FUNCTIONAL OUTCOMES OF PROXIMAL FEMUR LIMB SALVAGE SURGERY

A PATIENT SPECIFIC MUSCULOSKELETAL MODEL SIMULATION OF LIMB SALVAGE SURGERY TO INVESTIGATE HOW ALTERED HIP BIOMECHANICS IMPACTS FUNCTIONAL OUTCOMES

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Lay Abstract

Hip reconstructive surgery as treatment for bone cancer is a highly invasive surgery that negatively impacts patients walking patterns and ultimately quality of life. The current thesis investigates existing literature to determine if specific, innovative surgical techniques lead to better functional results for patients after surgery. A three-dimensional model of a patient who had hip reconstruction surgery for bone cancer was created using quantitative analysis of their walking patterns. The model was manipulated to simulate surgical intervention for hip cancer treatment. The model findings suggest when specific hip muscles are substantially affected by surgery, patients walking patterns are negatively impacted. Understanding how surgical intervention impacts walking patterns can inform surgical technique, implant design and physiotherapy programs leading to better quality of life for patients after surgery.

Abstract

Sarcoma cancer of the proximal femur is a bone tumor that develops near the hip joint. The most common method of treatment is limb salvage surgery (LLS), a highly invasive surgery that often leads to impaired movement including walking due to soft tissue resection. The current thesis focuses on 1) systematically reviewing current literature of functional outcomes after proximal femur LSS to determine if specific methods of muscle reattachment lead to better limb function, and 2) objectively analysing how reducing hip muscle strength impacts one's ability to achieve healthy gait. Findings from the systematic review suggest using artificial mesh or ligaments for LLS may be a good alternative to allograft prosthesis composites and trochanter osteotomy, producing good functional outcomes with low rates of complications. It was also determined current literature is lacking objective quantitative analysis of patients' limb function after surgery. Objective 2 was executed using instrumented gait analysis to record the gait kinematics, kinetics and EMG patterns of a patient who received LSS for proximal femur sarcoma. Data from the gait analysis was used to create a patient-specific musculoskeletal model. Healthy gait kinematics were applied to the model and specific hip muscle strengths were systematically reduced to simulate different surgical interventions. After an 85% reduction in gluteus medius and minimus muscle strength, healthy gait kinematics were not achieved. Reducing muscle strength of the gluteus medius and minimus together had a greater impact on the model's ability to achieve healthy gait kinematics then when reduced individually. An understanding of how patient's limb function is impacted after surgery can inform surgical technique, implant design and physiotherapy programs leading to better quality of life for patients after surgery.

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Table of Contents

Lists of Figures

Lists of Tables

List of Abbreviations and Symbols

LSS	Limb Salvage Surgery
PROM	Patient Reported Outcome Measure
MSTS	Musculoskeletal Tumour Society
TESS	Toronto Extremity Salvage Score
HHS	Harris Hip Score
EMG	Electromyography
sEMG	Surface Electromyography
MVIC	Maximum Voluntary Isometric Contraction
MSTS93	1993 version of Musculoskeletal Tumour Society Scoring System
ROM	Range of Motion
APC	Allograft Prosthesis Composite
TFR	Total Femur Replacement
LARS	Ligament Advanced Reinforcement System
Endo	Endoprosthesis
PFR	Proximal Femur Replacement
NP	Not Provided
TO	Trochanter Osteotomy
MP	Modular Prosthesis
TFL	Tensor Fasciae Latae
DOHM	Dynamics of Human Motion
SH	Shoulder
LE	Lateral Epicondyle
GT	Greater Trochanter
LM	Lateral Malleolus
ME	Medial Epicondyle
MM	Medial Malleolus
1MT	First Metatarsal
SM	Second Metatarsal
5MT	Fifth Metatarsal
FH	Fibular Head
TT	Tibial Tuberosity
ASIS	Anterior Superior Iliac Spine
PSIS	Posterior Superior Iliac Spine
VL	Vastus Lateralis
VM	Vastus Medialis
RF	Rectus Femoris
LH	Lateral Hamstrings
MH	Medial Hamstrings
LG	Lateral Gastrocnemius
MG	Medial Gastrocnemius

GM	Gluteus Medius
DOF	Degree of Freedom
MTP	Metatarsal-phalanges
PCSA	Physiological Cross-Section Area
GMRS	Global Modular Replacement System

Declaration of Academic Achievement

To execute the thesis presented, I took the lead on the ethics submission for data collection, musculoskeletal modeling, data analysis, and writing of the thesis. The gait data for the patient was collected at the DOHM lab at Dalhousie University, due to Covid-19 restrictions in Ontario. It was originally planned that I would stay in Halifax for 2 months to complete the data collection, but due to delays in ethics approvals we were not able to collect data on the participant until I left. Although I was unable to participate in the data collection of the participant, I received training on the gait analysis protocol at the DOHM and practised on other students. I also supported setting up the motion capture system implemented at St. Joseph's hospital when needed. Through working at St. Joseph's and the DOHM lab, I gained hands on experience of gait analysis data collection.

Chapter 1 Introduction

1.1 Introduction

Sarcoma cancer is a type of tumor that originates at the bone [1]. Approximately one per 100,000 Canadians are diagnosed with primary bone sarcoma each year [2]. It is most prevalent in individuals who are young and otherwise healthy [3]. Although a rare type of cancer, bone sarcoma requires a complex treatment usually involving a highly invasive surgery [4],[5]. Due to advancements in medical imaging, neoadjuvant treatment, surgical technique and implant design, limb salvage surgery (LSS) has become the standard of care [5],[6]. Limb salvage surgery entails surgically resecting the tumorous bone as well as soft tissues involved, to create a safe oncological margin. The resected bone is then replaced with an orthopedic implant, and preserved muscles are reattached to either bone, soft tissue, or the implant.

Sarcoma cancer of the proximal femur is a bone tumor at the hip joint. Proximal femur sarcoma presents as a particularly difficult location to treat, due to the amount of soft tissue and muscle attachments at the hip joint. During reconstruction of the hip, many muscle attachments are disturbed or resected, impacting the native musculature and ultimately the biomechanics at the hip. Hip abductors in particular are commonly impacted during proximal femur limb salvage surgery[7]. This leads to patients having abnormal gait patterns and limb function deficits [8].

To determine how patients' limb function are impacted after surgery, an assessment using functional outcome measures is completed. The most common functional outcome measures are subjective and do not provide quantitative evidence to inform surgical technique or implant design[9]. Currently, there is limited literature using objective quantitative analysis to understand how hip biomechanics are affected by limb salvage surgery[10].

Instrumented gait analysis provides objective outputs such as kinematic, kinetic and electromyography patterns which can be compared to healthy controls as well as pre and post operatively [11],[12],[13]. This allows for a comprehensive understanding of the impairments patients face. A limitation to using gait analysis alone with this demographic is the inherit variability between patients as oncological margins, surgical techniques and implants can all impact hip biomechanics. This makes it difficult to determine which aspect of the surgery causes a deficit in limb function.

Patient specific musculoskeletal models in combination with kinematics and kinetics from instrumented gait analysis allows for the simulation of surgical intervention[14],[15]. This technique provides an opportunity for specific elements of surgery to be manipulated to determine how model biomechanics are affected in a controlled environment [16],[17]. The results from this strategy allow us to form conclusions about the effect specific elements of limb salvage surgery have on functional outcomes. The insights provided from objective biomechanical analysis for proximal femur LLS can inform treatment and rehabilitation programs to improve limb function and quality of life for patients after sarcoma cancer.

1.2 Objectives

1.2.1 Objective 1

Objective 1 aims to review current literature to determine if specific methods of muscle reattachment during limb salvage surgery for proximal femur sarcoma lead to better limb function. Papers reporting functional outcomes for proximal femur LSS will be examined and main themes of muscle reattachment techniques and their outcomes will be synthesized.

Hypothesis:

1. Proximal femur limb salvage surgeries that result in good muscle strength preservation lead to better functional outcomes.

1.2.2 Objective 2

Objective 2 focuses on examining how reductions in hip muscle strength affects one's ability to achieve healthy gait. Kinematics and kinetics from a patient who received LSS for proximal femur sarcoma, were collected using instrumented gait analysis and applied to a patient specific musculoskeletal model. Surgical intervention was simulated by systematically reducing gluteus medius, gluteus minimus and piriformis muscle strengths, to determine if the model could achieve healthy kinematics.

Hypothesis

1. Large simultaneous reductions in gluteus medius, gluteus minimus and piriformis muscle strength prevent healthy kinematics from being achieved. Reducing muscle strengths individually will not impact healthy kinematics as much as reducing multiple muscle strengths together.

1.3 Structure of Thesis

This thesis will be structured into five chapters. Chapter 2 provides a background of bone sarcoma, gait analysis, functional outcomes of LLS, and potential for innovation. Chapter 3 addresses objective 1 with a semi-structured systematic review of functional outcomes related to muscle reattachment techniques for proximal femur limb salvage surgery. Chapter 4 addresses objective 2 by simulating surgical intervention using a patient specific musculoskeletal model and healthy kinematics to determine if healthy gait patterns are achievable after surgery. Chapter 5 provides conclusions of the thesis, summarizing the work presented, addressing the limitations of findings and implications of results, and suggesting areas to focus future work.

Chapter 2 Background

2.1 Sarcoma

Sarcoma is a rare cancer that forms in the bone or soft tissue of the body. Bone sarcoma tumours most commonly originate in the long bones of the extremities and have the potential to metastasise to other organs [18]. The proximal femur is the second most common location for primary bone tumors to form [19]. There are different types of bone sarcoma; the most common are osteosarcoma, Ewing sarcoma, and chondrosarcoma [1]. Bone sarcomas are usually grouped into two categories, primary and metastasis (secondary) bone sarcoma. Primary bone sarcomas are cancerous tumors that originates in the bone, whereas metastatic bone cancer occurs when a primary tumour that originated somewhere else in the body such as breast or lung cancer, spreads to the bone.

2.1.1 Incidence and Survival Rates

Roughly one in 100 000 Canadians are diagnosed with primary bone sarcoma each year [2]. In 2018, 285 Canadians were diagnosed with primary bone sarcoma, with a net 5-year survival rate of 62% [20]. People under the age of 20 are most commonly diagnosed with primary bone sarcoma, accounting for over 25% of all new cases [3]. Males are more frequently diagnosed with bone sarcomas than females; in 2016, 1.45 males were diagnosed with bone sarcoma for every 1 female diagnosed [21].

The incidence rates and demographics of sarcoma cancer vary depending on the specific type. Osteosarcoma and Ewing sarcoma often occur in people under the age of 20, whereas chondrosarcoma is more common in people over the age of 40 [3]. The incidence rates of sarcoma of bone diagnosed for people under the age of 20 is 1.46 and 1.89 per 100 000 for females and males respectively [3].

Metastatic bone cancer is more common than primary bone cancer. Bone metastasis most commonly spreads from primary breast, prostate and lung tumours [22]. The most frequent locations for bone metastasis to form is the spine, pelvis, femur and ribs respectively [23].

2.1.2 Treatment for Sarcoma Cancer

The treatment for sarcoma of bone can involve chemotherapy, radiation, and surgery. Chemotherapy is commonly used as part of the treatment plan for bone sarcoma, often used before and after surgery to reduce the rate of metastatic spread [24]. Radiation may be used to kill tumor cells and prevent them from reoccurring [4]. The use of radiation and chemotherapy vary depending on the type of sarcoma and the location. Chemotherapy is often used for osteosarcoma and Ewing sarcoma but is usually not effective treating chondrosarcoma [25]. Radiation can be used for specific cases of Ewing sarcoma. The two main methods of surgical removal of the tumour are amputation or limb salvage surgery (LSS). Amputation includes surgically removing the affected limb. Limb salvage surgery is a technique where the cancerous portion of bone is removed, with a safe surgical margin of surrounding soft tissues to prevent local reoccurrence. The limb is then reconstructed using either an endoprosthesis or bone graft. Due to advancements in imaging, surgical techniques, implant design and neoadjuvant treatment, limb salvage procedures have become more popular in recent years compared to amputation, and are now the standard of care [1]. During limb salvage surgery, muscle attachments are preserved when a safe surgical margin allows, but there are many cases when these muscle attachments cannot be preserved, which can impact the function of the patient's limb. Depending on the location and size of the sarcoma tumour, limb savage surgeries can represent large, complex procedures with more anatomical disruption than comparable surgeries such as joint arthroplasty.

2.1.3 Limb Salvage Surgery for Proximal Femur Sarcoma

Limb salvage surgery for sarcoma at the hip joint is particularly complex, where the resection of numerous soft tissue attachments leads to challenging reconstructions that have a particularly large effect on gait and function[8]. The muscles commonly disrupted and lost during proximal femur limb salvage surgery are the hip abductors, short external rotators, iliopsoas, and gluteus maximus (Figure 1, Figure 2). The hip abductors include the gluteus minimus, gluteus medius and the tensor fasciae latae. Loss of hip abductor function can lead to gait impairments such as Trendelenburg gait, where the pelvis drops down on the contralateral side during weight bearing, affecting the symmetry and efficiency of the gait cycle [26]. The iliopsoas are hip flexors. Weak iliopsoas muscles can lead to gait impairments including, stiff knee patterns, reduced gait velocity and reduce range of motion [27]. The action of the gluteus maximus is extension of the hip and external rotation. Impaired gluteus maximus muscle can lead to pelvis instability, and impact one's ability to climb stairs, walk and run [28]. If the gluteus maximus muscle does not function effectively, it can lead to compromised gait control and impact the function of distal joints [28].

Figure 1. Anterior and Posterior Views of Pelvic and Thigh Muscles. Extracted from [29]

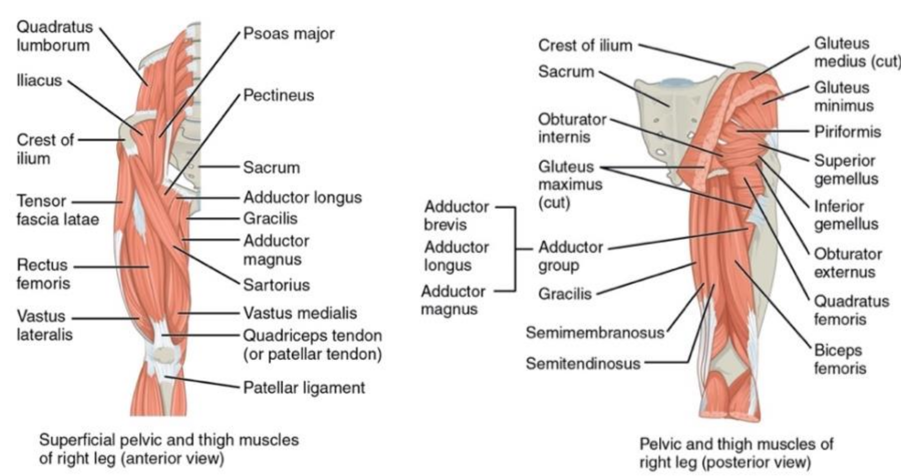
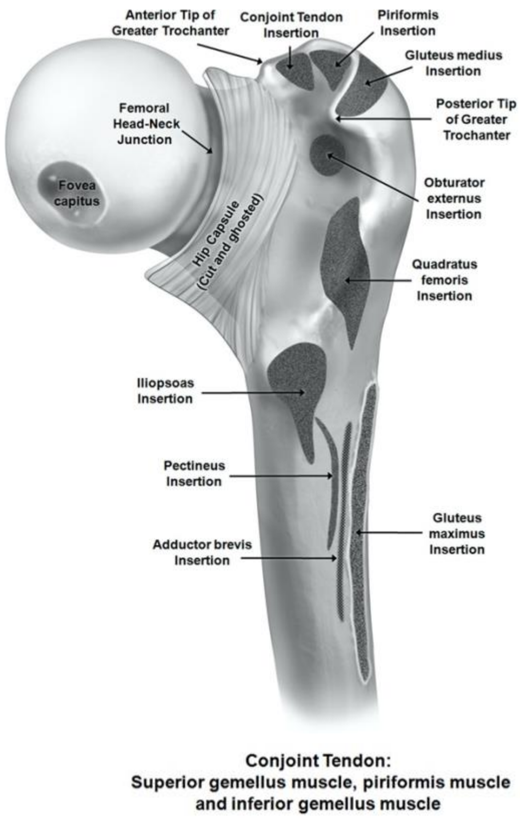


Figure 2. Femoral Head Muscle Insertion Locations. Extracted from [30]



2.2 Limb Salvage Functional Outcomes

The functional outcomes (i.e. mobility and movement characteristics after surgery) of limb salvage surgery vary depending on the size, location and type of tumour. The most frequently reported ongoing symptoms after lower limb salvage surgery include: stiffness, weakness, fatigue, pain, reduced range of motion and swelling [5]. Functional outcome measures after LSS can be categorized broadly into two groups, objective, or subjective. Subjective functional outcomes are often patient, or clinician reported, and typically in the form of questionnaires that tally to provide scores which can vary depending on the person assessing limb function. Objective functional outcomes include quantifiable analysis which focus on measured quantities such as gait spatiotemporal factors, kinematics, and kinetics typically recorded using instrumentation.

2.2.1 Subjective Outcome Measures

Functional outcomes of limb salvage surgery are most commonly captured by patient-reported outcome measures (PROMs) or clinician-reported outcomes, including the Musculoskeletal Tumour Society scoring system (MSTS) [5], [31], Toronto Extremity Salvage Score (TESS) [5] and Harris Hip Score (HSS) [32].

The MSTS is a subjective assessment tool where a clinician evaluates patient's physical functionality. The lower limb functional assessment of the MSTS is based on 6 different sections including pain, function, emotional acceptance, use of walking supports, walking ability, and gait [33], and provides a score out of 30 (each section 0-5), with a higher score representing better function, and often expressed as a percentage [5].

TESS is a subjective assessment tool made specifically for evaluating the physical function of the extremities of sarcoma patients who had limb salvage surgery [31]. TESS comprises of 30 questions, on a scale of 1-5, which patients complete individually. The questionnaire focuses on the patients' ability to perform daily activities including work, mobility, dressing, and sports [9], [34].

The Harris Hip Score (HSS) is an assessment tool that is administered by a clinician to evaluate a patient's function after hip surgery. The tool is comprised of 4 sections, function, range of motion, pain, and absence of deformity. The maximum score is 100. The higher the score the better the outcome. A rating less that 70 indicates a poor functional outcome, 70-80 indicates fair function, 80-90 shows good function and 90-100 is excellent function[32], [35].

Trendelenburg gait is another common subjective assessment for sarcoma patients after proximal femur reconstruction. Trendelenburg gait occurs when the abductor muscles are weak and results in a limp where the contralateral side of the pelvis drops while walking. Trendelenburg gait is typically clinically diagnosed visually, by having the patient raise one leg off the ground while standing, if the contralateral side of the pelvis drops then Trendelenburg gait is present [26][36].

Studies utilizing functional patient or clinician-reported assessments including the MSTS, TESS and the HSS have shown that functional scores for limb salvage surgery are overall superior to amputation [1], [5]. In a systematic review of outcomes for proximal femur reconstruction, the MSTS scores of the 17 papers included displayed a great amount of variability, with MSTS scores ranging from 56% to 94% [37]. Additionally, it has been shown compared to patients' perception, clinicians over estimate patients functional ability and emotional acceptance when using the MSTS score[33]. The subjective nature combined with significant patient variability makes it difficult to use patient or clinician reported outcomes to inform innovation for sarcoma surgery.

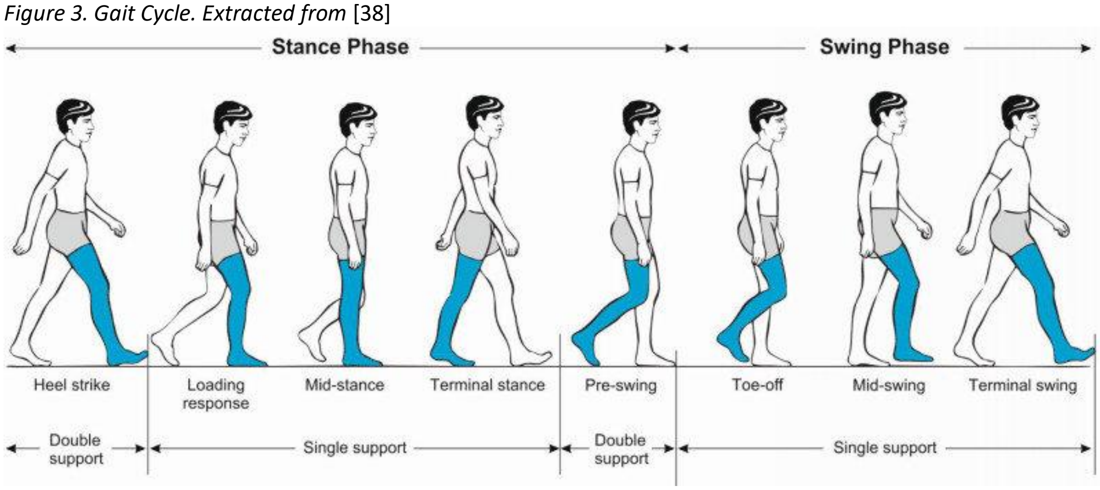
2.2.2 Objective Functional Outcome Measures

It is intuitive that disruption of musculotendon anatomy of the proximal femur would affect strength, the neuromechanics of periarticular muscle activation, and limb biomechanics; however objective assessment of functional outcomes is not routine clinically, and it remains unknown if prioritization of muscle attachments surgically could significantly enhance functional outcomes for patients. Objective functional outcome measures such as those from instrumented gait analysis provide specific quantifiable information about how a person moves after surgery. Utilizing objective functional and biomechanical testing after limb salvage surgery could provide the specificity not offered through PROMs to measure functional deficits allowing for innovation in surgical decision-making and implant augmentation to improve function.

2.2.2.1 Gait

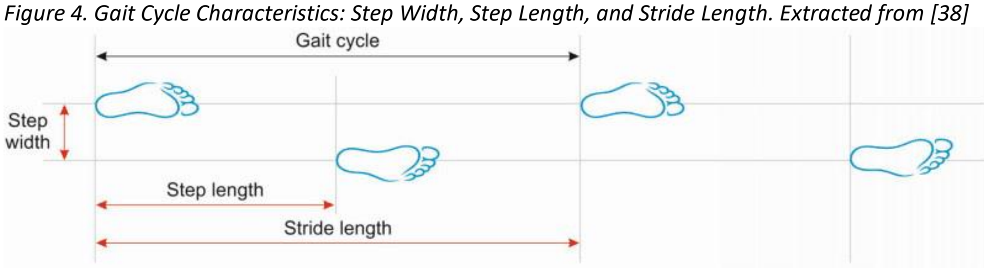
Gait refers to the manner in which a person walks. The gait cycle is measured from foot contact to foot contact of the same foot. There are two main phases of the gait cycle, the stance phase which makes up approximately 60% of the gait cycle during healthy walking and the swing phase which makes up the remaining approximate 40% (Figure 3). The stance phase refers to the period from heel strike to toe off when the foot is in contact with the ground. Stance phase is broken in to four components: loading response, mid stance, terminal stance and pre-swing. The swing phase is from toe off to heel strike when the foot is off the ground. Swing phase comprises of initial swing, mid-swing, and terminal swing.

Figure 3. Gait Cycle. Extracted from [38]



Stride characteristics of gait include step length, step width, velocity, cadence, and symmetry. Step length is measured from heel strike of one foot to the heel strike of the opposite foot. As shown in Figure 4, step width is the distance between the heels during double support in the medial/lateral direction. Velocity is the speed vector at which the person is walking. Cadence is the number of steps a person takes per minute and symmetry measures how similar gait outcomes of both legs are. Healthy walking gait is generally symmetric, periodic, and cyclic.

Figure 4. Gait Cycle Characteristics: Step Width, Step Length, and Stride Length. Extracted from [38]



2.2.2.2 Kinematics and Kinetics

Kinematics and kinetics can be determined through instrumented gait analysis. Kinematics is the study of how things move, more specifically in biomechanics we focus on how limb segments and joints move. Kinetics is the study of forces and moments that cause motion. When applied to biomechanics, we focus on joint net reaction forces and moments. Joint angles, forces and moments calculated from instrumented gait analysis provide a quantitative output to evaluate how people walk. Hip, knee and ankle joint kinematics and kinetics can be used to objectively compare patients' gait before and after surgery or to healthy controls, to determine how patients' gait are affected by surgery.

2.2.2.3 Instrumented Gait Analysis

Gait analysis is the study of locomotion, and because walking is the most common activity of daily living, there is an interest in understanding a person's joint-level biomechanics during gait as a reflection of their functional ability and mobility. Technology such as optoelectronic motion capture allows for vision-based capture of three-dimensional movement biomechanics during gait. Such technology can be combined with in-ground force platforms and biomechanical models to provide insight into the kinetics (forces, moments) that create motion, as well as synchronized electromyography (EMG) to provide simultaneous information on muscle activation patterns to interpret the neuromuscular control of movement during gait.

Optoelectronic motion capture uses high speed cameras (150-250 Hz) to visually record the position of individual markers placed on anatomical landmarks, and marker clusters placed on each limb segment. For passive motion capture, light emitted near the cameras is reflected off the reflective markers back to the cameras. Using multiple cameras to record the two dimensional position of the same marker allows for triangulation, which mathematically determines the (x,y,z) position of the intersection of two converging lines. Through direct linear transformation the two-dimensional coordinates are converted into three dimensional coordinates [39]. Each body segment is assumed to be a rigid body, maintaining the distances between the markers on one limb segment.

A cluster of a minimum of three non-collinear markers are placed on each limb segment of interest typically including the pelvis, thigh, shank, and foot. These markers allow for an arbitrary local coordinate system to be defined relative the stationary global coordinate system. The position and orientation of the clusters are tracked as the participant walks through the cameras field of view. The individual markers placed on anatomical landmarks, are used to define anatomical coordinate systems for each limb. The position and orientation of the local coordinate system relevant to the global coordinate system is transformed to the anatomical coordinate system such that results have anatomical meaning. Using the joint coordinate system [40], the rotation matrices of the anatomical to local coordinate system, and local to global coordinate system for the proximal and distal limb segments are used to calculate joint angles.

In addition to positional three-dimensional data, ground reaction data is often also collected simultaneously using instrumented force platforms. The force platforms are commonly integrated into the floor of the cameras viewing volume and synchronized with the motion capture system. Many force platforms use strain gauges connected to load cells at each of the four corners of the platform, to form six Wheatstone bridges, each outputting a force parallel to each axis, and a moment about each axis. The output data is often expressed as a voltage, which is converted to N or Nm.

Using the segmental inertial properties, kinematic accelerations and velocities, and ground reaction forces, the joint forces and moments can be calculated using inverse dynamics. Joint forces and moments are the external forces and moments acting at a joint. When calculated using inverse dynamics it is assumed that all forces acting at the joint simplify to one three-dimensional force and moment and that limb segments are rigid bodies.

The segmental inertial properties are determined from anthropometric data collected, including body mass, thigh length, midthigh circumference, calf length, calf circumference, malleolus width, malleolus height and foot length. Using total body mass, the mass of each body segment is determined using regression equations [41] based on cadaver measurements [42]. Body segment center of mass and moment of inertia are calculated using standard equations [41].

From motion capture data, linear and angular accelerations of body segments are determined. Joint forces and moments are calculated using a link segmented model of the body, starting at the most distal segment, the solving up the chain [41]. With all the information determined previously, joint forces and moments are solved using the following equations.

$$\sum F = ma \tag{1}$$

$$\vec{F}_{Prox} = m \times \vec{a}_{cm} - m \times \vec{g} - \vec{F}_{Dis} \tag{2}$$

$$\sum M = I\alpha \qquad (3)$$

$$\vec{M}_{Prox} = I\alpha - \vec{d}_{prox} \times \vec{F}_{Prox} - \vec{d}_{dis} \times \vec{F}_{Dis} - \vec{M}_{Dis} \qquad (4)$$

Where $\vec{F}_{Prox}$ is the force at a proximal joint, m is the mass of the body segment, $\vec{a}_{cm}$ is linear acceleration at the center of mass of the body segment, $\vec{g}$ is the acceleration of gravity, $\vec{F}_{Dis}$ is the force at the distal joint, in the case of the ankle ($\vec{F}_{Dis} = \vec{F}_{GRF}$) .
$\vec{M}_{Prox}$ is the moment at a proximal joint, *I* is the moment of inertia matrix, α is angular acceleration matrix, $\vec{d}_{prox}$ is the x,y,z distance from the center of mass to the proximal joint, $\vec{d}_{dis}$ is the distance from the center of mass to the distal joint, $\vec{F}_{Prox}$ is the force at the proximal joint, and $\vec{F}_{Dis}$ is the force at the distal joint

Simultaneous surface electromyography (sEMG) may also be recorded during instrumented gait analysis. Surface EMG is a non-invasive method of recording the electric signals produced by muscles as they contract. When normalized to maximum voluntary isometric contractions (MVIC), EMG shows the percentage of muscle activation as a person walks [11]. Muscles that commonly have EMG recorded during gait analysis include the rectus femoris, vastus lateralis, vastus medialis, bicep femoris, semimembranosus and semitendinosus and gastrocnemius. With the results from EMG, it can be determined when muscles are being activated throughout the gait cycle and how much they are being activated. This can provide insights to abnormal muscle activations including extended activation and co-contractions of muscles.

There has been minimal use of instrumented gait analysis and EMG for lower limb sarcoma surgery outcomes. A systematic review on quantifiable functional outcomes for sarcoma patients concluded that there is a deficit in studies utilizing objective quantifiable measurements for evaluating lower limb sarcoma patients after treatment. Furthermore, many studies have not used reliable, consistent or valid instruments to measure gait, balance, and physical abilities after surgery [10].

The few previous studies which utilized instrumented gait analysis with synchronized EMG for proximal femur LSS patients have reported worse stride characteristics and abnormal kinematic and kinetic patterns for patients compared to healthy controls. The studies found LSS led to an increase in energy cost during walking, as well as reduced gait velocity, stride length, symmetry, and cadence when compared to controls [34],[43]. Patients also demonstrated significantly less range of motion and smaller joint net reaction moments at the hip, reduced knee flexion during stance phase, and co-contraction of the flexors and extensors (hamstrings, quadriceps and gastrocnemius) during stance phase, a joint stabilizing strategy that can cause reduced knee flexion [8],[34]. The findings from these studies provides good evidence for the need to further understand how the loss of muscle attachments during surgery, or a reduction in muscle strength due to the surgery, can affect joint mechanics and general mobility of patients.

2.2.2.4 Musculoskeletal Modeling

Musculoskeletal modeling is a method of representing and analysing the biomechanics of the human body. Anatomical marker positions from gait analysis can be used to create patient specific musculoskeletal models, such that body segments, and actuators represent the anatomy of the participant. Kinematics and kinetic data from instrumented gait analysis can be used to generate patient specific dynamics, including joint net reaction forces and moments, which can be further reduced into individual muscle forces and activations.

The patient specific model can then be manipulated with iterative changes to the anatomy and/or muscle strength, to simulate surgical intervention. Muscle activations and forces can be monitored after each manipulation to determine how surgical intervention impacts participants' gait. This technique allows specific elements of limb salvage surgery to be isolated and altered to gain an understanding of how hip biomechanics are affected by surgery. This is particularly important for this demographic as limb salvage surgery varies greatly for each patient due to oncological margins, surgical technique, and implant design. These variations in surgery make it difficult to form conclusions on which element of the surgery caused a specific outcome in studies using only gait analysis or subjective outcome measures. This process can be done on a person-specific level or a broader level by generalising the results from several patients.

OpenSim [44], [45] is an open source platform for modeling, simulating and analysing the dynamics of the musculoskeletal system. Through OpenSim patient specific data from gait analysis trials can be imported and used to illustrate the patient's movement through the model. The utilization of these models allows for a non-invasive method of predicting joint contact forces, and understanding the relationships between muscle firing, muscle forces, ground reaction forces, and gait patterns [44], [45].

OpenSim musculoskeletal models have been used in previous research studies to predict different functional outcomes for hip arthroplasty. One particular study focused on simulating different rehabilitation interventions by creating patient specific models of people who received hip arthroplasty surgery [46]. The strength of the hip abductors was altered to determine how joint contact forces at the hip and other joints would be affected, they demonstrated that rehabilitation routines for hip arthroplasty should focus on the hip abductors strength in order to improve patients overall function after surgery [46].

There are multiple different generic musculoskeletal models that can be used as the basis for OpenSim simulations. Many models were created for investigations focusing on specific body functions such as analysing movement of the wrist, arm, spine, or legs. Depending on the intended purpose of the model, they have varying body segments, number of actuators and degrees of freedom. The number of actuators and degrees of freedom included in the model can impact how the model moves but can also increase complexity and computational processing. To our knowledge musculoskeletal modeling to simulate limb salvage surgery for proximal femur sarcoma has not been investigated previously, but musculoskeletal modeling has been used in studies focusing on hip biomechanics during walking.

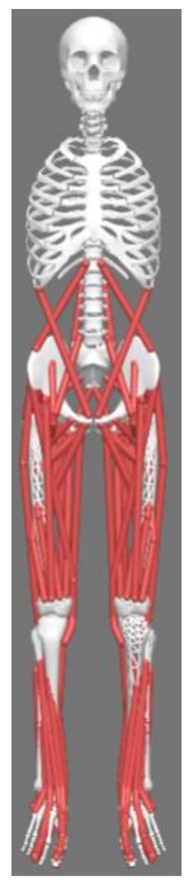
Musculoskeletal Model Validation

In particular, the generic Gait2392 (Figure 5) model which focuses on the lower limbs has been used in previous studies to analyse hip biomechanics simulations [47], [48]. The use of the Gait2392 model for hip simulations has been validated previously in literature. In-vivo hip joint contact forces recorded from an instrumented total hip implant and EMG data [49] were compared to Gait2392 modeling results. Hip joint contact forces and muscle activations predicted using the Gait2392 model were found to corroborate well with instrumented prosthesis joint contact forces and EMG results [50].

Gait2392 Model

The Gait2392 model comprises of 12 body segments with 23 degrees of freedom (DOF) (Table 1). The 12 body segments include the torso, pelvis, femurs, tibias, talus, calcaneus, and toes. The measurements of the Gait2392 body segments were based off of the Delp model [51]. The model utilises 92 musculotendon actuators to simulate 76 of the lower limb muscles (Table 2). The musculotendon actuators are the same as those used in the Delp [51] model, with the exception of 6 lumbar muscles which are from the Anderson model [52]. The hip joint is a ball-in-socket joint based off the Delp model [51], where the pelvis and hip frame of reference is centered between the ASIS and fixed at the femoral head respectively. The knee joint is a single degree of freedom joint as described by Yamaguchi et al.[53] and was adopted by Delp [51] where the tibial plateau is a flat line and the femoral condyles are ellipses. The tibial frame of reference is the centered between the lateral and medial epicondyles of the femur. The ankle, subtalar and metatarsophalangeal (MTP) are also single degree of freedom revolute joints. The location and orientation of the frame of reference for the 3 joints is based off Inman et al. [54], except for the MTP angle which was adjusted by 8 degrees to reduce unrealistic movement that caused separation between the metatarsal and phalanges. Inertial properties of the body segments except for the hindfeet and toes were based off of measurements taken from 5 subjects (age 25 $\pm$ 3 years, height 177 $\pm$ 3cm, and mass 70.1 $\pm$ 7.8kg) [52]. The muscle geometry of the model was created by replicating muscle attachment locations on the bone and wrapping the

Figure 5. Generic Gait2392 Model



muscle around the bone segment to prevent interference between muscle and bone[51].

Musculotendon parameters and physiological cross-section area (PCSA) were adapted from the Delp model. The Delp PCSA values were based off of combination of young [55] and elderly cadavers [56]. To produce muscle strength results similar to those reported by Anderson et al. [52] from healthy living subjects, the Delp model maximum isometric muscle strengths were scaled. The optimal fiber lengths for the Gait2392 model were based off of those described by Wickiewicz et al.[56]. The optimal fiber lengths were then scaled by 2.8/2.2, which is the ratio of sarcomere length measured by Wickiewicz et al. (2.2cm) divided by the sarcomere length at which muscle forces achieve peak force as reported in the sliding filament theory of muscle contraction (2.8cm).

Table 1. Gait 2392 Degrees of Freedom

Segment/Joint	Rotational DOF	Translational DOF
Lumbar	3	0
Pelvis	3	3
Hip	3	0
Knee	1	0
Ankle	1	0
Subtalar	1	0
Metatarsal phalanges	1	0

Table 2. Gait 2392 Muscles

Gait2392 Muscles			
Gluteus Medius 1	Adductor Brevis	Quadratus Femoris	Flexor Hallucis Longus
Gluteus Medius 2	Adductor Magnus 1	Gemellus	Tibialis Anterior
Gluteus Medius 3	Adductor Magnus 2	Piriformis	Peroneus Brevis
Gluteus Minimus 1	Adductor Magnus 3	Rectus Femoris	Peroneus Longus
Gluteus Minimus 2	Tensor Fasciae Latae	Vastus Medialis	Peroneus Tertius
Gluteus Minimus 3	Pectineus	Vastus Intermedius	Extensor Digitorum Longus
Semimembranosus	Gracilis	Vastus Lateralis	Extensor Hallucis Longus
Semitendinosus	Gluteus Maximus 1	Medial Gastrocnemius	Erector Spinae
Biceps Femoris-Long Head	Gluteus Maximus 2	Lateral Gastrocnemius	Internal Oblique
Biceps Femoris-Short Head	Gluteus Maximus 3	Soleus	External Oblique
Sartorius	Iliacus	Tibialis Posterior	
Adductor Longus	Psoas Major	Flexor Digitorum Longus	

2.3 Potential for Innovation

The utilization of musculoskeletal modeling allows for the simulation of different surgical outcomes, to determine the relationship between loss of muscle attachments during LSS and gait disability, with a goal of gaining insight that will inform surgical techniques to preserve patients' natural gait. LSS results in significant loss of muscle, tendon, and bone, and restoring muscular and tendonous anatomy is difficult and often not approached as a priority using currently available technology. However, there is motivation to improve functional outcomes for LLS, which requires an evidence-based approach. Therefore, there is a need to understand prioritization of muscles for reattachment. Understanding patient-specific biomechanics combined with computational musculoskeletal dynamic modeling will allow us to understand the functional constraints imposed by sacrificed muscle, and to non-invasively and rapidly optimize surgical approach by comparing functional outcomes with high throughput computing of different muscle reattachment combinations.

Chapter 3 A Systematic Review of Functional Outcomes Related to Muscle Reattachment for Proximal Femur Limb Salvage Surgery

3.1 Introduction

The proximal femur is one of the most common sites for sarcoma of bone to occur [19]. Proximal femoral sarcoma was historically treated with amputation, but with advances in neoadjuvant treatment, modern imaging, surgical technique and implant design, limb salvage surgery has become the standard of care [1]. Limb salvage surgery (LSS) is a highly invasive procedure that involves removing tumorous bone and affected soft tissue and replacing it with an orthopedic implant. The need to achieve good oncologic margins results in resection of soft tissue and important muscle attachments, which frequently leads to compromised functional outcomes[1].

As research in this field shifts focus from examining if limb salvage surgery provides good oncological results and concentrates on improving functional outcomes, there is a need to better understand how surgical technique and implant design affect patients' limb function. Currently the most commonly used functional outcome measures are patient or clinician reported outcome measures such as the Musculoskeletal Tumor Society (MSTS)[57], Toronto Extremity Salvage Score (TESS) [31], and Harris Hip Score (HHS) [32]. These scoring systems are helpful in providing global indicators of functional success; however, they are inherently subjective and do not provide the specificity necessary to understand how specific surgical and design decisions affect limb function.

There have been a few systematic reviews on proximal femur reconstruction surgery in previous literature [37],[58]. Thambapillary et al. summarized complication rates, MSTS and TESS scores from proximal femur reconstructions for sarcoma [58]. Janssen et al. focused on revision rates, implant survival, reasons for revision, reasons for amputation, limb salvage rate, and clinician/patient reported functional outcomes, providing MSTS scores for 24 relevant papers[37]. There is a gap in current literature summarising functional results along with details regarding the method of muscle reattachment. The objective of the current study is to perform a semi-structured review of recent literature (after 1998), concentrating on functional outcomes after proximal femur reconstruction surgery to understand how different approaches lead to improved functional outcomes. The papers included focus on muscle reattachment methods, including incorporating a mesh or artificial ligament, allograft prosthetic composite, and trochanteric osteotomy.

3.2 Methods

A semi-structured, limited time review of existing literature relevant to the objective was conducted. PubMed was searched for papers on proximal femur reconstruction for sarcoma where functional outcomes, and details on the approach of muscle reattachment, were specified. The search was limited to papers written in English and published after 1998, as the majority of papers reporting functional outcome measures from the two previous systematic reviews were after 1998 [37], [58]. The papers had to include the following terms in the title or abstract: ((femur and proximal) or hip) and (tumor or sarcoma), and the following terms had to be included in the paper: (surgery) and (abductor or muscle). The abstracts of the search results were reviewed to determine if the papers focussed on proximal femur reconstruction for sarcoma cancer and provided clinician/patient reported or other functional outcomes. All important details relating to the procedure and functional results were extracted from the papers and synthesized for comparison and interpretation.

3.2.1 Outcome measures

The papers needed to include at least one of the following functional outcome measures: Musculoskeletal Tumor Society (MSTS)[57], muscle strength, Trendelenburg gait or active range of motion.

The MSTS is a subjective assessment tool where a clinician evaluates patient's physical functionality. The lower limb functional assessment of the MSTS is based on 6 sections including pain, function, emotional acceptance, use of walking supports, walking ability, and gait [33], and provides a score out of 30 (each section 0-5), with a higher score representing better functionality, and often expressed as a percentage [5]. The MSTS scoring system is the most common patient/clinician reported outcome measure, therefore it will be the focus subjective outcome measure in the current review.

Active range of motion (ROM) is another measure used to characterize a patient's functional ability after surgery. Active ROM of the hip is the maximum angle a patient can move their limb using voluntary muscle activation without assistance. ROM is typically measured using a goniometer with the patient laying down or standing [59]. In this study, we are interested in the ROM in all three planes of the hip including flexion/extension, adduction/abduction, and internal/external rotation.

Trendelenburg gait is a common assessment for sarcoma patients after proximal femur reconstruction. Trendelenburg gait occurs when the abductor muscles are weak and results in a limp where the contralateral side of the pelvis drops while walking. Trendelenburg gait is typically diagnosed visually, by having the patient raise one leg off the ground while standing, if the contralateral side of the pelvis drops then Trendelenburg gait is present [26][36].

3.3 Results

The Pubmed structured search criteria produced 145 papers in English published after 1998. The titles and abstracts of all 145 papers were reviewed by a single author, and those that did not include proximal femur reconstruction for sarcoma were excluded, reducing the total number of papers to 27. The 27 papers were reviewed and papers that did not include any of the indicated outcomes were removed. After this process, 14 papers remained to be included in this review (Table 3). Information from the 14 papers was summarized and categorized according to three general themes focusing on improving muscle reattachment including artificial ligament/mesh, allograft prosthesis composite (APC), and trochanter osteotomy (TO). Thematic summary tables based on these identified themes were generated.

Table 3. Study Demographics, Implant Design and Mean Follow up

Authors	Number of Patients	Mean Age (Age Range)	Sex	Implant Info	Bipolar or THA	Metastasis	Mean Follow Up (Range)
E. R. Henderson et al.[60]	2	63 (60-65)	1 Female (50%) 1 Male (50%)	Endoprosthesis with Aortograft	100% Bipolar	1 (50%)	2.2 years (2-2.4 years)
T. Ji et al. [61]	3	32 (19-41)	1 Female (33%) 2 Male (66%)	LARS and capsulotomy	2 Bipolar (66%) 1 THR (33%)	0	2.4 years (2-3 years)
Z. Du et al. [62]	58	23 (9-79)	22 Female (38%) 36 Male (62%)	Endoprosthesis (TFR) 12 with LARS (21%) 46 without LARS (79%)	100% Bipolar	0	LARS = 3.1years Without LARS = 3.75 years (0.5-10.75 years)
M. Benedetti et al. [63]	1	4	1 Female (100%)	Custom APC	100% Bipolar	0	7 years
Y. Farid et al. [64]	72	APC: 44 (17-64) Endo: 36 (16-87)	APC: 7 Female (35%) Endo: 28 Female (54%)	20 APC (28%) 52 Endoprosthesis (72%)	APC: 19 Bipolar (95%) Endo: 40 Bipolar (77%)	APC: 0 (0%) Endo: 18 (35%)	APC: 5.2 years Endo: 10.9 years (2-27.9 years)
A. Dubory et al. [19]	46	34 (7-71)	20 Female (43%) 26 Male (57%)	APC	14 Bipolar (30%)	2 (4%)	14.7 years (6.3-32.6 years)
F. Langlais et al.[65]	21	38 (14-77)	13 Female (62%) 8 Male (38%)	APC	100% THR	0	Short term group: 1 year Long term group: 10 years (0.5-15 years)
D. Luis Muscolo et al.[66]	38	46 (13-76)	26 Female (68%) 12 Male (32%)	APC	100% THR	2 (5%)	7.5 years (3-17 years)
D. Donati et al. [67]	27	32 (11-64)	14 Female (52%) 13 Male (48%)	APC	24 Bipolar (89%) 3 THR (11%)	1 (4%)	4.8 years (3-10.5 years)
V. Crenn et al. [68]	31	45 (18-80)	15 Female (48%) 16 Male (52%)	Modular Endoprosthesis	8 Bipolar (25%) 23 THR (75%)	6 (19%)	2.2 years (0.5-8.6 years)
J.-M. Philippeau et al. [69]	71	54 (15-86)	38 Female (54%) 33 Male (46%)	Dual Mobility Endoprosthesis	100% THR	38 (54%)	2.2 years (0.2-7.9 years)
C. M. Ogilvie et al. [70]	33	46 ± 17.6	12 Female (36%) 21 Male (64%)	Endoprosthesis	21 Bipolar (64%) 12 THR (36%)	2 (6%)	3.2 ± 1.9 years
J. Groundland et al. [71]	53	55 (13-85)	19 Female (36%) 34 Male (64%)	Endoprosthesis	48 Bipolar (91%) 5 THR (9%)	26 (49%)	1.9 years (0.17-11 years)
J. Bickels et al. [72]	57	41 (5-85)	22 Female (39%) 35 Male (61%)	Endoprosthesis 39 PFR (68%) 18 TFR (32%)	49 Bipolar (86%) 8 Fixed Unipolar Head (14%)	6 (11%)	6.7 years (2-18.2 years)

Abbreviations. THA, Total Hip Replacement; APC, Allograft Prosthesis Composite; Endo, Endoprosthesis; TFR, Total Femur Replacement; PFR, Proximal Femur Replacement; NP, Not Provided

3.3.1 Artificial Ligament or Mesh

Three of the 14 papers used an artificial ligament or aortograft for muscle reattachment [60]–[62] (Table 4). Two of the papers used the Ligament Advanced Reinforcement System (LARS), a synthetic ligament that has been used in other surgical reconstructions such as Achilles tendon, anterior cruciate ligament (ACL) and rotator cuff repairs [61][62]. In both cases, the abductor muscles were reattached to the LARS, if no native greater trochanter remained for reattachment. The third paper used an aortograft, a synthetic mesh sleeve used with the goal to improve hip function and stability [60]. The abductors, iliopsoas and, when possible, the vastus lateralis and external rotators were reattached to the aortograft. The mean MSTS scores when a mesh or artificial ligament were used ranged from 78.9-80%. Zero dislocations occurred in all patients who received the LARS or aortograft. The mean active ROM of the three studies ranged from 73.3-90 ° for hip flexion and 28.3-48° for abduction. Two of the three papers reported zero Trendelenburg gait and zero patients requiring supports during walking [60], [61]. The third paper did not report Trendelenburg gait, but did find that patients who received the LARS had a mean score of 3.98/5 for the “use of supports” section in the MSTS [62]. Du et al., compared reconstruction with LARS verses without, and found the group with LARS had higher MSTS scores, better function, gait, and hip flexion and abduction range of motion [62].

Table 4. Mesh and Artificial Ligament Outcomes

Author	Number of Participants	Type of Mesh/ Artificial Ligament	Muscle attachments	Dislocation	Mean MSTS93 (Range)	Active Hip ROM (Range)	Trendelenburg gait	Use of supports
E. R. Henderson et al.[60]	2	Aortograft	Reattached to aortograft: • Abductors, Iliopsoas • When present vastus lateralis, external rotators	0	80% (77-83%)	Flexion = 90 ° (90°) Abduction = 48 ° (45-50°)	0	0
T. Ji et al. [61]	3	LARS	Reattached to prosthesis wrapped in LARS: • Abductors Sutured to hip capsule: • Pectineus, external rotators, and psoas Sutured to LARS • gluteus tendon	0	78.9% (70-90%)	Flexion = 80° (60-100°) Extension = 10° (5-15°) Abduction = 28.3° (20-35°) Adduction = 16.7° (10-25°) Internal Rotation = 18.3° (10-3°) External rotation = 26.7° (20-30°)	0	0
Z. Du et al. [62]	58	LARS verse without LARS	Reattached to LARS: • Gluteus medius • Gluteus maximus • Iliopsoas If LARS was not used: • Abductors were sutured to either tensor fasciae latae or prosthesis directly or by trochanter osteotomy	LARS: 0% NonLARS: 26%	LARS = 80$\pm$3.7% NonLARS = 70.4$\pm$4.3% (NP)	LARS: Flexion = 73.3° Abduction = 39.3° External Rotation = 18.8° (NP) NonLARS: Flexion = 61.6° Abduction = 26.1° External Rotation = 17.7° (NP)	N/a	LARS = 3.92/5 NonLARS = 3.65/5

Abbreviations. MSTS93, Musculoskeletal Tumour Society Score 1993 Version; NP, Not Provided

3.3.2 Allograft Prosthesis Composite

Six papers used an allograft prosthesis composite (APC) to reconstruct the proximal femur [19], [63]–[67] (Table 5). An APC is comprised of a prosthesis inserted into a harvested cadaver bone such that the patients' muscles can be reattached to the cadaver tendons. Muscle strength was measured in different ways among the studies, including the manual muscle test (rated 0-5)[73], maximum isometric hip abduction using a dynamometer and resistance to hip abduction in lateral position (rated 0-5). Reattachment of the muscles to the APC also varied, including suturing the host tendons to the allograft tendons, attaching host tendons to allograft bone and trochanter osteotomy. APC reconstructions resulted in high MSTS scores (study means ranging from 75 to 90%) and good abductor strength (Table 5). Four of the papers showed resulting abductor strength ranging from 3.5-4.5 out of 5 [19], [63]–[65]. Muscolo et al. and Donati et al. reported marked Trendelenburg gait was present in only 26% (7/27) and 9% (2/22) of their cohorts respectively and Benedetti et al. showed no Trendelenburg gait present with their patient. Farid et al. found over 50% (11/20) of their APC group had abductor strengths of 5/5 and no Trendelenburg gait present, compared to their endoprosthesis group which had only had 2% (1/52) without Trendelenburg gait and abductor strength of 5/5.

Table 5. APC Muscle Details and Outcomes

Authors	**Number of Participants**	**Muscle Info**	**Mean MSTS93 Scores** (Range)	**Muscle Strength**	**Implant survival**
M. Benedetti et al. [63]	1	Reattached to insertion of allograft: • Iliopsoas muscle tendon • Gluteus max • Gluteus med Partially removed: • Vastus lateralis muscle • Vastus medialis muscles Not Reattached • External rotators	77%	Flexors 5/5 Extensors 4/5 Abductors 4/5 Adduction 5/5 Internal Rotator 4/5 External Rotator 0/5 (detached)	
Y. Farid et al. [64]	72	Allograft abductor reattachment techniques included: • Reattached to the allograft greater trochanter through drill holes (n=9) • Tendon to tendon reattachment (n=7) • Fixation of a host greater trochanter remnant to the allograft (4 patients) Attachment of abductor to endoprosthesis techniques included: • Tendon to prosthesis (36 patients) • Tendon to prosthesis suturing augmented with tenodesis to the iliotibial band (11 patients) • Reattachment of remnant greater trochanter to the prosthesis with sutures (5 patients)	APC = 82% Endo = 70% (NP)	Endo Abductor Strength= 3.3/5 APC Abductor Strength= 4.45/5 55% of allograft group had 5/5 abductor strength, verse 4% of the endo group	Endo: 5 year = 85.7 $\pm$ 0.06% 10 year = 85.7$\pm$ 0.07% 15 year = 81.8$\pm$ 0.07% APC: 5 year = 100% 10 year = 85.7$\pm$ 0.13% 15 year = 85.7$\pm$ 0.13%
A. Dubory et al. [19]	46	• Gluteus Medius muscle was attached at the corresponding allograft ligament or fixed on the allograft GT if the gluteal bone insertion had been preserved • Iliopsoas was sutured to allograft lesser trochanter • 84% of patients had insertion of gluteus medius muscle tendon to tendon • 15% had insertion of gluteus medius muscle bone to bone • 15% of patients had a bone graft at the junction allograft to host bone	75% (15-29)	Abductor Strength = 3.5/5 (2-5)	Overall revision-free survival at: 5 years = 73$\pm$ 0.07% 10 years = 54.1$\pm$ 0.8% Femoral stem survival at: 15 years 81.4$\pm$ 0.6% 10 years = 91.3$\pm$ 0.4%
F. Langlais et al[65]	21	Three techniques of abductor reattachment were used: • 1: trochanteric osteotomy (5/11) • 2: tendon reattachment to combined allografts (5/11) • 3: miscellaneous reinsertion (1/11)	77% (43-97%)	Long term patients: • Average abductor strength 4.36/5 (2-5) Short term patients (<2 years) • Abductor strength = 3/5 or 4/5 in 8 patients, and non-functional in two patients who	10 years = 81%

				had excision of the gluteus muscles	
D. Luis Muscolo et al.[66]	38	• 73% of patients had the abductor mechanism sutured to the corresponding tendons of the allograft (tendon on tendon) • 26% of patients had abductor muscles reattached to the graft through a wire to screw	90% (77-100%)		5 year survival = 72% 10 year survival = 69%
D. Donati et al. [67]	27	• Rectus femoris was spared • Vastus lateralis was partially or mostly sacrificed • Vastus med and adductor muscles were only partially removed • Tendons of the gluteus maximus, medius, minimums and iliopsoas muscles were preserved as much as possible and sutured to the corresponding tendons of the allograft (tendon on tendon) • Glute max tendon was not reattached to its anatomical place, and the tensor fasciae latae was closed around the reconstruction	92% (75-100%)	All patients had good strength of quadriceps, iliopsoas, and glute muscles	

Abbreviations. MSTS93, Musculoskeletal Tumour Society Score 1993 Version; NP, Not Provided; GT, Greater Trochanter; Endo, Endoprosthesis; APC, Allograft Prosthetic Composite

3.3.3 Muscle Reattachment

Nine papers used three different approaches of muscle reattachment [64]–[72], [74] (Table 6), including reattaching abductor tendons directly to endoprosthesis or allograft [64], [69], [71], [72], [74], tendon to tendon/muscle [64]–[67], [70], and trochanter osteotomy[64], [65], [68]–[71]. MSTS scores for all three groups ranged from 59-91% depending on the muscle reattachment approach (Table 6).

Of the papers that reported results for direct muscle to endoprosthesis attachment, the MSTS scores were good, but rates of positive Trendelenburg gait were high. Bickels et al. found 81% of their direct to prosthesis attachment group to have excellent or good MSTS scores and none of the patients needed walking assistive devices. Groundland et al. reported that 62.5% (15/24) of those with their abductors attached directly to the prosthesis had Trendelenburg gait, and 66% (16/24) of these patients required walking supports.

Four papers specified results for soft tissue repair, including muscle/tendon reattached to muscle or allograft tendon. The mean MSTS scores for the four papers with soft tissue repair ranged from 70-92%. Langlais et al. reported abductor strength of 4.4/5 after soft tissue repair and Donati et al. found all soft tissue repair patients to have good strength of the quadriceps, glutes, and iliopsoas.

3.3.4 Trochanter Osteotomy

Trochanter osteotomy (TO) was commonly used when tumor margins and soft tissue involvement allowed the greater trochanter to be preserved. Although trochanter osteotomy was the preferred method for some surgeons in an effort to preserve as much of the native anatomy as possible, in many cases TO did not produce superior results to other techniques such as soft tissue repair, or direct to prosthesis [70],[71]. Langlais et al. was the only study to report better MSTS scores for TO compared to soft tissue reconstruction of the abductors (83% and 77%), but also noted that the soft tissue group had a more extensive resection than the TO group, and still maintained a high MSTS score. Abductor strength was also similar between TO and soft tissue repair in the study by Langlais et al. Ogilvie et al. found TO repair MSTS and TESS scores to be similar to those who received no soft tissue repair. Muscolo et al. had a mean MSTS of 86% for those with TO but found 50% (3/6) to have Trendelenburg gait. Groundland et al. found that 89% (26/29) of the TO group had Trendelenburg gait and 82% (23/29) needed an assistive device for walking.

Complications after TO were not uncommon in the papers included in the review. Muscolo et al. TO cohort had 83% (5/6) with non-union of the greater trochanter. Oglivie et al. had 11% (1/9) loss of trochanter screw fixation. Langlais et al. reported non-union at the trochanter in 18% (2/11) of the long term follow up patients at a mean of 10 years post-op. Groundland et al. found 44.8% (13/29) of those with TO had disassociation and migration of the trochanter from the endoprosthesis.

Table 6. TO, Soft Tissue Reattachment and Direct to Prosthesis Muscle Details and Outcomes

Author	Number of Participants	Muscle Info	Mean MSTS93 (Range)	Muscle Strength	Trendelenburg Gait	Functional Outcome
V. Crenn et al. [68]	31	Trochanter osteotomy maintaining glute medius and vastus lateralis attachments (digastric reinsertion) in 68% of patients	Digastric: 75.6% (27-100%) Non-Digastric: 75.1% (53-97%)	Digastric muscle strength conservation: • Abduction = 66% • Adduction = 78% • Flexion = 66% • Manual muscle test = 4/5 Non-Digastric: • Abduction = 36% • Adduction = 75% • Flexion = 72% • Manual muscle test = 3.5/5		• Severe limp (19% verses 60%) and medallion migration were less common with digastric reinsertion • Those with digastric trochanteric reinsertion with standard offset showed the best abduction conservation (76.7%) • No significant difference was seen in MSTS, TESS or adduction and flexion strength between groups • Those with digastric reinsertion had significantly better abductor strength conservation
J.M. Philippeau et al. [69]	71	3 types of surgical methods: • type 1 (28 cases) (25/38 metastasis, 3 primary): preserve abductor muscles • type 2 (21 cases) (8 MS, 13 P): gluteus medius tendon to prosthesis or greater trochanter osteotomy • type 3 (22 cases) (5MS, 17P) resection of gluteus medius muscle or nerve	Metastasis = 68$\pm$23.5% (majority had type 1) Primary = 59$\pm$17.5% (majority had type 2 or 3)			• Major dislocation risk was the weak hip abductor muscles • Primary tumor group had majority of type 3 surgery (17/22) and had poorer functional outcomes • Type 3 surgery was associated with dislocation • 30 metastasis patients required walking supports • 26 primary tumor patients required walking supports
Y. Farid et al. [64]	72	APC: • reattachment direct to allograft (n=9) • direct tendon to tendon reattachment (n=7) • trochanter osteotomy (n=4) Endo: • direct tendon to prosthesis (36 patients) • direct tendon to prosthesis augmented with tenodesis to the iliotibial band (11 patients) • trochanter osteotomy (n=5)	APC = 82% Endo = 70% (NP)	Endo Abductor = 3.3/5 Allograft Abductor = 4.45/5	•Over 50% of allograft group had no Trendelenburg gait •All but 1 patient in an endoprosthesis walked with Trendelenburg gait of varying severity	• Type of abductor tendon attachment was not associated with differences in hip abduction strength • Majority of endoprosthesis group had reattachment tendon to prosthesis (47/52) and had lower MSTS than allograft group • 55% of allograft group had 5/5 abductor strength, verse 4% of the endo group

C. M. Ogilvie et al. [70]	33	• Type 1: No soft tissue repair was done (n=8) • Type 2: Patients had soft tissue repair (n=16) (tendon to muscle) • Type 3: Trochanter was reconnected (n=9) (trochanter osteotomy)	Type 1= 64.1% Type 2= 70.4% Type 3 =66.0% (40-93%)			• Trend towards better function in patients with type 2 than type 1 but not statistically significant • Strength and use of supports scored higher for type 2 than type 1 • Stability scored better for type 3 than type 1
J. Groundland et al. [71]	53	• Type 1: reattach abductors to endoprosthesis via soft tissue repair only (45%) • Type 2: greater trochanter osteotomy with reattachment of the bony greater trochanter to the proximal femur endoprosthesis (54%)			Type 1 = 62.5% had Trendelenburg gait Type 2 = 89% had Trendelenburg gait	• Type 2 had a trend of increased need for assistive ambulatory device compared to type 1 group • 44% of those who had type 2 had subsequent dissociation and proximal migration of the greater trochanter from the endoprosthesis • Type 2 had 48% trochanteric failure • No statistical difference in need for assistive device or Trendelenburg gait between trochanter group with bony failures and not •Type 1: 66% need an assistive ambulatory device •Type 2: 82% needed an assistive ambulatory device
F. Langlais et al. [65]	21	• Type 1: trochanteric osteotomy (5/11) • Type 2: tendon reattachment to combined allografts (5/11) (tendon to tendon) • Type 3: miscellaneous reinsertion (1/11)	Type 1 = 83.2% Type 2 = 77.4% (43-97%)	Mean abductor Strength Long term patients (10 years): • Type 1: 4.8/5 • Type 2: 4.4/5 Short term patients (<2 years) • 8 patients had 3/5 or 4/5 and 2 patients had non-functional abductors due to excision of the gluteus muscles		• Abductor function had the greatest effect on results • Type 2 group tumors required more resection of the gluteal muscle tendons
D. Luis Muscolo et al. [66]	38	• Type 1: 73% tendon on tendon • Type 2: 26% trochanter osteotomy	Entire group =90% Type 1 =91% Type 2 = 86% (77-100%)		• Type 1: 19% had Trendelenburg gait •Type 2: 50% had	83% of Type 2 group had non-union

					Trendelenburg gait	
D. Donati et al. [67]	27	• Spared: Rectus femoris • Partially/mostly sacrificed: Vastus lateralis • Partially removed: Vastus medialis and adductor muscles • Gluteus maximus, medius and minimus and iliopsoas tendons were preserved as much as possible and sutured to the allograft tendons (tendon on tendon)	92% (75-100%)	All patients had good strength of quadriceps, iliopsoas, and glute muscles	• 52% had no Trendelenburg gait • 22% had slight Trendelenburg gait • 7% had a marked Trendelenburg gait and needed a cane for walking indoors	• zero patients had pain or an unstable joint • passive ROM of the hip was similar to normal • active abduction of the hip exceeded 30 degrees
J. Bickels et al. [72]	57	• Reattachment of the abductor mechanism to the prosthesis and extracortical bone fixation • If possible greater trochanter is osteotomized • Vastus lateralis was preserved and overlie the abductor muscles fixation • Capsule and acetabulum were spared • Psoas muscle was reattached the anterior capsule • Remaining muscles are sutured to the vastus lateralis anteriorly and the hamstrings posteriorly	81% of patients had a good to excellent functional outcomes, and 19% had fair outcomes (NP)		16% had Trendelenburg gait	• None of the proximal femur group needed walking aids

Abbreviations. NP, Not Provided; MS, Metastasis; P, Primary; Endo, Endoprosthesis

3.4 Discussion

3.4.1 Artificial Ligament or Mesh

In all three cases, the use of a mesh or artificial ligament provided good functional outcomes with high MSTS scores, absent Trendelenburg gait, and low instances of walking supports required [60]–[62]. Similar results were found by Bugelli et al. when analysing outcomes for ACL repair using LARS, attributing good kinematic results to the LARS ability to support tissue regrowth [75]. Not only did the mesh and LARS produce good MSTS scores and low incidence of Trendelenburg gait, but also reduced incidents of dislocations, one of the most common complications for hip reconstructions, especially when soft tissue resection is involved [62],[76],[77],[78],[79]. Henderson et al. and Ji et al. had no dislocations in their cohorts. Du et al. found their cohort with LARS had significantly reduced rates of dislocations compared to the cohort without LARS. Xin et al. had similar findings when using a mesh for participants with a high risk of dislocation after hip arthroplasty, resulting in zero (0/51) dislocations in their mesh cohort [80]. Frequent dislocations after proximal femur reconstruction are linked to abductor deficiency, hip joint capsule, tension of muscles across the hip joint, and acetabulum shape [81],[82]. Synthetic materials support hip stability by providing additional fixation about the hip to supplement the soft tissue resected during surgery, resulting in a more stable hip joint capsule and stronger muscle reattachments. The ability to securely reattach muscles to the synthetic material while supporting tissue ingrowth for additional strength over time allows for a superior mechanical advantage than reattaching impacted native muscles to an endoprosthesis alone.

A limitation of the studies on mesh and LARS is the small cohort sizes. Henderson et al. and Ji et al. had 2 and 3 participants in their study respectively. In the study by Du et al. they recommended all patients to receive the artificial ligament, but only 12 of the 58 consented to receiving it. Although synthetic materials such as the LARS have been around since the 1990s there is a lack of uptake for proximal femur reconstructions, resulting in patients' hesitancy towards receiving it as seen in Du et al [83]. Continued research is required to gain a better understanding of the potential benefits of using synthetic materials for limb salvage procedures.

3.4.2 Allograft Prosthesis Composite

The six APC papers included in the current study resulted in low incidences of Trendelenburg gait, as well as good MSTS scores and muscle strength. Farid et al. showed that APCs have potential to provide better functional outcomes than endoprosthesis, with the APC group producing higher MSTS scores and abductor strength. Farid's link between high abductor strength and absent Trendelenburg gait also highlights the importance of abductor reattachment on functional ability [64]. Benedetti et al. found similar results when comparing functional outcomes of modular prosthesis (MP) to APCs for proximal femur sarcoma reconstructions. Benedetti et al.

found the MP group to have a greater reduction in hip strength, walking speed, cadence and stride length compared to the APC group. The group contributed the reduction in hip muscle strength in the MP patients to the reattachment of the hip muscles to the prosthesis, potentially changing the muscle tension and lever arm, effectively altering the muscles' ability to produce the same moment at the hip [8]. The force output required by the hip muscles needs to increase to compensate for reduced lever arm of the abductors. This results in less efficient mechanics around the hip, that require more effort from the impacted abductor muscles. In addition, altering the muscle tension can negatively impact a muscles ability to produce a larger force. The high functional scores associated with APC are attributed to the ability to reattach the native muscles to the corresponding anatomical attachment sites or tendons [8]. This method creates good fixation for the muscles to reattach which results in high abductor strength conservation after reconstruction [19], [64], [65], [67].

Due to better muscle reattachment, APCs have been reported to provide more stability at the hip and reduce the likelihood of dislocation [58]. The average dislocation rate for the six APC papers was 3.1%. All dislocations occurred in implants with an acetabular component. Low dislocation rates for allografts have been reported in other series, including Fox et al. who reported zero dislocations in a group of 137 APC patients at a mean of 7.9 years follow up [84]. Min et al. had similar findings with zero dislocations at a mean of 4.7 years post-op in their cohort of 28 patients who received a proximal femur APC for sarcoma [85].

Although APCs provide good functional outcomes with high MSTS scores and abductor strength, they do have common complications to consider as well, such as infection, non-union, and allograft fracture. While infection is a common concern for allografts, as APC procedures are time consuming and involve a large amount of dead bone, the infection rates for the six APC papers reviewed were low, ranging from 0-8% with an average of 4%. In Janssen et al.'s 2019 systematic review, APC patients had three times as many incidences of infection requiring revision as endoprosthesis patients, with APCs having an infection rate of 6.5% verses endoprostheses which only had 2.1% [37]. In Janssen et al.'s, APC reconstructions had a revision rate of 19% whereas endoprostheses had a revision rate of 10%. In the systematic review, structural failures such as peri-prosthesis or prosthesis fracture were the cause of 2.2% of endoprosthesis revisions compared to the 8.3% of APC revisions, which were related to fracture, non-union and resorption [37]. In the APC papers reviewed in the current study, structural failures were common, non-union ranged from 8-36% and allograft fracture ranged from 5-63%. In a study of APCs by Hornicek et al., it was found that patients with non-union had worse functional outcomes than those without. The study also showed that receiving chemotherapy increased patients' risk of non-union, and that patients with adjuvant radiation had less union with the allograft [86]. APCs may have potential to provide better functional outcomes than endoprosthesis, but high rates of complications negatively affect functional results and implant survival commonly leading to revision. Endoprosthesis complication rates tend to be lower providing better long-term results even though MSTS scores may not be as high.

In addition to the difficulties that arise from complications, allografts are not always an option due to limited supply. APCs require harvested cadaver bone that is appropriately sized for the patient, thus are not as readily available and can be harder to supply then off the shelf endoprosthesis. Ropars et al. reported in France the availability of bone grafts for APC's is poor, which is one of the reasons why endoprostheses are more common [7]. Ultimately endoprostheses tend to be used more often than APCs because of their reduced risk of complications and off the shelf availability.

3.4.3 Trochanter Osteotomy

Trochanter osteotomy allows for a reconstruction that preserves more patient anatomy, but the current review found that TO produced similar or inferior results to soft tissue repair. Poorer than anticipated outcomes may be due to the high incidences of complications as seen in the papers reviewed in the current study including non-union and trochanter migration. Non-union of the greater trochanter can lead to dislocation, pain and reduced strength of the abductor muscles [87].

To reduce common complications of TO, Crenn et al. analysed a group who had digastric TO, maintaining glute medius and vastus lateralis attachments to the greater trochanter and non-digastric reconstruction. Digastric reinsertion significantly reduced trochanter medallion migration as well as severe limp and improved abductor strength conservation (36.0% vs 66.6% conservation). Even with significant improvements in trochanter migration and abductor strength similar MSTS and TESS scores were reported for digastric and non-digastric groups. Within the study's cohort there was a mix of standard and small femoral offset prosthesis used, which can impact abductor lever arms and ultimately hip moments. Similar MSTS and TESS outcomes may be due to the variation in femoral offsets used which were distributed amongst both cohorts.

Bal et al. used an anterior trochanteric slide osteotomy for THA and found that non-union rates were less than 10% but hardware fixation complication rates were too high to recommend the surgical technique [87]. Even when using different variations of TO such as a digastric approach or TO slide, superior patient/clinician reported functional scores to alternative techniques are not achieved. Beck et al. determined that greater trochanter position after osteotomy can negatively affect the balance of the gluteus medius muscle leading to an undesirably lever arm, and both stretching or shorting of the muscle causes a reduction in muscle strength [88]. Although TO may produce good fixation between the abductor muscles and greater trochanter leading to the assumption that better strength would be achieved, the location of the greater trochanter can negatively impact abductor moment arms often leading to worse outcomes than reattaching the abductors to soft tissue or directly to prosthesis.

It has been shown in the literature reviewed that abductor muscle strength can impact MSTS scores, and Trendelenburg gait. The constant factor throughout the three themes presented is the focus on conserving muscle strength through secure muscle reattachments. TO produces a secure attachment of the muscles to the native greater trochanter, but complications related to the union of the greater trochanter to the prosthesis are common. Additionally, abductor lever arms are greatly affected by greater trochanter location, often leading to reduced abductor moments causing poor functional outcomes. APCs produce secure muscle reattachment by allowing native muscles and tendons to connect to cadaver tendons, producing a result that resembles natural anatomy and joint biomechanics. For these reasons APC tend to produce advantageous functional outcomes compared to endoprostheses, but high rates of complications negatively impact limb function and often lead to revision. The use of synthetic materials such as LARS and mesh provide an interesting alternative to TO and APC. The synthetic materials improve hip stability and allow for secure muscle reattachment that encourage muscle regrowth, strengthening the muscle attachment over time. Synthetic materials also had low complication rates unlike TO and APCs. Although synthetic materials have been around for decades and have the potential to produce better functional outcomes for LSS there is a lack of uptake for proximal femur reconstructions. We recommend that future work incorporate synthetic materials for limb salvage surgery to gain a better understanding of the potential benefits.

3.5 Limitations

There are limitations to comparing the muscle attachment approaches for the papers included in the review. Many of them had small cohorts or a large group who received one approach and a very small group who received another approach such as Muscolo et al. study. As well, there are many factors involved in limb salvage that impact the ability to accurately compare two methods. In Langlais et al., the trochanter osteotomy group had slightly better MSTS scores than those with soft tissue reattachment, but the soft tissue group had on average a more invasive surgery with more muscle resected. Studies also use different prosthesis, some using a mix of total hip and bipolar [19], [64], [67], [70], [71] which may affect rates of hip instability [89]. Within study cohorts, there tends to be a lot of variability in the methods used for proximal femur reconstruction including implant type, muscles sacrificed and method of reattachment. This variability makes it difficult to form conclusions within study cohorts and especially when comparing different study results.

As reporting functional outcomes has begun to be a focus for limb salvage research, subjective patient or clinician reported outcomes are the most common measures of limb functionality. These scoring systems such as MSTS, TESS and HHS can vary from study to study and do not provide granular detail on what caused improvements [8]. Other areas of research including hip arthroplasty for osteoarthritis have been utilizing technologies such as instrumented gait analysis to objectively analyse the kinematics and kinetics of patients gait before and after surgery[46],[90]. Even though gait analysis has been used for decades for hip and knee arthroplasty, it is not as commonly used for sarcoma patients after limb salvage surgery [8]. In the current review Benedetti et al. was the only study that used instrumented gait analysis, but only included one participant. In a recent systematic review by Filis et al. on studies analysing functional outcomes after limb salvage surgery for the lower extremities with gait analysis, 8 studies were found that used gait analysis for this population, just one of which exclusively focused on proximal femurs. Filis et al. found that limb salvage surgery negatively impacted patients gait compared to healthy controls resulting in significantly reduced gait velocity, cadence and stride length, as well as an increase in cycle time [91]. The group that focused on the proximal femur found that sagittal and coronal plane hip range of motion, and hip flexion, adduction and external rotation moments were significantly reduced compared to controls [8]. Kinematic and kinetic outcomes from gait analysis provide information that is not only objective but can show more joint-specific differences in results between participants.

Due to small cohorts and variability between patients' procedures, forming conclusions on improvements in surgical approach can be very difficult. There is potential to gain an objective understanding of the effects of implant design and surgical approach on functional outcomes when utilising computational modeling powered by instrumented human movement analysis, such as gait analysis [45], [44]. Musculoskeletal computational modeling has been used in hip and knee arthroplasty to simulate surgical outcomes and explore the effect of musculature on gait kinematics and kinetics. Myers et al. used computational musculoskeletal modeling to simulate the effect of hip abductor strengthening on joint reaction forces of the hip, knee, ankle and back [46]. Myers et al. not only determined that increased abductor strength reduced peak joint contact forces in all four joints when compared to pre-operative data, but also found that reductions in joint reaction forces were most sensitive to strengthening of the tensor fasciae latae (TFL) and gemellus. This is interesting as a lot of focus on abductor strength is placed on the larger gluteus medius and minimus, potentially overlooking the effects of the TFL and gemellus on hip biomechanics. Information on how the TFL and gemellus affect joint reaction forces have the potential to help inform surgical approaches for limb salvage reconstruction. Musculoskeletal modeling can be used in future work to explore if prioritizing specific hip muscles during limb salvage surgery and post operative rehabilitation produces better functional outcomes.

Bahl et al. conducted a study using data from CT scans and instrumented gait analysis to create musculoskeletal models of patients before and after total hip arthroplasty [90]. Bahl et al. concluded from their modeling that increasing abductor lever arm length by changing the center of rotation at the hip, reduced abductor muscle force and hip joint contact forces during walking. Musculoskeletal modeling that simulates gait dynamics could be used to inform proximal femur reconstruction for sarcoma, where weak abductor muscles are common after surgery. Increasing lever arms of abductor muscles, in turn reducing required abductor force could reduce incidences of Trendelenburg gait and improving limb function. Elements of limb salvage surgery such as implant selection can affect hip joint center offset and femoral neck length impacting joint moments and ultimately muscle force requirements [92]. These small changes between implants may have larger influences on functional results that could be overlooked when using subjective or more global functional outcomes.

Using musculoskeletal models to predict patient post-op function, can remove the complexities of LSS variability, to allow for isolated changes in hip musculature to simulate the impact on hip biomechanics. Using technology to simulate surgical interventions removes uncertainties in results caused by additional surgical factors such as implant design and varying oncological margins. This understanding can inform improvements in surgical technique and implant design based on objective biomechanical analysis, that is capable of utilising muscle lever arms and muscle tensions to the patients' advantage leading to more efficient hip biomechanics that compensate for muscle defects due to resections.

3.6 Conclusion

Proximal femur reconstruction surgery for sarcoma is a complex procedure with constraints that vary from patient to patient to achieve good oncological outcomes. Trochanteric osteotomy does not necessarily provide better outcomes than soft tissue or direct to prosthesis muscle reattachment, despite preserving more of the natural anatomy. APCs have been shown to produce high MSTS scores, high muscle strength, and low Trendelenburg gait. However, they can have high rates of complications and issues with availability of cadaver bone. LARS and mesh produce good hip stability, high MSTS scores due to the ability to reattach muscles securely to the synthetic material and low incidences of complications unlike APC and TO. There is a gap in current literature on analysing functional outcomes of proximal femur sarcoma with objective technology such as instrumented gait analysis and computational modeling simulations. Further research should explore using objective tools to analyse functional outcomes to gain a better understanding proximal femur reconstruction, to produce better outcomes for patients.

Chapter 4 Impact of Limb Salvage Surgery for Proximal Femur Sarcoma on Healthy Gait Patterns Using a Patient Specific Musculoskeletal Model

4.1 Introduction

Sarcoma of the proximal femur is a cancerous bone tumor that occurs at the hip joint. It is most common in people under the age of 20 who are otherwise healthy [3]. The main method of treatment for proximal femur sarcoma is lower limb salvage surgery (LSS), a highly invasive procedure where the cancerous bone is removed and replaced with an orthopedic implant[1]. During limb salvage surgery, the natural anatomy of the hip is greatly impacted and varies patient to patient depending on oncological implications, surgical technique, and implant design. These changes affect hip joint biomechanics and ultimately gait patterns of patients after surgery. Compared to healthy controls, patients have been found to have lower walking speeds, stride lengths, and hip range of motion[8].

Previous studies focusing on functional outcomes after LSS for proximal femur sarcoma have primarily used subjective patient or clinician reported functional outcomes, with the most frequently used being the Musculoskeletal Tumor Society Score (MSTS)[57]. The MSTS score comprises of six sections, each with a maximum score of five. MSTS scores are often presented as a percentage with higher scores representing better limb function. In a 2019 systematic review, it was reported that MSTS scores ranged from 56-94% after proximal femur limb salvage surgery for sarcoma[37]. The subjectivity of functional outcome measures like the MSTS score can cause results to vary greatly between studies. These outcome measures do not provide the specificity of the impact on hip biomechanics required to provide useful insights for surgical technique and implant design innovations that could improve functional outcomes for patients.

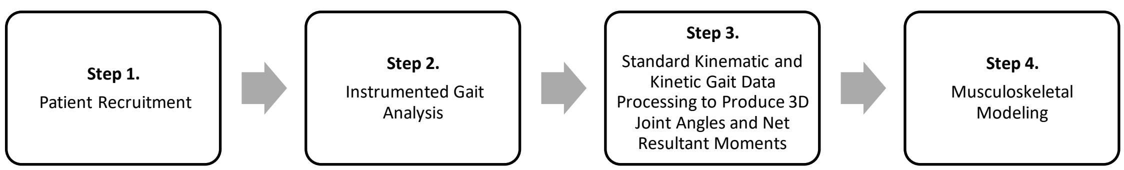
Tools such as instrumented gait analysis can provide objective functional outcomes after LSS including spatiotemporal factors, joint angles, and joint reaction moments. Although gait analysis has the potential to provide objective insights to proximal femur LSS, it has not been widely used for this patient cohort and is limited by small cohort size and patient variation. Typical gait parameters such as spatiotemporal factors, joint angles, and net resultant moments alone do not provide a comprehensive understanding of which element of LSS caused an improvement in function, as cohorts tend to vary in oncological margins, soft tissue resection, implant design and surgical technique. Computational musculoskeletal modeling is a tool that allows for the simulation and study of dynamic human movement biomechanics [44]. Musculoskeletal modeling takes instrumented gait analysis one step further, using kinematic and kinetic data from instrumented gait analysis to simulate a specific component of surgery on patient specific models. Surgical simulations provide the specificity and control to determine how altering hip biomechanics impacts patients' gait. These modeling techniques have been used extensively in other applications, including hip arthroplasty for osteoarthritis [46], but have not been widely used to simulate proximal femur limb salvage surgery.

The objective of the current study is to use a patient-specific musculoskeletal model to investigate how simulated limb salvage surgery for proximal femur sarcoma impacts the ability of a patient to achieve healthy gait kinematics. This will be achieved using a musculoskeletal model and recorded gait kinematics, kinetics, and surface electromyography specific to a single participant who received limb salvage surgery for proximal femur sarcoma. It is hypothesized after a large reduction in gluteus medius, gluteus minimus and piriformis muscle strength due to LSS, healthy gait kinematics will not be achievable.

4.2 Materials and Methods

Figure 6 provides the workflow used for the current study.

Figure 6. Workflow of Simulating Surgical Intervention on Patient Specific Model



Step 1. Patient Recruitment

The goal for recruitment was to collect comprehensive data from one participant. The inclusion criteria were proximal femur reconstruction for oncologic indication, at least 1-year post-operative from surgery, no history of infection/re-operation, available pre-operative imaging, detailed operating room notes to determine resected musculature and reconstruction techniques, ability to ambulate down a walkway independently without an assistive device, and over the age of 18 years. The exclusion criteria included proximal femoral reconstruction for non-oncologic indications, local recurrence or infection requiring re-operation/re-resection, radiotherapy given in the perioperative period to the affected limb and history of neurological disease that would affect gait (i.e. neurological disease). The study was approved by the local ethics board.

Step 2: Instrumented Gait Analysis

At 16 months after surgery, the participant visited the Dynamics of Human Motion (DOHM) lab at the School of Biomedical Engineering at Dalhousie University for instrumented gait analysis. The participant’s demographic and anthropometric data were collected.

Before starting the gait analysis, calibration of all equipment was completed. A four-camera bank (12 camera) Optotrak^{TM} Certus system (NDI) synchronized with an in-ground AMTI^{TM} (AMTI) force plate was used to record the three-dimensional kinematic and kinetic data throughout the gait cycle. 16 infrared markers were placed on the participant, including anatomical landmarks on the shoulder (SH), lateral epicondyle (LE), greater trochanter (GT), lateral malleolus (LM), and three-infrared marker triads on the sacrum, thigh, shank, and foot of the surgical limb. During a quiet standing trial, 12 virtual markers were defined including medial epicondyle (ME), medial malleolus (MM), first metatarsal (1MT), second metatarsal (SM), fifth metatarsal (5MT), heel, fibular head (FH), tibial tuberosity (TT), left and right anterior superior iliac spine (ASIS), and posterior superior iliac spine (PSIS).

In addition to gait kinematic and kinetics, muscle activation patterns of major lower extremity muscles were measured using simultaneous surface electromyography (EMG). EMG data was recorded for 8 muscle sites: the quadriceps (vastus lateralis, VL; vastus medialis, VM; rectus femoris, RF), hamstrings (lateral, LH; medial, MH), gastrocnemius (lateral, LG; medial, MG), and gluteus medius (GM), with waveform signals calculated from the raw EMG signals using standard procedures previously reported [11]. Silver/silver chloride bipolar surface electrodes (0.79 mm^2 contact area, Bortec Inc, Calgary, Alberta) were placed in line with the muscle fibres of each muscle. A reference electrode was placed on the tibial shaft.

Once the markers and EMG electrodes were secured at the appropriate anatomical locations, the gait analysis began. A one second standing calibration trial with the participant standing comfortably in the middle of the viewing volume was recorded. After a brief warm-up including a few lengths of the room, the participant completed five recorded walking trials along a six-meter walkway, at a self-selected speed that reflects their natural gait patterns. The Optotrak system collected three-dimensional positional data of the infrared markers at 100 Hz. The inground force plate synchronized with the motion capture system recorded the ground reaction force and moment data at 2000 Hz. The EMG system was also synchronized with the motion capture system and recorded signals at 2000 Hz. The raw EMG signals were pre-amplified 500x then further amplified (bandpass 10 – 1000 Hz, CMRR = 115 dB (at 60 Hz), input impedance ~ 10 Gohm) using an eight-channel surface EMG system (AMT- 8 EMG, Bortec Inc., Calgary, Alberta).

After the walking trials, a participant bias and noise trial in which the participant was lying supine and completely relaxed was recorded. The participant then completed a series of EMG normalization exercises using a Biodex^{TM} dynamometer designed to elicit maximum voluntary isometric contractions (MVICs) and muscular strength of quadriceps, hamstrings, gastrocnemius and gluteus muscle groups [93]. Exercises consisted of knee extension and flexion during sitting with the knee at 45 and 55 degrees, respectively, long sitting plantar flexion, and hip abduction in side-lying.

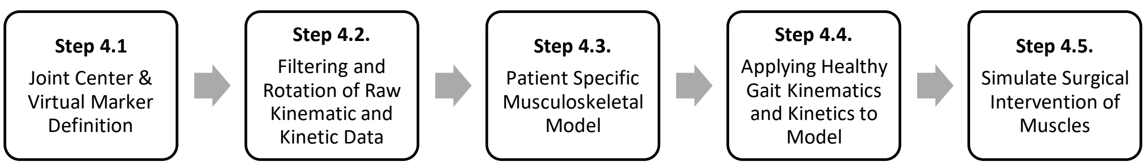
Step 3: Standard Kinematic and Kinetic Gait Data Processing to Produce 3D Joint Angles and Net Resultant Moments

Standard 3D kinematic and kinetic modeling algorithms were used to provide 3D lower extremity joint angles and net resultant joint moments during gait. Angles were calculated using a Cardan sequence consistent with the Joint Coordinate System [40], and net resultant kinetics were calculated based on an inverse dynamics procedure [13][94][95]. EMG signals were also processed using a standard procedure, where signals were full wave rectified, low pass filtered at 6 Hz, corrected for subject bias and amplitudes were normalized to maximum voluntary isometric contractions [93]. All EMG, and kinematic data except for knee adduction and rotation angles were time normalized to 100% of the participant's gait cycle. Kinetic data, as well as knee adduction and rotation angles were time normalized to 100% of the participant's stance phase of their gait cycle.

Step 4: Musculoskeletal Modeling

A patient specific model was created using the workflow in Figure 7.

Figure 7. Patient Specific Musculoskeletal Model Workflow



Step 4.1: Joint Center & Virtual Marker Definition

Visual3D (C-Motion Inc.), a software for biomechanical modeling, analysis, and processing, was used to calculate joint centers, and apply virtual markers from the static trials to the motion trials. The patient's raw positional data from the static and motion trials was imported to Visual 3D and interpolated to solve for gaps in marker data. A third order polynomial spline interpolation, using three data points before and after a gap in data to determine the polynomial coefficient and allowing a maximum of 10 frames of data to be interpolated ensured all markers were present throughout the entire gait cycle. Virtual markers recorded during the standing trials including ME, MM, 1MT, SM, 5MT, left and right ASIS, and PSIS were defined relative to the triad markers and applied to the motion trials in Visual3D. Hip, knee and ankle joint centers were calculated for the static, and motion trials. Hip joint centers were defined based on the CODA pelvis (Charnwood Dynamics)[96], [97]. The knee joint center was calculated to be halfway between the lateral and medial epicondyles. The ankle joint center was created halfway between the lateral and medial malleolus. Joint centers were calculated using the following equations.

$$Right\ Hip\ Joint\ Center\ (x, y, z) = ([0.36 * ASIS\ Distance], [-0.19 * ASIS\ Distance], [-0.3 * ASIS\ Distance]) \quad (5)$$

$$Left\ Hip\ Joint\ Center(x, y, z) = ([-0.36 * ASIS\ Distance], [-0.19 * ASIS\ Distance], [-0.3 * ASIS\ Distance]) \quad (6)$$

$$Knee\ Joint\ Center\ (x, y, z) = ([0.5 * Knee\ Distance], [0.5 * Knee\ Distance], [0.5 * Knee\ Distance]) \quad (7)$$

$$Ankle\ Joint\ Center\ (x, y, z) = ([0.5 * Ankle\ Distance], [0.5 * Ankle\ Distance], [0.5 * Ankle\ Distance]) \quad (8)$$

Where *ASIS distance* is the distance between the right and left anterior iliac spine, *knee distance* is the distance between the medial and lateral epicondyles, and *ankle distance* is the distance between the medial and lateral malleoli.

Step 4.2: Filtering and Rotation of Raw Kinematic and Kinetic Data

Once the joint centers and virtual markers were present throughout all the trials, they were exported to Matlab. Opensim [44], an open-source musculoskeletal modeling software, was used to create a patient specific model to analyse the patient's motion and simulate surgical outcomes. The DOHM laboratory global coordinate system was oriented relative to the participant with x backwards, y right and z up. OpenSim's coordinate system is x forward, y up and z right. In Matlab the experimental data was rotated 270 degrees about the x axis and 180 degrees about the y axis to be compatible with OpenSim. Matlab was also used to filter the raw kinematic and kinetic data from the motion and static trials with a dual pass second order Butterworth filter with a cut off frequency of 6Hz. The filtered data were then exported as .trc files to be compatible with OpenSim.

$$[b, a] = butter(n, Wn) \quad (9)$$

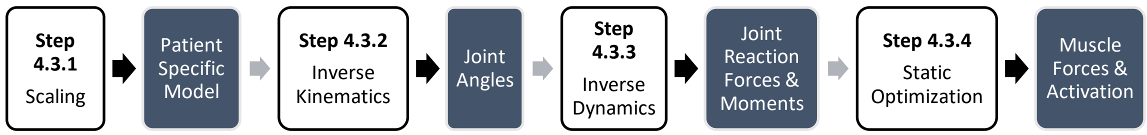
$$Filtered\ Data = filtfilt(b, a, data) \quad (10)$$

Where W_n is the cut off frequency, *n* is the filter order, *b* and *a* are the transfer function coefficients.

Step 4.3: Patient Specific Musculoskeletal Model

Opensim was used to create the patient specific model utilising the filtered kinematic and kinetic data. The generic Gait2392 model which focuses on the lower limbs and has been used in previous studies to analyses hip biomechanics simulations was selected as the basis of the patient specific model [47], [48]. Once the Gait2392 model was selected, the following workflow (Figure 8) was used to create the patient specific model. The modeling steps are shown in the white boxes, and the output of each step is shown in the navy boxes.

Figure 8. Musculoskeletal Modeling Workflow



Step 4.3.1: Scaling

The generic Gait2392 model was scaled to simulate the participants anatomy, including height, mass, and limb segment lengths. 20 virtual markers representing the anatomical markers applied to the participant at the DOHM were added to the model including the shoulder, left and right ASIS, left and right PSIS, greater trochanter, medial and lateral epicondyles, medial and lateral malleoli, fibular head, tibial tuberosity, heel, and toes. Markers were added to the model at the origin of the femur, tibia, and talus for the hip, knee, and ankle joints centers respectively. The model markers were used to scale the model body segments, muscles, and mass to the anatomy of the patient. The scale factors for each body segment were determined by dividing the distance between two markers on the model by the distance of the same markers from the static trial. The pelvis, femur and tibia were scaled using the hip, knee, and ankle joint centers. The torso scale factor was calculated using the shoulder and left hip markers. All segments were scaled uniformly in the x, y, and z directions except for the foot. The model's foot was wider than the patient's foot, so the x and y directions were scaled uniformly using the heel and first metatarsal, and the z direction was scaled using the first and fifth metatarsal. Static pose weights that prioritized joint center locations were applied, to ensure the model joint center positions closely represented those recorded from the lab.

Step 4.3.2: Inverse Kinematics

Inverse kinematics was used to determine the coordinates of the model markers in each frame of data such that the model's movement simulated the movement of the participant in the lab. Inverse kinematic uses the experimental marker data from the motion trials to determine joint angles and translations throughout the gait cycle. These calculated joint angles and positions are later used to determine joint forces, joint moments and muscle forces and activations. A least square function is used to reduce the squared error between the model marker coordinates and the corresponding experimental marker coordinates recorded in the lab. Specific weights were prescribed for each marker, causing the error value for a marker to be penalised more heavily when given a higher weight during the least square solution. Joint center marker weights were reduced to zero, and anatomical markers were given specific weightings depending on how much we trusted the accuracy of their position. The positions of the pelvis markers were prioritized over the greater trochanter marker, the lateral and medial epicondyles markers were prioritized over the tibial tuberosity and fibular head markers. The heel, medial and lateral ankle, first and second metatarsal markers were prioritized over the fifth metatarsal marker. Providing higher weightings to specific markers prioritizes reducing the least square error between the model and lab marker positions. Due to marker data only being collected for the left leg, the pelvis will tilt downwards on the left side because of the other anatomical markers pulling the model towards them. To ensure the pelvis was balanced and tracking the ASIS and PSIS markers more accurately, higher weights were allocated for the ASIS and PSIS markers, than the rest of the markers. The same least square weighting system is used for coordinate values that represent the 23 degrees of freedom of the model, listed in Table 1. Each coordinate value that is weighted greater than others, prioritizes reducing the error between the experimental and model coordinate value. Coordinate values were not provided weights, allowing marker position to be prioritized.

$$Squared\ Error = \sum_{markers} w_m \left(x_m^{exp} - x_m\right)^2 + \sum_{coordinate\ values} w_j \left(\theta_j^{exp} - \theta_j\right)^2 \qquad (11)$$

Equation 11 describes the least squared error function used in inverse kinematics, where w_m and w_j are the weights assigned to each marker position and coordinate value respectively. x_m^{exp} is the 3D experimental marker position, and x_m is the 3D model marker position for the m^th^ marker. θ_j^{exp} is the experimental value and θ_j is the model value for the coordinate j.

Step 4.3.3: Inverse Dynamics

Inverse dynamics uses the estimated mass and inertial properties of limb segments from the model, joint angles from inverse kinematics and ground reaction forces from the lab force plate to solve for three-dimensional joint forces and moments. Using all three inputs (model mass/inertia, inverse kinematics, and ground reaction forces) creates an over determinant problem which is solved iteratively using a least square approach as describe by Kuo et al [98]. The least square approach adjusts the measured ground reaction forces and angular accelerations iteratively, such that one solution for joint torques can be found, while minimizing the adjustments made to the measured values [98].

Step 4.3.4: Static Optimization

The resulting inverse dynamics net reaction forces and moments at the joints are used to determine specific muscle forces and activations. Static optimization further reduces the generalized inverse dynamics result into individual muscle forces for muscles that are included in the model. Static optimization uses the known joint forces from inverse dynamics to solve for individual muscle forces by determining the optimized solution for minimizing the sum squared muscle activations. Solving for equation 12 while minimizing equation 13 distributes the joint force across the muscles at that joint.

Static optimization is governed by the following equations:

$$\tau_j = \sum_{m=1}^{n} (a_m F_m) r_{m,j} \qquad (12)$$

While minimizing the following equation:

$$J = \sum_{m=1}^{n} (a_m)^p \quad (13)$$

Where a_m is the muscle activation ($a_m = F/F^0_m$), F^0_m is the maximum isometric force, and $r_{m,j}$ is the length of the moment arm for muscle m. τ_j is the generalized joint force for the jth joint axis from the inverse dynamics solution. P the is power of the optimization function, the higher the p value the more equally distributed the load is between the muscles.

Reserve actuators can provide additional actuation at a particular degree of freedom if the model muscle actuators are not capable of achieving an acceleration [99]. Reserve actuators were created for all 23 degrees of freedom of the model and were appended to the model's force set as backups to the model's muscles. The reserve actuators were recruited by the model if the muscles were not strong enough to achieve the required forces. The reserve actuators have a maximum control and optimal force that affect the way they are used by the model. The optimal force setting of the reserve actuators was set to be low (1N) with minimum and maximum control of +/-infinity. Having a low optimal force with a maximum control of +/-infinity allows the model to recruit the reserve actuator when needed, but the cost will be much higher than using the model muscles, thus the model will prefer to use the model muscles and only recruit the reserve actuators when needed.

Residual actuators are similar to reserve actuators except they are only applied to the 6 pelvis degrees of freedom. Residual actuators account for the discrepancies between the model and experimental lab data as shown in equation 14.

$$\vec{F}_{External} = \sum_{i=1}^{Segments} m_i \vec{a}_i - \vec{F}_{Residual} \quad (14)$$

$$\vec{F}_{External} = F_{grf} - \vec{F}_B \quad (15)$$

Where $\vec{F}_{grf}$ is the 3D experimental ground reaction force vectors, $\vec{F}_B$ is the subject's body weight vector. m_i is the mass and $\vec{a}_i$ is the acceleration of the i^{th} body segment from the model and $\vec{F}_{Residual}$ is the residual forces.

The residual actuators for the 6 pelvis degrees of freedom were given high optimal forces with low controls, to account for errors between measured ground reaction forces and model accelerations. High optimal force and low controls reduces the penalty of using the residual actuator and allows for high force to be recruited by the model. Static optimization was completed to determine the model muscle activation and forces throughout the gait cycle. The results from inverse kinematics, inverse dynamics and static optimization were compared to the joint angles, moments and EMG results found in Step 3 to confirm the model represented the patient's anatomy and movement.

Step 4.4: Applying Healthy Control Kinematics and Kinetics to Patient Specific Model

To determine how a reduction in specific muscle strength impacts one's ability to achieve healthy gait, healthy control kinematic and kinetic gait data from a previous study were applied to the model [100]. The participant involved in the previous study at the DOHM followed similar gait analysis process and consented to having their data used for future studies. The healthy data was from an adult male participant whose height and mass were similar to the recruited sarcoma patient.

Step 4.4.1: Scaling

The kinematics and ground reaction force data of the control participant were filtered and processed with the same workflow as the patient. The scaled model with the anatomy of the sarcoma patient and default Gait2392 muscle strengths was used to simulate the healthy control data. The patient-specific model was scaled again using the static trial from the control participant data to adjust the mass and model marker positions while keeping body segments the same. The same markers were used in both gait trials except the PSIS markers which were included in sarcoma patient trials but not the control trials. Instead of the PSIS marker for the control trials, a sacrum marker was used. The same marker weights that were used for scaling the first participant were used again, but additional manual coordinate values were used. The coordinate values represent the 23 degrees of freedom of the model and allow a manual value to be specified and given a specific weight to be considered when scaling. Target angles were specified for hip flexion, hip rotation, knee angle, ankle, angle, lumbar rotation, pelvis tilt, pelvis list and pelvis rotation in the static trial. Target positions were also specified for the pelvis x and y positions. Because the control kinematics were applied to a model that reflected the patient's anatomy, scaling then inverse kinematics and inverse dynamics was run iteratively, comparing inverse kinematic and inverse dynamics results to joint angles, forces and moments produced for the control participant using a standard protocol from Step 3.

Step 4.4.2-4.4.4 Inverse Kinematics, Inverse Dynamics, and Static Optimization

Once the final coordinate values were determined and the model had been scaled, the same workflow with the same settings previously described for the first participant including inverse kinematics, inverse dynamics, and static optimization, was completed using the healthy control data. When confirming model muscle activations against the EMG results, it was determined the muscle activations were higher than expected when compared to EMG results. To ensure the model produced accurate muscle activations the model maximum isometric strength was scaled by a factor of 1.9. The factor of 1.9 was selected by dividing the peak muscle activation from the EMG results, by the peak muscle activation from static optimization for the same muscle, then averaging these scale factors for the muscles listed in Table 7. Vastus Medialis was an outlier that created a much larger scale factor than the others, so it was removed when averaging the scale factors for the other six muscles. Table 7 shows the unscaled peak activations of the model, compared to the EMG peak activations, then the peak activations after scaling which are much closer to the EMG results. After the muscle strength scaling the simulated joint angles, forces, moments, and muscle activations were similar to those produced from patient recorded EMG data.

Table 7. EMG Activations Before and After Scaling Muscle Strengths

Muscle	Unscaled Peak Activations	Subject 2 Peak EMG	Scaled Peak Activations
Medial Gastrocnemius	27%	55%	52%
Lateral Gastrocnemius	14%	20%	27%
Rectus Femoris	15%	30%	29%
Semimembranosus & Semitendinosus	29%	55%	56%
Biceps Femoris-Long & Short Head	14%	30%	28%
Vastus Lateralis	9%	25%	17%
Vastus Medialis	6%	35%	11%

Step 4.4.5 Simulating Maximum Isometric Muscle Strength Reduction Due to Surgical Intervention

To ensure the model represented the patient's muscle anatomy after surgery, the patient's chart was referenced to determine which muscles were impacted from surgery. The chart reported that there was loss of the insertion of the gluteus maximus, iliopsoas, short external rotators, adductor brevis and longus and pectineus. The residual abductor tendons were reattached directly to the endoprosthesis. In the model, the iliopsoas, adductor brevis, and pectineus were removed by reducing each muscles maximum isometric force to 0. The gluteus medius, gluteus minimus and piriformis muscles were the focus of surgical intervention simulations for the current study.

In order to simulate the reduction in muscle strength incrementally the maximum isometric muscle force for the gluteus minimus, gluteus medius and piriformis were reduced in percentages starting at 25% reduction to 100%. Table 8 shows the original maximum muscle strength of the model, then the maximum muscle strengths after each incremental reduction. The effect each muscle and muscle combinations had on kinematics was also explored by reducing the muscle strengths of all three muscles, then only two of the three muscles at a time, then each muscle individually.

Table 8. Reduction in Muscle Strength

Subject 2	**% Reduction**						
Muscle	0%	25%	50%	75%	85%	90%	100%
Gluteus Medius 1	1556	1167.1	778.1	389.0	233.4	155.6	0
Gluteus Medius 2	1089	816.5	544.4	272.2	163.3	108.9	0
Gluteus Medius 3	1241	930.5	620.4	310.2	186.1	124.1	0
Gluteus Minimus 1	513	384.8	256.5	128.3	77.0	51.3	0
Gluteus Minimus 2	542	406.1	270.8	135.4	81.2	54.2	0
Gluteus Minimus 3	614	460.3	306.9	153.4	92.1	61.4	0
Piriformis	844	632.7	421.8	210.9	126.5	84.4	0

The cases of muscle reduction are illustrated in Table 9. By reducing the maximum isometric force of the muscle, we are affectively weakening the muscle, until the maximum force is less than the force required to achieve the healthy kinematics, at which point the reserve actuators will be recruited by the model. As previously reported by van der Krogt et al. once the reserve actuator moment exceeds 5% of the required moment from inverse dynamics, the model muscles are deemed not strong enough to achieve the desired motion [99], [101]. This technique was therefore applied throughout the gait cycle where the inverse dynamics moment was greater than 1Nm [101]. The reserve actuator moment was divided by the inverse dynamics' moment at every point in the stance phase of the gait cycle to determine if reserve actuator moment was more than 5% of inverse dynamics moment. This approach allowed us to determine how much the three muscles can be impacted before healthy gait cannot be achieved.

Table 9. Muscle Combinations for Strength Reduction

Case	Muscle Strengths Reduced
Case 1	Gluteus Medius, Gluteus Minimus & Piriformis
Case 2	Gluteus Medius & Gluteus Minimus
Case 3	Gluteus Medius & Piriformis
Case 4	Gluteus Minimus & Piriformis
Case 5	Gluteus Medius
Case 6	Gluteus Minimus
Case 7	Piriformis

4.3 Results

The recruited sarcoma surgical patient was a 54-year-old male. The participant's diagnosis was grade 2 chondrosarcoma. Treatment was limb salvage surgery of the hip with the Stryker Global Modular Replacement System (GMRS), a total hip replacement with a constrained liner. The length of proximal femur resected was 200mm. The insertion of the gluteus maximus, iliopsoas, short external rotators, adductor brevis and longus and pectineus were not preserved, and the residual abductor tendon was sewn into the implant without augmentation. The participant signed the consent form and then demographic and anthropometric data (Table 10) was collected.

Table 10. Demographic and Anthropometric Data Collected for Patient and Control

Demographic & Anthropometric Data	Patient	Control
Age	54	56
Sex	Male	Male
Hand Dominance	Right	Right
Study Leg	Left	Left
Mass (kg)	91.5	93
BMI	28.56	30.54
Height (cm)	179	175
Waist Circumference (cm)	99	100
Hip Circumference (cm)	100	102
Thigh Circumference (cm)	50	54
Distance From Thigh Circumference to Fibula Head (cm)	23.5	22
Calf Circumference (cm)	34.5	43
Distance From Calf Circumference to Fibula Head (cm)	7	8
Foot Width (cm)	9.5	11
Shoe Size	10.5	11

4.3.1 Patient and Control Kinematics, Kinetics and EMG

Compared to the healthy control participant, the patient who received limb salvage surgery had a smaller stride length and slower speed while walking (Table 11). The patient also had a smaller range of motion at the hip, knee, and ankle joint while walking than the healthy control (Figure 9, Figure 10). The patient only had a larger range of motion than the control for knee adduction. The patient and control's range of motion throughout the gait cycle is described in Table 12. The patient also demonstrated lower joint moments at all three joints while walking, shown in Table 13 (Figure 11, Figure 12). When comparing EMG results the patient had higher activation of the lateral gastrocnemius, vastus lateralis, vastus medialis, and hamstrings (Figure 13, Figure 14). Visual inspection of patient EMG may show signs of extended activation of the gastrocnemius, vastus lateralis, vastus medialis, and hamstrings. The patient also may have patterns of co-contraction of the rectus femoris, vastus lateralis, vastus medialis, and the hamstrings.

Table 11. Stride Characteristics Results

Stride Characteristics	**Patient**	**Healthy Control**
Stride Length (m)	0.93	1.49
Stride Time (s)	1.23	1.09
Stance Time (s)	0.81	0.71
Stance Percent	66	65
Swing Percent	34	35
Speed (m/s)	0.76	1.37

Table 12. Patient and Control Peak Joint Angles (Degrees) During Walking

Participant	**Maximum/ Minimum Joint Angle**	**Hip**			**Knee**			**Ankle**		
		Adduction	**Flexion**	**Rotation**	**Adduction**	**Flexion**	**Rotation**	**Inversion**	**Flexion**	**Rotation**
Patient	**Maximum (°)**	3.41	13.24	11.89	8.68	43.43	4.43	1.18	14.30	2.34
	Minimum (°)	-1.03	2.00	0.40	-1.98	-11.68	-3.93	-7.00	-12.78	-5.73
	Range of Motion (°)	4.44	15.24	12.29	10.66	55.11	8.36	8.18	27.08	8.07
Control	**Maximum (°)**	4.82	33.49	12.84	0.86	72.82	19.16	10.43	16.10	2.08
	Minimum (°)	-6.90	-11.73	-19.40	-4.51	3.87	2.5	-11.71	-15.95	-17.34
	Range of Motion (°)	11.72	45.22	32.24	5.37	76.69	21.66	22.14	32.05	19.42

Table 13. Patient and Control Peak Joint Moments Normalized to Body Mass (N/Kg) During Walking

Participant	**Maximum/ Minimum Joint Moment**	**Hip**			**Knee**			**Ankle**		
		Adduction	**Flexion**	**Rotation**	**Adduction**	**Flexion**	**Rotation**	**Inversion**	**Flexion**	**Rotation**
Patient	**Maximum (Nm/Kg)**	0.73	0.35	0.02	0.09	0.19	0.04	0.13	0.03	0.02
	Minimum (Nm/Kg)	-0.05	-0.31	-0.14	-0.06	-0.12	-0.03	-0.01	-1.22	-0.05
Control	**Maximum (Nm/Kg)**	1.63	0.86	0.39	0.55	0.27	0.28	0.24	0.14	0.02
	Minimum (Nm/Kg)	-0.42	-0.47	-0.20	-0.17	-0.78	0.00	-0.02	-1.38	-0.14

Patient and Control Kinematics

Figure 9. Patient Hip, Knee, and Ankle Joint Angles

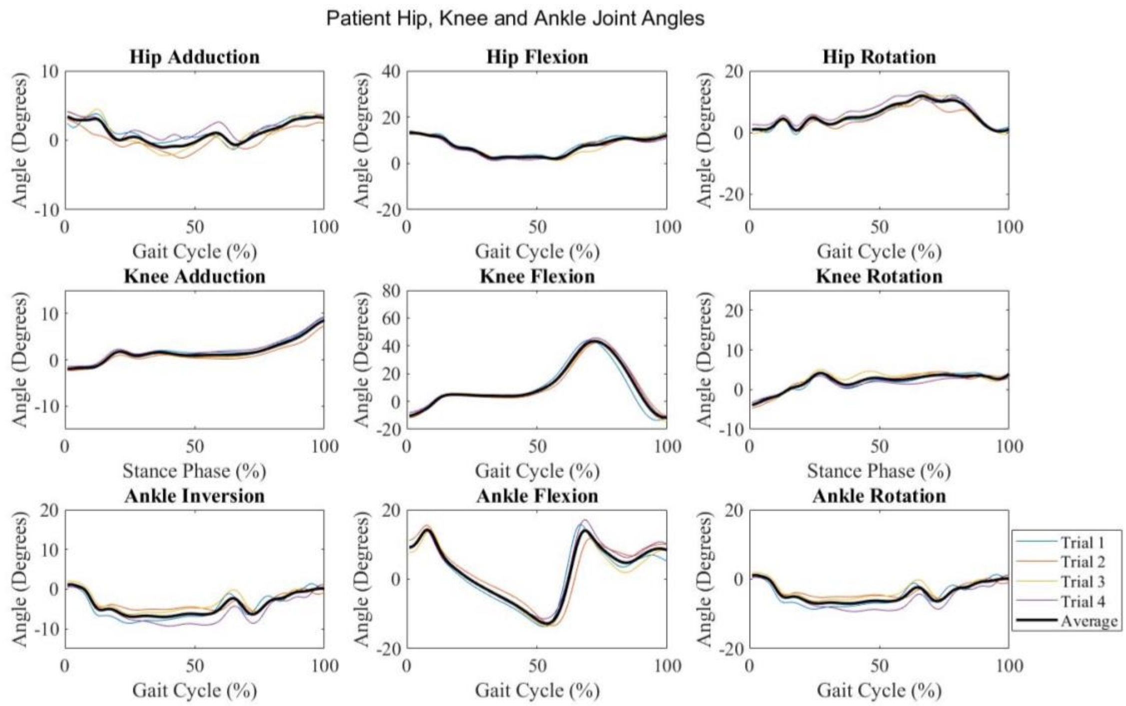
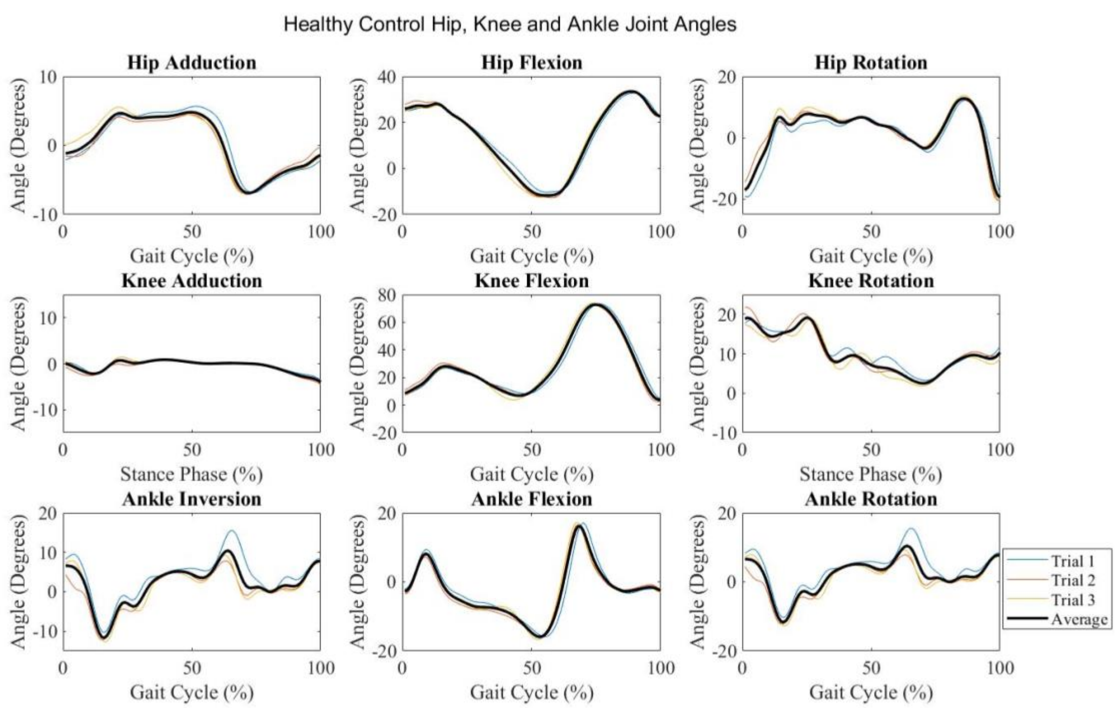


Figure 10. Healthy Control Hip, Knee, and Ankle Joint Angles



Patient and Control Kinetics

Figure 11. Patient Hip, Knee and Ankle Moments Normalized to Body Mass and Stance Phase

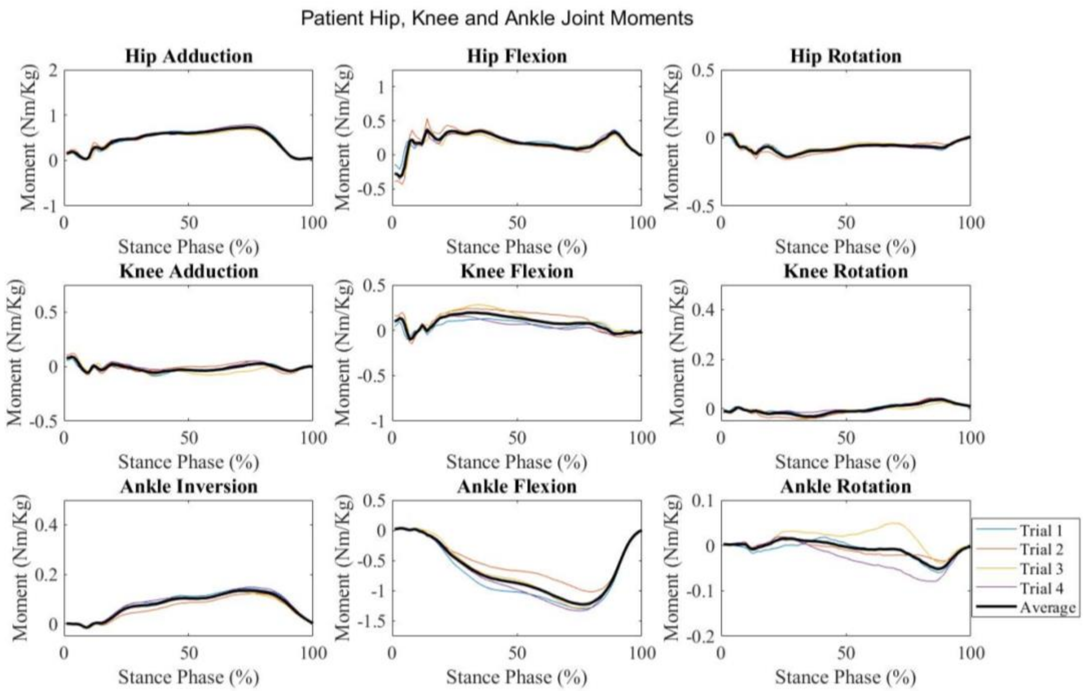
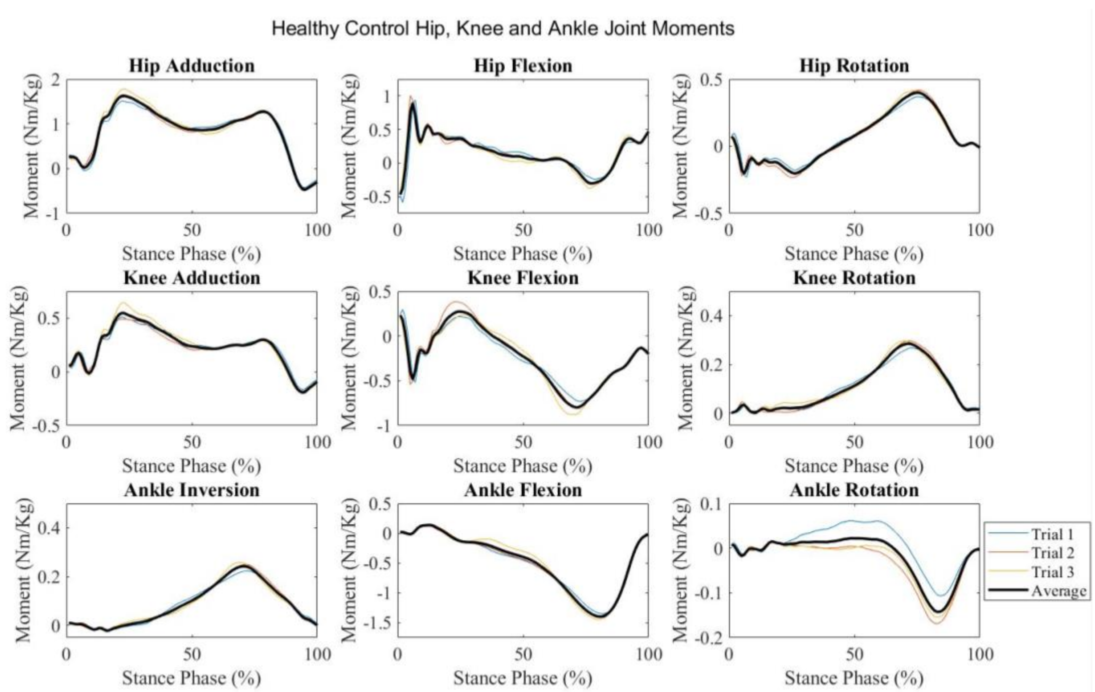


Figure 12. Healthy Control Hip, Knee and Ankle Moments Normalized to Body Mass and Stance Phase



Patient and Control EMG

Figure 13. Patient EMG

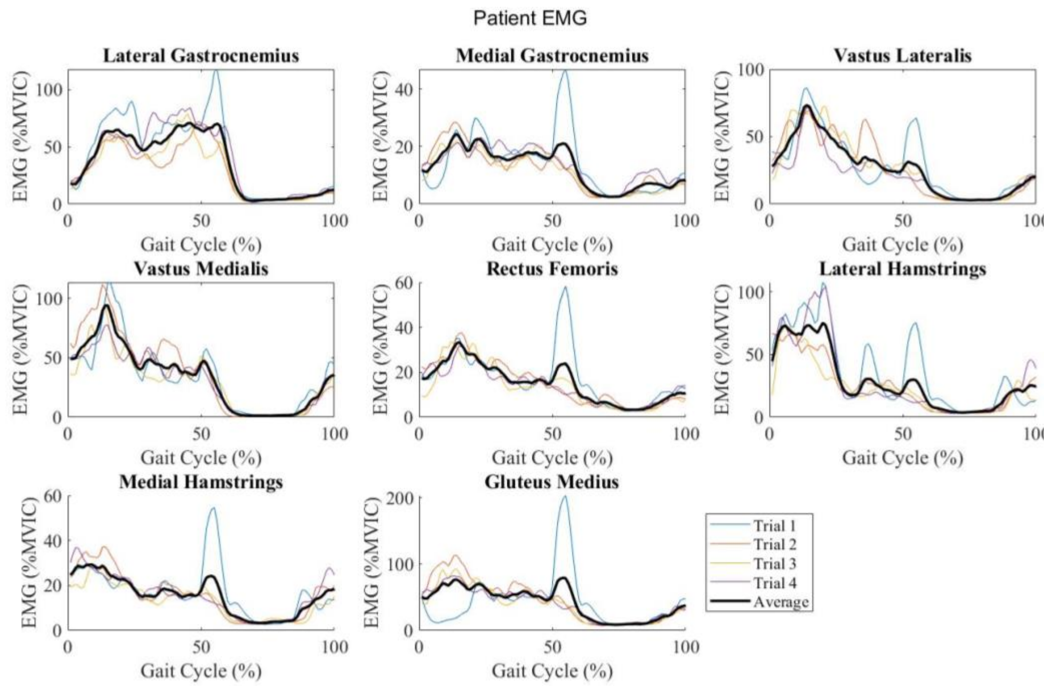
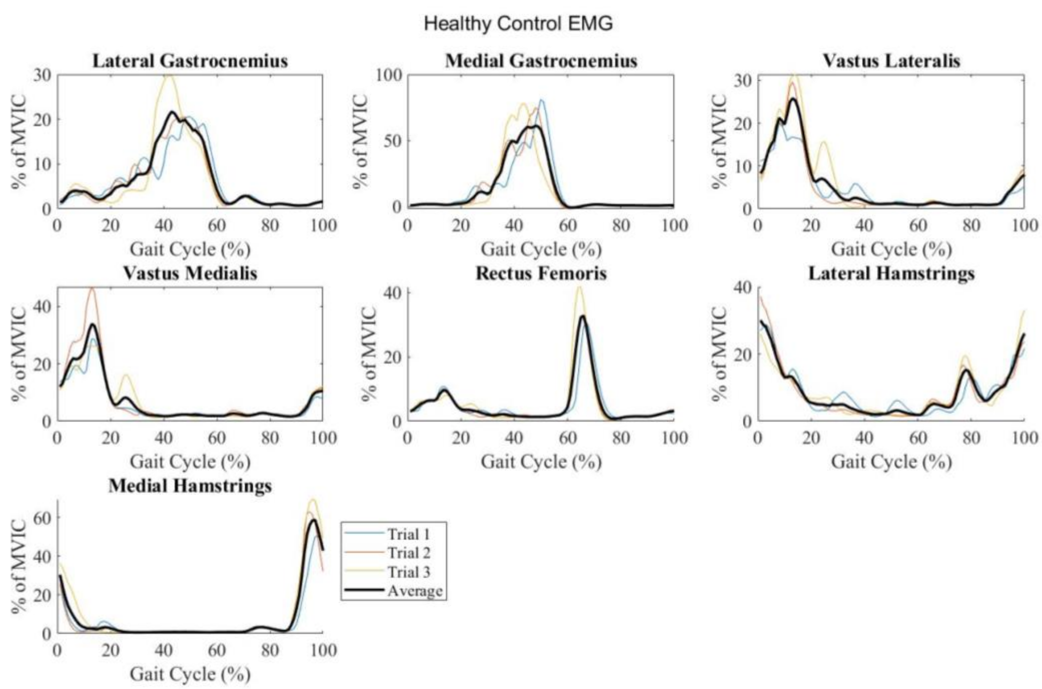


Figure 14. Healthy Control EMG



4.3.2 Model Results

After systematically reducing the gluteus medius, gluteus minimus and piriformis (case 1, Figure 15) muscle strengths by 85% it was determined that the patient specific model could not achieve healthy kinematics without recruiting reserve actuators to produce a moment more than 5% of the inverse dynamics moment at a given point in the gait cycle. When reducing two out of the three muscles of interest it was found with an 85% reduction in only the gluteus medius and gluteus minimus, that healthy gait was unachievable without recruiting reserve actuators more than 5% of the inverse dynamic moment (case 2, Figure 16). When reducing the muscle strength of the gluteus medius, gluteus minimus and piriformis individually, healthy gait was achievable with reserve actuator moments less than 5% of the inverse dynamic moments in all cases even when each muscle was set to maximum isometric force of 0. When gluteus medius and piriformis (case 3, Figure 17) or gluteus minimus and piriformis (case 4, Figure 18) were reduced together, healthy gait was still obtainable.

The maximum percentages of reserve actuator moment relative to inverse dynamics moment throughout the stance phase of the gait cycle are shown for all cases after an 85% (Table 14), 90% (Table 15) and 100% (Table 16) reduction in muscle strength. For cases 1 and 2, after an 85% reduction in muscle strength, the hip rotation reserve actuator produced a peak moment 26.3% of the inverse dynamics' moment. In the same two cases, when muscle strength was reduced by 90%, hip adduction and hip rotation reserve actuators were recruited to provide peak moments 6.8% and 81.7% of the inverse dynamics' moment respectively. Finally, when muscle strengths were reduced by 100% for case 1 and 2, in addition to increases in hip adduction and rotation moments, the hip flexion reserve actuator provided a peak moment 21.8% of the inverse dynamics' moment.

Table 14. Percentage of Reserve Actuator Moment to Inverse Dynamics Moment for 85% Reduction in Muscle Strength

Reduction	Hip Flexion	Hip Adduction	Hip Rotation	Knee	Ankle	Subtalar
Case 1	0.7%	2.2%	26.3%	0.4%	0.0%	0.2%
Case 2	0.6%	2.2%	26.3%	0.3%	0.0%	0.2%
Case 3	0.8%	0.0%	0.9%	0.4%	0.4%	0.2%
Case 4	1.1%	0.0%	0.4%	0.3%	0.0%	0.2%
Case 5	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Case 6	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Case 7	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Case 1: Gluteus Medius, Gluteus Minimus & Piriformis; Case 2: Gluteus Medius & Gluteus Minimus; Case 3: Gluteus Medius & Piriformis; Case 4: Gluteus Minimus & Piriformis; Case 5: Gluteus Medius; Case 6: Gluteus Minimis; Case 7: Piriformis

Table 15. Percentage of Reserve Actuator Moment to Inverse Dynamics Moment for 90% Reduction in Muscle Strength

Reduction	Hip Flexion	Hip Adduction	Hip Rotation	Knee	Ankle	Subtalar
Case 1	1.8%	6.8%	81.7%	0.4%	0.0%	0.2%
Case 2	1.8%	6.8%	81.9%	0.3%	0.0%	0.2%
Case 3	0.8%	0.0%	0.9%	0.4%	0.4%	0.2%
Case 4	1.1%	0.0%	0.4%	0.3%	0.0%	0.2%
Case 5	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Case 6	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Case 7	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Table 16. Percentage of Reserve Actuator Moment to Inverse Dynamics Moment for 100% Reduction in Muscle Strength

Reduction	Hip Flexion	Hip Adduction	Hip Rotation	Knee	Ankle	Subtalar
Case 1	21.8%	19.1%	200.6%	0.5%	0.3%	0.6%
Case 2	22.2%	19.2%	200.4%	0.5%	0.3%	0.6%
Case 3	0.8%	0.0%	1.0%	0.4%	0.4%	0.2%
Case 4	1.1%	0.0%	0.4%	0.3%	0.0%	0.2%
Case 5	0.8%	0.0%	0.4%	0.3%	0.0%	0.2%
Case 6	1.1%	0.0%	0.3%	0.3%	0.0%	0.2%
Case 7	1.0%	0.0%	0.4%	0.3%	0.3%	0.2%

In situations where healthy kinematics were not obtainable (case 1 & 2), the reserve actuators recruited that exceeded 5% of the inverse dynamics moment were hip rotation, hip adduction and hip flexion depending on the reduction in muscle strength. When the gluteus medius and gluteus minimus were reduced together by 75% (case 1 & 2), the TFL and gluteus maximus 1 (the posterior component of the gluteus maximus muscle) reached a maximum activation of 1, using 100% of the muscle strength to achieve the healthy kinematics. When reducing gluteus medius and minimus muscle strength together by 100%, a peak muscle activation of 1 was found in the TFL, gluteus maximus 1, semimembranosus, bicep femoris short head, rectus femoris and gastrocnemius medial (Figure 19).

Figure 15. Case 1: Inverse Dynamics verses Reserve Actuator Moments for Reductions in Gluteus Medius, Gluteus Minimus and Piriformis Strength

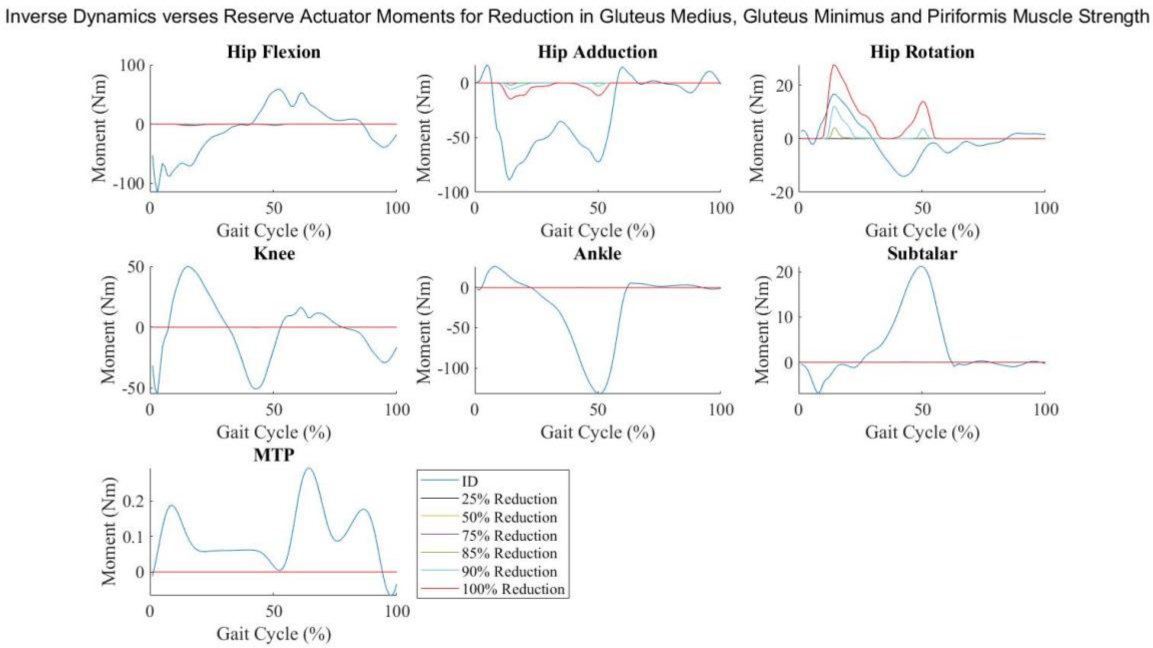


Figure 16. Case 2: Inverse Dynamics verses Reserve Actuator Moments for Reductions in Gluteus Medius and Gluteus Minimus Strength

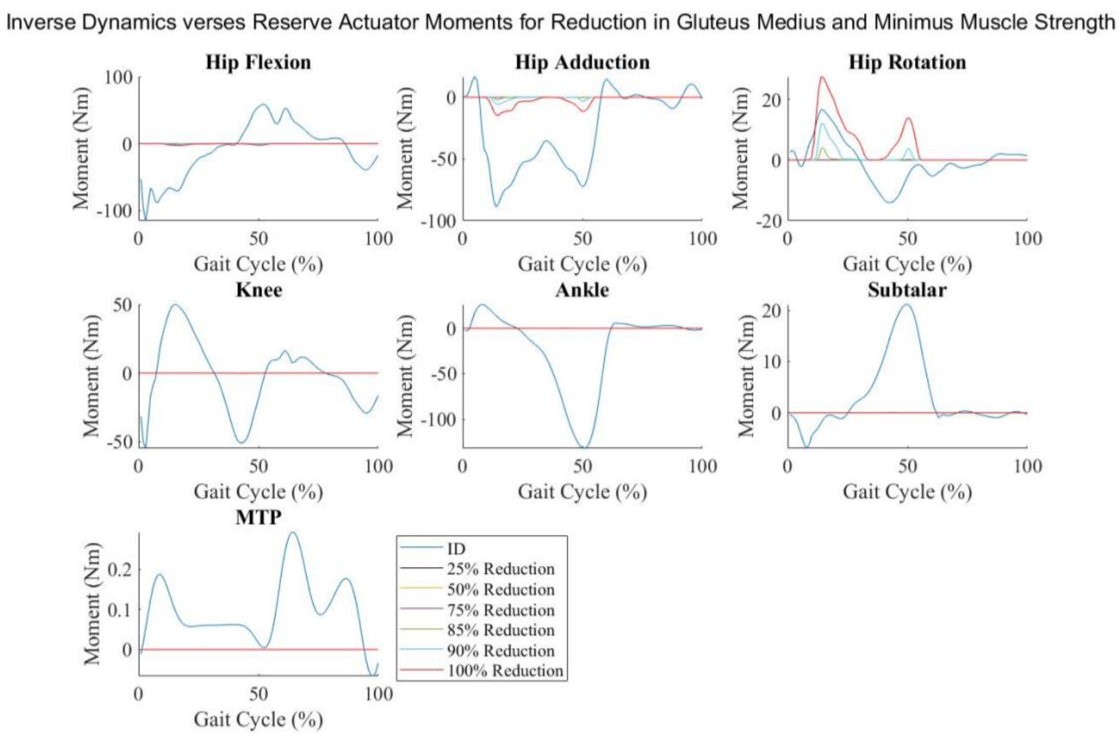


Figure 17. Case 3: Inverse Dynamics verses Reserve Actuator Moments for Reductions in Gluteus Medius and Piriformis Strength

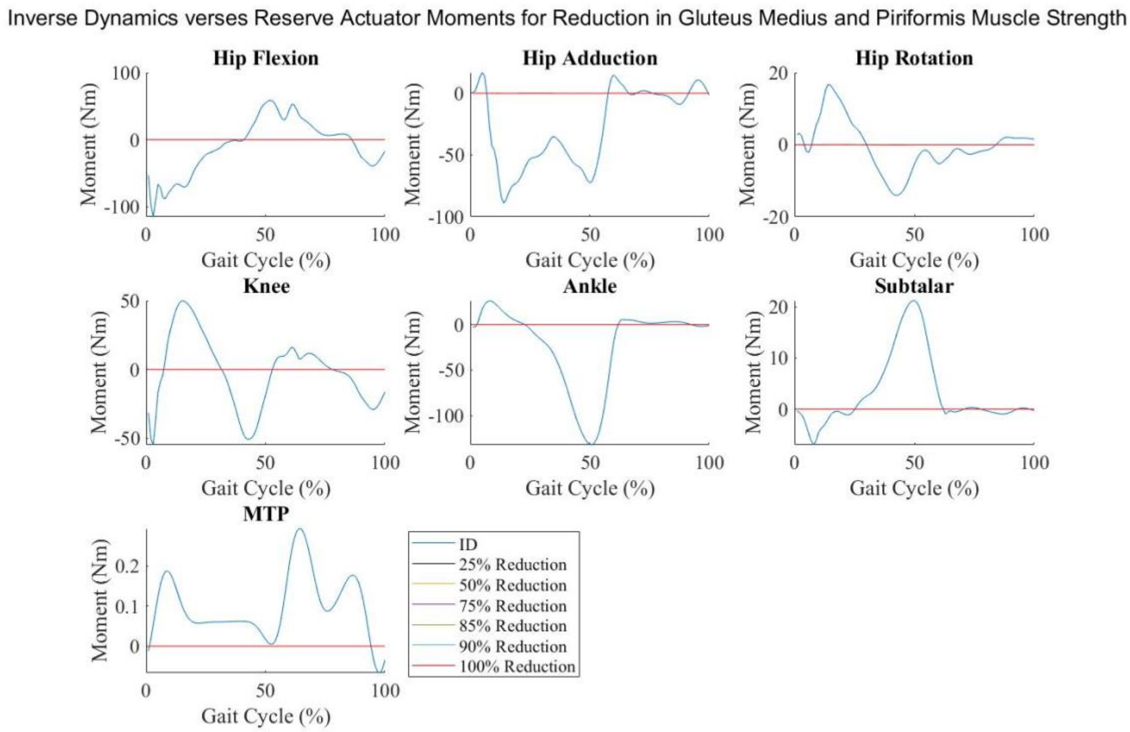


Figure 18. Case 4: Inverse Dynamics verses Reserve Actuator Moments for Reductions in Gluteus Minimus and Piriformis Strength

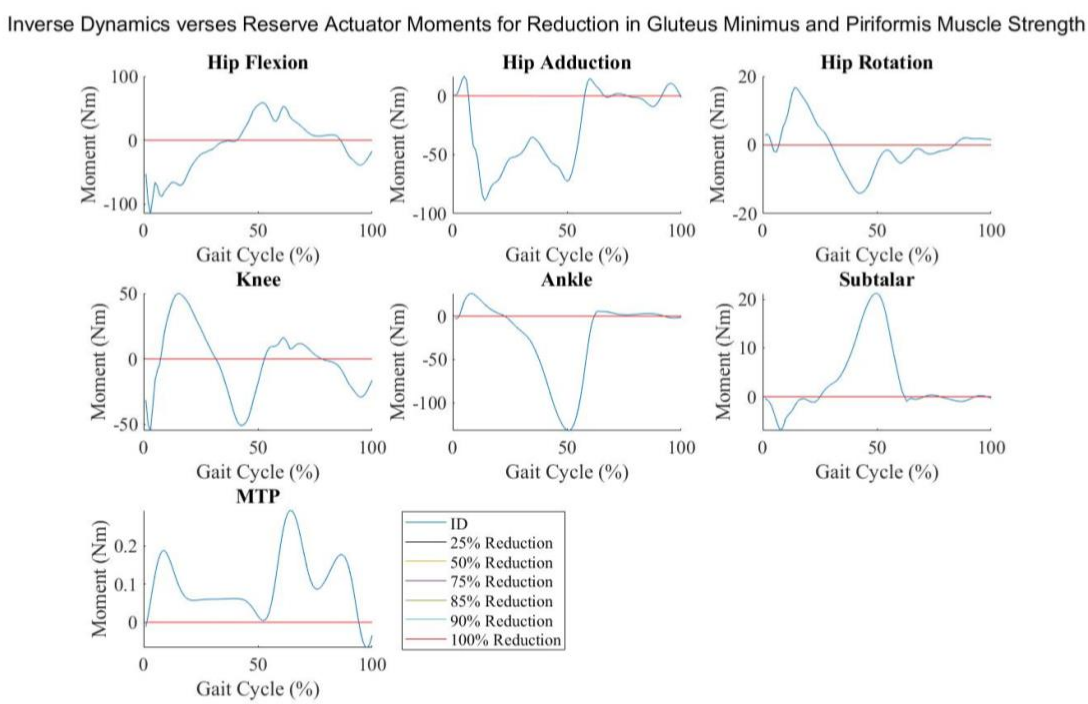
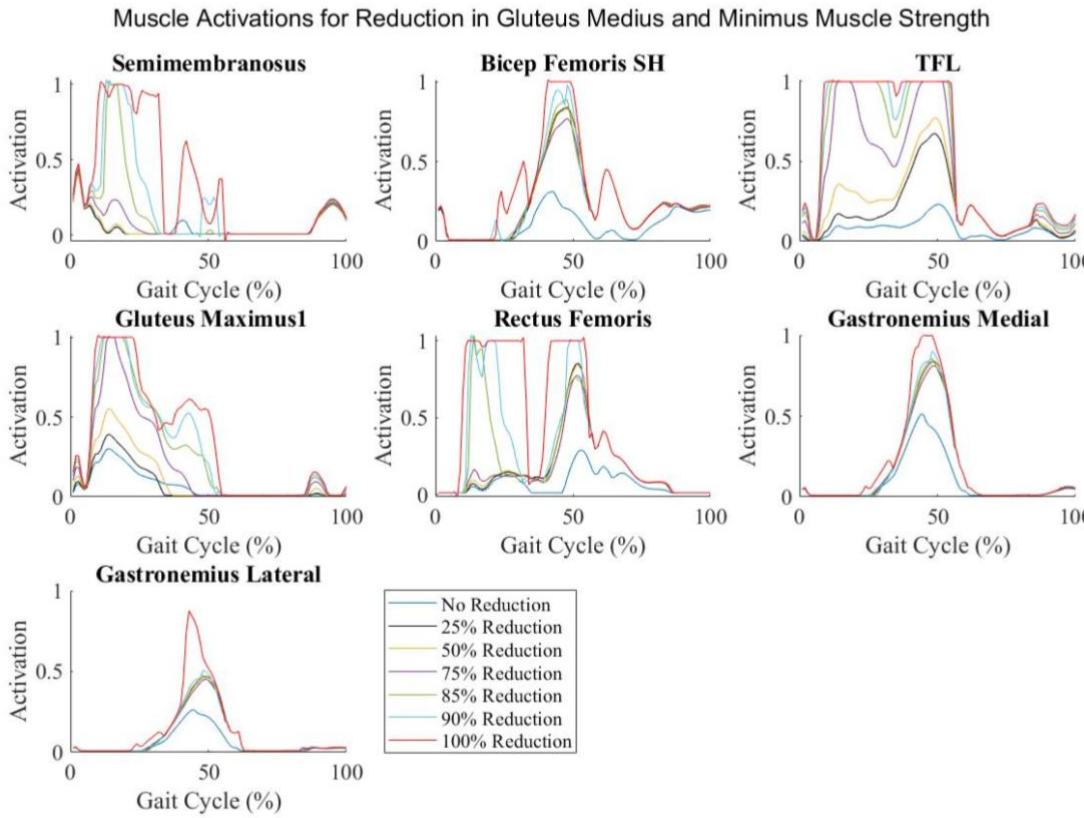


Figure 19. Muscle Activations for Compensatory Muscles Recruited After Reduction in Gluteus Medius and Minimus Muscle Strengths



4.4 Discussion

Through the use of a patient specific model, surgical intervention for limb salvage surgery was simulated to determine how a reduction in strength in the gluteus medius, gluteus minimus and piriformis muscles affect one's ability to achieve healthy gait kinematics and kinetics. The findings from the simulation have the potential to inform surgical technique by prioritizing the gluteus medius and gluteus minimus together as the results show that reducing the strength of the gluteus medius and gluteus minimus simultaneously can inhibit a patient from being able to achieve healthy gait patterns, whereas defunctioning them individually does not. This result shows that during surgical intervention impacting both the gluteus medius and minimus together has more effect on gait patterns than individually, if possible, an effort should be made to preserve the strength in at least one of the two muscles as much as possible. Additionally, the findings highlight the importance of the tensor fasciae latae and gluteus maximus as muscles that help compensate for weakened abductors.

When gluteus medius and gluteus minimus muscle strengths were reduced substantially, the TFL, gluteus maximus, semimembranosus, bicep femoris short head, rectus femoris and gastrocnemius medial muscles were recruited to compensate for weakened abductors. The TFL and gluteus maximus in particular were recruited heavily allowing healthy gait to be achieved after a 75% reduction in gluteus medius and minimus muscle strength. Valente et al. conducted a comparable study manipulating gluteus medius, gluteus minimus and TFL maximum muscle strengths. Using a probabilistic approach, Valente et al. found healthy kinematics was possible for their model in all combinations of reduced strength of the abductors. The group determined that the rectus femoris, bicep femoris, gastrocnemius and the anterior and middle components of the gluteus maximus were recruited to compensate for weakened abductors and resulted in increased hip and knee contact forces[14]. From Valente et al. and the current study, it is shown that an extreme reduction in abductor strength does not necessarily prevent healthy kinematics when compensatory muscles are able to be recruited.

The strength of muscles recruited to compensate for weak abductors influences whether the model is able to achieve healthy gait. In the current study the model's default maximum isometric muscle strengths were scaled by 1.9 to replicate EMG activations. This effectively strengthened the muscles that were recruited to compensate for the weakened gluteus medius and minimus. van der Krogt et al. simulated the impact of weakening lower extremity muscles on the model's ability to achieve healthy kinematics. In their cohort of 6 participants, one was unable to achieve healthy kinematics after 60%, two after 80% and the remaining three after 100% reduction in gluteus medius strength[101]. Their result contrasts with the current study's findings that healthy kinematics are achievable without the gluteus medius. The differences between the two studies ability to achieve healthy kinematics without gluteus medius is attributed to the muscle strengths used. They used the Delp model[51] with default muscle strengths which as described previously, are weaker than the Gait2392 default model muscle strengths. This resulted in the current study's compensatory muscles having higher strengths than the model used in van der Krogt et al [101]. In our model, when default muscle strengths are used and the gluteus medius is removed, healthy kinematics are not achievable. This difference in results highlights that other muscles compensate for the removal of the abductors in order to achieve healthy gait patterns, and the ability to actually achieve healthy gait is dependent on the compensating muscles strengths. This has interesting implications for those who received limb salvage for sarcoma, as many current physiotherapy programs focus only on restrengthening the impacted abductor muscles[102]. The findings of the current study suggest physiotherapy programs that additionally emphasize increasing muscle strength of these key compensatory muscles may allow improvements in kinematics patterns after surgery.

Kinematic results showed the largest difference in range of motion between the two participants was at the hip joint. Changes in hip musculature not only altered hip range of motion but also knee and ankle range of motion, which can lead to future pathologies such as arthritis at these joints if functional limitations are not addressed[103]. The patient also had smaller net reaction moments across all joints compared to the control. Benedetti et al. found similar results when using instrumented gait analysis on a population level for those who received proximal femur limb salvage surgery[8]. In their study hip abduction/adduction and flexion/extension was reduced, along with reduced hip flexion, abduction and external rotation moments compared to healthy controls. Their cohort had an average manual muscle strength score of 4/5. Participants were able to achieve abductor muscle strengths greater than 15%, but still had altered kinematics that led to a restriction of activities. The findings of the current study suggest the good muscle strength found in Benedetti et al. cohort should have led to gait kinematics and kinetics that resembled healthy gait but did not. This result may be due to reduced range of motion about the hip due to the method of muscle reattachment. Reducing the range of motion about the hip during gait leads to reduced step length, gait cadence and joint kinematics and kinetics. This restriction in range of motion was not considered in the current study's model and may limit the patient's ability to achieve normal gait kinematics even with good abductor muscle conservation.

Reduced range of motion commonly seen after proximal femur reconstruction may also be a protective behaviour. As seen with the patient in the current study, when hip flexion, adduction, rotation, and knee flexion range of motion decreases the moment arm between the joint and ground reaction force decreased leading to smaller joint reaction moments and ultimately a smaller required force from the muscles. The reduction in range of motion during gait may be a behavior to reduce the force required by reattached muscles as the patients do not trust the limb after surgery. In a systematic review of patients after THA, Bahl et al. found similar patterns with lower ranges of motion at the hip in the sagittal and coronal planes after THA compared to healthy controls [104]. Bahl et al. found that coronal abduction range of motion was not improved after surgery compared to pre-op, suspecting the result was related to abductor muscle weakness. Bahl et al. questioned if the reduction in hip range of motion was related to strategic gait patterned developed before surgery to reduce pain at the joint. To determine if a reduction in range of motion during gait is a protective behaviour or a physical limitation it is recommend future studies record range of motion at the hip and knee using voluntary muscle activation prior to gait analysis. This will provide insight to whether the changes in gait kinematics are due to physical constraints of the musculature that prevent healthy kinematics or other factors like adapted gait patterns prior to surgery, and protective behaviors.

There are limitations to the current study. The current study was focussed on only changing abductor strength by altering maximum isometric muscle forces and not insertion location. During limb salvage surgery, the location of the abductor reinsertion location greatly varies depending on oncological implications, implant design and surgical technique. Abductor reinsertion location has a great impact on the muscle lever arm, and ultimately the ability to achieve desired abductor moment. The current study shows, when the abductor muscles are in the natural anatomical locations and compensatory muscles are strong enough, healthy gait can be achieved even after substantial decreases in abductor strength. The impact of changing muscle insertion locations on muscle moment arms and ultimately muscle strength was not investigated. Hu et al. used CT scans and DFIS surveillance of patients while walking on a treadmill to create 3D models of the patients after hip arthroplasty for osteoarthritis[105]. When comparing the operated leg and non-operated leg, the group found abductor moment arms were reduced and abductor muscle lengths on the operated leg were longer compared to the non-operated leg during the support phase of the gait cycle. They also found adductor muscles lengths were significantly shorter on the operated leg than the non-operated leg. This combination of adductor and abductor musculature results in undesirable hip joint biomechanics that require a higher force generated from the abductor muscles to compensate for a reduction in hip abduction moment arm but shortened adductors and elongated abductor muscle length lead to weaker abductor muscles. This situation causes a reduction in the maximum abduction moment the operated leg can generate. Hu et al. findings highlight how abductor moment arms are impacted after hip arthroplasty. Although the current findings may inform surgical technique in terms of prioritizing the gluteus medius and minimus together instead of individually, insights on how changes in muscle insertion locations specifically reduces muscle strengths cannot be concluded from the current study. Future studies should continue to explore the impact altered hip musculature has on gait to inform surgical technique and implant design, by simulating how changes in specific muscle insertion location impact muscle strengths and ultimately gait.

The current study was also limited to patient gait data after proximal femur limb salvage surgery without pre-operative gait data. Because we did not have gait data for the patient before their limb salvage surgery, we used healthy kinematic and kinetic data from a control who was of the same sex, and similar height and weight to the patient. Using kinematic and kinetic data from a healthy control instead of the patient prior to surgery could affect modeling outcomes, as the model's maximum isometric muscle strengths were scaled based on the control's EMG data. It is possible that basing the maximum isometric muscle strengths from the control could result in a model that was stronger than the patient was prior to their surgery. As stated previously increasing the model's muscle strengths results in stronger compensatory muscles that are recruited to supplement weakened abductors. If the patient had weaker muscles before surgery than the model, they may not be able to recruit their compensatory muscles to the same extent, influencing their ability to achieve healthy gait.

Another limitation of the current study is the sample size of one. The current study presents objective analysis of the functional outcomes and impact of abductors on gait kinematics and kinetics but may not be applicable to all patients who received LSS for the proximal femur. LSS for the proximal femur varies substantially from patient to patient thus gait patterns vary greatly as well. The current case study provides initial insights to objective analysis of hip biomechanics after proximal femur reconstruction. Further research should examine variability associated with multiple patients to determine if a patient-specific approach is required to inform surgical decision making based on the specific anatomy and surgical constraints of the patient and their diagnosis or if modeling can be generalized. Studies should continue to utilise computational biomechanics to objectively analyse hip biomechanics for limb salvage surgery to inform surgical technique and implant design.

4.5 Conclusion

Hip biomechanics are greatly impacted after limb salvage surgery of the proximal femur, leading to abnormal gait patterns after surgery. Analyses using patient specific musculoskeletal models to simulate surgical interventions provides objective biomechanical insights that can inform surgical technique and implant design. Using a model representing the anatomy of a participant after proximal femur reconstruction, it was determined that healthy kinematics can be achieved when the gluteus medius, gluteus minimus and piriformis are individually removed. We also found that the gluteus medius and gluteus minimus maximum isometric strength could be reduced by 75% while still achieving healthy gait kinematics. Decreasing the strength of the gluteus medius and minimus together had a greater impact on healthy kinematics than reducing strength individually. The gluteus maximus, rectus femoris, bicep femoris, and gastrocnemius were recruited to compensate for weakened gluteus minimus and medius. This simulation study therefore suggests that surgical techniques should prioritize preserving one of the gluteus medius or gluteus minimus over reducing both of their strength together. Future work should use musculoskeletal modeling to investigate how altered abductor moment arms impacts one’s ability to achieve healthy gait.

Chapter 5 Conclusion

5.1 Thesis Summary

Proximal femur limb salvage surgery (LSS) as treatment for sarcoma cancer is a highly invasive procedure due to the amount of soft tissue resected. Patients tend to have abnormal gait patterns after surgery [106], but it is not understood what aspect of LSS has the greatest impact on patients gait [10]. The current thesis is focused on understanding which elements of limb salvage surgery impact patients' gait, through investigating current literature and objective analysis using musculoskeletal modeling.

The first objective of the thesis focused on synthetizing functional outcomes after proximal femur LSS from current literature to determine if specific surgical techniques produced superior functional results. Literature after 1998 was systematically reviewed by a single author and narrowed down to 14 papers to be evaluated. Three main themes of muscle reattachment were presented in the 14 papers, including allograft prosthesis composite, trochanter osteotomy, and artificial mesh or ligament. Results from the studies showed that APC allowed for secure muscle reattachment and tend to have good functional outcomes, but common complications and allograft availability make endoprosthesis the more popular choice of implant design. Trochanter osteotomy also had common complications, associated with the fixation of the trochanter to the implant. Additionally greater trochanter position greatly influences moment arms and muscle tension often leading to undesirable hip biomechanics and functional outcomes. Artificial mesh and ligaments presented as a good alternative to APC and TO, producing good functional outcomes and low complication rates. Ultimately current literature of proximal femur LSS is lacking objective analysis of functional outcomes to provide the qualitative evidence required to inform innovation.

The second objective of the thesis aimed to objectively analyse how changes in muscle strengths about the hip induced by LSS impact one's ability to achieve healthy gait. This was executed using instrumented gait analysis to record the gait kinematics, kinetics and EMG patterns of a patient who received LLS for proximal femur sarcoma. The data from the gait analysis was used to create a patient specific musculoskeletal model to simulate surgical intervention. The gluteus medius, gluteus minimus and piriformis maximum isometric muscle strengths were systematically reduced, and reserve actuator moments were compared to inverse dynamic moments to determine if healthy gait would be achievable for each simulation. It was determined after an 85% reduction in the gluteus medius, and gluteus minimus healthy gait was no longer achievable. It was also found, the tensor fasciae latae and gluteus maximus played a large role in compensating for weak gluteus medius and minimus after a 75% reduction in muscle strength, allowing healthy gait to be achieved.

5.2 Implications

Objective one of the thesis revealed that the use of synthetic materials may produce better functional outcomes than allograft prosthesis composites and trochanter osteotomy. The papers included in the review that used synthetical materials, produced strong muscle reattachments due to the synthetic materials ability to allow tissue regrowth. Complication rates were also low for this group unlike with APCs and TO. When reviewing the 14 papers included in the study it was evident focus was placed on creating secure muscle attachments and preserving natural anatomy. Although these components are important aspects of LSS the impact surgical approaches have on hip biomechanics (ability to produce force, and moments at the joint) cannot be overlooked. Even if certain surgical approaches produce good muscle force conservation, if moment arms are severely reduced, patients' ability to achieve healthy kinematics and kinetics will still be limited. Currently functional outcomes after LSS are often reported using subjective measures which do not provide insights on the biomechanics at the hip joint. These subjective outcome measures lead to great variability between studies as well as contradicting findings, making it difficult to form conclusions about superior approaches and inform innovation [33],[37].

To address the limitations of literature, objective two focused on objective quantitative analysis of surgical intervention for proximal femur sarcoma. Objective two presented joint kinematics, kinetics and EMG for a patient after proximal femur LSS, which have only been reported by a limited amount of authors previously [8], [10], [63], [107]. It is well known that patients walking patterns after proximal femur LSS are abnormal, but the findings from objective two describe specifically that joint angles and moments were lower for the LSS patient than the healthy control. EMG results also described that the patient had higher activation of the lateral gastrocnemius, vastus lateralis, vastus medialis, and hamstrings than the control. Using objective technology like gait analysis provides a quantitative understanding of the exact deficits in limb function patients face after surgery.

Additionally, it was found through musculoskeletal modeling simulations that gluteus medius and gluteus minimus together had a greater impact on gait than the gluteus medius, gluteus minimus and piriformis individually and gluteus medius or gluteus minimus and piriformis together. The insights found in objective two have the potential to inform surgical technique, prioritizing preserving the strength in at least one of the two muscles as much as possible. It was also found the model's ability to achieve healthy gait with weakened gluteus medius and minimus was dependent on the strength of compensatory muscles. The muscles recruited to compensate for weakened gluteus medius and minimus include the tensor fasciae latae, gluteus maximus, semimembranosus, bicep femoris short head, rectus femoris and gastrocnemius medial. These findings can inform physiotherapy rehabilitation programs after proximal femur

LSS to focus on strengthen these muscles. The findings from objective two demonstrate the insights that utilizing patient-specific musculoskeletal modeling can provide if applied clinically and integrated into surgical planning to simulate possible outcomes.

5.3 Limitations

Limitations of objective one includes the process of selecting papers to review. In the systematic review only one database (Pubmed) was used. Additionally, the search criteria may have limited the results as all papers needed to include the terms *femur* and *proximal* or *hip* and *tumor* or *sarcoma*, in the title and *surgery* and *abductor* or *muscle* in the paper. This may have prevented some relevant studies from being captured in the search and included in the review. Additionally, other outcome measures such as TESS and HHS were included in some of the studies, but the MSTS score was the only clinician/patient reported outcome included in our results, as it was the most popular. This allowed clinician/patient reported outcomes to be compared between studies but did not provide additional insights from other outcome measures reported.

The results of objective two are limited by their ability to be generalised to a greater population. The objective focuses on a case study of one patient who had limb salvage surgery and one participant with healthy gait. Originally the goal was to recruit 20 patients who received proximal femur LSS but due to Covid-19 restrictions, and later hesitancy to participate in an in-person study from patients who had received cancer treatments, only one participant was able to be recruited in our timeline. As mentioned previously, limb salvage surgery varies greatly between patients which limits the outcomes presented in the thesis to be applied to other patients who received LSS.

There are also inherit errors in data collection using instrumented gait analysis. Marker placement, in addition to soft tissue and skin movement during data collection can cause discrepancies between anatomical landmarks and marker positions[108]. These errors can be amplified when participants have more adiposity, which may have occurred in the current study as both participants had a BMI greater than 28 [109]. When participants have excess adiposity the use of the rigid body assumption while walking can be questionable. This would impact multiple steps of the modeling workflow including, inverse kinematics, inverse dynamics, and static optimization. These errors could affect joint angles and moment results as well as muscles forces and activations.

EMG recorded during gait analysis also is prone to errors due to signal attenuation and cross talk which can also be amplified with higher adiposity [110], [111]. As well, EMG was not wireless and required cables connecting to the skin over the muscles of interest. The cables may have influenced how participants walked. EMG data for the healthy control was used to determine the scale factor of 1.9 for the models' maximum muscle strengths. Errors in EMG could affect the scale factor used, making the model muscles stronger or weaker than they actually were. This would impact the compensatory muscle strengths, which were shown to influence the model's ability to achieve healthy gait even with large reductions in gluteus medius and minimus strength.

Although the results from instrumented gait analysis provide a quantitative understanding of the patients gait after proximal femur LSS, we only recorded data for the one limb due to instrumentation constraints in the DOHM and did not have gait data recorded prior to surgery. Thus, we were unable to form conclusions of how the patient's gait was specifically altered from surgery, we were limited to comparing their gait patterns to a healthy control. Data collected before and after surgery, or for the surgical and non-surgical leg could give an understanding of the changings in gait patterns due to surgical intervention. Additionally, because we did not have gait data prior to surgery for the patient, healthy control data were used to simulate healthy gait patterns. The model's muscle strengths were scaled based on the healthy control's EMG patterns, which may have resulted in a model that was stronger than the patient was prior to surgery. As mentioned previously strengthening the model's muscles influences the model's ability to compensate for weakened abductors impacting the ability to achieve healthy gait.

Lastly, the results presented in objective two are limited as only maximum isometric muscle forces were manipulated, but the impact that changing muscle insertion locations has on muscle strength was not investigated. In limb salvage surgery, many muscles are reattached to either the implant, soft tissue or bone changing not only muscle force generating ability but also insertion location. When the muscle insertion location is changed the moment arm is also changed, which can limit the patient's ability to generate a specific moment at that joint. Investigating the impact changing muscle insertion location has on muscle strength can provide additional insights to inform surgical technique and implant design.

5.4 Future Directions

The thesis revealed there is a deficit of objective quantitative understanding of the impact proximal femur limb salvage surgery has on patient's limb function. To inform innovation, future work should focus on using technology to objectively analyse limb function using techniques such as gait analysis. It is recommended that gait patterns before and after surgery for both legs be recorded for a more comprehensive assessment. This information can be used to compare EMG patterns, as well as joint angles and moments to determine specific deficits in limb function and compensatory behaviours. Future work should also focus on having a larger cohort size, with an age distribution that includes people under the age of 20 as sarcoma cancer is most prevalent in this demographic.

Due to the inherit variability of LSS between patients musculoskeletal modeling provides a unique opportunity to understand how specific elements of the procedure impact hip biomechanics. Future work should continue to utilize musculoskeletal modeling for this demographic. Patient specific musculoskeletal models have the potential to be used clinically to inform surgical approach. It is recommended that future studies continue the current work presented by adjusting muscle reinsertion locations to understand how altered muscle moment arms limits one's ability to achieve healthy gait.

Chapter 6 Bibliography

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