information including time since amputation and OI surgery, amputation cause, and current prosthetic components will also be collected.

To determine the sample size required for the proposed project, an *a priori* power analysis was completed using G*Power 3.1 (Heinrich Heine University Dusseldorf, Dusseldorf, North Rhine-Westphalia, Germany). Data investigating the hip

range of motion in individuals who use an OI prosthesis (K Hagberg et al., 2005) and peak vertical ground reaction force differences between limbs across walking speeds in individuals who use a socket (Schaarschmidt et al., 2012) was used for the power analysis. For a power level of 0.8, an alpha level of 0.05, and moderate effect size, the *a priori* power analysis to detect differences in the means in a repeated measures ANOVA indicated a sample size ranging between 8 and 19 participants. However, due to the limited number of individuals who undergo the OI procedure, and because other studies with individuals who use OI prostheses have sample sizes between 9 and 12 (L. Frossard et al., 2020; Lee et al., 2007), we will plan to recruit a sample size N = 10 individuals

3.2.2. Data collection

Our protocol was approved by the University of Maryland IRB. After the informed consent process, participants changed into lab provided clothing, but used their own shoes. Participants had 77 markers placed on relevant bony and physiological landmarks, following a modified Rajagopal model (Rajagopal et al., 2016). The modifications for the marker model consisted of adding markers for the amputee population on a force transducer placed in the prosthesis system and the addition of markers on the feet and hands. After marker placement, participants performed a static calibration trial at the origin of the force platforms, and then three different walking conditions across the force platforms. The three walking conditions consisted of participants walking at self-selected preferred, fast, and slow speeds for 4 – 7 trials. The fast and slow speeds were counterbalanced across participants. During the walking

trials, marker data was collected at 200 Hz using 13 infrared motion capture cameras (Vicon, Oxford, UK), and force data from ground contact was collected at 1000 Hz using eight 6DoF piezoelectric force platforms (Kistler, Switzerland) arranged in a single row located within a raised platform.

3.2.3. Data processing and analysis

After the data collection, the ground reaction force (GRF) for each limb during the stance phase of the three walking speeds will be extracted using Visual3D (C-Motion, Germantown, MD, USA). Three clean foot strikes for each limb during each walking speed condition were selected for analysis, and smoothed using a 4^{th} order dual-pass Butterworth filter with a cutoff frequency of 45 Hz. The average GRF for each limb over the three clean foot strikes will be computed for the vertical, anterior-posterior (AP), and medial-lateral (ML) direction, as well as the overall GRF.

3.2.4. Statistical analysis

To test for differences between the limbs across walking speeds, the time-dependent GRF for each walking speed condition was compared using Statistical Parametric Mapping with a 2-way ANOVA with an interaction effect. The two within-factors for the ANOVA were the walking speed and the limb of the individual, and the interaction effect consisted of the effect of limb*walking speed. Statistical Parametric Mapping allows comparison of each percentile of stance to identify where within the stance phase an interaction or main effect such as limb and walking speed may result in statistically different GRF. If the interaction effect of limb*walking speed was significant, the simple main effect within walking speeds and between limbs was tested

using two sample t-tests with a Bonferroni correction. Because the simple main effect required comparing 3 different paired groups (intact limb versus amputated limb during the fast, preferred, and slow speed each), the Bonferroni correction will set the p-value to 0.016.

3.3. Results

Participants (Table 1) consisted of 7 males (51.71 ± 11.94 years old, 1.78 ± 0.16 m, 83.44 ± 25.63 kg, 2.89 ± 1.27 years since OI surgery) and 4 females (50.25 ± 11.35 years old, 1.65 ± 0.09 m, 54.93 ± 14.97 kg, 2.54 ± 2.38 years since OI surgery). Participant demographics did not differ between the male and female groups (p<0.05), indicating the two groups could be aggregated into a single group for analysis.

Table 1. Participant demographics as averages (SD) within groups by sex, and then as a whole sample

Gender	Age	Height (m)	Weight (kg)	Etiology	Time since amputation (years)	Time since OI surgery (years)	K Level	Residual limb length (cm)
N = 7 men	51.71 (11.94)	1.78 (0.16)	83.44 (25.63)	4 trauma, 2 cancer, 1 infection	7.02 (2.64)	2.89 (1.27)	3.71 (0.49)	21.22 (5.36)
N = 4 women	50.25 (11.35)	1.65 (0.09)	54.93 (14.97)	2 trauma, 2 cancer	22.14 (15.5)	2.54 (2.38)	3.50 (0.58)	16.70 (4.84)
N = 11	51.18 (11.17)	1.73 (0.15)	73.07 (25.86)	6 trauma, 4 cancer, 1 infection	12.52 (11.6)	2.76 (1.64)	3.64 (0.5)	19.41 (5.41)

The average walking speed (Table 2) for each walking condition was 0.76 ± 0.15 m/s, 0.94 ± 0.14 m/s, and 1.22 ± 0.23 m/s for the slow, preferred, and fast walking speeds

respectively. Statistical tests indicate that the slow speed is significantly different from the preferred (p<0.001) and the fast (p<0.001) speeds, and that the preferred is significantly different from the fast speed (p<0.001).

Table 2. Average walking spatiotemporal data (SD) for three walking conditions

Gender	Slow	SSW	Fast
Average walking speed (m/s)	0.76 (0.15)	0.94 (0.14)	1.22 (0.23)
Average stance time (s)	0.87 (0.3)	0.77 (0.14)	0.67 (0.16)
Average stride length (m)	1.03 (0.08)	1.15 (0.16)	1.37 (0.29)

When comparing the amputated and intact limb GRF (Fig. 2, dashed lines = amputated limb, solid lines = intact limb), the general shape of the curve in each axis direction appears to be similar, but the effect of walking speeds on each limb appears to be statistically different for the medial-lateral (F> 8.011, p<0.05, vertically shaded region in Fig. 2) and vertical direction (F> 8.488, p<0.05, vertically shaded region in Fig. 2). Specifically, the interaction effect of walking speed on each limb is statistically different between 6 and 23% of stance, and between 73% and 91% of stance in the ML direction, and between 8 and 23%, 46 and 57%, and 71 and 89% of stance in the vertical direction. However, in the AP direction, there was not an interaction effect of walking speed and limb for any of the stance phase.

To determine at what walking speeds each limb had statistically different GRF, simple main effects were determined for the ML and vertical direction, but not the AP

direction, indicating that the intact and amputated limb were statistically different at each walking speed in the regions where an interaction effect was found. Specifically, the ML direction had statistically greater GRF on the intact limb when compared to the amputated limb during the fast (F> 3.418, p<0.016, black horizontal bar in Fig. 2), preferred (F> 3.407, p<0.016, dark gray horizontal bar in Fig. 2), and slow (F> 3.433, p<0.016, light gray horizontal bar in Fig. 2) walking speeds for the early stance and late stance periods. In

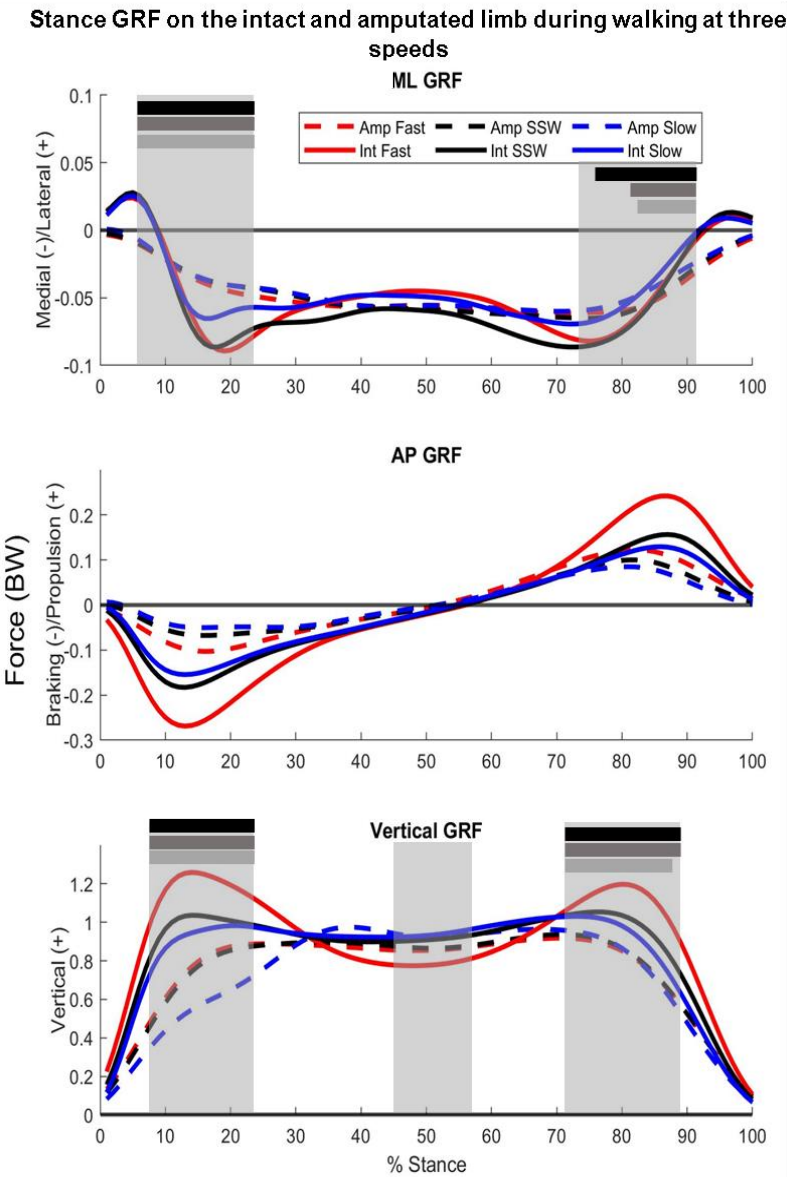

Figure 2. Average GRF in the three component directions when walking at three speeds Gray shaded regions indicate an interaction effect of limb*walking speed, while the horizontal bars indicate statistical differences between the intact and amputated limb during the fast (black), preferred (dark gray), and slow (light gray) walking speeds. Line colors and styles are the following: **Slow** = slow walking speed, **SSW** = preferred walking speed, **Fast** = fast walking speed, **—** Int = intact limb in (A), **---** Amp = amputated limb

the vertical direction, the GRF was statistically greater in the intact limb when compared to the amputated limb for the fast ($F > 3.498$, $p < 0.016$, black horizontal bar in Fig. 2), preferred ($F > 3.503$, $p < 0.016$, dark gray horizontal bar in Fig. 2), and slow ($F > 3.531$, $p < 0.016$, light gray horizontal bar in Fig. 2) walking speeds for the time periods where the peak GRFs occurred in the early and late stance periods. To summarize, in the vertical and ML directions during early and late stance, the intact limb generally had GRF which was statistically greater on the intact limb when compared to the amputated limb at all walking speeds, but the intact and amputated limb had similar GRF in the AP direction for the entire stance phase.

3.4. Discussion

The purpose of this study was to identify how individuals with a transfemoral amputation who use an OI prosthesis generate ground reaction force and share the force between the limbs when walking at three different speeds. Because the OI prosthesis uses a more rigid connection to the skeleton, we expected that the GRF on the intact and amputated limbs would be statistically diffeent during faster walking, but that the GRF on both limbs would be similar when walking at slower or preferred speeds. Our results indicate that our hypothesis of similar GRF on the intact and amputated limbs during slow and preferred speed, different GRF on the intact and amputated limbs when walking at a faster speed was partially supported. Specifically, in contradiction with our hypothesis of similar GRF on both limbs during slow and preferred speed walking, but statistically different GRF on the intact and amputated limb during faster walking,

our results found that, at all walking speeds, the GRF was statistically greater on the intact limb during all walking speeds for the medial-lateral and vertical direction, but similar at all speeds for the anterior-posterior direction. Overall, these results contradict the expectation that the rigid connection between the prosthesis and skeleton would afford an individual with a transfemoral amputation improved sharing of the GRF between the limbs when walking at different speeds, while providing evidence that these individuals use an intact limb reliance strategy at all walking speeds.

One of the primary reasons for using the OI prosthesis is that initial evidence suggests that the rigid connection provides improved function and performance based on clinical tests (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013). Whether this improvement is extended to the biomechanics is largely uninvestigated in this population. However, the results of this investigation indicate that using an OI prosthesis may not mitigate the intact limb reliance strategy required to compensate for inability of the prosthesis to mimic the intact limb. Specifically, our results indicate that, in both the medial-lateral and vertical direction at all walking speeds, the interaction of walking speed on the limbs results in statistical differences in the GRF on the intact and amputated limbs (Fig. 2), with individuals producing greater force with their intact limb at all walking speeds. The statistically greater force on the intact limb at all walking speeds for the ML and vertical direction indicates individuals are using an intact limb reliance strategy to compensate for limitations in the amputated limb which may be due to prosthesis componentry, and the missing muscle and tissue of the amputated limb.

Previous literature has established there are interlimb asymmetries in the GRF during walking in individuals who use a socket-based prosthesis (Lee Nolan et al., 2003; Rutkowska-Kucharska et al., 2018; Winiarski et al., 2021). These asymmetries are generally due to lower magnitude forces placed on the amputated limb in comparison to the intact limb, with the peak vertical forces on the amputated limb ranging between 96% and 123% of the body weight and the forces on the intact limb between 99% and 160% of the body weight, depending on the walking speed (Lee Nolan et al., 2003; Rutkowska-Kucharska et al., 2018; Winiarski et al., 2021). In contrast, in this study, the peak vertical GRF was generally lower in magnitude when compared to the previous literature, on the order of 89% to 98% of the body weight on the amputated limb during early stance, and 97% to 125% of the body weight on the intact limb, depending on the walking speed. These differences between the GRF magnitudes for this study and the previous literature are likely related to the differences in the suspension methods used by each population, as there are differences in sensation between the groups (Örgel et al., 2021), and specific differences in characteristics such as residual limb length which may influence the GRF which is placed on the limb. When using a socket-based prosthesis, the individuals largely has lowered sensation of the amputated foot, resulting in lower perception of the force placed on the residual limb outside of the pressure from the socket (Örgel et al., 2021). However, when using an OI prosthesis, initial evidence suggests there is increased sensation of the amputated limb (Örgel et al., 2021), referred to as osseoperception, where the individual is able to perceive sensation from mechanical stimuli such as impact with the ground. The

osseoperception available with an OI prosthesis has been suggested to possibly compensate for the missing cutaneous sensation after amputation (Stenfelt et al., 1998) and is believed to provide significantly more information to the individual about the contacting surface when compared to individuals with a socket-based prosthesis (Örgel et al., 2021). Lowered cutaneous sensation in the foot during gait has been found to result in greater forces placed on the foot (Hohne et al., 2012), perhaps explaining partially why the GRF is lower on the amputated limb in this study when compared to the previous literature. In addition, in research with diabetic individuals who have neuropathy, evidence suggests that the GRF may increase when the individuals wear shoes, perhaps due the shoe further decreasing the sensory capability of the foot (Sacco et al., 2010). Therefore, the decrease in the GRF on the amputated limb of the individuals in this study may be related to the individual choosing a more cautious gait pattern due to the additional sensation provided by the rigid connection between the prosthesis and the body via the OI implant.

In addition to the greater sensory capability provided by the OI implant, the greater force on the intact limb of the individuals in this study may be related to specific characteristics differences between the investigated populations. When comparing the demographics of the studied population to the demographics in the prior literature, there is a clear difference in the length of the residual limb. Specifically, in the Winiarski et al. (2021) study, the average residual limb length was 27.07 cm, and in the Nolan et al. (2003) study, the average residual limb length was not reported. However, the participants in this study had residual limbs which were only 19.41 cm or

approximately 46% of the intact femur length on average. This difference in residual limb length could contribute to the greater differences in GRF magnitude in our results, as residual limb lengths on the order of 40 ± 11% of the intact femur length have been previously found to correlate with increased gait deviations such as trunk flexion and lean, and pelvic tilt and obliquity (Bell et al., 2013). In addition, shorter residual limbs have been found to increase the difference in joint kinetics (Jaegers et al., 1995b) and to be associated with muscle atrophy at the hip (Jaegers et al., 1995a), perhaps requiring compensations for the limitations of the amputated limb through reliance on the intact limb during locomotion. Therefore, due to the short residual limbs of the individuals in this study, the individual may rely more on the intact limb for motion generation, resulting in greater differences in the GRF placed on each limb.

This study is one of the first to investigate the differences in the GRF of the intact and amputated limbs during walking at different speeds in individuals who use an OI prosthesis. And, while the OI prosthesis was expected to improve the performance due to the rigid skeletal attachment, our results indicate there may be limitations in the amputated limb such as a short residual limb, and muscle atrophy, as well as the use of a potentially more cautious gait due to the increased sensory feedback provided by the OI implant which result in increased reliance and greater GRF on the intact limb during locomotion. As a result of this increased loading placed on the intact limb, individuals who use an OI prosthesis may also still be at risk for overuse injuries in the intact limb such as knee osteoarthritis. Therefore, it may be important to establish with future work whether the intact limb reliance results in greater risk to the intact

limb's joint cartilage, and increased risk for knee osteoarthritis, as has been found with individuals who use a socket-based prosthesis (Norvell et al., 2005). However, while it appears that the more rigid connection with the skeleton afforded by the OI prosthesis does not fully mitigate the limitations of the amputated limb, and the intact limb reliance may potentially lead to overuse injuries in the intact limb, using an OI prosthesis may provide performance improvements and solutions to patient specific problems such as an inability to wear a socket which make the OI fixation a valuable option for individuals with transfemoral amputation.

4. CHAPTER 4: STUDY 2 INVESTIGATING SPECIFIC AIMS 2.1 AND 2.2

4.1. Introduction

Individuals with lower extremity amputation commonly report dissatisfaction with their current prosthesis, and general discomfort with their socket. The discomfort and dissatisfaction are associated with skin ulcers and irritation (K. Hagberg & Brånemark, 2001; Lyon et al., 2000), volume changes throughout the day (Sanders et al., 2018), and difficulty putting on and taking off their prosthesis (K. Hagberg & Brånemark, 2001), resulting in decreased time wearing and using their prosthesis throughout the day. Concurrently, individuals with lower extremity amputation have also been found to take only between 1500 and 5500 steps per day (Bussmann et al., 2004; Pepin et al., 2019), a number which is much lower than the recommendation that individuals walk 10,000 steps per day to have a healthy lifestyle. The combination of the discomfort, decreased wear time, and fewer steps per day generally results in decreased physical activity and increased risk for chronic health problems such as cardiovascular disease and obesity (Naschitz & Lenger, 2008b; Saris et al., 2003; Singh et al., 2007).

In addition to the risk for cardiovascular disease and obesity, individuals with lower extremity amputation typically develop overuse syndromes such as osteoarthritis in the intact limb (Gailey et al., 2008; Norvell et al., 2005; Struyf et al., 2009), and

chronic low back pain (Gailey et al., 2008; Hammarlund et al., 2011; Highsmith et al., 2019; Stam et al., 2004) as the result of relying on their intact limb for propulsive work during walking (Bonnet et al., 2014; Kobayashi et al., 2022; Pinhey et al., 2022), and various interlimb asymmetries at the joint kinematic (M. Finco et al., 2022; Kaufman et al., 2012; Winiarski et al., 2021) and kinetic (Harandi et al., 2020; Kobayashi et al., 2020; Seroussi et al., 1996) level. Specifically, individuals with lower extremity amputation have been found to have greater joint angles and ranges of motion at the ankle, knee and potentially the hip of the intact limb (M. Finco et al., 2022; Kaufman et al., 2012; Winiarski et al., 2021), as well as increased plantarflexion moments, hip extensor moments, and knee extensor moments on the intact limb side, and greater hip flexor moments on the amputated side (Harandi et al., 2020; Kobayashi et al., 2020; Seroussi et al., 1996). These kinematic and kinetic asymmetries are expected to be the result of the inability of the prosthesis to fully mimic the intact limb and the missing muscle and tissue on the amputated side, and would be expected to be exacerbated when individuals are required to walk faster. As walking speed increases, the joint kinematics and kinetics have relative changes that are unequal between the limbs (Bonnet et al., 2014; Frigo & Tesio, 1986), which would be expected to result in increased asymmetries between the limbs. While the changes to the joint kinematic asymmetries have not been explicitly investigated with walking speed, a single study found qualitative differences between the joint kinematics as individuals with lower extremity amputation walked faster (Frigo & Tesio, 1986). In addition, while the joint kinetics increase with walking speed, the kinetics on the amputated side have been

found to generally be smaller in magnitude than the intact limb, resulting in joint asymmetries at all walking speeds (Bonnet et al., 2014). However, whether these asymmetries can be reduced or removed entirely is largely unknown.

One potential mechanism to reduce not only the joint kinematic and kinetic asymmetries, but also the general discomfort and dissatisfaction with their prosthesis reported by individuals with amputation is to remove the socket entirely, and instead use the innovative osseointegrated (OI) fixation method. Recent innovations in prosthesis fixation methods have introduced the OI prosthesis, which uses a titanium implant anchored in the medullary canal of the residual limb bone. This results in more anatomically correct positioning of the residual limb (Ranker et al., 2021), as well as a direct and rigid connection between the prosthesis and the body. When compared to their peers who use a socket, individuals with lower extremity amputation who have an OI prosthesis have performance and functional improvements on clinical tests (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), as well as hip range of motion, sitting comfort, and basic kinematic measures such as walking speed (K Hagberg et al., 2005; Tranberg, Zugner, et al., 2011). In addition to the clinical tests, initial evidence suggests that using an OI prosthesis improves the peak knee extension, and hip extension moments, as well as the decreasing the asymmetry between the limbs during preferred speed walking (Davis-Wilson et al., 2023). These improvements are largely believed to be due to the direct fixation between the prosthesis and the skeleton, but whether these improvements are reflected in the interlimb asymmetries during the entirety of stance is essentially uninvestigated, and

whether the interlimb asymmetries become worse at faster walking speeds is unknown. It would be expected that the direct fixation should reduce some of the interlimb joint asymmetries found when using a socket-based prosthesis, but whether individuals still use compensation strategies such as relying on their intact limb after undergoing the OI procedure is not known, despite the claims for functional and performance improvements with the OI implant.

Therefore, the purpose of this study is to investigate the differences in the (1) joint kinematics and (2) joint kinetics in the intact and amputated limb of individuals with a transfemoral amputation who use an OI prosthesis while walking at three different speeds to determine whether an OI prosthesis influences the kinematic and kinetic strategies used for locomotion. We hypothesized that (1) joint kinematics, and (2) joint kinetics will be similar between the intact and amputated limb while walking at the slower than preferred and preferred walking speed as a result of the improved function afforded by the OI prosthesis through the rigid attachment, muscle re-attachment, rehabilitation and training, and more natural anatomical positioning around the hip, but that the kinematics and kinetics will be different between the intact and amputated limbs during faster than preferred walking as an intact limb reliance strategy is required to compensate for the limitations of the residual limb and prosthesis.

4.2. Methods

4.2.1. Population of interest and power analysis

Ten individuals with transfemoral amputation who use an OI prosthesis will be

recruited for this study. Inclusion criteria will consist of the following. Participants will be recruited if they (1) between the ages of 18 and 70, (2) are at least 1 year post-OI surgery, (3) are cleared by their medical professional for ambulation, (4) present no functional limitations which would affect their ability to walk or complete activities of daily life unaided, and (5) have at least 6 months' experience with their definitive prosthesis. Demographic and health information, including age, body weight, height, gender, and other relevant information including time since amputation and OI surgery, amputation cause, and current prosthetic components will also be collected.

To determine the sample size required for the proposed project, an *a priori* power analysis was completed using G*Power 3.1 (Heinrich Heine University Dusseldorf, Dusseldorf, North Rhine-Westphalia, Germany). Data investigating the hip range of motion in individuals who use an OI prosthesis (K Hagberg et al., 2005) and peak vertical ground reaction force differences between limbs across walking speeds in individuals who use a socket (Schaarschmidt et al., 2012) was used for the power analysis. For a power level of 0.8, an alpha level of 0.05, and moderate effect size, the *a priori* power analysis to detect differences in the means in a repeated measures ANOVA indicated a sample size ranging between 8 and 19 participants. However, due to the limited number of individuals who undergo the OI procedure, and because other studies with individuals who use OI prostheses have sample sizes between 9 and 12 (L. Frossard et al., 2020; Lee et al., 2007), we will plan to recruit a sample size N = 10 individuals

4.2.2. Data collection

Our protocol was approved by the University of Maryland IRB. After the informed consent process, participants changed into lab provided clothing, but used their own shoes. Participants had 77 markers placed on relevant bony and physiological landmarks, following a modified Rajagopal model (Rajagopal et al., 2016). The modifications for the marker model consisted of adding markers for the amputee population on a force transducer placed in the prosthesis system and the addition of markers on the feet and hands. After marker placement, participants performed a static calibration trial at the origin of the force platforms, and then three different walking conditions across the force platforms. The three walking conditions consisted of participants walking at self-selected preferred, fast, and slow speeds for 4 – 7 trials. The fast and slow speeds were counterbalanced across participants. During the walking trials, marker data was collected at 200 Hz using 13 infrared motion capture cameras (Vicon, Oxford, UK), and force data from ground contact was collected at 1000 Hz using eight 6DoF piezoelectric force platforms (Kistler, Switzerland) arranged in a single row located within a raised platform.

4.2.3. Data processing and analysis

After the data collection, marker position data and ground reaction force (GRF) for each limb during the stance phase of the three walking speeds will be exported from Nexus (Vicon, Oxford, UK) to Visual3D (C-Motion, Germantown, MD, USA). Three clean foot strikes for each limb during each walking speed condition were selected for analysis, and smoothed using a 4^{th} order dual-pass Butterworth filter with a cutoff frequency of 6 and 45 Hz for the marker position data and the GRF data respectively.

A linked segment model containing a foot, shank, and thigh for both the amputated and intact limbs, as well as a pelvis, was created for each participant using a standing static calibration trial and the marker position data. Segment properties were estimated using standard equations from Dempster (1955) for segment masses, and Hanavan Jr. (1964) for segment moment of inertias (Dempster, 1955; Hanavan Jr, 1964). The standardized segment moment of inertia properties are acceptable to model the gait of individuals with amputation during the stance phase, so only the stance phase for each walking condition will be analyzed in this analysis. Joint kinematics and kinetics were calculated using 3D inverse dynamics to output the ankle, knee, and hip joint angles and moments in the sagittal plane. Joint angles were calculated in the proximal segment reference frame, while joint moments were calculated in the distal segment reference frame. The joint angles and moments will be normalized to percent stance, as the absolute time spent in the stance phase differs both between limbs and at different walking speeds.

4.2.4. Statistical analysis

To test for differences between the limbs across walking speeds in the joint kinematics and kinetics, the time-dependent joint angles and moments for each limb at each walking speed condition were compared using Statistical Parametric Mapping with a 2-way ANOVA. The two within-factors for the ANOVA were the walking speed and the limb of the individual, and the interaction effect consisted of the effect of limb*walking speed. Statistical Parametric Mapping allows comparison of each percentile of stance to identify where within the stance phase an interaction or main

effect such as limb and walking speed may result in statistically different joint angles or moments. If the interaction effect of limb*walking speed was significant, the simple main effect within walking speeds and between limbs was tested using two sample t-tests with a Bonferroni correction. Because the simple main effect required comparing 3 different paired groups (intact limb versus amputated limb during the fast, preferred, and slow speed each), the Bonferroni correction will set the p-value to 0.016.

4.3. Results

Participants (Table 3) consisted of 7 males (51.71 ± 11.94 years old, 1.78 ± 0.16 m, 83.44 ± 25.63 kg, 2.89 ± 1.27 years since OI surgery) and 4 females (50.25 ± 11.35 years old, 1.65 ± 0.09 m, 54.93 ± 14.97 kg, 2.54 ± 2.38 years since OI surgery). Participant demographics did not differ between the male and female groups (p<0.05), indicating the two groups could be aggregated into a single group for analysis.

Table 3. Participant demographics as averages (SD) within groups by sex, and then as a whole sample

Gender	Age	Height (m)	Weight (kg)	Etiology	Time since amputation (years)	Time since OI surgery (years)	K Level	Residual limb length (cm)
N = 7 men	51.71 (11.94)	1.78 (0.16)	83.44 (25.63)	4 trauma, 2 cancer, 1 infection	7.02 (2.64)	2.89 (1.27)	3.71 (0.49)	21.22 (5.36)
N = 4 women	50.25 (11.35)	1.65 (0.09)	54.93 (14.97)	2 trauma, 2 cancer	22.14 (15.5)	2.54 (2.38)	3.50 (0.58)	16.70 (4.84)
N = 11	51.18 (11.17)	1.73 (0.15)	73.07 (25.86)	6 trauma, 4 cancer, 1 infection	12.52 (11.6)	2.76 (1.64)	3.64 (0.5)	19.41 (5.41)

The average walking speed (Table 4) for each walking condition was 0.76 ± 0.15 m/s, 0.94 ± 0.14 m/s, and 1.22 ± 0.23 m/s for the slow, preferred, and fast walking speeds respectively. Statistical tests indicate that the slow speed is significantly different from the preferred (p<0.001) and the fast (p<0.001) speeds, and that the preferred is significantly different from the fast speed (p<0.001).

Table 4. Average walking spatiotemporal data (SD) for three walking conditions

	Slow	SSW	Fast
Average walking speed (m/s)	0.76 (0.15)	0.94 (0.14)	1.22 (0.23)
Average stance time (s)	0.87 (0.3)	0.77 (0.14)	0.67 (0.16)
Average stride length (m)	1.03 (0.08)	1.15 (0.16)	1.37 (0.29)

4.3.1. Ankle

At the ankle, there was a significant interaction effect at the ankle during early stance for the angle (Fig. 3, $F > 7.491$, $p < 0.05$) and late stance for the moment (Fig. 4, $F > 7.722$, $p < 0.05$). During early stance, the intact limb had a significantly more dorsiflexed ankle for the fast ($F > 3.258$, $p < 0.02$) and preferred speed ($F > 3.322$, $p < 0.02$), while the intact limb had a significantly more plantarflexed ankle during the slow

speed walking condition ($F > 3.287$, $p < 0.02$).

The ankle moment (Fig. 4) was significantly greater in the intact limb for the fast and preferred walking speeds during late stance, with greater ankle plantarflexion moments during each condition. The ankle moments were not statistically different between the limbs for the slow walking condition.

4.3.2. Knee

At the knee, there was a significant interaction effect between the limbs and walking speeds for both the angle (Fig. 3, $F > 7.558$, $p < 0.05$) and moment (Fig. 4, $F > 7.687$, $p < 0.05$). When comparing between the limbs at each walking speed, the intact limb had a greater flexion angle

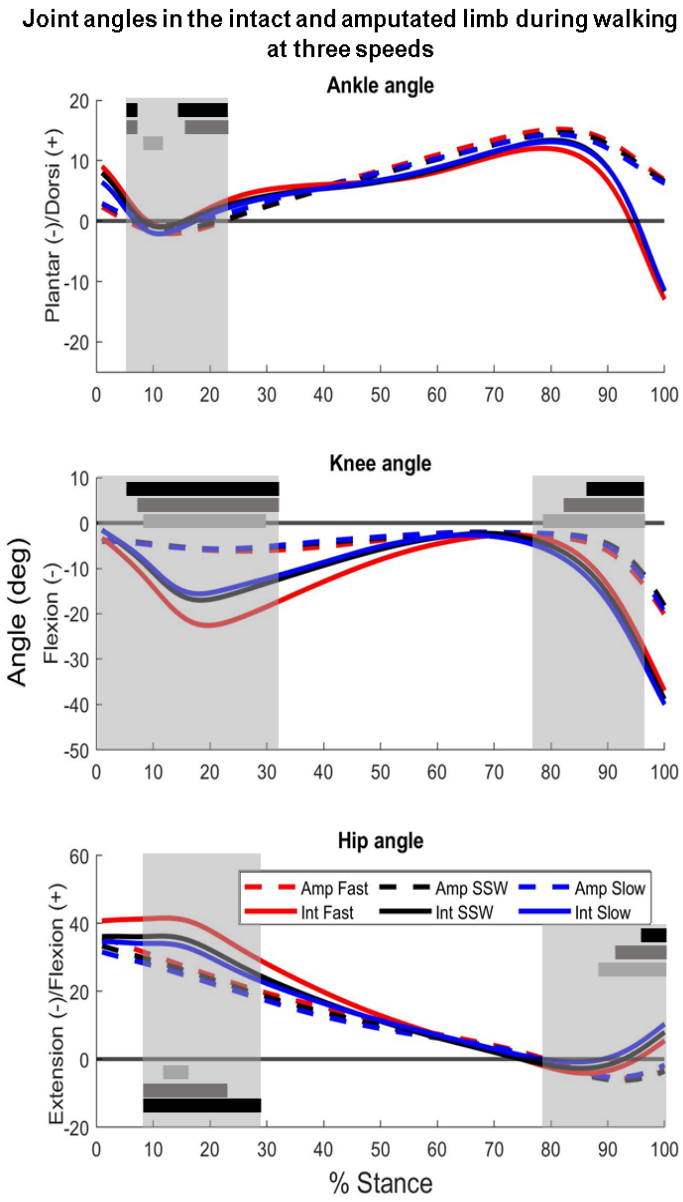

Figure 3. Average joint angles in the ankle, knee, and hip when walking at three speeds. Gray shaded regions indicate an interaction effect of limb*walking speed, while the horizontal bars indicate statistical differences between the intact and amputated limb during the fast (black), preferred (dark gray), and slow (light gray) walking speeds. Line colors and styles are the following: **Slow** = slow walking speed, **SSW** = preferred walking speed, **Fast** = fast walking speed, — Int = intact limb, --- Amp = amputated limb

during early and late stance for the fast (F > 3.078, p < 0.02), preferred (F > 3.058, p < 0.02), and slow (F > 3.067, p < 0.02) walking speed conditions. Similarly, when comparing the knee moment between the limbs at each walking speed (Fig. 4), there was a significantly greater flexion moment for the intact limb at the fast (F > 3.358, p < 0.02), preferred (F > 3.367, p < 0.02), and slow (F > 3.385, p < 0.02) speeds during early stance. However, during late stance, the moments at the knee were not statistically different between the limbs at each walking speed.

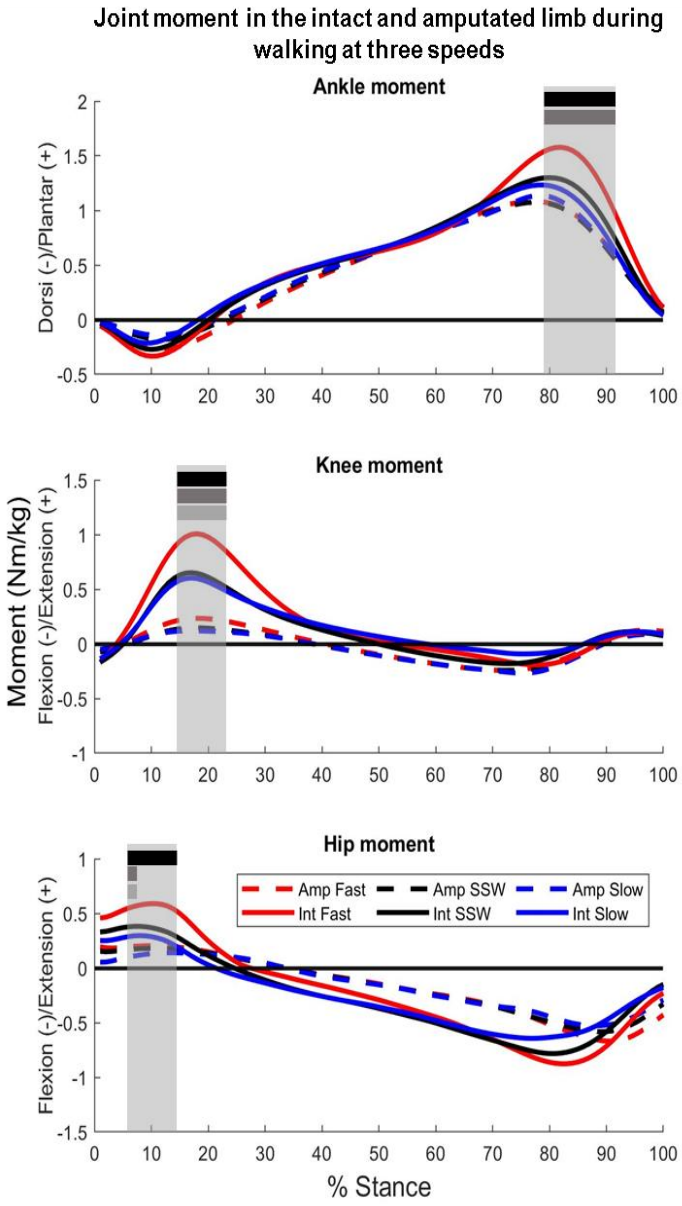

Figure 4. Average joint moments in the ankle, knee, and hip when walking at three speeds. Gray shaded regions indicate an interaction effect of limb*walking speed, while the horizontal bars indicate statistical differences between the intact and amputated limb during the fast (black), preferred (dark gray), and slow (light greay) walking speeds. Line colors and styles are the following: **Slow** = slow walking speed, **SSW** = preferred walking speed, **Fast** = fast walking speed, **—** Int = intact limb, --- Amp = amputated limb

4.3.3. Hip

At the hip, there was a significant interaction effect between the limbs and walking

speed for both the angle (Fig. 3, $F > 7.202$, $p < 0.05$) and moment (Fig. 4, $F > 7.802$, $p < 0.05$). When comparing between the limbs at each walking speed, the intact limb hip was significantly more flexed during early stance and into toe off for the fast ($F > 2.967$, $p < 0.02$), preferred ($F > 2.943$, $p < 0.02$), and slow ($F > 2.971$, $p < 0.02$) walking speed conditions. Similarly, during early stance, the intact limb hip had a significantly greater hip extension moment for the fast ($F > 3.315$, $p < 0.02$), preferred ($F > 3.300$, $p < 0.02$), and slow ($F > 3.314$, $p < 0.02$) walking conditions. During late stance, there was not a significant difference between the limbs at each walking speed for the hip moment.

4.4. Discussion

The purpose of this study was to investigate the differences in the joint angles and moments in individuals who use an OI prosthesis when walking at three different speeds in order to establish foundational knowledge surrounding the biomechanics of using an OI prosthesis. Because the OI prosthesis uses a more rigid connection to the skeleton, we expected that the interlimb joint (1) kinematics and (2) kinetics would be similar between the intact and amputated limbs during walking at the slow and preferred speed, but that the joint angles and moments would be greater in magnitude for the intact limb when compared to the amputated limb during the fast speed walking. Our results (Fig. 3 and 4) indicate that our hypothesis of similar joint angles and moments during slow and preferred speed walking, but significantly greater angles and moments when walking at a faster speed was partially supported. Specifically, in contradiction with the first half of our hypothesis of similar joint angles and moments

during slow and preferred speed walking, our results found that the intact limb joint angles and moments were significantly greater for the ankle, knee, and hip at the slow and preferred speeds. However, the second half of our hypothesis postulating that the joint angles and moments would be significantly greater in the intact limb when compared to the amputated limb during fast speed walking was supported. Overall, these results contradict the expectation that the rigid connection between the prosthesis and skeleton would afford an individual with a transfemoral amputation improved interlimb symmetry and biomechanics when walking at different speeds, while providing evidence that these individuals may still use compensatory strategies during locomotion.

Previous research has found that using an OI prosthesis results in improvements to the performance on clinical tests and basic spatiotemporal measures during gait (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), as well as improvements in peak hip and knee moment asymmetry when compared to their joint kinetics pre-OI surgery (Davis-Wilson et al., 2023). However, it is largely unknown how using an OI prosthesis influences the biomechanics of both the intact and amputated limb, as well as the effect of walking speed in these individuals. The results of this study found that, despite the belief that the more rigid skeletal connection would provide improved mechanics during locomotion, there still exist kinematic and kinetic differences between the limbs which result in greater joint angles and moments at the ankle, knee, and hip, and that walking faster may increase the differences between the limbs. Due to the limited research investigating interlimb asymmetries in

individuals with OI prostheses, it is difficult to compare these results to the literature. However, when comparing the results of this study with individuals who use socket-based prostheses, the general differences between the limbs for the joint angles and moments are similar. Specifically, previous literature reported that with a microprocessor knee, the limbs generally have differences with respect to joint kinematics, with the differences the greatest at the knee during the early and midstance periods (Harandi et al., 2020; Kaufman et al., 2012; Winiarski et al., 2021). This is similar to our results, which found significant differences in the knee flexion between the limbs during early and midstance, regardless of walking speed. In addition, previous literature has found that, at the hip, individuals with a socket-based prosthesis generally have a smaller flexion angle on the amputated side and have an amputated limb which reaches extension sooner than the intact limb (Harandi et al., 2020; Kaufman et al., 2012; Winiarski et al., 2021). Our results how agreement with the previous results, as individuals with an OI prosthesis generally have a smaller hip flexion angle during early stance, and hip kinematics which more quickly progress toward extension in the amputated limb when compared to the intact limb, resulting in significant differences between the limbs during early stance (Harandi et al., 2020; Kaufman et al., 2012; Winiarski et al., 2021).

With regard to joint kinetics, previous literature has found that individuals with a socket-based prosthesis generally have decreased ankle moment during late stance, decreased knee moment during early stance, and decreased hip moment during late stance, along with other changes between the limbs (Carse et al., 2020a). Our results

found similar differences at the ankle and knee, but not at the hip, where the individuals with an OI prosthesis had decreased hip moments during early stance. The differences in our results may be due to the use of the bone-anchored prosthesis allowing the individual better hip extension during late stance when compared to a socket-based prosthesis. The results of this study also showed agreement with the literature comparing asymmetry indices between socket-based and OI prosthesis. Specifically, during walking, the peak kinetic interlimb asymmetries decreased slightly when using an OI prosthesis at the hip and knee, but there were still differences between the limbs in the joint kinetics (Davis-Wilson et al., 2023). Overall, our results show agreement with the literature that interlimb differences in both the joint kinematics and kinetics still occur in individuals with a transfemoral amputation who use an OI prosthesis.

No research has been conducted investigating the effect of walking speed on interlimb kinematic and kinetic asymmetries in individuals who use an OI prosthesis, making this the first investigation to systematically quantify how walking speed influences the biomechanics of this population. The results of this study largely find there is an increase in the interlimb kinematic and kinetic differences when individuals walked at a fast speed, but that interlimb differences at all three lower limb joints occur at all walking speeds. Specifically, the interlimb kinematic differences increased at early stance for the ankle, and at midstance and toe off for the knee and hip (Fig. 3), while the interlimb kinetic differences (Fig. 4) increased during late stance for the ankle and early stance for the knee and hip. The increase in interlimb differences with faster walking largely appears to be the result of a larger relative increase in joint angle or

moment magnitude for the intact limb, while the angle and moment on the amputated limb stays relatively constant with walking speed. At the ankle and knee, the interlimb differences are likely related to limitations within the prosthetic system, as the prosthetic components are unable to increase their contribution to the joint kinematics and kinetics as walking speed increases. Prosthetic feet generally act in a passive energy storage and return manner, and result in a net energy loss during the energy return phase of gait (Czerniecki et al., 1991; Rigney et al., 2017). The passive characteristic of the prosthetic foot likely results in an ankle dorsiflexion angle at heel strike that is a function of walking speed, as walking faster leaders to a greater initial dorsiflexion angle with loading. In addition, the passive property of the prosthetic foot results in an inability of the amputated limb to match the plantarflexion angle of the intact limb, limiting the joint kinematics and kinetics during late stance. Similarly, even the most efficient microprocessor knee limits the knee flexion at all speeds during most of stance, generally to approximately 5 to 10 degrees (Creylman et al., 2016; Harandi et al., 2020; Johansson et al., 2005), resulting in increasing difference between the limbs when the individual walks faster, as the knee flexion angle on the intact limb side increase with walking speed, but the amputated limb's knee flexion angle does not. To confirm there were limitations in the prosthesis system which may have created the kinetic differences, the joint power was computed between the limbs. At the ankle and knee, the joint power in the amputated limb was smaller in magnitude than the intact limb, indicating that the prosthetic knee and ankle are unable to match the energy generation and absorption of the intact limb. As a result of these limitations in the

prosthetic system, and the poor imitation of the intact limb these components provide, there are interlimb kinematic and kinetic differences at the ankle and knee which increase with walking speed.

However, at the hip, the inability of the amputated limb to match the joint kinematics and kinetics of the intact limb with increasing walking speed may be due to the residual limb length. Previous literature investigating gait deviations, as well as joint moments with residual limb length found that, as the residual limb gets shorter, the kinematic differences between the intact and amputated limb at the knee and hip also increases (Jaegers et al., 1995b). In addition, short residual limbs have been associated with weakness and atrophy of the hip stabilizing muscles, leading to large gait deviations such as trunk lateral lean during stance (Bell et al., 2013; Jaegers et al., 1995a). The participants in this study had residual limbs that were 19.41 cm on average, or approximately 46% of the intact femur length. The residual limb length is shorter than in previous research reporting interlimb kinematics and kinetics (Davis-Wilson et al., 2023; Winiarski et al., 2021), and the much shorter residual limb length in our participants may contribute to the increase in interlimb differences at the hip with walking speed. Overall, our results indicate that during walking, there are limitations in the prosthesis system and residual limb which result in interlimb asymmetries that the more rigidly connected, better performing OI fixation is unable to overcome, resulting in compensations or reliance on the intact limb during locomotion.

This study is one of the first to investigate the interlimb kinematic and kinetic asymmetries at different walking speeds in individuals who use an OI prosthesis. The

OI prosthesis is generally expected to improve performance as a result of the direct skeletal fixation, but our results indicate there are interlimb kinematic and kinetic asymmetries at the ankle, knee, and hip at all walking speeds, and that these asymmetries generally increase with walking speed. The existence of these asymmetries may be due to the poor imitation of the intact limb provided by the prosthesis, a shorter residual limb length, and the muscle atrophy at the amputated hip combining to result in an inability of the amputated limb to match the relative increases in the joint kinematics and kinetics of the intact limb as walking speed increases. However, while our results find that using an OI prosthesis may not necessarily improve the interlimb biomechanics, there may be other performance and self-evaluated criteria such as an inability to wear a socket which make the OI fixation a valuable option for individuals with a transfemoral amputation.

5. CHAPTER 5: STUDY INVESTIGATING SPECIFIC AIMS 3.1, AND 3.2

5.1. Introduction

Individuals with lower extremity amputation commonly report discomfort with their socket and problems with skin irritation as a result of their socket fit (Berke et al., 2010; Pezzin et al., 2004). This discomfort may make it difficult for the individuals to use or wear their prosthesis for long periods of time, potentially resulting in decreased physical activity throughout the day and increased risk for chronic health problems such as cardiovascular disease (Naschitz & Lenger, 2008b; Saris et al., 2003; Singh et al., 2007). One innovative solution which removes the socket and socket-related complaints entirely is an osseointegrated (OI) or a bone-anchored prosthesis. An OI prosthesis uses a titanium implant which is surgically placed in the medullary canal of the residual limb bone. This implant then extends out of the bone, muscle, and tissue to create an external attachment point for the prosthesis, referred to as the abutment. The use of an OI prosthesis creates a more direct and rigid connection between the body and the prosthesis, ostensibly resulting in improved performance and function when compared to using a socket-based prosthesis.

Research has indicated that using an OI prosthesis improves the performance on clinical tests such as the Timed Up and Go and the Six Minute Walk Test (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), as well

as on basic kinematic measures such as walking speed and hip range of motion (K Hagberg et al., 2005; Tranberg, Zugner, et al., 2011). The use of an OI prosthesis also appears to improve the asymmetry at the hip and knee when compared to pre-surgery mechanics (Davis-Wilson et al., 2023), but may still result in interlimb asymmetries in the GRF, and the lower limb kinematics and kinetics that are individual specific (Studies 1 and 2). And, while these clinical performance improvements are promising, the use of the OI implant also may introduce a long-term concern surrounding the health of the residual limb bone over the individual's lifetime. This concern is directly related to the rigid connection between the bone and prosthesis, as high impact forces may transfer into the OI implant and bone with minimal damping from the ground contact of the prosthesis. Previous research investigating the force at the abutment and risk to the bone during walking have indicated that the force is not at a level that is expected to injure the bone (L. Frossard et al., 2013, 2021a; L. A. Frossard, 2010; Lee et al., 2007; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P. K. Tomaszewski et al., 2010), and the bone stress and strain are below the bone's yield strength or point where plastic deformation will occur (Newcombe et al., 2013; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P K Tomaszewski et al., 2010; Xu et al., 2006). These initial results, therefore, indicate that the health of the bone is not expected to be compromised during a single loading phase, making it likely that walking will not result in a traumatic injury to the bone.

However, the current literature is limited in its application, as the force and bone strain during walking has only been investigated during specific time points of a single

stance phase at the individual's preferred walking speed. In addition to the current limitations in the literature surrounding walking speed and the loading placed on the bone and OI implant, there are activity restrictions which acknowledge the potential danger of increasing locomotion speed on the longitudinal health of the bone, including the recommendation that individuals with an OI prosthesis not participate in running or high impact activities. The activity restrictions are essentially uninvestigated and are largely based on the assumption that as locomotion speed increases, the ground reaction force (Lee Nolan et al., 2003), and force which may be transferred to the bone via the prosthesis and implant are expected to increase as well, potentially leading to high impact forces which are directly placed on the bone and increased strain on the bone. However, despite this assumption, minimal research has been conducted to understand how locomotion speed influences the forces which are transferred to the bone via the OI implant and the resulting strain on the bone. Therefore, before expanding the recommended activities available to individuals with an OI prosthesis to include running, it is important to first understand the influence of walking speed on the force which is transferred to the abutment and OI implant and the loading which occurs on the bone in order to provide foundational knowledge about potential risk to the bone during activities of daily living such as variable speed walking.

Therefore, the purpose of this study is to investigate (1) the abutment force during walking at different speeds, and (2) the strain on the bone during walking at different speeds to determine the risk for bone-OI implant degeneration over time. We hypothesized that (1) the forces at the abutment will increase with walking speed, as

ground reaction force increases as individuals walking faster and there will be minimal damping of the ground reaction force by the prosthesis, and (2) the peak strain on the bone during a single stance phase will increase with walking speed as the magnitude of the input forces increase with walking speed but that the strain pattern across the bone will be similar on the diaphysis, internal boundary between the bone and implant, and the femoral neck due to the abutment force being directed almost completely in the axial direction.

5.2. Methods

5.2.1. Population of interest and power analysis

Eleven individuals with transfemoral amputation who use an OI prosthesis were recruited for this study. Participants were recruited if they (1) were between the ages of 18 and 70, (2) are at least 1-year post-OI surgery, (3) are cleared by their medical professional for ambulation, (4) present no functional limitations which would affect their ability to walk or complete activities of daily life unaided, and (5) have at least 6 months' experience with their definitive prosthesis. Demographic and health information, including age, body weight, height, gender, and other relevant information including time since amputation and OI surgery, amputation cause, and current prosthetic components was also collected.

To determine the sample size required for the proposed project, an *a priori* power analysis was completed using G*Power 3.1 (Heinrich Heine University Dusseldorf, Dusseldorf, North Rhine-Westphalia, Germany). Data investigating the hip

range of motion in individuals who use an OI prosthesis (K Hagberg et al., 2005) and peak vertical ground reaction force differences between limbs across walking speeds in individuals who use a socket (Schaarschmidt et al., 2012) was used for the power analysis. For a power level of 0.8, an alpha level of 0.05, and moderate effect size, the *a priori* power analysis to detect differences in the means in a repeated measures ANOVA indicated a sample size ranging between 8 and 19 participants. However, due to the limited number of individuals who undergo the OI procedure, and because other studies with individuals who use OI prostheses have sample sizes between 9 and 12 (L. Frossard et al., 2020; Lee et al., 2007), we planned to recruit a sample size of at least N = 10 individuals

5.2.2. Data collection

Our protocol was approved by the University of Maryland IRB. After the informed consent process, participants changed into lab provided clothing, but used their own shoes. Prior to collecting data, a certified prosthetist placed the iPECS Lab, a 6DoF force sensor (RTC Electronics Inc., Dexter, MI, USA) within the prosthesis system, just below the Axor II. This sensor will allow the measurement of the forces and moments that are placed on the abutment, with the assumption of rigidity between the Axor II and abutment. The prosthesis was aligned by our prosthetist and adjusted based on feedback from the participant after fitting the iPECS in the prosthetic system, and before any walking data was collected.

After placing the iPECS force sensor and aligning the prosthesis, participants had 77 markers placed on relevant bony and physiological landmarks, following a

modified Rajagopal model (Rajagopal et al., 2016). The modifications for the marker model consisted of adding markers for the amputee population on the iPECS to define the axis system, and the addition of markers on the feet and hands. After marker placement, participants performed a static calibration trial at the origin of the force platforms, and then three different walking conditions across the force platforms. The three walking conditions consisted of participants walking at self-selected preferred, fast, and slow speeds for 4 – 7 trials. The fast and slow speeds were counterbalanced across participants. During the walking trials, abutment force data as raw strain data was collected at 1000 Hz using the iPECS Lab force sensor (RTC Electronics Inc., Dexter, MI, USA), marker data was collected at 200 Hz using 13 infrared motion capture cameras (Vicon, Oxford, UK), and force data from ground contact was collected at 1000 Hz using eight 6DoF piezoelectric force platforms (Kistler, Switzerland) arranged in a single row located within a raised platform.

5.2.3. Data processing

Due to limitations with placing the iPECS Lab force sensor within the prosthesis system of the participants, abutment force data was only able to be collected for three participants. Five participants had residual limbs that were too long to fit the

sensor above the knee, while three participants data were unavailable for analysis. Therefore, for the participants which had both the iPECS and GRF data, a comparison was done testing the differences between the peak force as measured by the iPECS Lab, and an estimation of the abutment force done by transforming the GRF into the iPECS axis system (Fig. 5). Previous research has indicated there is minimal differences in the force measured by the iPECS Lab and the transformed GRF in individuals with transtibial amputation (Koehler et al., 2014), so this method may provide acceptable estimations of the force at the abutment. Statistical tests of the peak forces from both the measured abutment force from the iPECS and the estimated force using the transformed GRF indicated there was no difference in the peak force across all walking speeds, indicating the transformed GRF may be used as an acceptable estimation of the abutment force, allowing use of the full data set of eleven participants for this analysis.

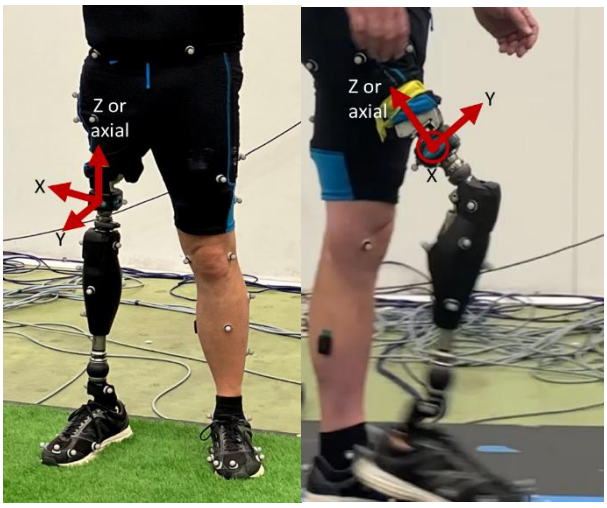

Figure 5. iPEC sensor axis system definition during static standing (left) and walking (right).

To do the analysis for Aims 1 and 2, the iPEC Lab forces and moments were imported into Visual3D (C-Motion, Germantown, MD, USA), along with the marker position and ground reaction force data, to define stance phases. The iPEC force and GRF were smoothed using a 4th order Butterworth filter with a cutoff frequency of 45

Hz, and then three stance phases for the amputated limb were exported for analysis in Matlab. The rotation matrix between the iPEC axis system, and the GRF axis system was identified in Matlab for the three participants who had both data sources. This rotation matrix was used to transform the GRF from the lab axis system to the iPEC axis system for the three stance phases of the eleven participants at each walking speed, and this data was used for analysis for Aim 1, and as the input for the finite element analysis in Aim 2.

5.2.4. Finite element analysis

To address Aim 2, a custom finite element model (FEM) of the femoral bone and implant was built in Comsol Multiphysics 6.0 (Comsol Inc, Stockholm, Sweden). The details of the model are briefly described below, with additional details in Appendix A. The final FEM was built with three different domains, a cortical external bone structure, a cancellous internal structure in the femur head, and a titanium alloy implant which shared internal walls. The geometries of each the femur-implant system was based upon an open source femur model generated by MacLeod et al., (2016) in ANSYS, and an implant model provided for research purposes by Integrum (MoIndal, Sweden) (MacLeod et al., 2016). The open source femur model was converted from an ANSYS model to a SolidWorks (Dassault Systemes, Waltham, MA, USA) model, and then validated in Comsol using the loads referenced in MacLeod et al., (2016) (MacLeod et al., 2016). Results for this validation are in Table 11 in Appendix A, with the Comsol model in good agreement with both the experimental data, and the ANSYS model. The validated femur only model was then used to generate the geometry

representing the bone and implant of an individual who uses an OI prosthesis.

The femur-OI implant geometry was then built in SolidWorks by positioning the OI implant within the medullary canal of the femur, and then cutting the femur such that the threads on the OI implant was countersunk by 20 mm. A mesh file was exported from SolidWorks to create the geometry in Comsol. After importing the mesh file to Comsol, the geometry (Fig. 6A and B) was finalized as a union of the bone and implant such that they shared an internal wall.

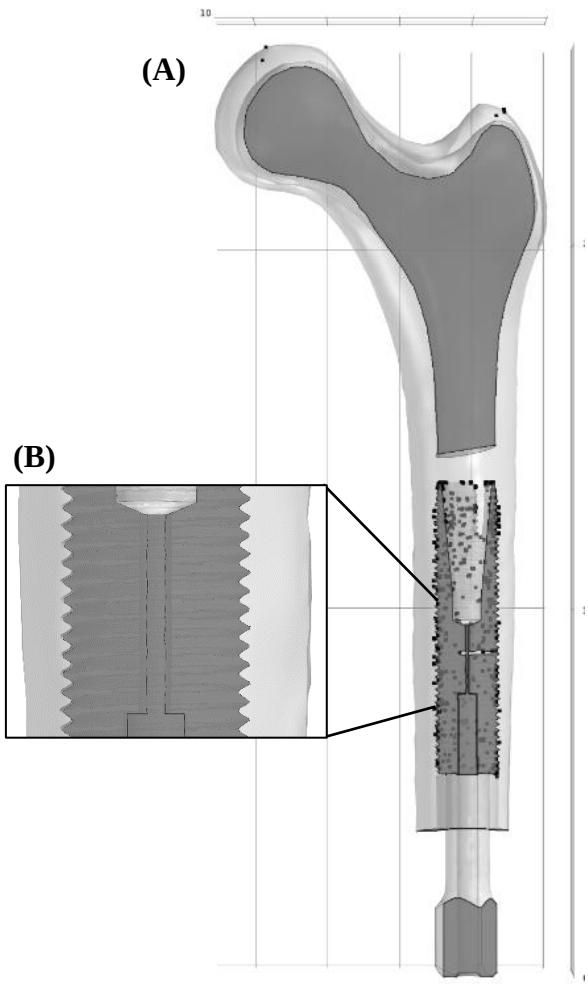

Figure 6. Geometries of the finalized femur-implant model with (A) cross section and (B) zoom to show the internal boundary shared between the bone and implant.

The material properties for each domain of the model (Table 5 and 12 in Appendix A) were based on values from MacLeod et al., (2016) and the standard properties of Ti6Al4V, the titanium alloy used for the implant (MacLeod et al., 2016). This model assumed isotropic material properties, as is common in the literature.

Table 5. Bone and OI implant material properties used for this dissertation's Comsol model of a residual limb femur which contains an OI implant for prosthesis fixation

Body	Young's Modulus (Pa)	Poisson's Ratio	Density (kg/m^3)
Cortical Bone[1]	$1.635e^{10}$	0.26	1932
Cancellous Bone[1]	$1.37e^{8}$	0.3	1750
Titanium Implant[2]	$1.15e^{11}$	0.342	4430

Properties are referenced from [1]MacLeod et al. (2016) and [2]Standard material properties for Ti6-Al4-V

After defining the material properties, the model was fully constrained on the proximal portion of the femur at five nodes, two on the femoral head and three on the trochanter. While the femur is not fully constrained at the hip in reality, similar models such as those conducted by Tomaszewski et al. (2010) have used a fixed constraint to simply the complexity of the model, and a similar constraint was used in this simulation. Boundary loads representing the input forces were added on the distal end of the abutment for each percentile of stance.

After finalizing the physics section of the model, the model was meshed with triangular elements on the boundaries, and tetrahedral elements in the domains. The mesh on the boundary between the implant and femur was created with a higher element density to ensure convergence and accurate simulation results. The finalized mesh contained 191,150 tetrahedral elements, and 33,096 triangular elements for the whole bone-implant structure, and a total degrees of freedom of 785,625. To confirm an appropriate mesh density was chosen, models with a more complex element density were investigated, and differences in the peak strain on the femoral neck, bone diaphysis, and bone-implant interface between the chosen mesh density and a much

more complex mesh density (698,152 tetrahedral elements, 84,891 triangular elements, 2,854,518 degrees of freedom in the model) were found to be at least one order of magnitude smaller than the peak strains on the bone. For example, the peak strains on the femoral neck for the chosen mesh density and the much more complex mesh density were 0.00130 and 0.00155 during the first half of stance, and 0.00123 and 0.00141 for the second half of stance, indicating there was a difference of 0.00025 and 0.00018 for each half of the stance phase respectively. Therefore, using a more complex mesh density does not appear to appreciably change the results and implications for the strain on the bone, and the less complex density was chosen to reduce the solution computation time and power required for the simulations of the bone strain for each walking speed condition.

Prior to using our experimental data, the femur-OI implant model was validated using input forces (Table 13) from Tomaszewski et al. (2010) (P. K. Tomaszewski et al., 2010). Our model (Fig. 14A in Appendix A) was found to have general agreement with the results of Tomaszewski et al., (2010) (Fig. 14B in Appendix A) in terms of the stress range and distribution along the bone. Minor differences in stress magnitude occurred, but may be due to the choice of material properties, length of the residual bone (Andrango Castro et al., 2017), implant characteristics, and other modeling choices.

After comparing the validation case from Tomaszewski et al. (2010), a time-dependent solver was used to identify the time point where the greatest peak strains occurred on the bone, and this time point was isolated for analysis. The input forces for

the time-dependent model consisted of the group average abutment forces during each percent of the stance phase, as discussed in Section 5.2.3. After identifying the time point with the peak stress for each walking speed, the peak strain in the femoral neck, along the femur diaphysis, and along the interior boundary between the bone and implant and the strained volume of the bone for each walking speed was output for analysis. The strained volume represents the volume of the model which is above a threshold strain value. Previous research has indicated this may be a better way of identifying the mechanical fatigue with a repetitive loading (Haider et al., 2021). For this particular analysis, the strain threshold was set at 0.001 strains, as this represents the approximate maximum strain which may occur during walking in healthy bone (Lanyon et al., 1975).

5.2.5. Statistical analysis

Outcome variables for Aim 1 are the time course of the force estimated at the abutment when individuals walked at the three different speeds. The abutment force is determined for each participant, and then three stance phases will be used for statistical analysis. For Aim 2, the outcome variables were the peak strain on the femur diaphysis, internal bone-implant boundary, and femoral neck, and the strained volume above 0.001 strains at each walking speed. The peak strain and strained volume were computed using the average input abutment force for each walking condition.

To test for difference in the abutment force across walking speeds, Statistical Parametric Mapping with a 1-way ANOVA of walking speed was used to determine differences across the time course of the abutment force during stance. If a main effect

of walking speed was found, post-hoc testing used two sample *t* tests with a Bonferroni correction for multiple group comparisons. Because the two sample tests used three pair group comparisons (fast v slow, fast v preferred, slow v preferred), the Bonferroni correction set the *p* value to 0.02.

For Aim 2, because the ensemble averaged abutment force was used as the input the finite element analysis, statistical analysis was not possible for the peak strain, and strained volume.

5.3. Results

Participants (Table 6) consisted of 7 males (51.71 ± 11.94 years old, 1.78 ± 0.16 m, 83.44 ± 25.63 kg, 2.89 ± 1.27 years since OI surgery) and 4 females (50.25 ± 11.35 years old, 1.65 ± 0.09 m, 54.93 ± 14.97 kg, 2.54 ± 2.38 years since OI surgery). Participant demographics did not differ between the male and female groups ($p<0.05$), indicating the two groups could be aggregated into a single group for analysis.

Table 6. Participant demographics as averages (SD) within groups by sex, and then as a whole sample

Gender	Age	Height (m)	Weight (kg)	Etiology	Time since amputation (years)	Time since OI surgery (years)	K Level	Residual limb length (cm)
N = 7 men	51.71 (11.94)	1.78 (0.16)	83.44 (25.63)	4 trauma, 2 cancer, 1 infection	7.02 (2.64)	2.89 (1.27)	3.71 (0.49)	21.22 (5.36)
N = 4 women	50.25 (11.35)	1.65 (0.09)	54.93 (14.97)	2 trauma, 2 cancer	22.14 (15.5)	2.54 (2.38)	3.50 (0.58)	16.70 (4.84)
N = 11	51.18 (11.17)	1.73 (0.15)	73.07 (25.86)	6 trauma, 4 cancer, 1 infection	12.52 (11.6)	2.76 (1.64)	3.64 (0.5)	19.41 (5.41)

The average walking speed (Table 7) for each walking condition was 0.76 ± 0.15 m/s, 0.94 ± 0.14 m/s, and 1.22 ± 0.23 m/s for the slow, preferred, and fast walking speeds respectively. Statistical tests indicate that the slow speed is significantly different from the preferred (p<0.001) and the fast (p<0.001) speeds, and that the preferred is significantly different from the fast speed (p<0.001).

Table 7. Average walking spatiotemporal data (SD) for three walking conditions

	Slow	SSW	Fast
Average walking speed (m/s)	0.76 (0.15)	0.94 (0.14)	1.22 (0.23)
Average stance time (s)	0.87 (0.3)	0.77 (0.14)	0.67 (0.16)
Average stride length (m)	1.03 (0.08)	1.15 (0.16)	1.37 (0.29)

5.3.1. Abutment force

Overall, the estimated resultant force (Fig. 7) was found to decrease in stance time as individuals walked faster, as is expected when individual walk faster. However, the resultant force also indicates that that the abutment force magnitude does not increase with walking speed, as would be expected (Fig. 7, Table 8).

Table 8. Peak resultant abutment forces (SD) during walking at three different speeds for the loading period and push-off period of stance.

	Walking Condition	Peak Abutment Force (BW)
Loading Period	Slow	0.95 (0.04)
	SSW	0.87 (0.07)
	Fast	0.87 (0.15)
Push-off Period	Slow	0.80 (0.04)
	SSW	0.81 (0.05)
	Fast	0.82 (0.07)

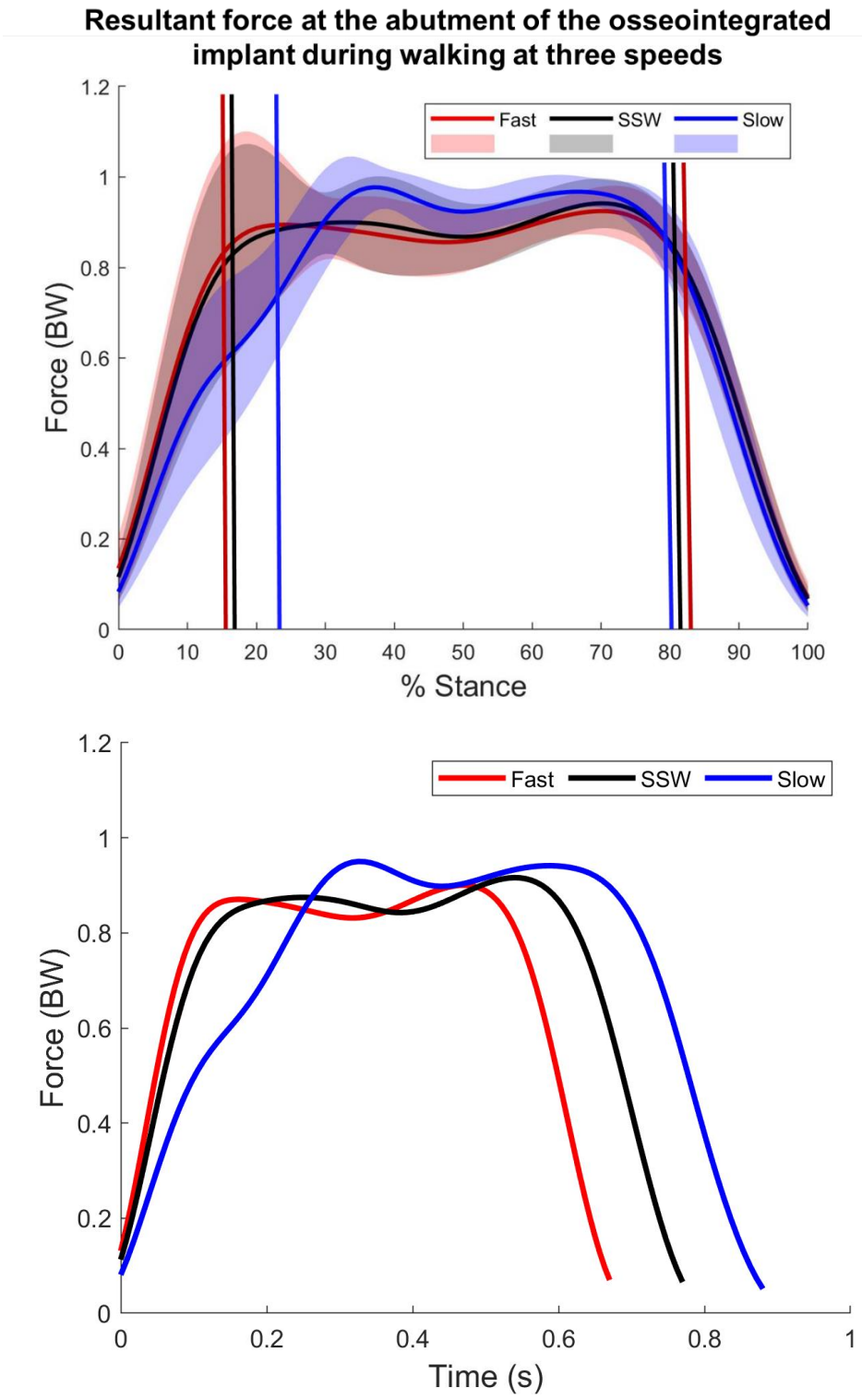

Figure 7. Resultant force at the abutment for three different walking speeds. Abutment force is normalized to stance length for each walking speed (top), and then plotted against time (bottom) to show how the abutment force changed with time across walking speeds. The line colors are defined as: **Slow** = slow walking speed, **SSW** = preferred walking speed, **Fast** = fast walking speed, and the vertical lines in the top figure indicate the timing of the peak strain in the finite element analysis.

Instead, the greatest magnitude abutment force occurs during the slow walking, with a slightly smaller magnitude force during the preferred and fast walking conditions. However, this unexpected relationship with walking speed is not fully translated to each component of the abutment forces, with each component direction defined as in Fig. 5 in the methods. Our results did find a main effect of walking speed in each component of the abutment force (Fig. 8), but the main effect indicates there is a decreased force magnitude with walking speed in the X (F>7.158, p<0.05, shaded regions in Fig. 8) and axial

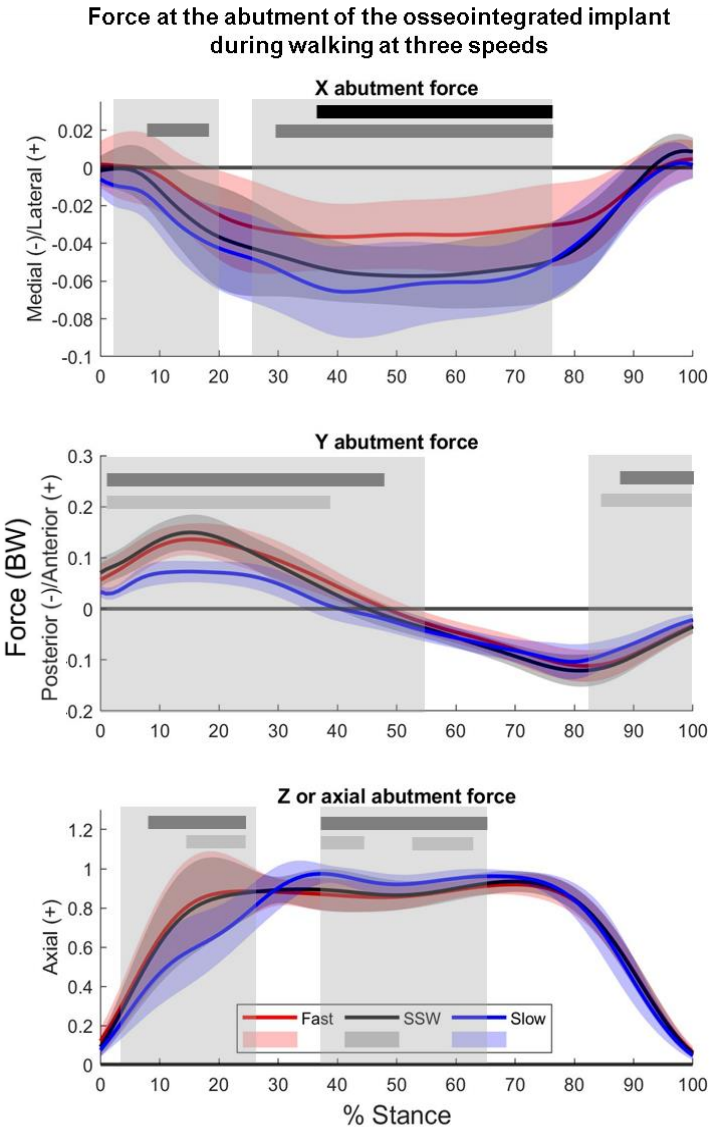

Figure 8. Average abutment force estimated from the transformed GRF when walking at three different speeds. The directions of the abutment force correspond to the axis system defined in Fig. 5 in the methods. Gray shaded region indicates a main effect of walking speed, while the black horizontal bar indicates statistical differences between the Fast and SSW walking speed, the dark gray bar indicates statistical differences between the Fast and Slow, and the light gray bar indicates differences between the SSW and Slow condition. The line colors are defined as: **Slow** = slow walking speed, **SSW** = preferred walking speed, **Fast** = fast walking speed.

(F>8.269, p<0.05, shaded regions in Fig. 8) directions, but an increased magnitude in the Y direction (F>7.659, p<0.05, shaded regions in Fig. 8). The X and axial directions had a main effect of walking speed during early stance and midstance, while the Y direction had a main effect of walking speed in early and midstance, as well as toe off.

Post-hoc testing found that the X force was significantly smaller in the regions of interest in the fast speed condition when compared to both the preferred speed condition (F>3.301, p<0.02, black bar in Fig. 8), and the slow speed condition (F>3.289, p<0.02, dark gray bar in Fig. 8). In the Y direction, post-hoc testing indicated that the abutment force was significantly greater in the fast walking condition when compared to the slow walking condition (F>3.331, p<0.05, dark gray bar in Fig. 8), and in the preferred walking condition when compared to the slow walking condition (F>3.387, p<0.05, light gray bar in Fig. 8). Finally, in the axial direction, the abutment force was significantly different in the slow walking condition when compared to both the fast (F>3.497, p<0.05, dark gray bar in Fig. 8) and preferred walking condition (F>3.495, p<0.05, light gray bar in Fig. 8). In the early stance, the slow walking condition was smaller in magnitude when compared to both the fast and preferred speed conditions, but during the midstance region, the slow walking condition had an abutment force that was significantly greater than both the fast and preferred walking conditions.

Therefore, to summarize, with respect to the X direction, the abutment force was statistically different across walking speeds with the following general relationship: Fast < SSW = Slow. Similarly, in the vertical direction, the abutment force

was statistically different with the following relationships: Fast = SSW > Slow during early stance and Fast = SSW < Slow during midstance. However, in the Y direction, the abutment force was statistically different across walking speeds with the following relationship: Fast = SSW > Slow.

5.3.2. Finite element analysis

Overall, there appears to be similar trends regarding the strain distribution across all walking speeds. Regardless of walking speed, the peak strain is greatest on the femoral neck, followed by the bone diaphysis, and then the bone-implant interface (Table 9), with the particular location of the peak strain within the region of interest generally similar. The only condition that had a slightly different peak strain location was within the femoral neck during the loading period or first half of stance (Fig. 9). The peak strain in the slow speed condition is slightly shifted to the anterior side of the femoral neck (black circle, Fig. 9).

Table 9. Peak equivalent strain on the residual bone during three different walking speeds and two time points during stance

	Walking Condition	% Stance of Peak Strain	Diaphysis Peak Equivalent Strain (strain)	Bone-Implant Interface Peak Equivalent Strain (strain)	Femoral Neck Peak Equivalent Strain (strain)
Loading Period	Slow	23	3.65E-04	3.10E-04	6.65E-04
	SSW	17	6.54E-04	5.63E-04	1.30E-03
	Fast	16	6.04E-04	5.15E-04	1.16E-03
Push-off Period	Slow	80	5.11E-04	3.61E-04	1.07E-03
	SSW	81	5.82E-04	4.03E-04	1.23E-03
	Fast	82	5.28E-04	3.65E-04	1.15E-03

While the distribution appears generally unaffected by walking speed, the magnitude (Table 9, Fig. 9) of the peak strain appears to have a non-linear relationship with walking speed, as, regardless of bone location, the peak strain is lowest in the slow walking condition, followed by the fast walking condition, and greatest in magnitude for the preferred walking speed. Specifically, as the walking speed increased, the peak strain on the bone diaphysis during the loading period was 0.000365, 0.000654, and 0.000604 strains for the slow, preferred, and fast speed respectively. Similarly, at the bone-implant interface, the peak strain during the loading period was 0.000310, 0.000563, and 0.000515 strains during the slow, preferred, and fast walking respectively. Finally, during the loading period, the strain on the femoral neck was 0.000665, 0.00130, and 0.00116 strains respectively for the increasing walking speed. The trend of increasing peak strain with walking speed is not as clear during the push off period or second half of stance, where the peak equivalent strains were more similar across walking speeds. At the diaphysis, the peak strain was 0.000511, 0.000582, and 0.000528 strains, while the strain on the bone-implant interface was 0.000361, 0.000403, and 0.000365 strains, and the strain on the femoral neck was 0.00107, 0.00123, 0.00115 strains for increasing walking speed.

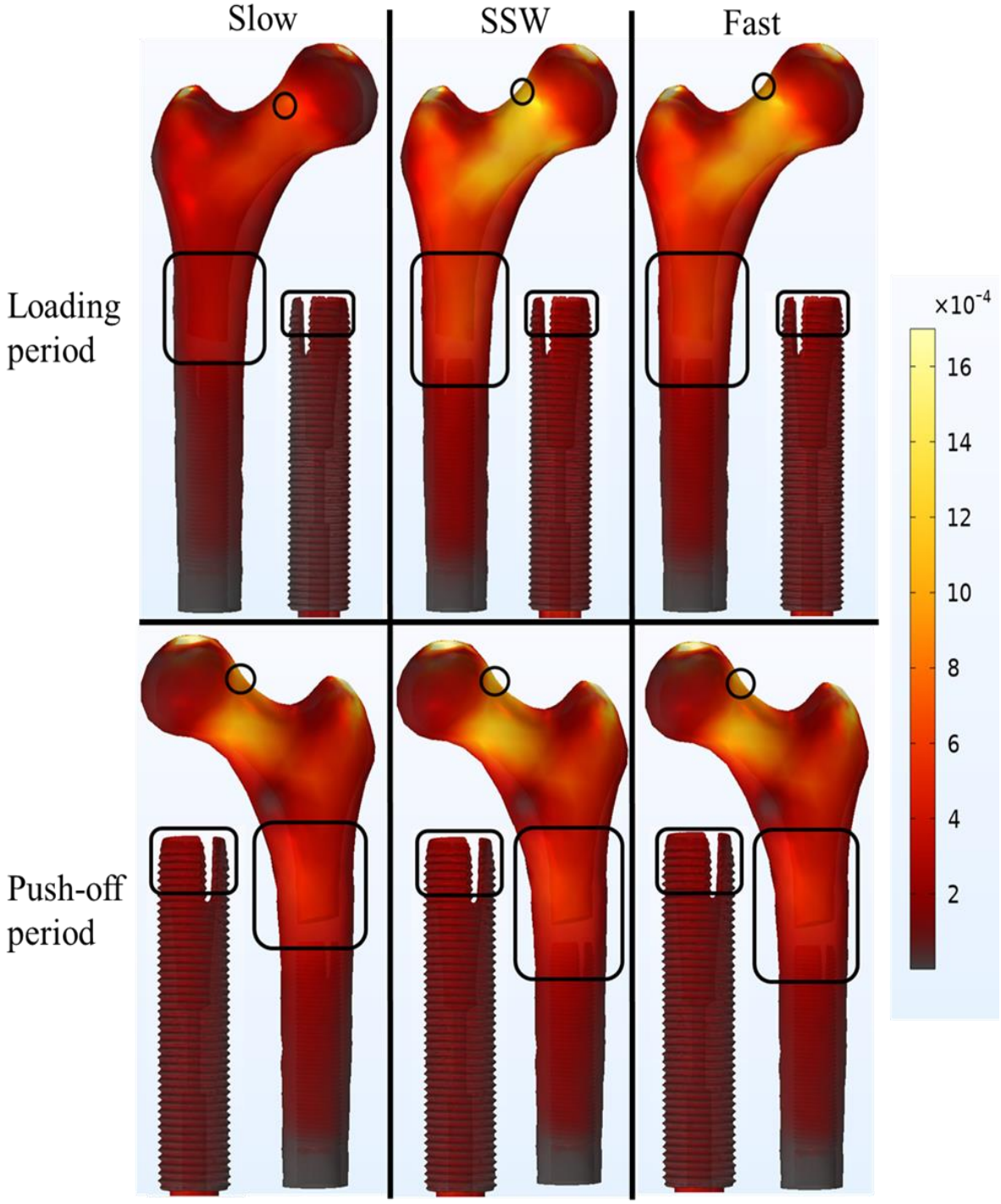

Figure 9. Peak equivalent strain (unit: strain) during first half (loading period) and second half (push-off period) of stance for three walking speeds (slow, preferred, and fast) in the femoral neck, bone diaphysis, and bone-implant interface. Peak strain locations are indicated by the circled regions on each area of interest.

Our results also indicate that the peak strain across stance may not coincide with the peak resultant forces, as indicated in Fig. 7. Instead, the peak strain appears to be more sensitive to the Y component magnitude of the abutment forces (Fig. 8), as the peak strain approximately coincides with the timing of the peak Y force for both the loading and push-off periods of stance.

The relationship between strain and walking speed is further shown in how the strained volume changes with walking speed (Table 10, Fig. 10). For each walking condition, the maximum volume of bone during the loading and push-off period coincided with the percentile of the peak strain during those periods. In addition, the volume of bone over the threshold, regardless of percent of stance and walking speed, was concentrated in the femoral neck of the bone (Fig. 10). When comparing the strained volume across walking speeds, as with the peak strain, there was a non-linear speed-strained volume relationship. The smallest volume of bone above the 0.001 strain threshold was during the slow speed condition, followed by the fast speed, and then the preferred speed condition. This non-linear relationship between strained volume and walking speed occurred during both time points of interest in the loading and push-off periods.

Table 10. Volume (mm^3) and percent of the bone with a strain greater than 0.001 strains during the first and second half of stance for three different walking speeds.

	Walking Condition	Volume of bone (mm^3)	Percent of total bone volume
Loading	Slow	204.81	0.22
	SSW	1425.6	1.50
	Fast	796.96	0.84
Push-off	Slow	700.1	0.74
	SSW	1079.00	1.14
	Fast	825.04	0.87

Specifically, during the slow speed, 204.82 mm^3 or 0.22% of the bone during the loading period, and 700.1 mm^3 or 0.74% of the bone during the push-off period had a strain greater than the 0.001 strain threshold. During the fast speed condition, 796.96 mm^3 or 0.84% and 825.04 mm^3 or 0.87% was greater than the 0.001 strain threshold during the loading and push-off periods respectively. Finally, in the preferred speed, the maximum volume of the bone with a strain greater than 0.001 strains was 1425.6 mm^3 or 1.50% and 1079 mm^3 or 1.14% during the loading and push-off period.

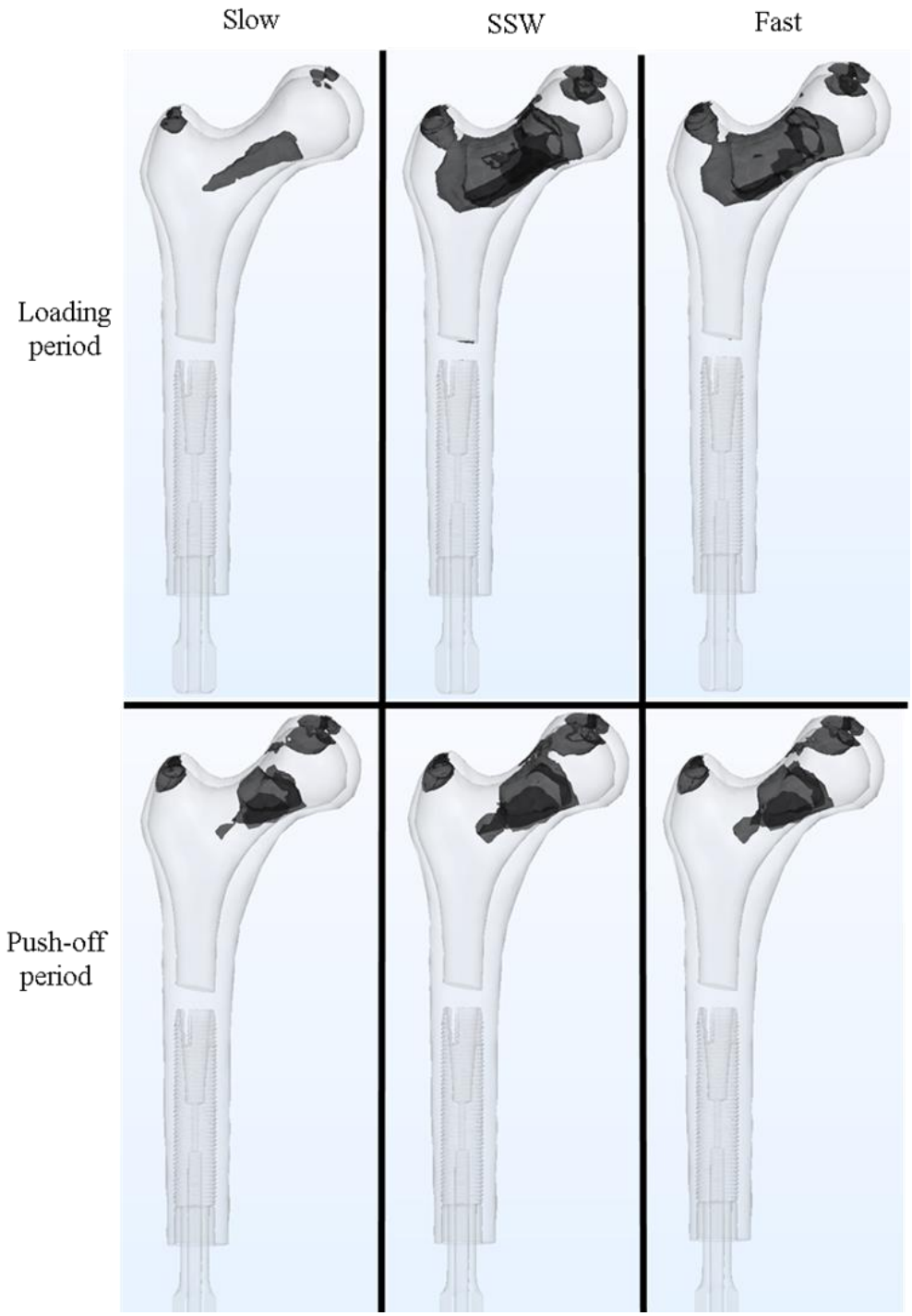

Figure 10. Bone volume with strain above 0.001 during loading (top) and push-off (bottom) periods when walking at three speeds. The strain threshold was set at 0.001 strains, as this is generally near the peak strains that may occur on the bone during walking.

5.4. Discussion

The purpose of this study was to investigate the connection between loads placed on the abutment and the probability of injury with a lifetime of OI prosthesis use by individuals with transfemoral amputation. Our hypotheses that (1) the forces at the abutment would increase with walking speed, and (2) that the peak strain on the bone during a single stance phase will increase with walking speed were partially supported. For our first hypothesis about abutment force of an increase in abutment force with walking speed, the results did not show an increase in abutment force with walking speed in all axis directions, indicating there may be some compensatory behaviors which shift some of the movement generation capacity to the intact limb. However, our second hypothesis was partially supported, as there appears to be some relationship between speed and peak bone strain, but it may be a non-linear relationship as individuals increase their speed from the preferred to fast speed. Overall, these results indicate there may be some relationship between walking speed, abutment force, and strain placed on the bone, but the relationship may not be strictly linear, perhaps due to the use of compensatory strategies.

Previous research has indicated that the abutment force, and strain placed on the bone are not likely to result in a traumatic injury, as the stress and strain on the bone during a single time point of stance is below that of the yield strength of bone (P. K. Tomaszewski et al., 2010). Our results largely agree with this previous research,

finding similar peak abutment forces during the loading and push-off periods of walking (Lee et al., 2007), and similar peak strains along the bone diaphysis and bone-implant interface during the preferred speed walking (Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P. K. Tomaszewski et al., 2010; Xu et al., 2006). In addition, when comparing the magnitudes of the abutment force components, our results have good agreement with previous data (L. Frossard et al., 2021b), with a magnitude of approximately 0.05 BW, 0.15 BW, and 0.87 BW for the loading period, and 0.05 BW, -0.15 BW, and 0.92 BW for the push-off period during the preferred speed walking for the X, Y, and axial directions respectively. However, in contradiction to the previous studies, the direction of the X and Y forces are switched for this study when compared to the previous literature. This change in sign could be due to the position of the force sensor within the prosthesis system. Previous literature had the transducer positioned slightly behind, and medial to the abutment end, while the iPEC within our study was position directly below the Axor II attachment and in line with the abutment. Additional factors which may contribute to the change in sign could biomechanical differences between the populations such as placing the prosthesis directly under the center of mass, rather than slightly laterally, as well as our use of the transformed GRF.

When investigating the influence of walking speed on the abutment force, our results found a non-linear relationship. This result was surprising, as it was largely expected that the ground reaction force would increase with walking speed, resulting in greater abutment forces with faster walking. However, the results instead indicate that the influence of walking speed largely results in decreased abutment forces in the

resultant abutment force, as well as the X and axial component forces. Only the Y component force showed an increase in abutment force for the preferred and fast conditions over that of the slow condition. The general decrease in abutment force with speed may be the result of compensatory strategies used by the individual, as they rely on their intact limb for movement generation and to generate compensations for the limitations of the prosthesis. The use of an intact limb reliance strategy is also supported by the results of the first study of this dissertation, as, when individuals walked faster, there were minimal increases, if not decreases, in the ground reaction force of the amputated limb, but increases in the ground reaction force placed on the intact limb. Therefore, it is likely that individuals with an OI prosthesis use an intact limb reliance during faster walking, resulting in the decreased ground reaction force placed on the prosthesis, and decreased abutment force. These results would largely lead to the conclusion that there would be lower risk to the longitudinal health of the bone during faster walking, as the offloading of the force to the intact limb leads to decreased abutment forces.

To establish the relationship between walking speed, abutment force, and stress on the bone, finite element analysis of a bone and implant system was completed, finding, in contradiction to the abutment force results, the greatest peak strain and the greatest volume of bone which has a strain over that of 0.001 occurred during the preferred and fast speed walking. Previous literature has assumed that the peak strain and stress placed on the bone would coincide with the peak forces at the abutment, and that there is a linear relationship between abutment force magnitude and bone stress.

Under that assumption, the results of the abutment force would lead one to believe that the greatest strain would occur during the slow walking condition, as the resultant force magnitude was the greatest during that condition. However, the results of this study indicate this may not necessarily be true. Instead, the greatest strain across all three regions of interest, and the greatest strained volume of the bone occurred during the preferred speed walking, followed by the fast speed walking. In order to understand why this might occur, the stride length during walking and the timing of the peak strain during the stance phase become particularly important. With faster walking, the stride length increased, placing the foot farther in front of the body, and resulting in a greater angle between the residual limb bone and the direction of the ground reaction force. The increase in angle between the residual limb and the ground reaction force also results in a greater magnitude of force in the Y direction of the abutment axis system, resulting in an abutment force vector that is directed further away from the long axis of the bone. The importance of the direction of the force relative to the long axis of the bone is corroborated by the timing of the peak strain. When comparing the peak strain timing within the component abutment forces, it is clear that the peak strain almost perfectly coincides with the peak force in the Y direction across all walking speeds, indicating that the direction of the resultant force may be as important, if not more, than the magnitude of the force. Therefore, these results indicate that a force that is directed farther away from the axial direction, even if the force magnitude is lower, may result in greater strain placed on the bone.

The importance of the force direction is further reflected in the relationship

between force and strain for the slow walking condition. In the slow condition, the stride length is the shortest of the three conditions, placing the foot more directly under the center of mass of the body, and resulting in a lower Y component force at the abutment. In addition, the peak resultant force occurs much later in the stance phase, during a time period when the Y component of the force is very small, resulting in a force that is almost entirely directed along the long axis of the bone. Therefore, even though the force magnitude is the greatest of the stance phase, the shorter stride length resulting in a force vector that is more aligned with the long axis of the bone, and a peak resultant force which occurs when the Y component force is close to zero results in largely compressive strain and lower strain on the bone. These results indicate that the direction of the force may be an important consideration for the longitudinal health of the bone with sustained OI prosthesis use, as experiencing forces which are directed farther away from the long axis of the bone may result in greater than expected strain on the bone, and increased risk for injury with repetitive loads.

This study is one of the first to systematically investigate the influence of walking speed on the load which is experienced by the residual femur when using an OI prosthesis. Due to the rigid connection between the prosthesis and the bone, and minimal damping of the force during ground contact, there is the possibility of greater risk to the bone with faster locomotion speed, as high magnitude forces are transferred through the prothesis and into the bone via the OI implant. Despite this concern, the results of this study indicate that, at all walking speeds, the abutment force is comparable to that which has been previously measured at the OI implant, and that the

bone strain magnitude is similar to that which is experienced by healthy bone during walking. However, a surprising result of this study indicated that, while the magnitude of the abutment force is important, the direction of the force relative to the long axis of the bone may be more important. This study found that, even with lower abutment force magnitude, greater bone strain occurred during walking conditions where the abutment forces were directed further from the long axis of the bone. Therefore, while abutment force magnitude may be important to take into consideration when making activity recommendations, it may be more important to make sure that activities which largely result in force which is directed along the axis of the bone are chosen for individuals with an OI prosthesis. However, because the bone strain during all walking conditions in this study were similar to that of healthy bone, walking appears to be a relatively safe way for individuals with an OI prosthesis to increase their physical activity, and individuals may confidently use an OI prosthesis to walk throughout the day with minimal concern surrounding the acute loading which is placed on the residual limb bone.

6. CHAPTER 6: STUDY INVESTIGATING SPECIFIC AIM 3.3

6.1. Introduction

Individuals with lower extremity amputation who use a socket-based prosthesis commonly report high rates of socket discomfort, as well as problems with skin irritation related to their socket fit (Berke et al., 2010; Pezzin et al., 2004). Because of the discomfort and skin irritation, it is often difficult for the individuals to use or wear their prosthesis for long periods of time, with the limited prosthesis use potentially leading to decreased physical activity and increased risk for chronic health problems such as cardiovascular disease (Naschitz & Lenger, 2008b; Saris et al., 2003; Singh et al., 2007). One innovative solution which circumvents the use of a socket, and avoides the socket-related complaints entirely is an osseointegrated (OI) or a bone-anchored prosthesis. An OI prosthesis uses a titanium implant which is placed in the residual limb bone during a surgical procedure, with the implant extending out of the bone, muscle, and tissue to create an external attachment point for the prosthesis, referred to as the abutment. The use of an OI prosthesis creates a more direct and rigid connection between the body and the prosthesis, ostensibly resulting in improved performance and function when compared to using a socket-based prosthesis.

Research has indicated that using an OI prosthesis improves the performance on clinical tests such as the Timed Up and Go and the Six Minute Walk Test (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), as well

as on basic kinematic measures such as walking speed and hip range of motion (K Hagberg et al., 2005; Tranberg, Zugner, et al., 2011). The use of an OI prosthesis also appears to improve the asymmetry at the hip and knee when compared to pre-surgery mechanics (Davis-Wilson et al., 2023), but may still result in interlimb asymmetries in the GRF, and the lower limb kinematics and kinetics that are individual specific (Ch. 3 and 4). And, while these clinical performance improvements are promising, the use of the OI implant also may introduce a long-term concern surrounding the health of the residual limb bone over the individual's lifetime. This concern is directly related to the rigid connection between the bone and prosthesis, as high magnitude forces may transfer into the OI implant and bone with minimal damping from the impact of the prosthesis with the ground. Previous research investigating the force at the abutment and risk to the bone during walking have indicated that the force is not at a level that is expected to injure the bone (L. Frossard et al., 2013, 2021a; L. A. Frossard, 2010; Lee et al., 2007; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P. K. Tomaszewski et al., 2010), and the bone stress and strain are below the bone's yield strength or point where plastic deformation will occur (Newcombe et al., 2013; Stenlund, Trobos, Lausmaa, Brånemark, et al., 2017a; P K Tomaszewski et al., 2010; Xu et al., 2006). These initial results, therefore, indicate that the health of the bone is not expected to be compromised during a single loading phase, making it likely that walking will not result in a traumatic injury to the bone.

However, the current literature is limited in its scope, as there has been minimal research establishing how the accumulated damage from repetitive actions such as

walking with an OI prosthesis may influences the longitudinal health of the residual limb bone. Instead, previous literature has tried to draw conclusions about the long-term health of the bone by measuring the abutment force and the bone strain during a single point of the stance phase when individuals walked at their preferred speed, and then drawing conclusions about the longitudinal bone health from the results. Drawing longitudinal conclusions from data collected at a single time point and walking speed does not have great validity, as individuals are expected to walk at variable speeds throughout the day and the cumulative effect of loading on the bone from the various walking speeds may not be strictly linear. Previous literature has established that there is a relationship between walking speed and the ground reaction force (Lee Nolan et al., 2003), abutment forces (Ch. 5 results), and peak strain on the bone (Ch. 5 results), and because specific circumstances throughout the day require individuals to walk faster or slower, the loading on the bone and longitudinal health of the bone is likely related to the proportion of time spent walking at the various speeds. However, it is difficult to directly measure the effect of walking speed on the longitudinal health of the residual limb bone throughout an individual's lifetime without large sample sizes, and extensive data collections and analysis. In order to circumvent the extensive and time-consuming data collections required for longitudinal research, mathematical simulations computing the probability of injury to the residual limb bone due to walking at different speeds over a lifetime of OI prosthesis use may be used. Probabilistic models allow the isolation of a specific factor such as walking speed to determine how this factor may influence to the probability of injury without requiring

longitudinal studies, with these methods used previously to investigate the probability of stress fractures in runners (B. W. Edwards et al., 2010a). Therefore, in order to understand if a lifetime of variable speed walking with an OI prosthesis may present an undue injury risk to the residual limb bone, probabilistic modeling of the residual limb bone may be done using data collected when individuals with an OI prosthesis walk at multiple speeds.

Therefore, the purpose of this study was to investigate the probability of bone failure over a simulated lifetime of OI prosthesis use when walking at different speeds to determine the risk for bone-OI implant degeneration over time. We hypothesized that the probability of bone injury will be low over the individual's lifetime due to the inherent strength and remodeling of the bone with loading, but that increasing the proportion of time spent walking at a faster than the preferred speed will result in bone failure at an earlier time of the simulated lifetime due to the increased peak stress and strain on the bone at faster walking speeds.

6.2. Methods

6.2.1. Population of interest and power analysis

Eleven individuals with transfemoral amputation who use an OI prosthesis were recruited for this study. Participants were recruited if they (1) were between the ages of 18 and 70, (2) are at least 1-year post-OI surgery, (3) are cleared by their medical professional for ambulation, (4) present no functional limitations which would affect their ability to walk or complete activities of daily life unaided, and (5) have at least 6

months' experience with their definitive prosthesis. Demographic and health information, including age, body weight, height, gender, and other relevant information including time since amputation and OI surgery, amputation cause, and current prosthetic components was also collected.

To determine the sample size required for the proposed project, an *a priori* power analysis was completed using G*Power 3.1 (Heinrich Heine University Dusseldorf, Dusseldorf, North Rhine-Westphalia, Germany). Data investigating the hip range of motion in individuals who use an OI prosthesis (K Hagberg et al., 2005) and peak vertical ground reaction force differences between limbs across walking speeds in individuals who use a socket (Schaarschmidt et al., 2012) was used for the power analysis. For a power level of 0.8, an alpha level of 0.05, and moderate effect size, the *a priori* power analysis to detect differences in the means in a repeated measures ANOVA indicated a sample size ranging between 8 and 19 participants. However, due to the limited number of individuals who undergo the OI procedure, and because other studies with individuals who use OI prostheses have sample sizes between 9 and 12 (L. Frossard et al., 2020; Lee et al., 2007), we planned to recruit a sample size of at least N = 10 individuals

6.2.2. Probabilistic model

Fatigue failure of a material, meaning the cycles or time it takes for a material to fail when placed under repetitive loads, is largely dependent on the strain level. At very high strain, the material cannot sustain very many loads before the accumulated damage results in permanent fatigue failure. However, at lower strains, the material

may never experience fatigue failure, and instead will be able to sustain the strain indefinitely. In addition, in biological materials such as bone, there is a delicate balance between the damage and repair cycles which allows repair of the accumulated damage and an extension on the fatigue life of the bone. The fatigue life can be mathematically simulated using different models and techniques, including estimated cycles to failure in finite element analysis and probabilistic modeling. One of these methods, using the probabilistic modeling, was investigated for Aim 1, the probability of bone failure with a lifetime of OI prosthesis use.

Briefly, probabilistic modeling requires the stress or strain as an input to a mathematical probability model, with this stress or strain generally computed using finite or discrete element analysis. To get the strain data for this analysis, abutment force (iPECS Lab, RTC Electronics Inc., Dexter, MI, USA) and ground reaction force (Eight 6DoF piezoelectric force platforms, Kistler, Switzerland) were collected while individuals walked at three self-selected speeds, referred to as fast, preferred, and slow from this point forward. The average force at the abutment was used as the input to a finite element model of the bone and OI implant (Comsol Multiphysics 6.0, Comsol Inc, Stockholm, Sweden), and the strain for each walking condition from the simulation solution was output for the volume of the residual limb bone. Additional details describing the data collection and finite element analysis are discussed in Chapter 5 and Appendix A.

To compute the probability of failure, a probability model similar to the methods of Edwards et al. (2009, 2010) and those of Taylor (1998), and Taylor et al.

(2004) was constructed which simulated the damage and repair which occurs on the bone with repetitive loading over time (B. W. Edwards et al., 2010b; W. B. Edwards et al., 2009; D. Taylor, 1998; David Taylor et al., 2004). A brief conceptual discussion of the probabilistic model is included below, with the mathematical details contained in Appendix A.

To determine the time dependent probability of fatigue failure of a bone model, a series of probability densities can be generated based on experimental data of the cycles to failure bone at specified strains. The strain-cycles to failure curve used for this probabilistic model was based on experimental data from Carter et al. (1981), with the data collected from materials testing of femur bones when cyclically loaded to failure at different strain levels (Carter et al., 1981). However, because there is generally wide scatter in the numbers of cycles at which a single bone section may fail when loaded repetitively at a specific strain magnitude, probability density functions (Fig. 11 from Taylor et al., (2004), dotted and dashed lines) are the best option to represent this scatter. Using a single probability density function

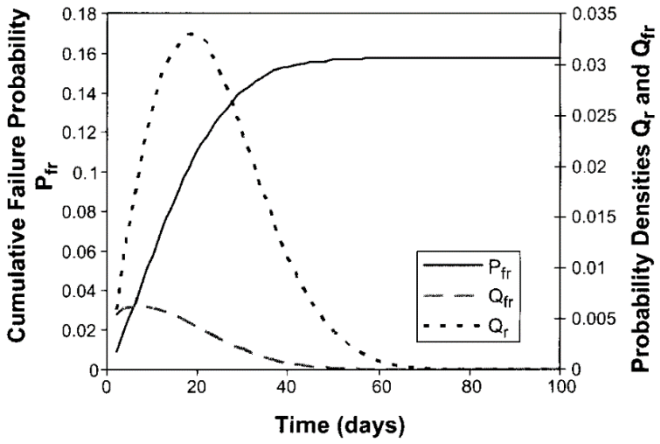

Figure 11. Probability density functions (Q_f and Q_{fr}) and cumulative failure probability (P_{fr}) for a probabilistic model of bone failure with (P_{fr}, Q_{fr}) and without repair (Q_f). The dashed line shows the probability density function accounting for repair, while the dotted line shows the density function without accounting for repair. The probability density function is integrated to get the cumulative probability of failure (solid line) for the bone. Figure taken from Taylor et al., (2004).

only represents a single time point where a single piece of the bone is loaded until failure. In order to effectively simulate the whole bone, and the probability of a fatigue failure over a lifetime, the probability density for each part of the bone must be computed (Fig. 11, dotted line), and then any additional responses of bone to loading over a period of time, such as repair of damage (Fig. 11, dashed line), must be incorporated.

Repair of the accumulated damage can be incorporated using a second probability density function (Fig. 11, dashed line). This probability density function represents the probability that, if damage occurs, the bone will be repaired, given some extended time period. But, to compute the probability of failure, the probability that damage will not be repaired is computed or one minus the probability density function. The probability that repair will not occur can be combined with the probability density function representing failure using the product rule of probability, where the probability density function is multiplied by probability that repair will not occur. However, this still is not the probability of failure, so to get the overall probability of failure, assuming repair does not occur, the combined probability density function is integrated over the specified time range, giving the cumulative probability of fatigue failure of the bone over the time range (Fig. 11, solid black line).

The probability of failure with repair will be computed over 50 years of simulated OI prosthesis use when individuals walk 1900 m a day. 1900 m has been previously found to be the median distance walked by individuals who use an OI prosthesis (Leijendekkers et al., 2019a). A custom Matlab script was written to compute

the probability of fatigue failure using the strain from the finite element model for each participant at each walking speed. The probability of injury was computed for each element within the bone model, and then an overall probability for the entire bone was computed as explained in Appendix A, Section 7.1.2.

To determine the effect of walking speed, the probability of failure with repair from the probabilistic model will be computed for each walking speed independently and compared. A summation model, referred to as the combined speed model, which combines the three walking speeds will also be investigated with the probabilistic modeling, as this likely is more reflective of the loading which happens throughout a specified time period such as a day or weeks. The combined speed model simulates the individual spending the 80% of their time walking at their preferred speed, and then 10% of their time walking at their faster and slower walking speeds respectively.

The outcome variables for this study were the time course of the probability of fatigue failure of the bone with a simulated lifetime of OI prosthesis use using the four different speed conditions (fast, preferred, slow, and combined speed). Because the probability of failure was computed using the averaged abutment forces as the input to the finite element analysis, statistical analysis was not possible.

6.3. Results

Participants (Table 11) consisted of 7 males (51.71 ± 11.94 years old, 1.78 ± 0.16 m, 83.44 ± 25.63 kg, 2.89 ± 1.27 years since OI surgery) and 4 females (50.25 ± 11.35 years old, 1.65 ± 0.09 m, 54.93 ± 14.97 kg, 2.54 ± 2.38 years since OI surgery).

Participant demographics did not differ between the male and female groups (p<0.05), indicating the two groups could be aggregated into a single group for analysis.

Table 11. Participant demographics as averages (SD) within groups by sex, and then as a whole sample

Gender	Age	Height (m)	Weight (kg)	Etiology	Time since amputation (years)	Time since OI surgery (years)	K Level	Residual limb length (cm)
N = 7 men	51.71 (11.94)	1.78 (0.16)	83.44 (25.63)	4 trauma, 2 cancer, 1 infection	7.02 (2.64)	2.89 (1.27)	3.71 (0.49)	21.22 (5.36)
N = 4 women	50.25 (11.35)	1.65 (0.09)	54.93 (14.97)	2 trauma, 2 cancer	22.14 (15.5)	2.54 (2.38)	3.50 (0.58)	16.70 (4.84)
N = 11	51.18 (11.17)	1.73 (0.15)	73.07 (25.86)	6 trauma, 4 cancer, 1 infection	12.52 (11.6)	2.76 (1.64)	3.64 (0.5)	19.41 (5.41)

The average walking speed (Table 12) for each walking condition was 0.76 ± 0.15 m/s, 0.94 ± 0.14 m/s, and 1.22 ± 0.23 m/s for the slow, preferred, and fast walking speeds respectively. Statistical tests indicate that the slow speed is significantly different from the preferred (p<0.001) and the fast (p<0.001) speeds, and that the preferred is significantly different from the fast speed (p<0.001).

Table 12. Average walking spatiotemporal data (SD) for three walking conditions

	Slow	SSW	Fast
Average walking speed (m/s)	0.76 (0.15)	0.94 (0.14)	1.22 (0.23)
Average stance time (s)	0.87 (0.3)	0.77 (0.14)	0.67 (0.16)
Average stride length (m)	1.03 (0.08)	1.15 (0.16)	1.37 (0.29)

6.3.1. Probability of injury

The probability of injury (Fig. 12) was investigated over 50 years of simulated walking 1900 meters a day at each walking speed and the combined model where individuals spent 80% of their time walking at the preferred speed and 10% at the fast and slow speed each. The model largely indicates there is a low chance of injury, as

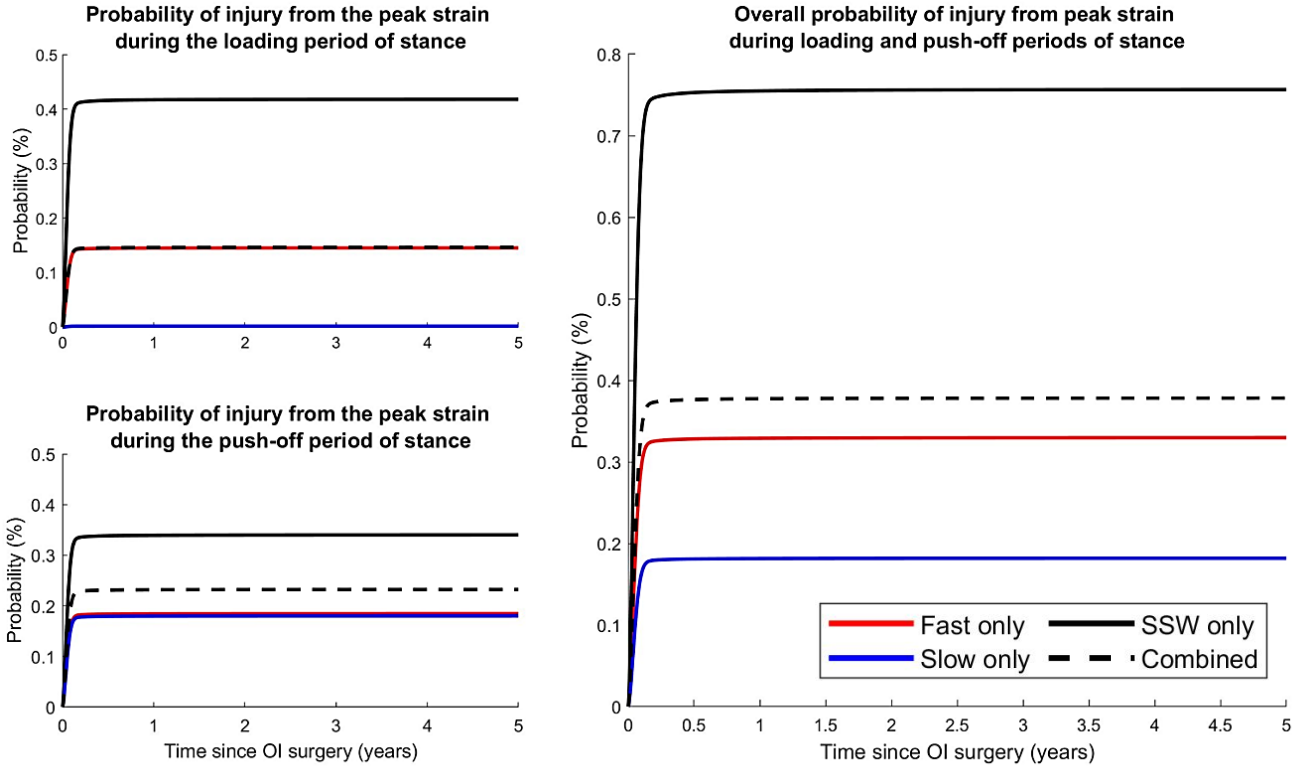

Figure 12. Probability of bone failure during three different walking speeds, and a combined speed model computed from the peak strain during the loading period of stance (top left), the push-off period of stance (bottom left), and then computed from the peak strains during both the loading and push-off periods of stance (right) together. For all figures, the line colors are defined as: **Slow** = slow walking speed, **SSW** = preferred walking speed, **Fast** = fast walking speed, and the combined speed model is shown with the black dashed line (**---**).

probability of injury in all walking speed and stance period conditions is under 1% for (Fig. 12). In addition, because the probability of repair reaches one very quickly due to the efficient response of bone to damage, the probability of failure plateaus after only

a short period of time, approximately 45 days, and stays constant for rest of the simulated lifetime. Therefore, the figures shown for this result were cropped to show only the first five years after an individual has undergone the OI surgery, completed their rehabilitation process, and has been cleared to walk by their medical provider.

The results of the probabilistic model (Fig. 12) indicate that, for all walking speeds, the probability of injury is very low; on the order of 0.0018% to 0.74%, depending on the walking speed condition and the period of the stance phase used to compute the probabilistic model. However, as with the abutment force and strain results, there does appear to be some relationship between walking speed and probability of injury, where the highest probability of injury occurs in the preferred walking condition, followed by the fast walking condition, and then the slow only walking condition. However, because individuals rarely walk at one speed throughout the day, a combined speed model was also analyzed, finding that, by walking for small periods of time at the fast and slow speed, the probability of failure is shifted down from the preferred condition probability by approximately 0.32% and 0.12% for the loading and push-off period strain respectively, and by approximately 0.38% for the probability computed from using the peak strains during both the loading and push-off periods. Overall, the results of the probabilistic model find that there may be a very low probability of injury with a lifetime of OI prosthesis use.

6.4. Discussion

The purpose of this study was to investigate the connection between walking

speed and the probability of injury with a lifetime of OI prosthesis use by individuals with transfemoral amputation. Our hypothesis that walking at the faster than preferred speed would result in a greater probability of injury, but that the probability of bone injury will be low over the individual's lifetime were partially supported. Specifically, our hypothesis that the probability of injury would be low over an individual's lifetime was supported, but the belief that the probability of bone failure would increase with walking speed was not supported. Overall, these results indicate that, while there may be some relationship between walking speed and the probability of injury with a lifetime of OI prosthesis use, the relationship may not be strictly linear and the probability of an injury to the bone as a result of walking is extremely low.

A probabilistic model which included repair was used to analyze the probability of injury using the bone strain during walking from the finite element analysis. From the probabilistic model, our results indicate that, across all walking speeds, the probability of injury to the bone over a simulated lifetime of use is extremely low, with a probability under 1% for all conditions. This low probability was not unexpected, as walking generally results in low strain on the bone, on the order of 0.001 strains (Lanyon et al., 1975). At that level of strain, the bone would be expected to sustain the loads for up to 10^7 cycles before fatigue failure (Swanson et al., 1971), indicating, even without taking into account the repair capacity, the bone is able to sustain the strain from walking for a long period of time. Therefore, with repair accounted for, the bone has a very low probability of injury due to its ability to heal the accumulated damage sustained during walking over long periods of time such as days.

While the probability of failure is low for all walking speed conditions, there does appear to be small increases in probability with the preferred speed walking when compared to the fast and slow speed conditions. The preferred speed walking indicates that, for 10000 people who have an OI prosthesis, between 33 and 74 individuals would be expected to experience an injury from walking over a lifetime of OI prosthesis use. In contrast, between 14 and 33 people would be expected to experience an injury from walking at their fast speed only, and between 1 and 18 people would be expected to experience an injury when walking at their slow speed only. This decrease in the probability of injury in the fast and slow speed conditions is largely related to the lower strain placed on the bone, and lower forces in the axial and anterior-posterior force relative to the long axis of the bone for those two conditions. When comparing the abutment forces during the time point of peak strain (Ch. 5, Fig. 8), the resultant force magnitude for the fast condition, and the force in the anterior-posterior direction relative to the long axis of the bone for both the fast and slow conditions are lower in comparison to the preferred condition. This lower magnitude force, as well as anterior-posterior component force, are likely the result of the intact limb reliance during the fast speed walking, and the smaller stride length during the slow condition placing the foot more underneath the center of mass of the body. These biomechanical differences in the walking kinematics and kinetics during the time point of peak strain results in not only lower magnitude forces placed on the bone, but also force which is directed more in line with the long axis of the bone. The direction of the forces more in line with bone axis results in lower strain on the bone, which then leads to lower probability of

failure with repetitive loading. Therefore, when an individual walks at only the slow or fast speed for their lifetime, the probability of injury would be expected to be slightly lower than if they walked at only their preferred speed.

However, individuals generally walk at different speeds throughout the day, and to account for variable speed within the probabilistic model, a combined speed condition where individuals walked at their preferred speed for 80% of the time, and then at the fast and slow speeds for 10% of the time was investigated. For this condition, the strain placed on the bone was computed as the weighted average of the three conditions determined by the stride length and number of strides that would be required to cover the daily distance. This weighting procedure accounts for the time spent in each condition, and therefore weighs the influence of the strain during each condition accordingly. As a result of spending a small portion of time at the fast and slow speed, the weighted or equivalent strain results in a strain for the combined speed condition that is lower than the preferred, but slightly greater than the fast and slow condition. This decrease in strain then results in a lower estimated probability of injury, with between 14 and 38 people in 10,000 people expected to experience an injury to the bone with a lifetime of OI prosthesis use. This probability is lower than the probability of injury from walking only at the preferred speed, but similar to the probability of injury for walking at the fast speed only. Therefore, the results of the combined speed model indicate that spending small periods of time walking at the slow and fast speed reduces the probability of injury to a level that is slightly greater than walking at only the slow speed. This reduction is likely due to the compensatory actions and kinematic

differences which occur during the fast and slow speed, such as some of the force being offloaded to the intact limb during the fast speed condition, and forces which are more aligned with the long axis of the bone during the slow speed condition.

This study is one of the first to systematically investigate the influence of walking speed on the longitudinal risk to residual limb bone when using an OI prosthesis over a lifetime. Due to the rigid connection between the prosthesis and the bone, and minimal damping of the force during ground contact, injury to the bone may be increased when individuals walked faster, resulting in a greater probability of injury with a lifetime of OI prosthesis use. However, the results of this study indicate that, regardless of walking speed, the inherent repair capacity of the bone provides significant protection against injury as a result of walking. In addition, the results indicate that spending small periods of time walking at speeds other than an individuals preferred speed may not be different than walking at only a slower speed for the lifetime a result of the kinematic differences which occur at the fast and slow speed. Overall, the results of this study indicate that the repair ability of the bone appears to provide substantial protection against injury to the residual limb bone and individuals may confidently use an OI prosthesis with minimal concerns surrounding their longitudinal bone health due to a lifetime of walking.

7. CHAPTER 7: SUMMARY

7.1. Summary

The overall purpose of this dissertation was to investigate how individuals with an OI prosthesis walk at different speeds. The use of an OI prosthesis has been previously associated with performance improvements during clinical tests (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013), as well as self-evaluated quality of life (Al Muderis et al., 2017; Leijendekkers et al., 2019a; Van De Meent et al., 2013). However, there has been minimal research investigating whether the performance improvements are extended to the kinematics and kinetics of the lower limb, as well as research which has established the longitudinal safety of the residual limb bone with sustained use. Therefore, the studies in this dissertation were designed to establish how using an OI prosthesis influences the (1) ground reaction force asymmetry of the lower limbs when walking at different speeds, (2) the asymmetry in the joint kinetics and kinematics, and (3) the longitudinal probability of bone failure with a lifetime of walking and OI prosthesis use. Chapter 3 investigated how walking speed and the use of an OI prosthesis influenced the interlimb ground reaction force asymmetries which are commonly found in individuals with a socket-based prosthesis due to their reliance on the intact limb to compensate for the inability of the amputated limb. Chapter 4 extended the research into interlimb asymmetries to investigate how the use of an OI prosthesis influenced the joint kinematics and kinetics for the intact and amputated limb when individuals walked at different speeds. Chapter

5 investigated the longitudinal health of the residual limb bone when using an OI prosthesis by establishing the connection between walking speed, abutment forces, and the simulated strain placed on the bone, and Chapter 6 used the result of Chapter 5 and probabilistic modeling to investigate the probability of bone failure when individuals with an OI prosthesis walked at different speeds over the lifetime.

Chapter 1 of this dissertation presented hypotheses for Chapters 3, 4, 5, and 6, which are explored in detail in their respective chapters, and then summarized below.

7.1.1. Dissertation limitations

This dissertation had several limitations, with the first limitation that the results of this study are only directly generalizable to those who have a transfemoral amputation and use an OI prosthesis. In addition, these results should not be used to conclude whether using an OI prosthesis is the best choice for each individual. While using an OI prosthesis appears to afford improvements when compared when the individual used a socket-based prosthesis, no data was collected with this dissertation's population when they used a socket-based prosthesis. Therefore, conclusions cannot be drawn about whether using an OI prosthesis directly changed or improved the mechanics of the studied population from when they used a socket. Instead, the conclusions of this research simply inform the reader about the relationship between walking speed, and the biomechanical strategies which may be used when an individual has an OI prosthesis, as well as to inform about potential unique concerns surrounding the longitudinal health of the residual limb bone due to the direct transfer of forces from the ground contact into the bone via the OI implant. In addition, there were limitations

in the data collections where several participants had prostheses which made it impossible to use the iPEC force transducer to collect the abutment forces directly. However, previous literature has used the transformed ground reaction force to verify the accuracy of the abutment forces measured by the iPEC, and using the ground reaction force transformed from the lab axis system to the abutment axis system was found to be an acceptable proxy for the direct measurement of the abutment forces.

Additional limitations are the related to the modeling choices in Chapters 5 and 6. Within the finite element analysis, the limitations in the modeling choices include choosing only one material property for the cortical, cancellous, and titanium implant respectively, using a full constraint at the proximal end of the femur, and neglecting muscle forces and attachments on the bone. These choices were largely based on both the literature and limitations within the study protocol. First, because the study protocol did not include any imaging of the residual limb bone, it was impossible to use customized and location dependent material properties for the bone. Second, the choice to use a fully constrained greater trochanter and femur head is not anatomically accurate, as the femur translates and rotates relative to the hip center. However, this constraint has been used previously in the literature, and matches the constraints of the model used for validation in this dissertation. Therefore, despite the constraint's inaccuracy, it was used to ensure comparison was possible between models. Finally, the choice to not include muscle forces was based on the significant individual differences in residual muscle mass, attachment point, and contraction capability which occurs after amputation. However, as with the constraint, neglecting muscle forces is a

common choice in the literature for modeling the bone and OI implant, and this modeling choice was also used to allow validation and result comparison. Addressing these model limitations will be done in future studies.

Within the probabilistic model, there were modeling choices which also limit the generalizability of the results, including not accounting for adaptation of the bone to repetitive loads over time, only using walking data as the input, and not accounting for changes to the bone as individuals aged. First, the model did not include adaptation of the bone to the loads over time. However, it is likely that including adaptation would only improve the longitudinal projections about the bone health, and decrease the probability of failure. Therefore, the results of this dissertation about probability of injury are a more conservative estimation of probability of injury, and the probability of injury may actually be slightly lower when accounting for adaptation. Second, this investigation only estimated the probability of bone failure from walking, and does not include other activities individuals may perform throughout the day such as climbing the stairs. However, it is likely that individuals will complete other activities such as stair climbing only a few times throughout the day, with the number of load cycles placed on the bone from those activities significantly smaller than those of walking throughout the day. Therefore, the accumulation of damage likely is related to the activity which individuals perform the most within a day, which would be expected to be walking, and this dissertation chose to focus on the highest volume daily activity. Finally, the repair capability of bone within the model was constant for the simulated lifetime, which may not be accurate for aging. Including age related changes to the

repair ability of bone will be explored in future studies.

7.1.2. Chapter 3

Because the OI prosthesis provides a more rigid connection to the skeleton, we hypothesized that the interlimb GRF would be significantly different during faster walking, but that the GRF would be similar when walking at slower or preferred speeds. At all walking speeds, the interlimb GRF was greater in the intact limb than the amputated limb in the medial-lateral and vertical directions, supporting part of the hypothesis of this study. However, the expectation of similar GRF magnitudes during the slow and preferred speed conditions was not supported, as the interlimb GRF was found to be different during all walking speeds. These results suggest that individuals who use an OI prosthesis may rely on their intact limb when walking at all speeds to compensate for the poor imitation of the intact limb provided by the prosthesis, as well as the limitations of the prosthesis with regard to producing net positive work.

The intact limb reliance in ground reaction force suggest that there may be other factors which limit the mechanics of the amputated limb beyond that of the fixation method, and that a more rigid connection to the skeleton cannot fully reduce or remove those limitations. Instead, these limitations may be the result of the inability of the prosthesis to provide positive work, as well as individual characteristics such as having a very short residual limb, which result in differences between the limbs and increased ground reaction force asymmetry during walking.

7.1.3. Chapter 4

To investigate whether the intact limb reliance strategy may be explained by

limitations at the joint level, the interlimb kinematics and kinetic asymmetries were investigated at different walking speeds for individuals with an OI prosthesis. Because the OI prosthesis uses a more rigid connection to the skeleton, we hypothesized that the interlimb joint (1) angles and (2) moments would be significantly different during faster walking at the ankle, knee, and hip, but would be similar between the limbs when walking at slower or preferred speeds. Our results indicate that, at all walking speeds, there are significant differences in the joint kinematics and kinetics between the limbs at each joint, contradicting our expectation that the preferred speed and slow speed walking would be similar. However, because there were significant differences in the interlimb kinematics and kinetics at each joint when individuals walked faster, our hypothesis was partially supported. Overall, it appears that the use of the OI prosthesis, with a more rigid attachment to the skeleton, cannot fully remove the previously established intact limb reliance and compensation strategies found in individual who use a socket-based prosthesis.

In addition, these results suggest that the use of an intact limb reliance may be partially due to the inability of the prosthesis to produce positive work at the ankle, and the limitations of the prosthetic knee flexion capability during stance, as these joints on the amputated side resulted in similar joint kinematics and kinetics at all walking speeds, creating large differences between the limbs as the intact limb joint kinematics and kinetics increased with walking speed. In addition, individual characteristics such as a short residual limb may reduce the ability of the amputated hip to compensate for the prosthetic knee and ankle, as well as create large differences between the limbs.

Therefore, the results suggest that the use of an OI prosthesis may result in biomechanical differences between the limbs which require an intact limb reliance and compensation strategies at the joint level, with these differences becoming occurring at all walking speeds. However, the joint level differences may not negatively affect the overall performance during functional tasks and the quality of life of the individual, as previous literature has established that the use of an OI prosthesis resulted in improved clinical test performance and self-efficacy.

7.1.4. Chapter 5

The hypotheses of Chapter 5 stated that, for individuals who use an OI prosthesis, it would be expected that the (1) abutment force magnitudes would increase when individuals walked faster, and (2) that the peak strain on the bone during a single stance phase will increase with walking speed. When walking at faster speeds, individuals with an OI prosthesis appear to still use an intact limb reliance strategy, leading to decreased peak abutment force magnitude during faster walking, contradicting the first hypothesis. In addition, the direction of the resultant abutment force may be more important than the magnitude of the resultant force, as the peak strain on the bone was greater for the walking speeds which had greater Y force magnitude. Therefore, despite the decrease in peak resultant abutment force magnitude during faster and preferred speed walking, the peak strain and volume of bone with a strain greater than 0.001 was greater during those conditions when compared to the slow speed condition, partially supporting hypothesis two for this study. The increase in strain during the fast and preferred speed conditions would be expected to lead to

greater injury risk to the bone, but the risk may not be significantly greater than that of experienced by the healthy bone, as the peak strain on the bone was similar to that which has been previously measured on healthy bone. In summary, while there may be some concern surrounding the longitudinal health of the residual limb bone with an OI prosthesis due to the direct transfer of forces from the prosthesis and into the bone, it appears that the strain experienced by the bone during all walking speeds is comparable to that which is found on healthy bone, and individuals who use an OI prosthesis are unlikely to experience a traumatic injury to the bone simply from their daily walking.

7.1.5. Chapter 6

The hypotheses of Chapter 6 stated that, for individuals who use an OI prosthesis, it would be expected that walking at the faster than preferred speed would result in a greater probability of injury, but that the probability of bone injury would be low over the individual's lifetime. The probability of bone failure when accounting for repair with a lifetime of OI prosthesis use was under 1% for all walking speeds, finding that between 18 and 74 individuals within 10000 who use an OI prosthesis would be expected to experience a bone injury due to walking over many years. However, while the probability of injury was low for all walking speeds, the largest probability of injury occurred due to the preferred speed walking rather than the fast speed walking, indicating that the hypothesis for this study was partially supported. However, when modeling the ability of individuals to walk at different speeds throughout the day, the probability of bone failure decreased, indicating that walking for small time periods at a slow and fast speed may result in greater protection to the bone than walking at only

a moderate speed for their entire lifetime. In summary, while there may be some concern surrounding the longitudinal health of the residual limb bone with an OI prosthesis due to the direct transfer of forces from the prosthesis and into the bone, it appears that the inherent repair ability of the bone provides much protection, and individuals who use an OI prosthesis would be expected to have a very low probability of injury to the bone simply from daily walking.

7.2. General Conclusions

The findings of this dissertation suggest that the more rigid connection afforded by the OI implant cannot fully remove the interlimb differences which occur as a result of the poor imitation of the intact limb provided by the prosthesis and prosthesis components. In addition, this dissertation suggests that there is minimal risk to the bone with a lifetime of sustained walking with an OI prosthesis due to the inherent ability of the bone to repair and adapt to variable loads over time. These findings are noteworthy for several reasons: (1) Individuals who use an OI prosthesis have been previously found to improve their performance on clinical tests and their self-efficacy and quality of life. However, even with the more rigid OI implant, there may exist limitations within the prosthesis and individual specific characteristics such as residual limb length which result in compensation strategies and intact limb reliance. Therefore, despite the functional improvements, there may still be concerns surrounding overuse injuries such as knee or hip osteoarthritis in the intact limb as a result of the chronic overloading and intact limb reliance of the intact limb. (2) The influence of walking speed may result in

a variable effect on the ground reaction force, joint kinematics and kinetics, and abutment force, with faster walking increasing the interlimb differences at all lower limb joints and in the ground reaction force, but decreasing the resultant force which is transferred up the prosthesis and into the abutment of the OI implant as a result of increased intact limb reliance during faster walking. (3) However, while the abutment force decreases with faster and preferred speed walking, the strain placed on the bone in those conditions may increase as a result of the resultant force direction. The findings of this dissertation suggest that the direction of the abutment force may be of greater importance than the magnitude, as an abutment force that is directed further away from the long axis of the bone may result in greater strain and probability of injury, even with a lower peak resultant force. However, the strain on the bone during walking at all speeds is comparable to that which has been found on healthy bones. (4) Despite concerns surrounding the direct transfer of force to the bone through the OI implant, the bone appears to have a strong repair capacity and significant protection against injuries due to the repetitive loads and accumulated damage which may occur during walking. This protection is largely due to the efficient repair ability of the bone which results in the deposition of new bone material to regions which experience strain, resulting in improved bone density and an extended fatigue failure life.

7.3. Future Work

As discussed above, the results of this study are limited in their generalizability to only individuals who use an OI prosthesis, and the results cannot be interpreted as

suggesting that using an OI prosthesis is better than a socket-based prosthesis. Future work will be conducted identifying how walking speed influences the biomechanics both before and after the OI procedure in order to establish how the prosthesis fixation method directly influences the interlimb asymmetries. In addition, because using OI prostheses results in activity restrictions such as not being able to run for exercise or participate in high impact sports, the finite element analysis and probabilistic modeling should be extended by investigating how loads which simulate those experienced during running may influence the longitudinal risk to the bone health. There also were several modeling choices which may limit the validity of the results from the finite element analysis and probabilistic model. These limitations will be explored in future studies by including location dependent material properties for the bone, more accurate constraints at the proximal end of the femur, and age-related physiological changes to the repair probability of the bone. Finally, because the results of this dissertation suggest that individuals who use an OI prosthesis may still be at risk for overuse injuries such as knee osteoarthritis in the intact limb due to the intact limb reliance and potential overloading of the intact limb, future work should be conducted to establish the knee kinetics and the correlations to osteoarthritis risk, as well as investigate any risks to the intact limb bones using finite element analysis and probabilistic models.

8. CHAPTER 8: APPENDIX A

8.1. Detailed methods for finite element analysis

The analysis proposed for this study uses finite element analysis of a bone-implant model to investigate the stress and strain during walking at three different self-selected speeds. The finite element model (FEM) bone-implant was built in Comsol Multiphysics 6.0 (Comsol Inc, Stockholm, Sweden) with three different domains, a cortical external bone structure, a cancellous internal structure in the femur head, and a titanium alloy implant. The geometries of the bodies were based upon an open source femur model generated by MacLeod et al., (2016) and an implant model provided for research purposes by Integrum (MoIndal, Sweden) (MacLeod et al., 2016). To convert the femur model from an ANSYS model to a Comsol model, the node positions were extracted to generate a 3D point map of the femur. The point map was divided into the two material bodies representing the cortical and cancellous bone, and meshed using SolidWorks (Dassault Systemes, Waltham, MA, USA) before being combined as a union. The full femur model was built such that the cortical and cancellous sections shared an internal boundary, and could be divided into parts with different material properties. Before creating the femur-OI implant model in Comsol, the femur only model was validated by comparing the results of our model with the ANSYS model using the same validation load, and the experimental results measured by MacLeod et al (2016). The validation load used in the original research consisted of a force ramped from 0 N to 500 N over 1 second, with the load placed at the proximal end of the femur

(MacLeod et al., 2016). The equivalent strain at four points on the femur surface was measured with strain gauges on the physical femur during the physical experiment, and the equivalent strain was computed for the FEA solution in ANSYS at approximately the same locations on the bone. To validate that our Comsol model converged to similar results, the validation force and constraints were repeated with the femur only model in Comsol, and the equivalent strain at the four locations, as well as the displacement of the loaded node was computed. The results from our femur model in Comsol are in Table 13 below, along with the experimental data and ANSYS results. The results for our Comsol model showed good agreement with both the experimental data and ANSYS model, with our femur model actually having smaller percent differences from the experimental data than the ANSYS model. Therefore, the next step in developing the femur-OI implant finite element model was to add the OI implant to the femur only model.

Table 13. Equivalent strain (percent difference from experimental results) for the validation of this dissertation's Comsol femur only model compared with the experimental and ANSYS results from MacLeod et al. (2016)

	Equivalent Strain at location 1	Equivalent Strain at location 2	Equivalent Strain at location 3	Equivalent Strain at location 4	Displacement at loaded location (mm)
Experimental	$5.63e^{-4}$	$3.93e^{-4}$	$4.60e^{-4}$	$3.82e^{-4}$	-
ANSYS	$6.27e^{-4}$ (11.37)	$3.44e^{-4}$ (-12.47)	$4.37e^{-4}$ (-5.00)	$4.88e^{-4}$ (27.75)	-0.633
Comsol	$6.03e^{-4}$ (7.10)	$3.77e^{-4}$ (-4.07)	$4.49e^{-4}$ (-2.39)	$4.74\ e^{-4}$ (24.13)	-0.652

Percent difference from experimental results is in parentheses for the ANSYS and Comsol results

After validating that the femur only Comsol model was still within an

acceptable range of the experimental results with the validation load, the femur and implant were imported into SolidWorks for easier residual limb length customization. After importing the CAD models into Solidworks, an assembly of the femur and the OI implant was built. The OI implant was moved and rotated until it was located in the medullary canal of the femur at the appropriate position for the length of the residual limb. Once positioning of the femur and implant were finalized in the SolidWorks assembly, the two structures were exported as mesh files for import into Comsol to build the FEA geometry.

The mesh files from SolidWorks were imported to Comsol as a mesh part and then two different FEA models were explored to determine the model for final analysis. The first model treated the bone and segment model as independent bodies which would need contact modeling between their boundaries. The second Comsol model generated a union of the femur and implant which simulated a single interior boundary in between the

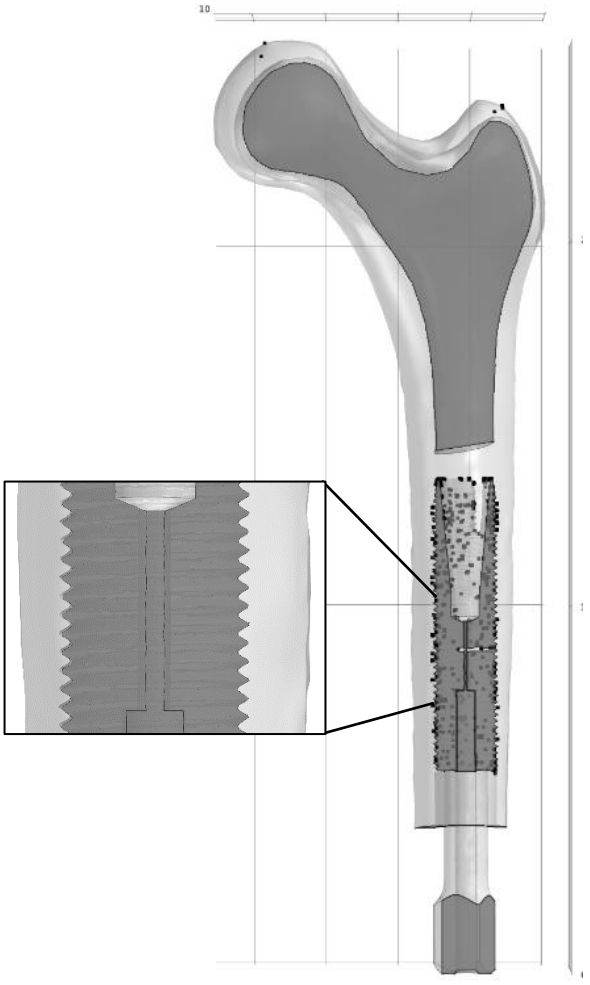

Figure 13. Geometries of the finalized femur-implant model with (A) cross section and (B) zoom to show the internal boundary shared between the bone and implant.

bone and implant (Fig. 13A and B). The two different Comsol models were explored to determine which was computationally efficient and could accurately model a fully osseointegrated implant and bone, with the second, union-based model less computationally complex and equally effective at modeling an initial validation load. The material properties for each domain of the model are contained in Table 14 below. The material properties for the bone sub-structures (MacLeod et al., 2016) were from MacLeod et al, (2016), while the material properties of the implant consisted of the standard properties for Ti6Al4V, the titanium alloy used for the implant material. The bone model uses isotropic material properties, but anisotropic material properties may be explored in the future.

Table 14. Bone and OI implant material properties used for this dissertation's Comsol model of a residual limb femur which contains an OI implant for prosthesis fixation

Body	Young's Modulus (Pa)	Poisson's Ratio	Density (kg/m^3)
Cortical Bone[1]	$1.635e^{10}$	0.26	1932
Cancellous Bone[1]	$1.37e^{8}$	0.3	1750
Titanium Implant[2]	$1.15e^{11}$	0.342	4430

Properties are referenced from [1]MacLeod et al. (2016) and [2]Standard material properties for Ti6-Al4-V

The boundary conditions fully constrained the proximal portion of the femur at two nodes, two on the femoral head and three on the trochanter. This constraint mimics the restriction created by the hip at the proximal end of the femur, and represents the boundary constraints used in the validation case from Tomaszewski et al. (2010). Boundary loads were added to the distal end of the abutment. The initial loading consisted of a validation case using data from Tomaszewski et al. (2010), with the

forces used in the model contained in Table 15 (P. K. Tomaszewski et al., 2010). For the validation case, the proximal end of the femur was constrained as in Tomaszewski et al. (2010), with three points fully constraining the head of the femur, and two points fully constraining the greater trochanter.

Table 15. Boundary load (N) used to validate this dissertation's Comsol model of the residual limb femur which contains an OI implant using input forces from Tomaszewski et al. (2010)

Axis	X	Y	Z
Boundary Load (N)	-20	100	780

After finalizing the physics section of the model, the model was meshed using triangular elements on the boundaries, and tetrahedral elements on within the domains. The meshing at the boundary locations between the implant and femur had a higher element density mesh to ensure convergence and accurate simulation results. The remaining boundaries for the bone and implant were meshed with a slightly larger element size to reduce the computational requirements when the model was being solved. Finally, after the boundaries were all meshed, the volumetric mesh was generated using tetrahedral elements for both the femur and implant. The finalized mesh contained 191,150 tetrahedral elements, and 33,096 triangular elements for the whole bone-implant structure, and a degrees of freedom of 785,625. To confirm an appropriate mesh density was chosen, models with a more complex element density were investigated, and differences in the peak strain on the femoral neck, bone diaphysis, and bone-implant interface between the chosen mesh density and a much

more complex mesh density (698,152 tetrahedral elements, 84,891 triangular elements, 2,854,518 degrees of freedom in the model) were found to be at least one order of magnitude smaller than the peak strains on the bone. For example, the peak strains on the femoral neck for the chosen mesh density and the much more complex mesh density were 0.00130 and 0.00155 during the first half of stance, and 0.00123 and 0.00141 for the second half of stance, indicating there was a difference of 0.00025 and 0.00018 for each half of the stance phase respectively. Therefore, using a more complex mesh density does not appear to appreciably change the results and implications for the strain on the bone, and the less complex density was chosen to reduce the solution computation time and power required for the simulations of the bone strain for each walking speed condition.

After meshing the bone-implant model, the model was validated using input forces from the literature. These input forces (Table 15) were taken from Tomazsewski et al. (2010), and used to compare our femur-OI implant model to a published model to check for validity of the model. The results for the validation case for our simulation (Fig. 14A) and from Tomazsewski et al. (2010) (Fig. 14B) show generally similar equivalent von Mises stresses and stress distributions. Note that, in the legends, the Tomaszewski et al. (2010) model's legend and the dissertation model's legend have similar blue, orange, and yellow points, but that the red in Fig. 14B corresponds to the pink in Fig. 14A. When comparing the stress distributions on each model, both have lower stress on the distal end of the bone, and increasing stress along the diaphysis as the proximal end of the implant is reached, with the greater magnitude stresses

generally above the proximal end of the implant. Above the proximal end of the implant, both models have two general stress concentration points, with one on the bone diaphysis and the second on the femoral neck. However, the peak stress in these two locations appears to be slightly different in magnitude, with the stress on the bone diaphysis at the proximal end of the implant approximately 6 to 8 MPa for the dissertation model, and 11 to 13.5 MPa for the Tomaszewski et al. (2010) model, and

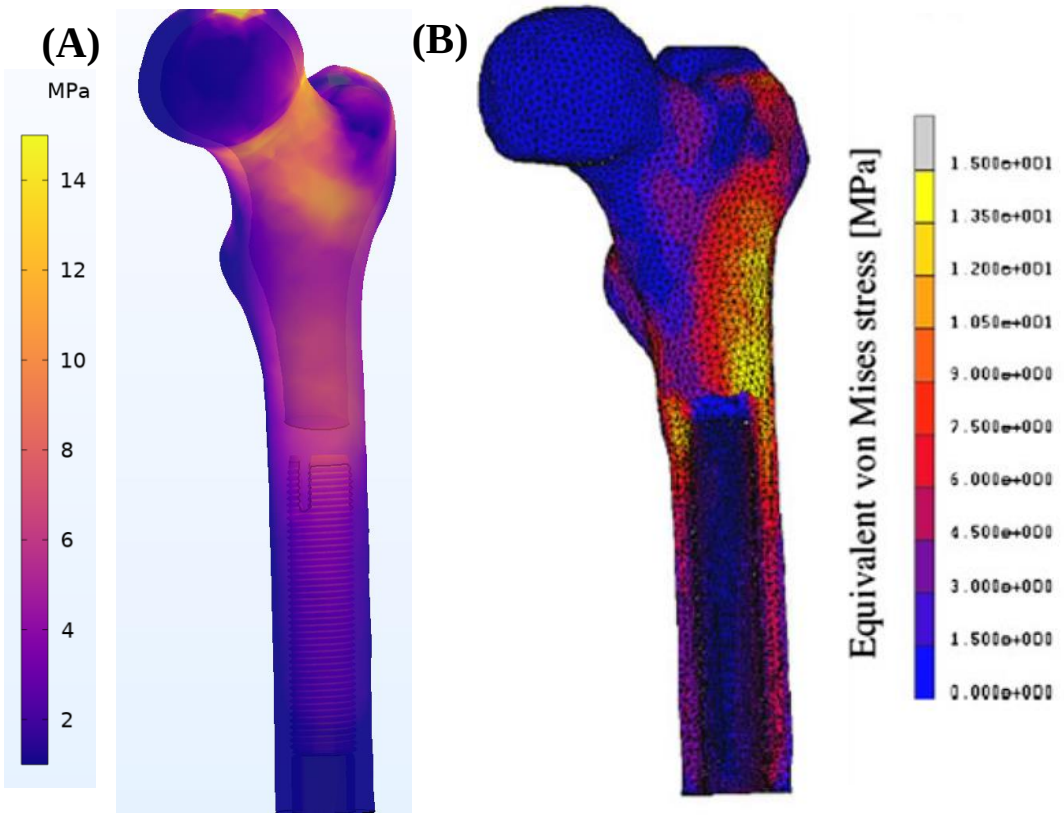

Figure 14. Equivalent von Mises stress for the (A) this dissertation's model of the residual limb femur which contains the OI implant and (B) the reference model from Tomaszewski et al. (2010). Note that the blue and yellow are similar in both figures legends, but the pink in (A) corresponds to the red in (B). Similar stress distributions occur in the diaphysis, but slight elevated stresses are on the femoral neck for this dissertation's model. Difference in stress distribution patterns may be due to material property choices, diaphysis length, and implant characteristics.

the stress on the femoral neck approximately 10 to 13 MPa for the dissertation model, and 6 to 9 MPa for the Tomaszewski et al. (2010) model. The differences in stress on the bone diaphysis and femoral neck between the two models is likely due to the choice of material properties, length of the residual bone, implant characteristics, and other modeling choices. In regard to material properties, our model uses a single isotropic material property for Young's modulus for each domain (Table 14), while the Tomaszewski model uses a variable Young's modulus determined from the relationship between CT scan value, ash density, and modulus. In addition, the length of the diaphysis included in our model is slightly longer than in the Tomaszewski model. The longer residual bone likely contributed to the difference in stress distribution patterns, as the length of the residual limb bone has been show to increase the stress on the bone, with increasing bone length potentially shifting the peak stress to the anterior side of the femoral neck (Andrango Castro et al., 2017). Finally, the specific implant models used in this dissertation and the Tomaszewski publication (2010) have different thread features. The implant used in this dissertation has external threads which are included in the interior boundary between the bone and implant, while the Tomaszewski model uses a smooth cylinder for the implant-bone boundary. This may have influenced the stress distribution between the two models slightly, but there is minimal evidence for how including a threaded implant changes the stress distribution when the implant is loaded. Overall, while the location of the peak stress is different between the models, the magnitude and general stress distribution pattern are similar between the two models, and the results from this dissertation are expected

to be comparable in magnitude, increasing confidence in the validity of the results.

After validating our model to show it has similar results to a previously published model, our experimental study investigating the effect of walking speed on the bone stress could be investigated. Using the previously validated geometry model, two different solution steps were used with the input forces the group averaged abutment force during each percent of stance in each walking speed. The first solution step used a time-dependent solver to identify when the highest peak stress occurred during the stance phase of each walking condition. For the second solution step, the abutment forces for the percent of stance with the highest peak stress were extracted, and then this three-dimensional force was used as the boundary load in a stationary solver. The FEM was solved using the averaged input forces for each participant at each walking speed, and then the output was the stress on the bone for each participant at each walking speed.

8.2. Detailed theory for probabilistic model

To investigate the probability of bone failure with a lifetime of OI prosthesis use, probabilistic modeling similar to the methods of Edwards et al. (2009, 2010) and those of Taylor (1998), and Taylor et al. (2004) accounting for bone repair was used (B. W. Edwards et al., 2010b; W. B. Edwards et al., 2009; D. Taylor, 1998; David Taylor et al., 2004). Briefly, the probability model is based on a material fatigue stress-life relationship

$$N_f = C\Delta\varepsilon^{-n}$$

where N_f is the number of load cycles to failure, $\Delta\varepsilon$ is the strain range, n is the slope of stress-life curve, and C is a constant. For bone, n has been previously observed to have a slope of 6.6 for cortical bone (David Taylor et al., 2004).

However, because the strain magnitude on the bone is location dependent, it is more realistic to use an equivalent strain instead of instantaneous strain. Equivalent strain represents the weighted average of the strain placed on the bone, with the weighting factor the load cycles at that strain, with equivalent strain $\Delta\varepsilon_{eq}$ calculated as

$$\Delta\varepsilon_{eq} = \left(\frac{1}{N_T}\sum_{i=0}^{j} N_i \Delta\varepsilon_i^n\right)^{1/n}$$

where N_t is the total number of load cycles over which the strain is applied, N_i is the number of load cycles at which the strain $\Delta\varepsilon$ is applied, and n is the constant from Equation 1. The equivalent strain $\Delta\varepsilon_{eq}$ can then be substituted into the first equation to replace the original strain $\Delta\varepsilon$, giving a cycles to failure model that accounts for the variability in the strain placed on the bone.

Because bone will fail at a wide band of cycles, with the number determined by the properties of that specific piece of bone, a Weibull equation or a probability distribution function can be used to account for the scatter. The Weibull equation determines the cumulative probability P_f at which a stressed volume will fail.

$$P_f = 1 - \exp\left[-\left(\frac{V_s}{V_{so}}\right)\left(\frac{\Delta\varepsilon_{eq}}{\Delta\varepsilon^*}\right)^m\right]$$

For the Weibull equation representing bone, the P_f is the probability that a volume of

bone V_s will fail at some strain $\Delta\varepsilon_{eq}$, with the exponential m determined by the width of the scatter. For bone, an m equal to 8 has been previously used (B. W. Edwards et al., 2010b). The denominators in both fractions represent a reference volume V_{so} which fails at a probability of 0.63 when exposed to a strain range $\Delta\varepsilon^*$.

To convert the Weibull distribution function from the cycles to failure at some strain range to probability of failure after a period of time, the equivalent strain $\Delta\varepsilon_{eq}$ can be solved for by re-arranging the first equation relating cycles to failure and strain, and estimating how many load cycles are completed during a given time period such as a day. The relationship between cycles to failure and the number of cycles during a given time periods will give an estimated time to failure, t_f. Using the re-arranged first equation, and the estimated time to failure, the equivalent strain and the strain range can be replaced in the Weibull function to give

$$P_f = 1 - \exp\left[-\left(\frac{V_s}{V_{so}}\right)\left(\frac{t}{t_f}\right)^w\right]$$

where t represents a time point during the period of interest, and w is the ratio of the scatter of the data m and the slope of the stress- life curve n or 1.2 for bone (David Taylor et al., 2004). The time to failure t_f was chosen to be 100 days, as this has been used previously in other probability models of bone (B. W. Edwards et al., 2010b; David Taylor et al., 2004).

In order to account calculate the probability of failure for the entire bone, rather than a single element, the probability of a single element failing within *k* independent elements is

$$P_f = 1 - (1 - P_1)(1 - P_2) \dots (1 - P_k)$$

where P_f is the probability of failure of any element within the bone, and P_k represent the independent probability of a single element failing within the k elements of the bone.

In order to account for bone repair, a third Weibull equation is used such that the probability of repair P_r is

$$P_r = 1 - \exp\left[-\left(\frac{t}{t_r}\right)^v\right]$$

where t_r is a reference time for repair, t is the current time point, and v is a modulus to account for scatter in the repair time. For bone, the reference time for repair is 26 days, and the scatter modulus is 2 (David Taylor et al., 2004).

To combine the probability of failure and the probability of repair, a probability density function for failure must be used in conjunction with the probability of repair not being done. A probability density function Q is the time differential of the probability P, with the general expression of

$$Q = \frac{dP}{dt}.$$

Therefore, the probability density function Q_f for failure is

$$Q_f = \frac{dP_{fa}}{dt} = \frac{Vw}{V_{so}t_f}\left(\frac{t}{t_f}\right)^{w-1} \exp\left[-\left(\frac{V}{V_{so}}\right)\left(\frac{t}{t_f}\right)^w\right].$$

To simplify the calculation, the assumption that V_s equals V_{so} can be made for the probability density function (David Taylor et al., 2004). This probability density function Q_f is then multiplied by the probability that repair is not completed or $(1 -$

P_r) to give the overall probability density function Q_{fr} of failure and a lack of repair or

$$Q_{fr} = Q_f(1 - P_r).$$

To calculate the final, overall probability P_{fr} that a single element will fail over a given time *t* while accounting for repair, the probability density function for failure with no repair must be integrated over time using

$$P_{fr} = \int_0^t Q_{fr} dt.$$

The probability of failure with repair will be computed over 50 years of simulated OI prosthesis use for each participant. The input data will be the grouped strain from the finite element model, and the probability model will be built using a custom Matlab script computing the probability of failure for the entire bone for each participant. To determine the effect of walking speed, the probability of failure will be computed for each walking speed independently, and then for a model which combines the three walking speeds. The combined model will simulate the individual walking for 80% of the time at their preferred speed, and then walking for 10% of the time at their faster and slower speeds respectively.

8.3. Additional results simulating materials testing of the bone

To understand the number of load cycles before which the bone would be expected to fail, simulated materials testing of the bone and OI implant system was conducted using the finite element model from Chapter 5. The Fatigue node within the

Comsol software was used to determine how many cycles to failure the bone would be expected to sustain with the stance phase abutment forces and strain. This node uses mathematical relationships between the simulated strain across the bone volume, a strain-cycles to failure model based on experimental data (Carter et al., 1981), and the material properties of the bone to estimate the fatigue life of the bone. The fatigue life of the bone when exposed to simulated cyclical loading for each walking condition (fast, preferred, and slow) was computed, finding that the estimated cycles to failure are on the order of 10 million or greater for all speeds (Table 16, Fig. 15). The number of cycles to failure for each walking condition was approximately 100 million for the slow walking condition, 10 million for the preferred speed condition, and 20 million for the fast walking condition (Fig. 15, Table 16).

Table 16. Results of the simulated materials testing of the bone as a result of walking at each speed. Distance and time to failure are computed assuming individuals walked with the average stride length of our participants, and walked 1900 meters per day.

	Slow	SSW	Fast
Cycles to failure	1e8	1e7	2e7
Average stride length (m)	1.03 (0.08)	1.15 (0.16)	1.37 (0.29)
Distance walked before failure (m)	1.04e8	1.15e7	2.75e7
Time to failure (years)	150	17	40

This indicates, based on the average stride length, individuals would be able to walk a distance of 104 million, 11.5 million, and 27.5 million m for the slow, preferred, and

fast walking conditions respectively, before a potential fatigue failure of the bone. In other words, assuming individuals walk 1900 m a day (Leijendekkers et al., 2019a) and the bone does not repair the accumulated damage over time, it would take

approximately 150 years of walking at the slow speed, 17 years of walking at the preferred speed, and 40 years of walking at the average fast speed before fatigue failure

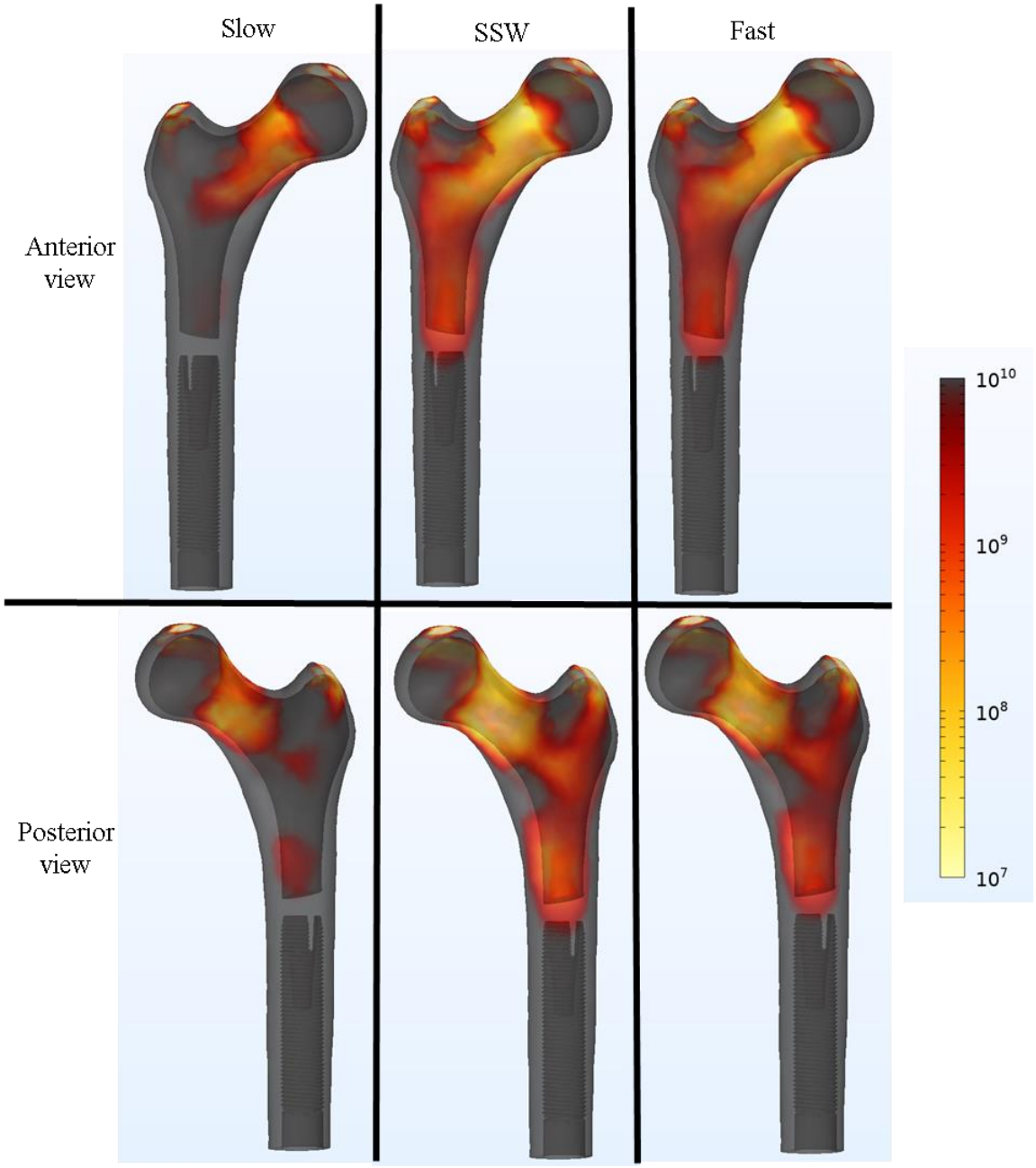

Figure 15. Simulated mechanical testing of cycles to failure for the strain computed on the bone during walking at three different speeds. The top row shows the anterior side of the bone, while the bottom row shows the posterior side of the bone. Due to the time scale, the color map is a logarithmic scale representing cycles to failure.

might occur in the femur. When considering the effect of walking speed, it appears that there is some influence of walking speed, but again, it is non-linear. Instead, the bone would be expected to fail first if the individual walked at the preferred speed, followed by the fast speed, and then finally the slow speed. However, it is important to note that the bone would only be expected to fail during an individual's lifetime if they walked only at the preferred speed, as many individuals expect to live more than 20 years after undergoing the OI procedure. There is a smaller chance of failure during an individual's lifetime if they walk only at the fast speed, as some individuals may live longer than 40 years with their OI prosthesis, but no chance of failure if individuals walk at only their slow speed, as 150 years is longer than the current average lifespan of people within the United States. However, it is important to note that, for some individuals, walking only 1900 meter may be a larger underestimation of the distance they walk each day. If individuals walk an average distance that is significantly farther, failure of the bone would be expected to occur sooner in the simulated lifetime. In addition, this model does not take into account the repair capability of the bone, which would be largely expected to extend the lifetime of the bone significantly longer than 17 years of walking. In order to account for the repair capacity, probabilistic modeling, as in Chapter 6, can be conducted.

Our results indicate that the number of cycles required to achieve mechanical fatigue were on the order of 10^7 to 10^8, depending on the walking speed, with the region of the bone which would be expected to fail largely coinciding with the region of the bone diaphysis and femoral neck which were highlighted by the strained volume. When

data from materials testing of femoral bones is compared to these results, previous literature indicates that bone will fail after approximately 10^7 cycles of loading for a stress of between 23.30 and 51.2 MPa, or strains of approximately 1.43e-3 and 3.13e-3 (Swanson et al., 1971). These stress and strain values are very similar to the stress and strains measured on the tibia during walking (Lanyon et al., 1975), and are also similar to the strains predicted by the finite element model simulation done in this study, indicating that the simulated failure testing done in this study agrees with the results of the mechanical tests. The results of the simulated mechanical testing done in this study indicate that the bone is unlikely to fail during a short period of time. Rather, the results find that, depending on the walking speed, the bone would be expected to fail after 17 to 150 years, assuming there is no capacity for repair of the bone.

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