Clinical, Kinematic, and Kinetic Analysis of Knee Arthrodesis in Support of the Design of a Novel Treatment Alternative

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CLINICAL, KINEMATIC, AND KINETIC ANALYSIS OF KNEE ARTHRODESIS IN
SUPPORT OF THE DESIGN OF A NOVEL TREATMENT ALTERNATIVE

A Dissertation
Presented to
the Graduate School of
Clemson University

In Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy
Bioengineering

by
Eric Montgomery Lucas
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ABSTRACT

The following body of work is the result of collaborative efforts between researchers at Clemson University and a team of practicing orthopedic surgeons. It begins with the identification of an inadequately addressed clinical need, the treatment of severe knee dysfunction, in the practices of our clinical collaborators. A case report, reviewing the condition of five affected patients, is presented to provide initial evidence for the existence of this need. A thorough review of the causes and currently available treatment options for knee dysfunction, including arthrodesis, is provided to clarify the need and establish its widespread significance, and a novel treatment model is proposed and discussed with respect to existing treatments.

In spite of a large number of recently published clinical case reports, the total number of affected patients has been heretofore unreported. In order to establish this figure in further support of the need for an alternative treatment, a large database of hospital discharge records is analyzed. An estimate of the frequency of knee arthrodesis is provided, and the affected patients are characterized.

Having quantified the incidence of the primary treatment method, and thus provided an estimate of the affected patient subpopulation, the effect of this treatment on lower body biomechanics is addressed. A gait analysis study was designed to simulate knee arthrodesis in normal, healthy subjects, providing a comprehensive quantification of joint kinematics and kinetics and allowing for the investigation of further hypotheses regarding the effects of treatment.
In spite of a number of reported cases of mechanical failure in knee arthrodesis implant designs, the robustness of these designs against such failure has been a neglected subject in literature. Data obtained from a previously conducted gait analysis study is used to estimate the loading conditions at an immobilized knee through the construction of a computational biomechanical model. The purpose of this model is to estimate the resultant effects of knee immobilization on the musculoskeletal system during gait, and estimates of muscle and joint loading patterns are provided.

Together, this knowledge is used to assist in the design and development of a novel treatment model, in the form of a salvage total knee replacement. This patent pending treatment is designed to subsume existing, less constrained treatment methods as well, broadening its applicability. It has been refined over the course of several design cycles, which were informed by the regulatory guidelines for medical device design in the United States. Prototyping techniques have been used throughout the design process to demonstrate proof of concept.

This work is intended to establish the significance of an unmet clinical need, characterize the patient subset and treatment patterns affected by the need, quantify the biomechanical conditions in the bodies of affected patients, and ultimately facilitate the translation of a proposed medical device from concept to clinical use.
DEDICATION

This work is dedicated to my parents, Stephen and Mary Lucas. You have always emphasized the importance of education and hard work, and you instilled the prerequisites for success in me from a young age. When you wanted me to stop watching television or playing video games as a child, an appeal to authority wasn’t enough. I still vividly remember all of the “studies” that you cited on the awful and addictive effects of “TVitis,” giving me the incentive to research the matter for myself (to find the opposite conclusion, I had hoped). I would not be where I am today without your unending support and encouragement. But just as importantly, you have been the best role models one could ever wish to have. You have served as a source of inspiration that I can only hope to live up to, providing examples of love, interdependence, support, drive, hard work, and self-discipline in every aspect of your lives, including your marriage, your work, your dedication to health and fitness, and even your leisure. And you were right about television.
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CHAPTER ONE
INTRODUCTION

The present body of work is introduced and its structure explained.

The central focus of this dissertation is the clinical treatment of severe knee dysfunction; its provenance was a meeting between researchers of the Laboratory of Orthopedic Design and Engineering at Clemson University and practicing orthopedic surgeons from the Moore Center for Orthopedics (Kim Chillag, M.D.) and the University of South Carolina School of Medicine (Frank Voss, M.D.). At this meeting, the clinicians identified an unmet clinical need among their patients and expressed a desire to further understand and address it. Thus began the series of research and design work documented herein. This dissertation is a culmination of that work, and it is divided into ten chapters.

At the first collaborative meeting, on August 10, 2010, Dr. Frank Voss and Dr. Kim Chillag conveyed the inadequacy of their armamentarium in addressing severe knee dysfunction among patients in their practice. The etiological origins of patients with this condition were diverse, but the available treatment options – high risk salvage knee replacement, transfemoral amputation, and knee arthrodesis – were limited. The conditions of five exemplary patients were subsequently reviewed to provide initial evidence of the existence of this limitation, and a Case Report of the findings is reported in Chapter 2. Limitations of existing treatment options are discussed, and development of an alternative treatment model is broached.
Having provided preliminary evidence for the existence of a clinical need through the Case Report, a thorough background analysis was conducted to document the various etiologies and currently available treatment options. The ideal treatment for knee dysfunction, from a patient’s and surgeon’s perspective, is salvage knee replacement. The nature of severe knee dysfunction, however, often means that this treatment option is inadequate or inappropriate. Alternative approaches include transfemoral amputation and knee arthrodesis, but these are undesirable and generally used as a last resort. In Chapter 3, a review of current literature is presented to clarify the etiologies of severe knee dysfunction, show that these etiologies often preempt salvage knee replacement, and discuss current surgical treatment options. A novel treatment model is proposed as an alternative to traditional knee arthrodesis. Under this model, an otherwise functional salvage knee replacement is capable of temporarily simulating knee arthrodesis. This model is intended to address the affected patient subpopulation by providing the benefits of a salvage knee replacement with the required stability of a knee arthrodesis.

The widespread applicability of any alternative treatment, however, is dependent on the overall size of the need. Despite the existence of a significant body of research on the various etiologies and treatment methods used to address knee dysfunction and knee arthrodesis, the number of patients who meet these criteria has been heretofore unquantified in published literature. Having established the existence of an unmet clinical need among a small number of patients, the next step was to quantify the overall size of this need. A large, nationally representative database of inpatient hospital records is analyzed in Chapter 5, and an estimate of the number of affected patients in the United
States is presented. In order to better understand this clinical need, the affected patients are further characterized by demographic and other clinically meaningful attributes. Characteristics of the hospitals where these patients received treatment are also analyzed, providing a deeper understanding of the condition through the identification of attributes that are common among hospitals where these patients seek treatment.

Rigid knee immobilization, such as in the existing application of knee arthrodesis or in the proposed treatment model, necessarily alters the kinematics and kinetics of gait. This appears to be well understood, but few publications have discussed these changes; of those discussions, gait changes are only described in abstract terms. No publications have quantified changes to gait kinematics or kinetics after knee arthrodesis in detail. Several studies have investigated rigid knee gait by other means, but these have been limited, and they have not fully quantified altered knee kinematics or kinetics. Those biomechanical changes have important implications, however, and knowledge of them is essential to fully understanding the consequent effects of such a treatment. One area where this is apparent is the suggested link between knee arthrodesis and early induced arthritis in other joints, such as the contralateral hip. While causation has been asserted, it has not been tested; such testing would require full consideration of biomechanical changes induced by such a treatment. A gait analysis study, simulating knee arthrodesis in normal, healthy subjects, was conducted in order to obtain this information, and this study is presented in Chapter 6.

Knee fusion by means of arthrodesis is generally assumed to be robust, which may explain why there is a dearth of information on the loading conditions of a fused
knee. Additionally, the difficulty of obtaining in vivo data measurements may contribute to the neglect of this subject. Regardless of this assumption of robustness, or the difficulty in obtaining data, there are a number of published reports of arthrodesis failure due to implant fracture or other mechanical failure modes. In order to predict and prevent failure in any engineered system, it is imperative to have an accurate understanding of the imposed loading conditions. In the study detailed in Chapter 7, kinematic and kinetic data obtained from the gait analysis study of Chapter 6 is used to drive a computational analysis consisting of dynamic simulations of a musculoskeletal model. The use of this model allows for estimates of joint loading conditions, the accuracy of which have been validated against instrumented joint replacements in other applications. In this chapter, the loading conditions at a rigidly immobilized knee are reported.

In parallel with investigations of the unmet clinical need, the treatment model proposed in Chapter 4 was explored and developed in the form of an implantable medical device. This work is documented in Chapter 8. Alternative designs, as well as the constraints of the treatment model itself, were investigated over the course of several design cycles. Recent advances in rapid prototyping techniques were used extensively to assist in design iterations and establish proof of concept. The resulting salvage total knee replacement design enables a patient to lock the knee in full extension with the use of a simple, handheld key, providing the passive flexibility of an existing knee replacement design in combination with the stability if an arthrodesis. This treatment is designed to subsume existing treatment methods, including knee arthrodesis and standard fully constrained salvage knee designs. Intellectual property created as part of this work fences
out this conceptual area and protects against others doing the same. Protection of this intellectual property has been secured with two separate patent applications through the United States Patent and Trademark Office. This work provides support for the translation of a proposed treatment solution to clinical use through intellectual property license.

A holistic discussion of the research described above is presented in Chapter 9. In Chapter 10, insight gained from this research is used to provide recommendations for future work.
CHAPTER TWO
RESEARCH OBJECTIVES

The content of this dissertation supports four specific aims.

Aim I: Establish the existence and quantify the size of the affected clinical population
Chapter 3 – Clinical Etiologies in the Loss of Knee Function: A Case Report
Chapter 4 – Background and Review
Chapter 5 – Quantifying the Affected Patient Population

Aim II: Quantify the changes to gait biomechanics induced by knee immobilization
Chapter 6 – Changes to Gait Kinematics and Kinetics Induced by Rigid Knee Constraint

Aim II: Estimate the joint loading patterns of a rigidly constrained knee
Chapter 7 – Estimated Joint Loading at a Rigidly Constrained Knee

Aim IV: Design an implantable device to serve as a proposed clinical treatment
Chapter 8 – Design of an Implantable Device to Satisfy the Proposed Treatment Model
CHAPTER THREE

CLINICAL ETIOLOGIES IN THE LOSS OF KNEE FUNCTION: A CASE REPORT

A local unmet clinical need is introduced and explored through the analysis of representative patients. The intention of this report is to present preliminary evidence of said need.

Abstract

In the course of collaborative research efforts, two practicing orthopedic surgeons describe an unmet clinical need among patients in their local practice. The commonality between these patients is severe knee dysfunction, defined as a loss of functional knee motion; the knee may become stiff with extreme limitation of flexion, or the extensor mechanism can become nonfunctional, resulting in a loss of the ability to actively flex and extend the knee. This condition is often irreversible, treatment options are limited, and the outcome is often poor quality of life. Five patients with lost functional knee motion, from diverse etiologies, are presented. These examples serve to demonstrate the limitations of existing treatment methods and the demand for a clinical solution. The potential for an alternative treatment approach is discussed.

Introduction

A loss of functional knee motion may be attributable to a variety of etiologies, including failed primary or revision total knee arthroplasty, osteosarcoma, virulent
infection, trauma, or neuromuscular disease, such as polio. Loss of knee function can be debilitating, limiting a patient’s ability to engage in activities necessary for a satisfactory quality of life. Compromised knee function can inhibit mobility, including walking, standing, and stair climbing, and can hinder basic activities of daily living such as bathing, dressing, and sitting [1]. Physical therapy is sometimes incapable of addressing the root causes of dysfunction, even when these causes are muscular weakness or inflexibility [2].

Total knee replacement is often contraindicated in the presence of knee dysfunction due to related factors, including lost anatomy, instability, infection, or muscular weakness [3]-[5]. The armamentarium available to orthopedic surgeons in these cases is typically limited to transfemoral amputation and knee arthrodesis. While knee arthrodesis can salvage the limb and enable a patient to walk independently, knee motion is completely eliminated. The resulting loss of knee function significantly interferes with activities of daily living, complicating activities as common as sitting. Reduced quality of life is associated with depression in patients following both amputation or arthrodesis [6], [7]. In a South Korean study, 30 patients with fused knees insisted on undergoing desarthrodesis (reversal) to a total knee replacement design to accommodate knee mobility; 17 of these patients had previously attempted suicide [7].

When faced with the prospects of these treatments, patients may adamantly insist on undergoing high risk salvage total knee replacement, in spite of the low chance of success. Treating physicians “have a responsibility to present their patients with treatment choices that have a reasonable chance of succeeding without causing undo harm,”
however, and knee arthrodesis or amputation may be the most appropriate treatment approach for these patients. This can result in an ethical dilemma for the physician, as these cases raise considerations of “informed consent, patient education, autonomy, decisional capacity, paternalism, and physician responsibilities” [8].

Current available treatment methods for lost knee function, regardless of cause, are unsatisfactory to surgeons and patients alike. This dissatisfaction indicates an opportunity for an improved treatment approach. The following case examples demonstrate patients with severe knee dysfunction resulting from various causes.

**Case Description**

**Patient 1** is a 69-year-old male who first underwent arthrodesis for osteoarthritis at age 51. This surgery was conducted at the US Department of Veteran Affairs, and fusion was performed using a Neff femorotibial nail.

![Neff Femorotibial Nail](image)

**Figure 1 - Neff Femorotibial Nail (Zimmer, Warsaw, Indiana)**

Subsequent to knee fusion, the patient developed osteoarthritis of the right hip, requiring a total hip replacement. The patient then developed osteoarthritis of the left hip, requiring a total hip replacement for that joint. While the left total hip replacement was
principally successful, the patient exhibits painful left hip range of motion. The right total hip replacement has failed, requiring revision.

Other medical problems include diabetes, hypothyroidism, hypertension, and gastroesophageal reflux disease. Patient was diagnosed with prostate cancer in 2007 and was treated with a series of 40 radiation treatments.

The patient is currently presenting with a stiff, fused knee and secondary pain.

**Patient Two** is a 70-year-old obese (BMI: 45, and Weight > 300 lbs.) male, and has undergone multiple failed total knee replacement surgeries. Other medical problems have included gastroesophageal reflux disease, hypertension, hyperlipidemia, and morbid obesity (but not diabetes.) Patient exhibited a 25 degree extensor lag, and his left knee was larger than his right.

Initial surgery was in 2001 for a primary total arthroplasty of the left knee. In 2003, patient underwent total knee arthroplasty for the right knee. Patient had a stroke in 2007, but did not have much residual deficit. Difficulties with the left knee began to accelerate in June 2009 when the femoral component was revised due to generalized pain, and the femur fractured at the end of the new femoral component’s stem in July 2009. Left knee pain continued, and the tibial component was revised in February 2010. During surgery, the patellar tendon was detached at the tibial tubercle and reattached with a Stone staple.

Two months later, in April 2010, the patient presented with loose femoral and tibial components, and was referred to a specialist. Specialist noted induration and
tenderness at the tibial tubercle, and aspiration revealed a purulent infection. The staple was removed, and the patient was given two days of IV antibiotics, followed up with 7 days of Keflex oral antibiotic. Gross purulence continued along with chronic avulsion of the patellar tendon.

Infected tibial and femoral components were removed, and ‘artificial fusion’, as described previously in the literature [9], was performed. Complex stabilization of the knee was achieved using a combination of an intramedullary rod and a large mass of PMMA, which was used to bridge the gap between the femur and tibia resulting from severe bone loss.

Figure 2 - Radiographs of the (A) Anteroposterior and (B) Mediolateral view of the knee (Patient 2)
**Patient 3** had a severe traumatic injury to the knee, requiring subsequent surgery for fracture. Patient underwent total knee replacement after the development of severe joint arthritis. Patient developed ankylosis at the knee, losing all mobility, and currently walks with a stiff leg gait. Heterotropic bone has formed posterior and medial to the knee, which can be seen in radiographs.

![Figure 3 - Radiographs of the (A) Anteroposterior and (B) Mediolateral view of the knee (Patient 3)](image-url)
**Patient 4** suffers from a congenital disease, which has resulted in knee problems, including a size differential between the left and right knees. The patient underwent total knee replacement, but subsequently developed severe postoperative joint stiffness. The subsequent surgical procedures were performed, but stiffness has not resolved. The knee has spontaneously fused in full extension, and heterotopic bone formation can be observed posteriorly.

![Radiographs of the (A) Anteroposterior and (B) Mediolateral view of the knee (Patient 4)](image-url)

*Figure 4 - Radiographs of the (A) Anteroposterior and (B) Mediolateral view of the knee (Patient 4)*
Patient 5 originally presented with an osteosarcoma, which was addressed with a total knee replacement. The primary total knee replacement procedure was complicated by the occurrence of infection, and required subsequent revision. Multiple surgeries have scarred the quadriceps muscle, and the patient has lost function of the joint. The patient currently has a hinged, rotating bearing total knee replacement, but has lost all flexion due to stiffness. The patient can walk with the knee in full rigid extension.

Figure 5 - Radiographs of the (A) Anteroposterior and (B) Mediolateral view of the knee (Patient 5)
Discussion

Two patients, Patients 1 and 2, present with a knee arthrodesis (traditional and “artificial” [9]). For these two patients, there is no current treatment available to improve the condition of the leg. The joint is pain-free, and there is no method of adjusting range of motion. Desarthrodesis to a total knee replacement, even one of constrained design, is not a viable option, especially without an intact extensor mechanism.

Treatment options for the three patients with an intact joint replacement (but without actual movement) are not significantly better. All three patients have formed heterotopic bone, and total knee replacement is contraindicated. The only appropriate treatment option available for these patients is knee arthrodesis, which would introduce surgical risks without any substantial benefit in outcome. The course of action with the most probable chance of success is to avoid surgical intervention.

Knee dysfunction manifests itself as immobilization of the joint in each of the presented cases, whether the joint is physically or functionally fused. Little to no flexion of the knee is achievable, but all patients are ambulatory with a stiff-knee gait. In this sense, all patients have the functional equivalence of knee arthrodesis. While this permanent extension enables these patients to be mobile, this mobility comes at the expense of the flexion required for some activities, such as sitting in close-quarter locations (vehicles, theaters), the ability to sit or lie comfortably, or the ability to engage in other activities of daily living [10], [11].

Knee desarthrodesis may offer these patients the ability to passively bend the knee, but it has a high risk of complications (upwards of 86%) and poor outcomes [12], [13].
Even in the presence of a functioning knee extensor mechanism, muscular weakness and joint stiffness may limit range of motion, and the loss of passive knee stability may prevent patients from standing or ambulating independently.

The present cases underscore the need for an alternative treatment method to address severe joint dysfunction. Without a functional knee extensor mechanism, current approaches force patients to choose (when they have a choice) between passive knee flexion and rigid knee stability. In all cases, patients would conceivably benefit from the ability to both passively bend the knee, such as while sitting or lying down, while maintaining the stability of rigid knee extension while standing and ambulating. A treatment that offered such an ability would be required to operate within the confines defined by the patient subset, whose knee extensors are weakened or completely missing. The treatment would necessarily include, at a minimum, an implantable medical device. Such a treatment would allow locomotion while reducing or eliminating the pain associated with the presented pathologies.

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CHAPTER FOUR
BACKGROUND AND REVIEW

The etiologies of knee dysfunction are addressed, current treatment methods are reviewed, and the potential for novel surgical treatments is discussed.

Abstract
A review of current literature suggests that total knee replacement surgery contributes to knee dysfunction, and that the additive dysfunction resulting from multiple failed total knee replacement surgeries is sometimes irreversible. The treatment options for severe knee dysfunction are limited; when surgery is required and total knee replacement is contraindicated, the options are typically limited to knee arthrodesis or transfemoral amputation. Knee arthrodesis has severe functional limitations, and is the subject of a relatively large number of published reports. Several alternative surgical approaches to traditional knee arthrodesis have been developed, but they all share the same functional limitations. A novel treatment model is proposed.

Rise in Primary Total Knee Replacement
Total knee replacement has proven to be a highly effective and successful means of treating joint disease, and the number of primary knee replacement surgeries has dramatically increased over time. According to Ong et al., 5 year survivorship of primary total knee arthroplasty is 97.2% [14], a high success rate and contributing factor to the
ready adoption of the surgery. Kurtz et al. estimated the number of arthroplasty surgeries in the United States between 1990 and 2002 using the Nationwide Inpatient Sample, and estimated that rate of total knee arthroplasties per 100,000 persons tripled in that time [15]. This increase can be attributed to a number of factors, including increased implantation in younger patients, an aging population, increased prevalence of obesity, and an “increased recognition [of need] by [both] the candidates for surgery and members of the orthopaedic community”.

Implicit in the high degree of success of total knee arthroplasty, however, is the fact that it is not an infallible treatment. In “Why Knees Fail,” Kelly Vince proposes nine causes of primary knee replacements failure [16]. These causes are aseptic loosening with or without osteolysis, tibial femoral instability due to ligament instability, patellar complications and malrotation, no diagnosis, structural failure of the implant, sepsis, extensor mechanism rupture, stiffness, and fracture. When a primary total knee replacement surgery fails, revision surgery is required. According to Vince, revision knee arthroplasty is not merely a repeat surgery, but “an opportunity to correct the shortcomings that lead to the initial failure [16].” This addresses a potential shortcoming of revision knee surgery: If the reason for the original prosthetic failure is not addressed, there remains a chance that it will also affect the results of the revision procedure.

**Rise in Revision Total Knee Replacements**

As the number of primary TKR surgeries in the United States has continued to rise towards a projected 3.48 million in 2030 [17], there has been a concomitant increase in the number and rate of revision procedures [15]. According to Kurtz et al., the
prevalence of revision total knee replacement surgery increased “by 5.4 procedures per 100,000 persons per decade,” increasing from 12,000 in 1990 to 35,000 in 2002. Without proper perspective, the growth of the sheer number of revision surgeries could indicate an alarming trend toward increasing failures of primary knee replacement. The authors account for this in the study through the calculation of “revision burden,” defined as the ratio of revisions to the sum of revision and primary procedures, and estimate the change in its rate over time.

While there are limitations to its use, revision burden is a measure of the quality of the primary treatment. Revision burden would increase over time if the primary treatment had an increased tendency to fail, including if treatment was expanded to use in patients less suited for treatment, or if the surgical implants reduced in quality over time. Revision burden would decrease over time with improvements of surgical technique, improvements implantable devices, or improved identification of appropriate patients for surgery. One shortcoming of this measurement is that revision burden also decreases if the rate of primary intervention increases in the short term, as the number of revisions is a lagging figure, based on historical primary intervention surgeries that occurred at the smaller intervention rate.

The Kurtz et al. study found that the revision burden for total knee replacement has remained constant over time for all patients except women in the 65-74 age group, who experienced a statistically significant annual increase of 0.5%. The authors thus attribute the increase in revision surgery to the large increase in primary procedures. This would indicate that the success rate of primary procedures has not improved, and that the
corresponding rate of patients who must undergo revision surgery has not been reduced. Kurtz et al. do not address the fact that the increases in primary surgery, which was identified, could have pushed down the revision burden, indicating the possibility that revision rate is actually *increasing*. It is noted that since revision burden is not decreasing (by their measure), a “greater number of revisions” should be expected without implementation of “some limiting mechanism… to reduce the future revision burden.” [15] This appears to be an appropriate assumption, and would indicate a growing population of patients undergoing revision.

In fact, in a subsequent 2007 study, Kurtz et al. projected a steep increase in the number of primary and revision arthroplasty surgeries between 2005 and 2030 [17]. The authors predict that revision knee arthroplasty will grow from 38,300 patients in 2005 to 268,299 patients in 2030. The group’s predictions were calculated by determining surgery prevalence by sub-group, and then applying those prevalence rates to “projected population data for each subgroup.” Subgroup covariates included age, gender, race, and census region, and the authors used projected population data from the United States Census Bureau. If these predictions prove accurate, there will be a sevenfold increase in the number of patients undergoing revision knee arthroplasty by 2030.

**Poorer Outcomes after Repeated Surgery**

In a meta-analysis of 42 articles published between 1973 and 1994, Saleh et al. investigated the long term outcomes of revision knee arthroplasty patients using Global Knee Scores (GKS) [18]. GKS were defined as “an instrument that measured patient outcomes in the domains of pain, function, and range of motion and combined these
domains in a summary scale,” [19] and include the Hospital for Special Surgery (HSS) and Knee Society (KS) scores. In their analysis, they found that patients undergoing revision surgery had a significant increase in GKS after their procedure, without a significant correlation between pre-revision surgery and post-revision surgery scores. This study supports the consensus that revision knee arthroplasty provides favorable outcomes when compared to no surgery at all.

The success of revision knee arthroplasty, however, has not matched that of primary knee arthroplasty, as outcomes after revision knee arthroplasty are typically worse than primary knee arthroplasty by every measure. Greidanus et al. assessed the outcomes of 159 patients undergoing primary and revision total knee arthroplasty using standardized and validated measures: The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Oxford-12 Knee Score, the Short Form-12, and patient reported satisfaction [20]. Deehan et al. studied the outcomes of 94 patients undergoing revision knee arthroplasty using standardized and validated measures: the Nottingham Health Profile (NHP) and Knee Society (KS) scores. The WOMAC, Oxford-12, NHP, and KS scores are each designed to capture health outcomes, though they do so in different ways. The WOMAC, Oxford-12, and KS specifically address knee arthroplasty, while the Short Form-12 and NHP measure generic quality of life. The conclusions of these studies show that results of revision knee arthroplasty are inferior to those of primary knee arthroplasty, even while adjusting for confounding factors [21]. The authors conclude “most revision patients will never experience an outcome as favorable as their primary procedure.” A number of physical and physiological factors
may contribute to diminished outcomes, including the compounding effects of multiple surgeries, increased loss of natural anatomy, and the difficulty of revision surgery. Other “factors that may contribute to this difference [may include] deconditioning, muscle impairment or atrophy, scar tissue, instability, and joint stiffness. [20]” With outcomes of revision knee arthroplasty measurably worse, patients whose primary surgery fails are subject to a reduced quality of life.

In addition to poorer functional scores after revision knee arthroplasty, Patients undergoing revision TKR are more likely to have complications such as periprosthetic fracture (0.78% vs. 0.08%), wound infection (0.78% vs. 0.12%), deep prosthetic infection (0.47% vs. 0.06%), major systemic complications (7.44% vs. 4.91%), and mortality (0.62% vs 0.12%) [14]. In addition to complications, revision knee arthroplasty is generally more likely to fail. While primary total knee arthroplasty has a 5-year survivorship of 97.2%, the same 5-year survivorship of revision knee arthroplasty is only 87.4% [14]. Ong et al. analyzed Medicare claims data to determine the “relative risk of revision surgery for primary and revision” total joint arthroplasty, and found that patients with a revision knee arthroplasty were 5.71 times more likely to undergo re-revision. Successive surgeries exacerbate damage as native anatomy is weakened, compromised, or removed. The result is a subset of patients who undergo a number of failed procedures and end up with severe and irreversible knee dysfunction.

With a growing population of patients undergoing revision knee arthroplasty, combined with poorer outcomes resulting from revision and the increased likelihood of a
subsequent surgery being necessary, the number of patients with serious complications, including severe knee dysfunction, is expected to rise as well.

Knee Dysfunction and Weakness

Weakness of the knee extensor mechanism is a debilitating condition that limits a patient’s ability to actively extend the knee, and thus the ability to stand, rise from a chair, and walk without assistance. In addition to allowing for independence, sufficient quadriceps strength is also essential in preventing injuries due to falls [22]. Extensor mechanism weakness can occur in patients with tumors, muscular diseases, neurological diseases, osteoarthritis of the knee, or in patients who have undergone knee replacement surgery. Quadriceps weakness has been closely linked to osteoarthritis of the knee, and it has been suggested that it may be a result, a risk factor, or both [23], [24].

To make matters worse, knee replacement surgery itself results in profound quadriceps weakness. While TKR is able to address pain associated with the disease, it does not address deficits in quadriceps function [25]. Physical therapy following TKR is standard care, but it is frequently unable to rehabilitate patients to full preoperative strength [2]. Walsh et al. examined the effect of TKR on 29 patients versus an age matched control group of 40 patients, and found that even one year after surgery patients exhibited strength deficits, physical impairments, and functional limitations, including reduced walking and stair climbing ability [26]. Mizner et al. subsequently demonstrated that reduced quadriceps strength correlated with reduced functional performance, loading, and moving patterns [1]. Loss of quadriceps strength can be significant after TKR
surgery; Mizner et al. studied a group of twenty patients and found an average loss of 62% of quadriceps strength after 1 month [27].

The causes of quadriceps weakness after knee surgery are multifactorial. In their investigation, Mizner et al. examined the causes of weakness, and found that failure of voluntary activation was the predominant cause, with muscle atrophy only a secondary cause. Together, failure of voluntary activation and atrophy caused 85% of postoperative weakness [27]. However, in another study, Lewek et al. examined 12 patients with osteoarthritis who had not undergone TKR, and found no statistically significant decrease in voluntary activation.

In cases where successive revision surgeries are required, weakness is exacerbated as damage to native anatomy is compounded. Severe weakness is often irreversible and prevents patients from walking without the use of assistive devices such as braces, canes, crutches, or wheelchairs. For these patients, activities of daily living become difficult or impossible, significantly reducing quality of life [25].

Extensor mechanism weakness is poorly addressed with reconstructive surgery, as existing total knee replacement designs require adequate muscular strength and joint stability to function. While some TKR systems are engineered to compensate for a loss of joint stability, no existing TKR designs compensate for a weakened, damaged, or missing quadriceps extensor mechanism. To date, the number of patients affected by this condition has not been well characterized in the literature.
Transfemoral Amputation

There are approximately 185,000 total lower limb amputations performed each year in the United States, and the procedure is associated with reduced function, reduced quality of life, and depression [6], [28], [29]. Transfemoral amputation is sometimes required after failed total knee replacement; one study of twenty-five patients showed that approximately 37% of amputations were attributable to complications of the replacement procedure itself [28]. If these figures are extrapolated to nationwide incidence, using projections of total knee replacement procedures, an estimated 4,900 amputations per year may occur as a result of complications attributable to knee replacement by 2030 [17].

Knee Arthrodesis

Arthrodesis, or complete fusion of the knee joint, is preferable to amputation but is still a treatment of last resort in patients where total knee replacement is contraindicated. While arthrodesis has an extensive history of use, it is currently most often used to treat pain and instability in the knee in cases of multiple failed total knee replacement surgeries, bone loss, infection, or loss of the quadriceps extensor mechanism [10], [11]. Arthrodesis maintains the anatomical structure of the lower limb, enabling patients to maintain mobility independent of assistive devices such as braces or wheelchairs.

While arthrodesis allows for patient mobility, it requires an altered gait as a result of the inflexibility of the knee and subsequently increased moment of the leg. It has been suggested that changes associated with arthrodesis include increased pelvic tilt, increased ipsilateral hip abduction, and increased ipsilateral ankle dorsiflexion [10], though the data
supporting this is unpublished. Walking with an arthrodesis is more physically demanding, with oxygen consumption shown to be 20% greater when walking with an immobilized knee [30], and energy use demonstrated to be 25-30% higher than that of normal walking [10]. However, arthrodesis is still preferable to amputation, however, which requires an additional 25% energy expenditure compared to arthrodesis.

Arthrodesis is not considered an entirely positive outcome, and it is often performed only because it is unavoidable or advisable compared with the alternatives, including amputation. Presence of arthritis in other joints of the leg are a contraindication for arthrodesis, as the altered gait may increase stresses in the hip and ankle [11] and may induce secondary arthritis. The permanence of the extended knee position complicates a number of activities of daily living. Simple tasks such as bathing, tying shoelaces, or sitting in close quarters become difficult or impossible. Travel can be significantly affected, as an extended leg interferes with the ability to sit in cars or planes.

Arthrodesis has been performed using a number of techniques and fixation methods, including bony fusion assisted by means of internal or external fixation devices [11]. Traditional arthrodesis is a technically demanding procedure, and can result in significant blood loss and operative time [10], [31]. In some cases, such as massive loss of bone stock, fusion with bone-to-bone contact is difficult or impossible. Traditionally, the loss of natural bone has been compensated with the use of allografts or autografts, which entails additional surgical time and associated difficulties [10], [11].
Alternative Surgical Approaches to Arthrodesis

Fusion can be performed without direct bone-to-bone contact, and several alternative approaches have been established to achieve full fusion. Voss demonstrated an ‘artificial fusion’ performed with an implantable rod passing through the intramedullary canal of both the femur and tibia, with polymethyl methacrylate cement used as a ‘spacer’ between the bones [9]. The rod and cement provided sufficient fixation for full weight bearing the day after surgery, and was still successful at four years, the latest follow up available. This technique was first shown by Campanacci and Casta [32] and has been subsequently used by a number of surgeons. One patient who underwent fusion by means of this technique is presented in Chapter 3. Success of this alternative to bone-to-bone arthrodesis is promising, as it demonstrates the potential for successful fusion using completely non-native materials to bridge the joint.

Following the development of “artificial fusion,” a number of implantable knee prosthetics have been designed specifically for knee arthrodesis [33]. At least one such device has taken a similar form to that of total knee replacement designs. Bartlett et al. reviewed ten cases of patients who underwent an arthrodesis using a Stanmore Custom Arthrodesis Prosthesis [31], consisting of cobalt chrome femoral and tibial components with stems that are mechanically locked together by means of an axle and circlip. This device compares favorably to traditional arthrodesis, as it allows for fusion using a less technically demanding technique and reduced blood loss. Additional benefits of using a device for knee fusion include allowing for the establishment of a precise limb length, deliberate limb alignment, and avoidance of amputation in patients who would be
otherwise unable to undergo fusion. Considering the success of these alternative procedures, it appears that good fusion results are possible with implanted orthopedic devices.

**Discussion**

With the recent success of implantable orthopedic joint devices designed for knee fusion, coupled with the long term success of standard total knee replacement designs, the prospects for a more fully functioning device appear promising. Such a device could be designed to address the previously defined patient subset, those with severe knee dysfunction.

The limitations imposed by knee dysfunction, as discussed in Chapter 3, have meant that some patients must choose between a treatment that offers little stability and a treatment that fully and permanently constrains the knee. The former, a total knee replacement of some form, enables a patient to bend the knee, but lacks the stability to provide adequate support in the presence of knee dysfunction. The latter, knee arthrodesis, provides the full stability needed to ambulate, but precludes any ability to bend the knee.

With consideration of the aforementioned limitations, we propose a novel treatment model. This treatment would take the form of a total knee replacement, but would incorporate an ability to simulate fusion by temporarily maintaining rigid extension. In this manner, this treatment model would eliminate many of the current limitations imposed on this patient group. Patients lacking knee stability or a knee extensor mechanism could stand and ambulate independently without forgoing the ability to otherwise bend the knee. The work of this dissertation, including the quantification of
the affected patient subset, the kinematics and kinetics of gait, and the resulting joint and muscle forces, supports the development of such a proposed treatment model. This proposed treatment model is explored and developed further in Chapter 8.
CHAPTER FIVE
QUANTIFYING THE AFFECTED PATIENT POPULATION

The number of patients undergoing knee arthrodesis in the United States is quantified and described in clinically relevant ways. The hospitals where these procedures are performed are further characterized.

Hypothesis
The number of patients undergoing knee arthrodesis in the United States, heretofore unquantified, is significant (greater than 100 procedures per year).

Abstract
Treatment options for severe knee dysfunction are limited, and include knee arthrodesis. Patient satisfaction after knee arthrodesis is generally low, making it a treatment of last resort. There is a high level of clinical interest in this procedure, however, as evidenced by the large number of recently published clinical case reports and reviews in peer reviewed orthopedic focused journals. In spite of this high degree of clinical interest, specific details about the affected patient population are largely unknown. The number of patients undergoing knee arthrodesis has not been previously quantified, the types of patients undergoing the procedure have not been characterized, and the hospitals where the procedure is performed have not been characterized. Two patients with a knee arthrodesis, from two clinical practices, were presented in Chapter 3 of this
dissertation. These patients provide initial evidence of an unmet clinical need, but the prevalence of similar patients is unknown. In Chapter 5, we investigate the incidence of knee arthrodesis procedures in the United States over the past two decades in order to further support this need. We further characterize the patients undergoing the procedure by demographic, and characterize the hospitals where the procedure is performed. Our estimates are based on data obtained from the Nationwide Inpatient Sample, a database of inpatient hospital discharge records, using the International Classification of Disease-Revision 9 medical billing code for knee arthrodesis (ICD-9-CM 81.22). We also estimate the per capita procedural rates for individual patient demographics using population data from the United States Census. We found that the annual number of patients undergoing knee arthrodesis in the United States remained relatively unchanged from 1993 to 2011, the latest year for which data was available, at a mean of 1,014 (Standard Deviation: 113) procedures per year. Over 80% of patients were aged 45 or above. Approximately 65% of patients utilized governmental payers for reimbursement, including 54% using Medicare, which cannot be accounted for by age alone. Nearly all of the procedures were performed in metropolitan area hospitals (92.5%), and a significant majority of the procedures were performed in teaching hospitals (62%). We conclude that the number of knee arthrodesis procedures performed in the United States is significant.

**Introduction**

Treatment options for patients suffering from severe knee dysfunction are limited. Salvage total knee replacement surgery is often contraindicated, requiring patients to choose between forgoing surgery, transfemoral amputation, or knee arthrodesis. While
the functional outcomes of knee arthrodesis are better than those of amputation, the outcomes of both are low. This often leaves arthrodesis as the best of poor alternatives.

Historically, knee arthrodesis has had a wide range of clinical indications, including advanced osteoarthritis, posttraumatic osteoarthritis, rheumatoid arthritis, tuberculosis, poliomyelitis, and syphilis\(^\text{[10], [34]}\). With the development and success of total knee replacement (TKR) surgery, along with advances in medicine eliminating the later stages of some diseases, the indications for arthrodesis have narrowed \(^\text{[10], [34], [35]}\). Current indications for this treatment include damage, weakness, or loss of the knee extensor mechanism, inadequate ligamentous constraint, substantial bone loss or defects, osteosarcoma, posttraumatic arthritis, arthrofibrosis, or infection \(^\text{[10], [11]}\) and the procedure is often performed after the failure of total knee replacements \(^\text{[5], [34], [36], [37]}\).

Perhaps due to a combination of the undesirability of knee arthrodesis and the limited treatment alternatives, there is a high degree of clinical interest in the procedure, as evidenced by the publication of more than 60 case reports and review articles on the subject in peer reviewed, orthopedic journals in the past five years. These include review articles \(^\text{[5], [10], [11], [36]-[38]}\) and case reports, some of which have focused on methods of achieving fusion, including external fixation \(^\text{[39]}\) and internal fixation by means of intramedullary nails \(^\text{[40], [41]}\) or dynamic compression plates \(^\text{[42]}\). Alternative methods of achieving fusion have been proposed \(^\text{[9]}\), including implantable prosthetics dedicated to knee arthrodesis \(^\text{[31], [33], [36], [43]}\). These dedicated implants can serve as a rigid spacer in the absence of sufficient bone stock and may improve the surgical
success rate, but they offer patients no functional advantages over traditional knee arthrodesis techniques. The functional limitations of knee arthrodesis have driven a strong desire among patients for desarthrodosesis, or reversal of a previous fusion, in spite of its high complication and poor success rate [12], [44], [45].

Even with such a high level of clinical interest, there are no published estimates of the incidence of knee arthrodesis; the figures are completely neglected in all six review articles referenced above. Evaluating and quantifying patient subsets is critical to fully understanding unique patient needs. In some cases, quantifying a patient subset provides justification for the development of new and improved treatments. There have been numerous estimates and characterizations of orthopedic patient populations published in the literature in recent years, including the number of patients undergoing primary and revision total knee, hip, and shoulder replacement surgery [15], [46]. That work has been influential, and has enabled further studies, such as estimations of economic burden [47], to build upon it. This type of study is also prevalent outside of orthopedics, such as in estimates of heart disease in the United States [48].

These estimates are most commonly made by searching inpatient hospital discharge records. When searching through this data, researchers may take advantage of the ubiquitous nature of the International Classification of Disease-Revision 9 (ICD-9) medical billing codes. Nearly all procedures and patient diagnoses have their own specific ICD-9 code, and each patient medical record contains their diagnoses and procedures listed by code. When patients medical records are aggregated, researchers can search these records to determine prevalence or trends in diseases or procedures.
Patient records may be aggregated in a number of ways and by a number of different entities, such as internally within a hospital system for their own records. A number of patient discharge records have been aggregated into larger and readily available databases, allowing for similar studies to be conducted using databases such as the Nationwide Inpatient Sample [49], the National Hospital Discharge Survey [15], or the Medicare claims database [50].

The Nationwide Inpatient Sample (NIS) is the “largest publically available all payer inpatient care database in the United States,” and is a part of the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality. The NIS database contains approximately 8 million inpatient hospital discharge records from approximately 1000 hospitals, and is intended to represent a 20% sample of community hospitals in the United States [51]. The NIS uses a two-stage stratified cluster design with five strata, consisting of hospital characteristics. These strata are hospital ownership/control (private or public), bed size, teaching status (teaching or non-teaching), urban/rural location, and U.S. region (Northeast, Southeast, Midwest, or West). A random sample of hospitals is selected from each stratum. Each individual hospital is considered a cluster, and every discharge record from selected clusters is included in the sample. Over one hundred data elements are included with each patient discharge record (case), including patient age, sex, payment method, diagnoses and procedures performed, and teaching status, location, and size of the admitting hospital. The latest available NIS dataset (2011) contains “all discharge data from 1,045 hospitals located in 46 states.”
Materials and Methods

Data from all available years of the Nationwide Inpatient Sample (1988-2011) was obtained from the Agency for Healthcare Research and Quality (AHRQ), a part of Healthcare Cost and Utilization Project (HCUP). The NIS sample design was changed in 2001, and supplementary data was provided to accommodate the investigation of trends spanning beyond that year. Linked patient and hospital database files were merged, and further merged with the provided supplementary files where appropriate. HCUP recommends against using data from years 1988 to 1992 for trends analysis due to its smaller sample size, and it was omitted from all final analyses.

The database was searched for all instances of knee arthrodesis by searching the procedural variables of all cases (inpatient records) for the presence of the ICD-9-CM medical billing code 81.22 – “Knee Arthrodesis,” and we distinguished cases where arthrodesis was coded as a primary or secondary procedure. This code does not distinguish between differing methods or types of implants used in knee fusion, such as external fixation or internal fixation using plates or nails. Our search was assumed to capture all instances of knee arthrodesis in the sample, as it was well established for all years of the study and was not prone to underreporting.

Cases including a knee arthrodesis procedure were further analyzed for the following information:

- Arthrodesis as a primary (PR1) or secondary procedure
- Patient demographic data:
  - Gender
Age – Binned into six groups

- 0 to 44 years
- 45 to 54 years
- 55 to 64 years
- 65 to 74 years
- 75 to 84 years
- 85+ years

- Characteristics of hospital stay:
  - Length of stay
  - Total number of procedures performed
  - Associated diagnoses
  - Associated procedures

- Payment:
  - Total hospital charges
  - Reimbursement method

- Hospital data:
  - Teaching status
  - Hospital location (urban/rural)
  - Region of the country

All data analysis for this work was performed using SAS software (Version 9 of the SAS System for Windows. Copyright 2013 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS
A complete program was coded in the SAS programming language to simplify analysis, and to facilitate future investigations of similar nature. Values of p<0.05 were considered statistically significant for all measures.

Nationwide estimates for each year of the study were determined with account for the NIS study design. The appropriate weighting factors were used for each case, and standard errors are reported with consideration of the stratified sample design using the SURVEYMEANS statement (See example code).
In cases where knee arthrodesis was recorded as a secondary procedure, frequency analysis was used to determine the most commonly performed primary procedures.
A Poisson distribution [15] was assumed for the total number of arthrodesis procedures, population based procedure rates, the total number of procedures on each discharge record, and the total length of stay. Procedure rates for each patient demographic were further analyzed by age and gender using publically available population figures from the United States Census Bureau. Estimates from July of each intercensal year were used. Poisson regression analysis allowed for the use of age and sex as covariates in determining the rate and rate ratio of knee arthrodesis, and provided age-gender specific procedure rates. An analysis of rate ratios across all years of study was used to determine the presence of annual trends.

The nature of our search and our use of an inpatient record database meant that there were no zero values for either length of stay or the total number of procedures within each discharge record of interest; our search for records with an arthrodesis procedure meant that no records had less than one procedure, and inpatient records, by definition, require a minimum length of stay of one. Zero-truncated Poisson regression was used to analyze these items to account for this.

Payment method, total hospital charges, hospital teaching status, hospital location, and hospital region were investigated, and trends were determined using linear regression. The diagnoses and procedures that were most commonly present in cases of knee arthrodesis were examined using frequency analysis.

**Results**

There were an average of 1,014 knee arthrodesis procedures performed in the United States each year from 1993 to 2011 (Table 1). Knee arthrodesis was recorded as
the primary procedure in over two-thirds of all cases (Figure 8); when recorded as a secondary procedure, the most commonly recorded primary procedure was “Arthrotomy for Removal of Prosthesis Without Replacement, Knee” (ICD-0-CM 80.06) and the second most commonly recorded primary procedure was “Excisional Debridement of Wound, Infection, or Burn” (ICD-9-CM 86.22). There was no statistically significant increase or decrease in the total number of knee arthrodesis procedures performed in this time.
<table>
<thead>
<tr>
<th>Year</th>
<th>All Procedures</th>
<th>Primary Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>Std. Error</td>
</tr>
<tr>
<td>1993</td>
<td>1,180</td>
<td>97</td>
</tr>
<tr>
<td>1994</td>
<td>952</td>
<td>98</td>
</tr>
<tr>
<td>1995</td>
<td>1,044</td>
<td>93</td>
</tr>
<tr>
<td>1996</td>
<td>1,021</td>
<td>91</td>
</tr>
<tr>
<td>1997</td>
<td>895</td>
<td>95</td>
</tr>
<tr>
<td>1998</td>
<td>922</td>
<td>88</td>
</tr>
<tr>
<td>1999</td>
<td>952</td>
<td>90</td>
</tr>
<tr>
<td>2000</td>
<td>1,021</td>
<td>117</td>
</tr>
<tr>
<td>2001</td>
<td>928</td>
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<td>2009</td>
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<td>89</td>
</tr>
<tr>
<td>2010</td>
<td>858</td>
<td>83</td>
</tr>
<tr>
<td>2011</td>
<td>1,122</td>
<td>163</td>
</tr>
<tr>
<td>Avg.</td>
<td>1,013</td>
<td>*</td>
</tr>
</tbody>
</table>

Table 1 – Estimated total number of knee arthrodesis procedures (ICD-9-CM 81.22) and those coded as the primary procedure, by year.
Figure 8 – Number of knee arthrodesis procedures performed in the United States.

The total population of the United States grew 19.9% over this time, from 260.0M in 1993 to 311.6M in 2011. Taking annual population data from the United States Census Bureau into account, there was a decrease in the per capita procedure rate observed during the years of this study (p<0.05) (Figure 9).
Patient Demographics

Both age and gender significantly affected the relative rate of knee arthrodesis procedures, with age having the largest influence. The procedure rate increased with increasing age group, and the relative risk was 15 times greater for persons aged 75 to 84 than for persons aged 0 to 45 (the absolute number of knee arthrodesis procedures in patients aged 85 and up was insufficient to allow for analysis.) Men are at greater risk of knee arthrodesis – the procedure rate was significantly higher for males than females at each age group (Table 2, Table 3).
Although there was no significant change in the overall number of procedures, and there was a significant reduction in overall per capita rate of knee arthrodesis over the years of study, patient demographics significantly affected these trends. Both the total number and per capita rate of knee arthrodesis dropped significantly in younger patients.
(0 to 44) over the years of study (p<0.001 and p<0.001), while the total number of procedures rose in patients aged 45 to 54 and 55 to 64 (p<0.01). There was no significant change in the total number procedures in older patients (aged 65 to 74 and 75 to 84), but the per capita procedure rate of this demographic dropped over the time of the study when accounting for population growth (p=0.02).

The average hospitalization length for patients undergoing knee arthrodesis was significantly affected by age (p<0.001), increasing by an average of 1.04 days with each increase in age group. Length of stay was not significantly affected by gender. There was a significant decrease in the overall average length of stay over the study period (p<0.01) (Figure 10).

Figure 10 – Average length of stay for a person undergoing knee arthrodesis.
Associated Procedures and Diagnoses

The total number of procedures that a patient undergoing knee arthrodesis will undergo (including knee arthrodesis itself) during his hospital discharge is positively correlated with age (p=0.014), but is not influenced by sex. The average number of procedures per discharge record also rose over the years of study, at a rate of 0.067 procedures per year (p<0.01) (Figure 11).

The diagnoses most commonly associated with knee arthrodesis in discharge records are “unspecified hypertension” (ICD-9-CM 4019), “infection and inflammatory reaction due to internal joint prosthetic” (ICD-9-CM 99666), and “acute posthemorrhagic anemia” (ICD-9-CM 2851). The procedure most commonly recorded alongside knee arthrodesis was “packed cell transfusion” (ICD-9-CM 9904), and the second most
commonly recorded procedure was “arthrotomy for removal of a prosthesis without replacement” (ICD-9-CM 8006).

Reimbursement and Charges

The charges associated with each hospital stay increased dramatically over the years of study \( (p<0.001) \), increasing from an average of $33k per stay to an average of $111k per stay in 2011 (Figure 12).

![Figure 12 – Average hospital charges for a discharge that includes a knee arthrodesis procedure.](image)

A significant majority of reimbursements came from government sources, including Medicare and Medicaid, while private insurance accounted for approximately 26% of payments (Figure 13).
Figure 13 – Number of discharge records billed to the top three payors from 1993 to 2011.

Figure 14 – Percentage of discharges including a knee arthrodesis procedure, by payor
Procedure Location

Knee arthrodesis was performed in a metropolitan hospital in nearly all cases (92%), and a significant majority (62%) of the admitting hospitals were classified as “Teaching” hospitals [“has an AMA-approved residency program, is a member of the Council of Teaching Hospitals (COTH) or has a ratio of full-time equivalent interns and residents to beds of .25 or higher”] (Figure 15). There were no significant trends over time.

Figure 15 – Percentage of knee arthrodesis procedures performed in a teaching hospital
There were fewer procedures performed in hospitals in the Western region of the United States (Figure 16, Figure 17, Table 4), even when accounting for population differences, than any other region of the country (p=0.05) (Figure 18).

Figure 16 – Average annual number of knee arthrodesis procedures, by region of the country
Figure 17 – Regions of the United States (Nationwide Inpatient Sample)

<table>
<thead>
<tr>
<th>Regions of the United States (Nationwide Inpatient Sample)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northeast</td>
</tr>
<tr>
<td>Midwest</td>
</tr>
<tr>
<td>South</td>
</tr>
<tr>
<td>West</td>
</tr>
</tbody>
</table>

Table 4 – Regions of the US as defined by the NIS
Discussion

The purpose of this work, having first identified an unmet need in the local practices of our clinical collaborators in Chaper 3, was to determine the broader significance of said need. This need – the limited number and undesirability of options available to patients with severe knee dysfunction – has been discussed in the literature from a number of perspectives. In one such publication, the most appropriate course of treatment is addressed as an ethical dilemma [8]. Knee arthrodesis is advocated as an option that will salvage the limb and allow for independent ambulation, but it is generally undesirable to patients. In spite of the large number of publications on knee arthrodesis in peer-reviewed journals, there are no reports or estimates of the actual number of
procedures performed. No recent review articles cite the commonness of the procedure [10], [11], [38], in stark contrast to those of other orthopedic procedures.

This study provides a robust estimate of the number of knee arthrodesis procedures performed in the United States, and was conducted by adopting and adapting methods used to quantify other patient population subsets. While there are relatively few knee arthrodesis procedures performed relative to total knee replacement procedures (0.14%), this study establishes that the number of procedures, at approximately 1,014 per year, is not insignificant. The results of this study further indicate, however, that the number of arthrodesis procedures performed in the United States has not significantly changed over the past two decades. A small reduction in the absolute number of procedures may have been prevented by population growth, as the per capita rate of knee arthrodesis procedures has fallen or remained unchanged for each individual age/gender demographic group. The continued use of knee arthrodesis as treatment, in spite of its undesirability, indicates an otherwise unmet need in the affected patients. This merits a closer look by clinicians, researchers, and medical device manufacturers.

The success of primary and revision total knee arthroplasty has significantly marginalized knee arthrodesis as treatment of choice in most cases[10], but has not completely eliminated it. Arthrodesis is indicated in patients with deficient or missing extensor mechanisms, as total knee replacement designs cannot compensate for the loss of function and stability and the risk of graft transfer may be unacceptably high [8]. Knee arthrodesis often follows failed knee arthroplasty, as determined by our procedure analysis, and it could be hypothesized that the incidence of arthrodesis will increase as
the number of revision arthroplasty procedures increases. This must be balanced against patients increasing expectations for higher quality of life, function, and mobility, however, for which arthrodesis technology has not kept pace. This could account for both the decrease in per capita arthrodesis rates and the observation that arthrodesis rates do not mirror increases in total knee revision rates. Given the steady number of knee arthrodesis procedures, it is likely that reconstructive knee replacement is already performed in as many cases as is feasible. It is also possible that high risk reconstructions are performed too often, and that knee arthrodesis should be attempted earlier in some cases to preserve bone stock and ensure the greatest chance of success [4].

We found that patients who do undergo arthrodesis are generally older, with over 80% of all patients above the age of 45, and over 41% of patients above the age of 65. Age alone does not fully explain the prominence of Medicare as a payment method, however. Assuming that all patients above the standard eligibility age of 65 utilized Medicare as a primary payment method, there was still a significant proportion (12.3%) of younger patients utilizing it. These patients most likely received Social Security Disability benefits prior to their knee arthrodesis procedure, an indication of the debilitating nature of the knee dysfunction and injuries that are present in patients who undergo the procedure.

We also found that a significant majority of arthrodesis patients obtained treatment in metropolitan areas and at teaching hospitals. This may be indicative of the complicated nature of the procedure, the severity of the negative side effects, and the severity of the potential complications. It is possible that only a small number of
orthopedic surgeons perform the majority of these procedures, but this was not explored in the current study. Patients appear to be much more likely to either receive referrals or actively seek out specialists in knee reconstruction.

Arthrodesis can enable a patient to ambulate independently, but permanent rigid knee extension has severe functional limitations and can make sitting uncomfortable. Simple activities of daily living, such as bathing or tying one’s shoes, can become difficult or impossible. Independence may be lost as patients have difficulty sitting in cars, busses, or planes, and patients may find it difficult to engage in activities in public such as in theaters. Some surgeons may request that a patient give fusion a test run by wearing a full leg brace for an extended period of time prior to surgery to see if permanent extension of the limb is acceptable, and it often isn’t.

These patients often face poor alternatives, however, including transfemoral amputation and resection knee arthroplasty [5]. Some patients may voice a preference for amputation, but functional outcomes are typically worse than those of arthrodesis [10]. And while resection arthroplasty both salvages the limb and enables a patient to bend the knee and sit comfortably, patients are typically unable to walk. At least one knee implant type design has been developed to address this population [31], but it offers patients no functional advantage over traditional fusion methods. When compared against these options, arthrodesis often offers the best combination of function and risk. Based on personal communication with orthopedic surgeons experienced in knee reconstruction and arthrodesis, we estimate that only one quarter to one third the number of patients who
are suitable candidates for knee arthrodesis actually undergo the procedure, often in an attempt to avoid its limitations.

This investigation shows that there is a relatively small, but significant number of knee arthrodesis procedures performed each year, and that this number has remained relatively steady over the past two decades. The average cost of these discharges has more than tripled (Figure 12) in that time, even as the average length of stay has gone down (Figure 10). The high level of interest in knee arthrodesis, as evidenced by the number of published articles, is likely due to both the undesirability of the procedure and the significant number of affected or candidate patients seen by publishing/researching clinicians.

Looking forward, we expect the number of knee arthrodesis procedures to remain steady and the associated costs to continue to rise. These trends could be affected by the development of technological or procedural advances to address the affected patient subpopulation. This could include implants specifically designed to provide limited knee function or modular implant systems to improve outcomes following massive knee reconstruction. The quantification and characterization of patients undergoing knee arthrodesis and the characterization of hospitals where it is performed provides researchers, clinicians, and medical device manufacturers with information critical to assessing the demand for new treatment approaches and implant design in this area.

The results of this study support the significance of the need.
Acknowledgements

The following people are gratefully acknowledged for their assistance in this work: William Bridges, Ph.D.
CHAPTER SIX

CHANGES TO GAIT KINEMATICS AND KINETICS INDUCED BY RIGID KNEE CONSTRAINT

In which the kinematics and kinetics of rigid knee gait are quantified.

“The true method of knowledge is experiment.” – William Blake Read

Hypothesis

Rigid immobilization of a single knee will induce immediate changes in gait kinematics and kinetics. Further, acclimation to rigid knee immobilization will have a continued effect on these kinematic and kinetic changes.

Abstract

The purpose of this study is to determine and quantify differences in human gait due to a ‘learning effect’ after complete constraint of a single knee. We hypothesize that with increased immobilization time, patients with a single immobilized knee will undergo changes in movement and muscular force generation (as measured by kinematics and ground reaction forces.) Ten healthy subjects (M/F, n=5/5; aged 18-23) with no history of gait abnormalities were recruited for this study, and knee arthrodesis was simulated for 0 through 24+ hours using an immobilizing knee brace. Gait analysis was conducted during level walking on a 15-meter walkway using an eight-camera motion tracking system with a six-axis ground reaction force platform. Normal gait served as each subject’s control, and multiple measurements of braced gait were taken immediately following fitting of the
brace, after walking 0.4 kilometers (0.25 miles) on a treadmill, after walking 1.2 kilometers (0.75 miles) on a treadmill, and after wearing the brace for 24 hours. Additionally, the percentage of lean muscle and fatty tissue were recorded for each body segment using dual energy x-ray absorptiometry. Results showed that simulated knee arthrodesis caused statistically significant and interrelated changes to gait kinematics when compared to normal gait, including increased ankle dorsiflexion and pelvic obliquity during swing phase of the braced limb, increased abduction of the left and right hip during stance of the braced limb, and an increase in the net joint reaction force at the contralateral hip. These changes facilitated ground clearance of the braced limb and minimized displacement of the center of gravity of the pelvis. Increased acclimation time was not found to significantly alter braced gait kinematics, supporting the use of short term bracing as a model for longer-term immobilization of the knee.

**Introduction**

Knee arthrodesis, or permanent fusion of the knee, is performed to treat pain and instability in cases of multiple failed knee replacement surgeries, bone loss, traumatic injury, infection, or loss of the quadriceps extensor mechanism [10], [11]. Knee arthrodesis can enable a patient to walk independently, and approximately one to two thousand procedures are performed in the United States each year. The inability to bend the knee can significantly affect patient quality of life, however, as patients can no longer bend their leg during activities such as sitting, bathing, and driving. In addition, the procedure necessarily affects gait biomechanics. Clinically, knee arthrodesis has been
hypothesized to increase loading and induce degeneration of the adjacent joints and spine [5], [11], [38]. There has been a high level of clinical interest in the procedure in the past five years, with over sixty case reports and review articles published in that time. The availability of detailed information on the resulting kinematic and kinetic changes, however, is limited [52], [53], potentially due to the difficulty in accessing the affected patient population. In addition, the diverse range of clinical indications for arthrodesis can introduce confounding factors that make meaningful comparison of the resulting pathologic gait difficult. This combination of current clinical interest, significant patient morbidity, and lack of quantitative biomechanical data necessitate the further study of this condition to improve treatment options and patient outcomes.

One potential, documented method of conducting arthrodesis studies is to temporarily simulate knee arthrodesis in normal, healthy subjects by applying an immobilizing brace or cast. This allows researchers to examine the effects of knee immobilization without the presence of confounding gait abnormalities, and increases the number of potential subjects. Subject-specific control data can be collected from the normal gait of each subject, enabling researchers to isolate changes solely attributable to joint immobilization. Some preliminary work has been done in this area, but most studies have focused on energy expenditure and there is a notable lack of reporting of comprehensive kinematic and kinetic data. The few studies that have included kinematic and kinetic data have limited their reporting to an undefined sagittal plane, and none have taken account of the importance of defining joint rotations [54], [55]. They have been limited by 2D data capture methods [56] or have otherwise not included kinematic and
kinetic measures outside of the “sagittal” plane [57], [58]. A comprehensive and well-defined account of lower body knee kinematics and kinetics is thus needed.

While immobilizing the knee will induce immediate biomechanical changes, it is possible that changes will continue to occur with long-term immobilization as subjects become accustomed to the newly immobilized joint. No studies, however, have investigated the potential for these changes. In nine studies involving gait after immobilization of the knee, the methods accounted for acclimation in only a limited manner (Table 5). Subjects walked until they reached a steady-state heart rate in three of these studies [30], [59], [60], subjects walked until they reached steady state oxygen consumption in two studies [57], [58], and subjects were given various, but limited accommodation in four studies [58], [61]-[63]. Given the absence of study into changes in gait kinematics with increased knee immobilization time, an appropriate acclimation protocol is unknown. If gait adaptation continues to cause kinematic changes after short-term immobilization of the knee, as could be the case with clinical knee arthrodesis, it is possible that the methods used in the above studies were insufficient to capture these changes. The poor functional outcomes in patients with arthrodesis necessitate the development of an immobilization protocol to appropriately model stiff knee gait.

<table>
<thead>
<tr>
<th>Peer-reviewed research studies utilizing knee immobilization in gait analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study</strong></td>
</tr>
<tr>
<td>Hanada and Kerrigan [59]</td>
</tr>
<tr>
<td>Abdulhadi et al. [30]</td>
</tr>
<tr>
<td>Mattson and</td>
</tr>
</tbody>
</table>
Brostrom[60]
Lewek et al.[57] Walk on treadmill until “metabolic” “steady-state” 5 min
Kerrigan et al.[64] Walk until steady-state oxygen consumption <2 min
Senden et al.[63] Familiarize with limitation Approx. 1 min
Boone[62] “The subjects were previously familiarized with the treadmill.” 10 min
Kerrigan et al.[58] “To allow some accommodation time, each subject walked up and down the length of the walkway approximately five times before data was collected.” No time given
Waters et al.[61] “The subjects were instructed to become accustomed to walking” No time given

Table 5 – Peer reviewed publications utilizing knee immobilization in gait

The objective of this research is to provide a definitive dataset quantifying the changes to gait kinematics and kinetics resulting from immobilization of the knee, as well as to quantify the influence of these changes on loading at the affected knee. To add to previous work utilizing short-term immobilization using a brace or cast, we will evaluate changes over distance and time to establish a robust model for representing long-term immobilization, as would be the case with clinical knee arthrodesis.

Materials and Methods

This study received approval from the Institutional Review Board (IRB) of Greenville Health System, Clemson University, and Furman University, and informed consent was obtained from each study subject. Gait analysis trials were conducted within the Molnar Human Performance Laboratory of Furman University (Figure 19), which was equipped with an 8-camera motion capture system (ProReflex MCU 240, Qualsys,
Gothenburg, Sweden (Figure 20) and 6-axis force platform (LG6-4-1, Advanced Mechanical Technology, Inc., Newton, Massachusetts).

Figure 19 – Gait analysis pathway instrumented with six-axis force platform
A total of ten subjects [(n=10), five male (n=5) and five female (n=5); Age range 18 to 23] with no history of joint or gait abnormalities were recruited for this study from a volunteer sample, which was solicited through Clemson University and Furman University campus email and bulletin posts.

Subjects were instructed to wear compression athletic clothing and low-cut athletic shoes prior to testing, which were provided if unavailable. Upon arrival at the gait laboratory, subjects were given all appropriate literature, including an informed consent
form. Testing did not proceed until any questions the subject had were answered, and the informed consent form was signed.

Designated anthropometric measurements of the subject, including age, mass, height, and body segment dimensions were taken and recorded. Tissue composition measurements were recorded using Dual Energy X-ray Absorptiometry equipment, including segmental tissue mass, fat mass, and lean mass. The provided report is included in each subject’s file.

Bony landmarks were identified with the assistance of a provided diagram.

![Bony Landmarks Diagrams](image)

**Figure 21 – Diagrams identifying bony anatomic landmarks used to locate and place reflective markers**

Reference Landmarks were marked with a $\frac{1}{2}”$ solid black dot using a permanent marker, mascara pen, or other method.

- Sacral Vertebrae
Reflective markers were placed over the following anatomic landmarks to facilitate motion capture:

- Anterior Spina Iliaca Superior
- Crista Iliaca
- Greater Trochanter
- Superior part of the Patella
- Lateral side of the Patella
- Medial Condylis of the Femur
- Medial Malleolus
- Lateral Malleolus

- Sternum
- C7 spine
- L5 spine
- Acromium (left and right)
- Humerus (left and right)
- Elbow (left and right)
- Radius (left and right)
- Ulna (left and right)
- Hand (left and right)
- Anterior spine of the iliac crest (left and right)
- Greater trochanter (left and right)
- Medial and lateral condyles of the knee (left and right)
- Medial and lateral malleoli (left and right)
- Proximal, distal, and lateral sides of the heel (left and right)
- First and fifth metatarsals (left and right)
- Toes (left and right)

A rigid polymer shell with four rigidly attached markers was secured to each thigh and shank via an elastic band (Figure 22).

Figure 22 – Researcher demonstrating placement of reflective tracking markers while wearing the immobilizing brace.
Data from each subject was collected on two consecutive days. The force plate and motion tracking equipment were calibrated each day prior to subject data collection. Six groups of trials were conducted. Prior to the start of each group of trials, the subject was asked to stand motionless in the anatomic position for the collection of calibration data.

<table>
<thead>
<tr>
<th>Trials</th>
<th>Experimental Condition</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 Control Trial 1</td>
<td>Normal gait, before fitting the immobilizing brace</td>
<td>Day 1</td>
</tr>
<tr>
<td>B1 Brace Trial 1</td>
<td>Immediately after subject is fitted with the brace</td>
<td>Day 1</td>
</tr>
<tr>
<td>B2 Brace Trial 2</td>
<td>After walking on treadmill for 0.402 kilometers (0.25 miles)</td>
<td>Day 1</td>
</tr>
<tr>
<td>B3 Brace Trial 3</td>
<td>After walking additional 0.805 kilometers (0.50 miles) on treadmill</td>
<td>Day 1</td>
</tr>
<tr>
<td>B4 Brace Trial 4</td>
<td>After wearing the brace for 24 hours</td>
<td>Day 2</td>
</tr>
<tr>
<td>C2 Control Trial 2</td>
<td>Normal gait, after removing the immobilizing brace</td>
<td>Day 2</td>
</tr>
</tbody>
</table>

Table 6 – Experimental trial names, conditions, and the day on which they occurred.

The subject was first asked to walk normally (at a self-selected speed) along a 15-meter, straight, level pathway for the collection of control data (C1 – Control Trial 1). Subjects were asked to repeat this motion until data was collected from five left and five right clean and complete foot strikes on the force platform were recorded. This data was used to establish the normal gait of each subject.

Upon completion of the first control trial, knee arthrodesis was simulated in the right knee of each subject using a locking knee brace (Telescoping IROM, DJO Global, Vista, California). The length of the brace was adjusted to extend from the ankle to the inseam of each subject, and the flexion angle was set to 0 degrees for all trials and all subjects. Data capture commenced immediately upon fitting the subject with the brace, preventing the subject from gaining any familiarity to walking with the brace. The subject
walked along the 15-meter pathway for data collection, as during the control trial. After completion of this experimental trial (B1), the subjects were instructed to walk on a level treadmill for 0.25 miles at 2.5 miles per hour.

After walking 0.25 miles in the brace on the treadmill, the second experimental trial (B2) was conducted in the same manner and data collection sequence as the first two trials. The subject was then instructed to walk an additional 0.50 miles on the treadmill, for a total of 0.75 miles, after which additional data was captured (B3). Motion tracking markers were removed and their locations marked. The subjects were instructed to wear the brace, which was fitted with a pedometer, for an additional 24 hours pending a return visit and additional trial measurements the next day.

Motion tracking markers were replaced on the second day, and a final set of experimental data was collected (B4.) The brace was then removed, the subject was asked to acclimate to normal gait for at least three minutes, and a second set of control data was then collected (C2.)

Three-dimensional motion capture and ground reaction force data was collected and processed using Qualisys Track Manager (Qualsys, Gothenburg, Sweden) and exported to Visual3D (C-Motion, Germantown, Maryland) for analysis. A rigid body model was created to correlate the location of motion tracking markers with anatomical landmarks, and was scaled to match subject-specific measurements. The Cardan rotation sequence described by Cole was used to describe hip, knee, and ankle joint rotations [65], while the convention proposed by Baker was used for the pelvis [66]. Net reaction forces
and moments of the ankle, knee, and hip were calculated using an inverse dynamics approach, and were normalized to subject mass[67].

The following kinematic and kinetic data was normalized to the gait cycle (0-100%) and output from Visual3D:
• Walking velocity (meters/second)
• Stance duration (seconds and percent of gait cycle)
• Swing duration (seconds and percent of gait cycle)
• Sagittal (x), Frontal (y), and Transverse (z) plane movement of the center of gravity of the pelvis
• Sagittal (x), Frontal (y), and Transverse (z) plane kinematics of the pelvis with respect to the lab
• Sagittal (x), Frontal (y), and Transverse (z) plane joint rotations of the hip, knee, and ankle
• Sagittal (x), Frontal (y), and Transverse (z) plane net reaction forces of the hip, knee, and ankle
• Sagittal (x), Frontal (y), and Transverse (z) plane net joint moments of the hip, knee, and ankle

Data from each subject (1-10), joint (pelvis, hip, knee, ankle), side (left/right), experimental trial (C1, C2, B1, B2, B3, B4), and rotation plane (x, y, z) were calculated for the entire gait cycle of each trial repetition. Data analysis was performed using SAS software (Version 9 of the SAS System for Windows. Copyright 2013 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.) A complete SAS program was coded to simplify analysis and to facilitate future investigations of similar nature, and is provided in the Appendices.
Figure 24 – Master program coded in SAS to analyze gait data

Kinematic and kinetic values of interest (e.g. peak knee flexion during stance phase) were calculated by determining the minimum, maximum, mean, or range of values within a specific range of the gait cycle. The times where minimum and maximum values occurred (in percent gait cycle or percent stance phase) were also recorded and compared. (e.g. peak knee flexion during stance was determined by finding the maximum value of knee flexion between 0% and 40% of the gait cycle for each trial.) Each value of interest was determined for every motion capture trial. Comparison of experimental conditions (C1, B1, B2, B3, B4, and C2) and sides (left/right) was performed using analysis of variance followed by Fisher’s Pairwise Comparison. Experimental conditions were compared against same-day control trials (C1 vs. B1, B2, B3; C2 vs. B4). Values of p<0.05 were considered statistically significant for all measures.
Figure 25 – SAS Program showing 24 of the 76 subfiles used to search for areas of statistically significant differences

```sas
/* Identify specific point of interest */
PROC SORT DATA=original_data;
    BY joint_name;
RUN;

%LET joint_name = PelvicCGRight;
%LET joint_name = PelvicCGLeft;
%LET joint_name = PelvicCGRange;
%LET joint_name = PelvicZLeftSwing;
%LET joint_name = PelvicZRightSwing;
%LET joint_name = PelvicZAfterLHS;
%LET joint_name = PelvicZAfterRHS;
%LET joint_name = PelvicRotationCCW;
%LET joint_name = PelvicRotationCW;
%LET joint_name = PelvicObliquityLIO;
%LET joint_name = PelvicObliquityLeft5Swing;
%LET joint_name = PelvicObliquityRight5Swing;
%LET joint_name = PelvicTiltLIO;
%LET joint_name = PelvicTiltPeakRTO;
%LET joint_name = PelvicMeanTiltRightswing;
%LET joint_name = HipExtensionStart;
%LET joint_name = HipFlexionStart;
%LET joint_name = HipAdductionMean;
%LET joint_name = HipAdductionFirstTO;
%LET joint_name = HipAdductionSecTO;
%LET joint_name = HipAddMeanSTLimbSup;
%LET joint_name = HipRotationMean;
%LET joint_name = HipRotMean;
```

Figure 26 – SAS code used to identify data to search for statistically significant differences (PelvicCGRight)
<table>
<thead>
<tr>
<th>Joint</th>
<th>Plane</th>
<th>Value of Interest</th>
<th>Range (% Gait Cycle)</th>
<th>(p&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic Center of Gravity</td>
<td>Side to Side Displacement [Right(+) / Left(-)]</td>
<td>Peak pelvic sway to the Right side</td>
<td>0% to 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak pelvic sway to the Left side</td>
<td>50% to 100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overall range of pelvic sway</td>
<td>0% to 100%</td>
<td>*</td>
</tr>
<tr>
<td>Vertical Displacement</td>
<td></td>
<td>Minimum after Right Heel Strike</td>
<td>0% to 25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum during Left Swing</td>
<td>10% to 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum after Left Heel Strike</td>
<td>35% to 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum during Right Swing</td>
<td>60% to 100%</td>
<td>*</td>
</tr>
<tr>
<td>Pelvis</td>
<td>Rotation [CCW(+) / CW(-)]</td>
<td>Peak towards Left side</td>
<td>0% to 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak towards Right side</td>
<td>25% to 75%</td>
<td>*</td>
</tr>
<tr>
<td>Obliquity</td>
<td></td>
<td>Minimum at Left Toe Off</td>
<td>0% to 25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum during Left Swing</td>
<td>0% to 45%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum at Right Toe Off</td>
<td>50% to 75%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum during Right Swing</td>
<td>50% to 95%</td>
<td>*</td>
</tr>
<tr>
<td>Rear(+)/Forward(-) Tilt</td>
<td></td>
<td>Maximum at Left Toe Off</td>
<td>5% to 30%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minimum at Right Toe Off</td>
<td>55% to 75%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean during Right Swing</td>
<td>55% to 100%</td>
<td>*</td>
</tr>
<tr>
<td>Hip</td>
<td>Flexion(+)/Extension(-)</td>
<td>Peak Extension</td>
<td>25% to 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Flexion before Heel Strike</td>
<td>75% to 100%</td>
<td>*Right</td>
</tr>
<tr>
<td>Adduction(+)/Abduction(-)</td>
<td></td>
<td>Peak Adduction in early stance</td>
<td>0% to 30%</td>
<td>*Left</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean during Single Limb Support</td>
<td>12% to 50%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Abduction in late stance</td>
<td>50% to 75%</td>
<td>*Left</td>
</tr>
<tr>
<td>Internal(+)/External(-) Rotation</td>
<td></td>
<td>Mean Rotation Angle</td>
<td>75% to 100%</td>
<td></td>
</tr>
<tr>
<td>Knee</td>
<td>Flexion (+)</td>
<td>Peak Flexion during early stance</td>
<td>0% to 40%</td>
<td>*Right</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Flexion during Swing</td>
<td>50% to 100%</td>
<td>*Right</td>
</tr>
<tr>
<td>Adduction(+)/Abduction(-)</td>
<td></td>
<td>Peak Abduction in early swing</td>
<td>60% to 80%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Abduction in late swing</td>
<td>70% to 100%</td>
<td>*Right</td>
</tr>
<tr>
<td>Internal(+)/External(-) Rotation</td>
<td></td>
<td>Peak External Rotation in late swing</td>
<td>75% to 100%</td>
<td>*Right</td>
</tr>
<tr>
<td>Ankle</td>
<td>Dorsiflexion(+)/Plantarflexion(-)</td>
<td>Peak Plantarflexion after Heel Strike</td>
<td>0% to 25%</td>
<td>*Right</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Plantarflexion at Toe Off</td>
<td>50% to 75%</td>
<td>*Right</td>
</tr>
<tr>
<td>Inversion(+)/Eversion(-)</td>
<td></td>
<td>Mean during Single Limb Support</td>
<td>12% to 50%</td>
<td>*Right</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Inversion at Toe Off</td>
<td>50% to 75%</td>
<td></td>
</tr>
<tr>
<td>FF Adduction(+)/FF Abduction(-)</td>
<td></td>
<td>Peak Abduction at Contralateral Toe Off</td>
<td>0% to 25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Adduction at Toe Off</td>
<td>50% to 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak Adduction before Heel Strike</td>
<td>90% to 100%</td>
<td></td>
</tr>
</tbody>
</table>

Table 7 - Kinematic values of interest that were analyzed to find statistically significant differences. Values that differed between "Control" and "Brace" trials are indicated with a "*" in the right column.
<table>
<thead>
<tr>
<th>Net Joint Reaction Force</th>
<th>Axis</th>
<th>Value of Interest</th>
<th>Range (% Stance)</th>
<th>(p&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak after Heel Strike</td>
<td>0% to 13%</td>
<td>*Left</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Minimum in early stance</td>
<td>15% to 25%</td>
<td>*Left</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean in midstance</td>
<td>25% to 75%</td>
<td>*Left</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peak in late stance</td>
<td>75% to 95%</td>
<td>*Left</td>
<td></td>
</tr>
<tr>
<td>Net Hip Reaction Force</td>
<td>Medial / Lateral</td>
<td>Peak in early stance</td>
<td>8% to 30%</td>
<td>*Left</td>
</tr>
<tr>
<td></td>
<td>Anterior / Posterior</td>
<td>Mean in midstance</td>
<td>35% to 65%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Axial</td>
<td>Minimum in late stance</td>
<td>65% to 90%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peak in early stance</td>
<td>10% to 35%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean in midstance</td>
<td>40% to 65%</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peak in late stance</td>
<td>65% to 90%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net Knee Reaction Force</td>
<td>Medial / Lateral Shear</td>
<td>Peak in early stance</td>
<td>10% to 35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anterior / Posterior Shear</td>
<td>Peak in early stance</td>
<td>10% to 35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Axial Compressive</td>
<td>Peak in early stance</td>
<td>10% to 35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean in midstance</td>
<td>40% to 65%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak in late stance</td>
<td>65% to 90%</td>
<td></td>
</tr>
<tr>
<td>Net Ankle Reaction Force</td>
<td>Medial / Lateral Shear</td>
<td>Peak in early stance</td>
<td>10% to 35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean in midstance</td>
<td>75% to 90%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak in late stance</td>
<td>65% to 90%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anterior / Posterior Shear</td>
<td>Mean in early stance</td>
<td>15% to 35%</td>
<td>*Right</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak in late stance</td>
<td>65% to 90%</td>
<td>*Right</td>
</tr>
<tr>
<td></td>
<td>Axial Compressive</td>
<td>Peak in early stance</td>
<td>10% to 35%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean in midstance</td>
<td>35% to 65%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peak in late stance</td>
<td>65% to 90%</td>
<td></td>
</tr>
</tbody>
</table>

Table 8 – Kinetic values of interest (Net Joint Reaction Force) that were analyzed to find statistically significant differences. Values that differed between "Control" and "Brace" trials are indicated with a "*" in the right column.
Table 9 – Kinetic values of interest (Net Joint Moment) that were analyzed to find statistically significant differences. Values that differed between "Control" and "Brace" trials are indicated with a "+*" in the right column.

**Results**

Kinematic and kinetic data was quantified, and mean values for combined data from Control (C1, C2) and Brace trials (B1, B2, B3, B4) are visualized with respect to the gait cycle for kinematics (Figure 27, Figure 28) and with respect to stance phase for kinetics (Figure 29, Figure 30). Statistically significant changes to gait kinematics and kinetics were observed when the knee was immobilized, and remained significant across all experimental trials (B1- B4) (Table 7, Table 8, Table 9). A small number of changes were only significant immediately after immobilization (Control vs. B1), but were no longer significantly different from control values in subsequent trials (Table 10). No significant differences were observed between braced trials (B1 vs. B2 vs. B3 vs. B4).
Figure 27 – Mean values (shaded regions represent standard deviation) of the pelvic center of gravity and pelvic rotation in three planes (Columns A-C). (Gait cycle displayed from ipsilateral heel strike to ipsilateral heel strike.)
Figure 28 – Joint Rotation Angle. Mean values (shaded regions represent standard deviation) of the Hip Rotation Angle (Row 1), Knee Angle (Row 2), and Ankle Angle (Row 3) in three planes (Columns A-C). (Gait cycle displayed from ipsilateral heel strike to ipsilateral heel strike.)
Figure 29 – Joint Reaction Forces. Mean values (shaded regions represent standard deviations) of the normalized (to subject mass) net joint reaction force of the hip (Row 1), knee (Row 2), and ankle (Row 3). (Legend: Control Trials – Right=Red, Left=Blue; Braced Trials: Right=Purple, Left=Cyan) (Stance phase displayed from ipsilateral heel strike to ipsilateral toe off.)
When braced, each subject’s self-selected gait speed and stride length was reduced (p<0.0001), while stride width was increased (p=0.0103). Right (braced) stance time, right (braced) swing time, and left stance time were increased (p<0.0001), but there was no difference in swing time of the left (unbraced) leg (p=0.6168). Some of the differences in kinematics can be observed relatively easily by overlaying a model of the braced subject on a model of the same subject during normal gait (Figure 32).
Figure 31 - A visual comparison of the relative stance and swing times of the left and right side during Control (C1, C2) and Experimental Trials (B1, B2, B3, B4).

Table 10 - The above values of interest were significantly different from Control values during the first brace trial (B1) but were no longer significantly different in subsequent trials.
Figure 32 – Posterior view visualization of a braced subject model (lighter) overlaid on the normal gait of the same model (darker) during (A) midstance and (B) midswing of the right leg. The left hip is more abducted and the pelvis is rotated obliquely during midswing, resulting in a rise of the center of gravity of the pelvis and the right hip joint center, helping the right foot to clear the ground as it is brought forward. Subject’s right and left feet are further away from the centerline of the body during their respective swing phases.

Significant kinematic differences between normal gait and immobilized trials (B1-B4) are listed below in the order in which they occur during a single gait cycle (The right knee was immobilized in all cases, and the gait cycle is listed from Right Heel Strike to Right Heel Strike).

- Following Right Heel Strike, the right foot plants flat on the ground with a greater degree of ankle plantarflexion (p=0.0014)
- Following Left Toe Off, the left hip abducts more than normal gait (p=0.0397)
- The right hip is more abducted through single leg stance (p=0.0020)
- Clockwise pelvic rotation reaches a greater peak immediately after Left Heel Strike ($p=0.0143$)
- The oblique pelvic dip towards the right foot is attenuated ($p=0.0005$)
- The right hip continues to extend longer into the gait cycle, until toe off ($p<0.0001$)
- With reduced heel rise, maximum plantar flexion of the right ankle is reduced ($p<0.0001$), and reaches its peak at Right Toe Off
- Dorsiflexion of the right ankle begins earlier, immediately at Right Toe Off rather than afterwards ($p<0.0001$), and neutralizes ankle plantar flexion more rapidly (Figure 8)
- The left hip is much more abducted through single leg stance ($p<0.0001$)
- Pelvic obliquity decreases (left side down, right side up) dramatically during right swing ($p<0.0001$)
- The center of gravity of the pelvis rises to a higher peak (along the vertical axis) as the rigidly extended right leg moves through swing phase ($p=0.0093$)
- The left ankle is more inverted as the right leg begins swing phase ($p=0.0059$)
- Pelvic tilt is reversed during right swing, tilting forward rather than towards the rear ($p<0.0001$)
- Maximum hip flexion prior to Right Heel Strike is reduced ($p=0.0496$) and occurs much closer to heel strike ($p<0.0001$)
Significant kinetic differences between normal gait and the immobilized trials (B1-B4) are listed below with respect to right and left stance phases:

Right Side – Early Stance

- Right ankle peak M/L force decreased (p=0.0046)
- Right ankle A/P force decreased (p=0.0007)
- Right hip peak adduction moment decreased (p=0.0004)
- Right knee peak flexion moment decreased (p=0.0109)

Right Side – Midstance

- Right hip axial compressive force increased (p<0.0001)
- Right knee axial compressive force increased (p<0.0001)
- Right ankle axial compressive force increased (p<0.0001)

Right Side – Late Stance

- Right ankle M/L force decreased (p=0.0063)
- Right ankle A/P force decreased (p=0.0003)

Left Side – Early Stance

- Left hip M/L force increased immediately after LHS (p=0.0010)
- Left hip M/L force remains increased as load transferred (p<0.0001)
- Left hip peak A/P force increased (minimum goes more negative) (p=0.0235)
- Left ankle peak M/L force decreased (p=0.0014)
- Left hip peak extension moment increased (p=0.0030)
• Left hip peak adduction moment decreased (p<0.0001)
• Left knee peak abduction moment decreased (p=0.0061)

Left Side – Midstance
• Left hip M/L Force increased (p<0.0001)
• Left hip axial compressive force increased (p<0.0001)
• Left knee axial compressive force increased (p<0.0001)
• Left ankle axial compressive force increased (p<0.0001)

Left Side - Late Stance
• Left hip M/L force increased (p=0.0031)

Discussion

This data confirms that gait kinematics and kinetics undergo immediate changes upon immobilization of a single knee. The most obvious change in kinematics is at the immobilized knee itself, which loses all range of motion. The effective length of the limb (the distance from the hip to most distal point of the foot) cannot be significantly reduced with the knee unable to bend, requiring subjects to compensate with kinematic changes in order for the foot to clear the ground during the swing phase of gait. While it may seem intuitive that increased adduction of the hip of the brace limb could help swing the leg out to assist in ground clearance, this does not occur. (In fact, there is slightly more abduction, though it is not statistically significant.)

The purpose of gait is forward motion, but the normal physiological modus operandi is to optimize energy expenditure by minimizing excess vertical and lateral
movement of the body’s center of gravity [68], [69]. Constraints on normal gait, such as an immobilized knee, will require simultaneous compensations to minimize energy use, and the gait alterations observed in this study may be understood as interrelated within this paradigm[69]. The most immediate impact of immobilizing the knee in full extension was during the two phases of gait where the knee normally flexes the most: midstance and swing phase (Figure 33). This is consistent with the fact that most of the statistically significant changes to gait kinematics correspond with these parts of the gait cycle (Figure 35).

![Figure 33](image)

**Figure 33 – Knee flexion during Brace trial, showing the significant difference in knee flexion between the left and right sides.**

Kinematic compensations are required to assist in clearing the floor with the limb, as noted previously [70], while simultaneously working to minimize energy expenditure. This is observable as a delay in the initiation of hip flexion in the right (braced) leg, immediate dorsiflexion of the ankle following Toe Off, left hip abduction, and a dramatic
increase in pelvic obliquity. Hip flexion typically occurs prior to Toe Off as the knee breaks, but when the knee is braced the hip cannot begin extending until the foot is lifted from the floor. Right ankle dorsiflexion minimizes the contribution of the foot to overall limb length as the leg begins swing phase, and pelvic obliquity helps ‘lift’ the limb over the ground. Although there is a significant increase in abduction of the left (unbraced) hip and obliquity of the pelvis, which serve to lift the right limb, this results in a wider stance, which keeps the body’s center of gravity low and centered. These observations are consistent with the conclusion that the observed gait changes minimize excess movement of the center of gravity.

Figure 34 – Plantarflexion of the ipsilateral ankle during normal gait (purple) and with simulated knee arthrodesis (red); Triangles denote Right Toe Off events.

Kinetic changes included a dramatic increase in the left hip extension moment, medial shear reaction force, and posterior shear reaction force during early stance as the opposite, braced leg was lifted from the ground and brought forward. The net medial reaction force in the left hip increased across the entire stance phase. In addition, axial
compressive loading during midstance increased in all joints. All other significant changes to joint kinetics were reductions in the magnitudes of joint reaction forces and moments. This suggest that contralateral hip extensors play an outsized role in the gait compensations required to bring forward an immobilized limb, and may help explain subsequent degeneration of this joint in patients with an arthrodesed knee [5], [11], [38].

Several kinematic and kinetic measures differed significantly from control values immediately after initial knee immobilization (C1 vs. B1), but were attenuated and no longer significantly different from control values in subsequent trials (Table 10). This suggests that acclimation has a limited effect on gait, but that directing subjects to ambulate 0.4 kilometers (0.25 miles) is sufficient to account for changes that would occur over a 24 hour immobilization time. This would appear to support the use of short-term bracing as a model (Table 5) for simulating long term knee immobilization, such as with knee arthrodesis. One limitation of this model, however, is that it does not take into account long-term, chronic changes in adjacent joint conditions that could affect patient kinematics. It is possible that long-term brace immobilization (greater than 24 hours) would result in significantly altered gait compared to the immediately braced and +24 hour braced knee, although no trends were noted in this study to support this hypothesis.

In spite of the high level of clinical interest in knee arthrodesis, as evidenced by the large number of published reviews and case reports, there is a notable lack of available information on the changes to gait kinematics and kinetics induced by the procedure, and a consequent lack of information on loading patterns at the affected knee. The goal of traditional methods of knee arthrodesis has been to fuse the femur and tibia
directly or with bone graft, and these fusions have generally been robust. This robustness has meant that there has been little need or benefit to quantifying the loading patterns of a fused knee, and may explain why there has been little interest in this subject.

When patients lack significant bone stock, however, new approaches to spanning the joint have been required [9], [33], and at least one total knee replacement like design has been developed to address knee arthrodesis [31]. With the development of these new implants, there have been examples of implant failure due to fracture [31], [33], which may suggest that the loading conditions used to design and test implants for use in knee immobilization were inadequate. There may be a question of quantifying the mechanics of knee arthrodesis to be used in the design of such devices. It is likely that the altered kinematics of arthrodesis gait play a significant role in altering the loading patterns at the knee. The development of detailed musculoskeletal models, using gait kinematics, has enabled researchers to create better informed finite element analysis models, and has been used in the testing of orthopedic implants [71]. Data from this study provides a robust account of the kinematic and kinetic gait resulting from knee immobilization, and can be used to assist in future computational modeling and testing of arthrodesis implants or implants that temporarily simulate arthrodesis.
Figure 35 – Phases of the gait cycle where lower body joint kinematics differed significantly from those of normal gait. Each row represents a joint of the lower body as it progresses through a single gait cycle, and is shaded in phases where the joint kinematics of the Experimental condition (right knee braced) differed significantly, in any plane, from the joint kinematics of the Control condition (normal gait). The gait cycle begins and ends with Right Heel Strike events, and Left Toe Off, Left Heel Strike, and Right Toe Off events are indicated with dashed lines. Significant differences at the right knee, which was braced, are more darkly shaded to emphasize its primacy in causing the other changes.

Acknowledgements

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CHAPTER SEVEN

ESTIMATED JOINT LOADING AT A RIGIDLY CONSTRAINED KNEE

In which the joint loading patterns of a rigidly constrained knee are estimated using a computational model incorporating musculoskeletal features and geometry.

Hypothesis

Knee joint reaction forces and moments during gait are significantly altered when the knee is fully constrained.

Abstract

Having established an unmet clinical need in support of a novel implantable medical device model in Chapters 3 through 5 of this dissertation, and having examined the kinematic and kinetic changes to gait that such a treatment model would induce in Chapter 6, this Chapter quantifies the mechanical loading patterns that would be present at such an implant.

Introduction

Knee arthrodesis, as reviewed in detail in Chapter 4, is a treatment in which the bones of the upper and lower leg are permanently fused, and may be used to salvage a leg that would otherwise require amputation. By imposing permanent rigidity at the knee, arthrodesis provides patients with the stability necessary to ambulate independently. This
independence can provide a greater level of function than amputation, as well as a better quality of life [38].

The inability to bend the arthrodesed knee, however, necessarily affects gait biomechanics. Some secondary effects of the biomechanical changes resulting from stiff-knee gait have been demonstrated, including increased energy expenditure and oxygen consumption [30], [57]-[59], [61], [62], [70], and pain in other joints and the lower back have been associated with knee arthrodesis. It has been asserted that knee arthrodesis may induce arthritis in other joints, including the contralateral hip, but no studies have established this causation or shown a conclusive link between the procedure and subsequent joint degeneration.

In addition to effects at other joints, there is a question of the robustness of a rigidly fused joint to bear the loading patterns produced by daily activity, such as during gait. The long term viability of some methods of knee fusion and their ability to withstand these loads has been questioned [9], and there have been published cases of knee arthrodesis implant fracture [31], [33]. It is common for orthopedic implants to undergo testing, but the in vivo mechanical failure of these implantable medical devices suggests that the parameters used for testing may have been inadequate. There have been no publications to date providing estimates of the loading patterns at an immobilized knee, and it is therefore necessary to undertake this quantification.

Measuring in vivo loading conditions, including the forces in muscles, ligaments, and joints, however, is often difficult or impossible. Instrumented total hip and total knee implant designs have been developed and used to acquire in vivo loading data in some
patients undergoing hip or knee arthroplasty, but this approach has not been used in knee fusion. Simplified net joint reaction forces and moments (net effect, neglecting musculature) can be calculated to balance a given load using an inverse dynamics approach with knowledge of the following information:

- **Body/Segment mass properties:**
  - Mass, \( m \)
  - Mass moment of inertia, \( I \)

- **Body segment kinematics (from 3D motion capture data):**
  - Position
  - Linear velocity
  - Linear acceleration
  - Angular Velocity
  - Angular acceleration

- **External forces (such as from force platform data)**

  This approach underestimates actual joint loads, however, by neglecting the contributions of musculature. Co-contraction, or simultaneous contraction of antagonist muscles about a joint, is physiologically common, and increases the magnitude of joint reaction forces without changing measured kinematics. This increase in magnitude goes undetected when musculature is ignored [72], [73].
The complexity of a biomechanical model can be increased to include musculature and detailed skeletal geometry Figure 36) using a system of equations of the following form:

\[ C\mathbf{f} = \mathbf{r} \]

Where \( \mathbf{f} \) is a vector of joint and muscle forces, \( \mathbf{r} \) is a vector representing the external and inertial forces, and \( C \) is a matrix of equation coefficients. In addition to the large increase...
in computational complexity, however, the redundant nature of musculature increases the number of unknowns beyond that of the number of equilibrium equations needed to balance a given set of loading conditions; the result is an unlimited number of potential solutions. An optimization function based on the minimization of muscle forces, and requiring that muscle forces are positive (can only contract), takes the following form:

\[ \text{Minimize: } G(f^M) \]

\[ \text{Subject to: } \quad Cf = r ; \quad f_i^{(M)} \geq 0, \quad i = 1..n^{(M)} \]

In order to solve this set of equations in a physiologically meaningful way, assumptions must be made about how the central nervous system recruits muscle activation. Published musculoskeletal models address this problem with the use of an optimization function that minimizes the overall muscle forces or muscle stress of the modeled system [74]-[77]. These functions have generally taken a single form, but with differences in polynomial order: (linear: p=1, quadratic: p=2, cubic: p=3 [78]-[80] … Min/Max: p essentially infinite) (Table 11):

\[ G = \sum_i \left( \frac{f_i}{N_i} \right)^p \]

Where \( f_i \) is muscle force, \( N_i \) is a normalization factor (such as muscle strength), and \( p \) is the order of polynomial. Put simply, the higher the order of polynomial, the more load sharing by synergistic muscles is predicted, as more highly loaded individual muscle terms are punished.
<table>
<thead>
<tr>
<th>Publication</th>
<th>Type</th>
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<tbody>
<tr>
<td>Grujicic, 2010; [81]</td>
<td>Min/Max</td>
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<tr>
<td>Grujicic, 2010; [82]</td>
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<td>Carbone, 2012; [78]</td>
<td>Cubic</td>
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<tr>
<td>Eltoukhy, 2011; [83]</td>
<td>Unspecified - “Postpone fatigue”</td>
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<tr>
<td>Grujicic, 2011; [71]</td>
<td>Unspecified – same as above</td>
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<tr>
<td>Anderson, 2011; [84]</td>
<td>Unknown</td>
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<tr>
<td>Damsgaard, 2006; [77]</td>
<td>All of them – balance, none proven superior</td>
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<tr>
<td>Wagner, 2010; [85]</td>
<td>Min/Max – “Minimum effort”</td>
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<tr>
<td>Holmberg, 2008; [76]</td>
<td>Min/Max</td>
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<tr>
<td>Erdemir, 2007; [86]</td>
<td>Review – Third Order Common for lower body</td>
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<tr>
<td>Crowninshield, 1981; [79]</td>
<td>Third Order</td>
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<tr>
<td>Seireg, 1975 [87]</td>
<td>Linear + 4M + Joint Force</td>
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<tr>
<td>Crowninshield, 1978 [88]</td>
<td>Linear</td>
</tr>
<tr>
<td>Patriario, 1981</td>
<td>Second Order + Power Output</td>
</tr>
<tr>
<td>Rohrl, 1984</td>
<td>Linear</td>
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<tr>
<td>Brand, 1986</td>
<td>Third Order</td>
</tr>
<tr>
<td>Collins, 1995;</td>
<td>Second Order, Linear, Etc.</td>
</tr>
<tr>
<td>Pederson, 1997</td>
<td>Third Order</td>
</tr>
</tbody>
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Table 11 – Optimization functions in peer reviewed publications
A number of analytical software packages have been developed over the past several years to assist in the creation and simulation of musculoskeletal models. These include AnyBody [77], LifeMod [89](since purchased by Smith & Nephew and no longer publically available), SIMM [90], and Open SIMM [91]. These software packages facilitate the construction of models and enable dynamic simulations of those models using motion capture data.

The relevance of any musculoskeletal model is its ability to accurately predict in vivo loading conditions. Confidence in the ability to do this requires validation of the model, which is complicated by the fact that models are often constructed to predict conditions that are difficult or impossible to measure in vivo. The assumptions, limitations, and uncertainties of a particular model must be assessed for its intended use [92]. Force and moment data acquired from subjects with instrumented joint replacements has been published, and this data has been used to validate and improve the construction of musculoskeletal models for gait analysis that are available to others [74].

Expected loading patterns are an important design parameter in engineered systems, and have been essential to the design and material selection of modern orthopedic implants. Musculoskeletal models have allowed researchers to predict how implanted prosthetics will perform [81], [93], [94], and have been used to assist in the design of new orthopedic implants [81], [82]. In order to either investigate the biomechanical effect of knee arthrodesis on other joints, or to accurately predict the mechanical failure of a knee arthrodesis implant due to local loading conditions, the
altered joint biomechanics resulting from knee arthrodesis must be known. These open questions demonstrate a compelling need for this data, which musculoskeletal modeling techniques are well suited to provide.

We hypothesize that joint reaction forces and moments at the knee in a patient with a single fully constrained knee are significantly different from the forces and moments at the knee in a patient without a fully constrained knee. Changes to gait kinematics and kinetics resulting from rigid knee immobilization were investigated and quantified in a study described in Chapter 6, and the kinematic and kinetic data gathered in that study was then used to construct a computational biomechanical model. This model was then used to drive a series of dynamic simulations, providing estimates of lower body reaction forces, including those at the immobilized knee, during walking with and without a single fully constrained knee.

**Materials and Methods**

The AnyBody Modeling System (Version 5.2.0) was used to construct a musculoskeletal model, which was subsequently driven through a series of dynamic simulations. These simulations were driven by three-dimensional kinematic and kinetic data obtained from a previously conducted gait analysis study, described in detail in Chapter 6. That study was designed and conducted to simulate arthrodesis in normal, healthy subjects using an adjustable locking knee brace, and three dimensional data was captured using an 8-camera motion capture system (ProReflex MCU 240, Qualsys, Gothenburg, Sweden) and a ground reaction force platform (LG6-4-1, Advanced Mechanical Technology, Inc., Newton, Massachusetts).
In that study, subjects were first instructed to walk normally, and the gait kinematics and kinetics captured were used as Control trials. Subjects were then fitted with an immobilizing brace on their right knee in all cases, and a series of trials were captured immediately after fitting of the brace, after walking 0.25 miles on a treadmill, and after walking an additional 0.50 miles on a treadmill. These distances were evaluated for effects due to acclimation to the immobilization. Three-dimensional motion capture data and force platform data from the preliminary Control trials (C1) and the third set of Brace trials (B3) was selected to create and drive a musculoskeletal model through dynamic simulations, providing estimates of knee joint reaction forces and moments during gait.

The musculoskeletal model constructed for the purpose of this study was based upon the Twente Lower Leg Model [95] (Figure 37) consisting of:

- 19 Rigid Segments – This included 5 segments in each of the lower extremities, 1 pelvis segment, and 8 segments in the spine, thorax, and skull.
- 18 Joints – The joints provide a total of 72 kinematic constraints to the model, and allow for 36 axes of rotation.
- 450+ Muscles – Muscle recruitment works both synergistically and antagonistically in order to reduce the total effort required by the system and to provide joint stabilization.

Model attributes, including total height and mass, were set to match those of the gait subjects from which kinematic and kinetic data was drawn, and the following model
segments were scaled to match subject anthropometry based on the placement of motion tracking markers:

- Upper Arm Lengths
- Lower Arm Lengths
- Trunk Height
- Pelvis Width
- Thigh Lengths
- Shank Lengths
Figure 37 – Musculoskeletal model consisting of 19 rigid segments, 18 joints, and 450+ muscles. The force platform, ground reaction force vector, and motion tracking markers are also visualized.

The model was used to run a series of dynamic simulations, including both normal and immobilized-knee gait. Fused knee conditions were simulated using a driver that locked the rotation of the right thigh and shank with respect to each other, and
determined the resultant joint moments.

Static optimization was used to calculate muscle activation at each time step of the simulation by minimizing the following fifth order objective function:

\[ G = \sum_i \left( \frac{f_i}{N_i} \right)^5 \]

Where \( f_i \) is force of the muscle and \( N_i \) is the normalization factor of the muscle [77]. The following lower limb muscle forces, joint reaction forces, and joint moments were collected for each trial (Control and Brace).

Ankle

- Joint Contact Forces
  - Proximal-Distal
  - Medial-Lateral
  - Anterior-Posterior

- Joint Moments
  - Plantarflexion/Dorsiflexion
  - Subtalar Inversion/Eversion
  - Axial (Forefoot Adduction/Abduction)

Knee

- Joint Contact Forces
  - Proximal-Distal
  - Medial-Lateral
  - Anterior-Posterior
• Joint Moments
  o Flexion/Extension
  o Adduction/Abduction
  o Internal/External Rotation

Hip

• Joint Contact Forces
  o Proximal-Distal
  o Medial-Lateral
  o Anterior-Posterior

• Joint Moments
  o Flexion/Extension
  o Adduction/Abduction
  o Axial (Internal/External Rotation)

Muscle Forces

• Quadriceps
  o Rectus Femoris
  o Vastus Lateralis
  o Vastus Medialis
  o Vastus Intermedius

• Sartorius

• Biceps Femoris

• Semitendinosus
- Semimembranosus
- Gastrocnemius
- Soleus

**Statistical Analysis**

Data analysis was performed using SAS software (Version 9 of the SAS System for Windows. Copyright 2013 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.) A complete SAS program was coded to simplify analysis and to facilitate future investigations of similar nature, and it is provided in the Appendices.

![Figure 38 - Display of heading code used in AnyBody to drive the musculoskeletal simulations](image-url)
Joint force and joint moment values of interest (e.g. peak Anterior-Posterior knee force during late stance) were calculated by determining the minimum, maximum, mean, or range of force/moment values within a specific range of the gait cycle. The times where minimum and maximum values occurred (in percent gait cycle) were also recorded and compared (e.g. peak Anterior-Posterior knee force during late stance was determined by finding the maximum value of the Anterior-Posterior knee force between 40% and 60% of the gait cycle and the moment when that maximum occurred in each trial.) Each value of interest was determined for every trial, and comparison of experimental conditions (Control vs. Immobilized Knee) and sides (left/right) was performed using analysis of variance followed by Fisher’s Pairwise Comparison. A value of $\alpha<0.05$ was considered statistically significant for all measures.

**Results**

Joint forces, joint moments, and muscle forces were quantified, and mean values (± standard deviation) for data from Control and Knee Immobilization trials are visualized below with respect to the gait cycle. Statistically significant changes to joint contact forces, joint moments, and muscle forces were observed when the right knee was immobilized. Areas where values of interest were examined are shaded, and the location of statistically significant differences are indicated with an (*). Detailed changes are described for each joint.
Statistically significant changes to loading at the right ankle (Figure 39).

- The maximum posterior joint force occurring between 40% and 60% of the gait cycle is increased to a mean of 670.6 N from 471.4 N (p=0.0297)
• The maximum forefoot adduction moment occurring between 40% and 60% of the gait cycle is decreased to a mean of 6.7 Nm from 10.4 Nm (p=0.0214) and occurs later in the gait cycle (p<0.0001)

• The minimum forefoot adduction moment occurring between 90% and 100% of the gait cycle is reduced to a mean of -0.156 Nm from -4.3 Nm (p=0.0014)
Figure 40 – Mean values of the right knee joint forces (Row 1) and right knee joint moments (Row 2) in three planes through the gait cycle. Mean and standard deviation values are shown for the control and immobilized knee trials.

Statistically significant changes to loading at the right knee (Figure 40).

- The peak compression joint force occurring between 5% and 20% of the gait cycle is reduced to -1180.0 Nm from -1534.7 Nm (p<0.0001)
The peak compression joint force occurring between 40% and 60% of the gait cycle is reduced to a mean of -2208.1 Nm from -2747.9 Nm, but this change is not statistically significant (p=0.0679)

The peak compressive joint force occurring between 90% and 100% of the gait cycle is reduced to a mean of -106.8 Nm from -771.9 Nm (p=0.0063)

The peak medial joint force occurring between 5% and 20% of the gait cycle is reduced to a mean of 208.8 Nm from 263.65 Nm (p=0.0057)

The peak medial joint force occurring between 90% and 100% of the gait cycle is reduced to a mean of 20.4 Nm from 114.2 Nm (p=0.0019) and occurs later in the gait cycle (p<.0001)

The peak posterior joint force occurring between 40% and 60% of the gait cycle is reduced to a mean of -318.9 Nm from -454.7 Nm, but this change is not statistically significant (p=0.0942), and this peak occurs earlier in the gait cycle (p=0.0068)

The maximum flexion moment occurring between 35% and 65% of the gait cycle is reduced to an average of 17.5 N from 33.9 N (p=0.0068) and occurs later in the gait cycle (p=0.0463)

The maximum abduction moment occurring between 40% and 60% is reduced to 39.9 Nm from 53.2 Nm (p=0.0385)

The maximum external rotation moment occurring between 35% and 50% of the gait cycle occurs later in the gait cycle (p=0.0080)
- The peak internal rotation moment occurring between 50% and 60% of the gait cycle is lost. The moment is increased to an 3.7 Nm external rotation moment from a 5.5 Nm internal rotation moment (p=0.0123)
Statistically significant changes to loading at the right hip (Figure 41).

- The minimum compressive joint load occurring between 10% and 45% of the gait cycle was reduced to a mean of 1075.9 N from 1507.8 N (p=0.0096)
- The maximum compressive joint force occurring between 40% and 60% of the gait cycle is reduced to a mean of 2420.9 N from 3341.5 N (p=0.0357)
- The maximum anterior joint force occurring between 5% and 20% of the gait cycle was reduced to a mean of 42.5 N from 227.5 N (p=0.0059)
- The minimum A-P joint force occurring between 20% and 40% of the gait cycle reversed direction and increased in magnitude to a mean 72.8 N posterior force from a 9.9 N anterior force (p=0.0162)
- The maximum anterior joint force occurring between 40% and 75% of the gait cycle occurred later in the gait cycle (p=0.0301)
- The maximum internal rotation moment occurring between 0% and 20% of the gait cycle increased to 23.2 Nm from 17.0 Nm (p=0.0355)
Figure 42– Mean values of the left ankle joint forces (Row 1) and left ankle joint moments (Row 2) in three planes through the gait cycle. Mean and standard deviation values are shown for the control and immobilized knee trials.

No statistically significant changes to joint loading were observed at the left ankle (Figure 42).
Figure 43 – Mean values of the left knee joint forces (Row 1) and left knee joint moments (Row 2) in three planes through the gait cycle. Mean and standard deviation values are shown for the control and immobilized knee trials.

Statistically significant changes to loading at the left knee (Figure 43).

- The minimum abduction moment occurring between 5% and 20% of the gait cycle is reduced to 29.6 Nm from 44.0 Nm (p = 0.0395) and occurs earlier in the gait cycle (p = 0.0234)
• The maximum internal rotation moment occurring between 50% and 60% of the gait cycle is reduced to 4.5 Nm from 10.7 Nm (p= 0.0281) and occurs earlier in the gait cycle (p= 0.0286)
Figure 44– Mean values of the left hip joint forces (Row 1) and left hip joint moments (Row 2) in three planes through the gait cycle. Mean and standard deviation values are shown for the control and immobilized knee trials.

Statistically significant changes to loading at the left hip (Figure 44).

- The maximum anterior joint force occurring between 5% and 20% of the gait cycle is reduced to 329.4 N from 391.2 N (p<0.0001)

- The maximum abduction moment occurring between 0% and 20% of the gait cycle was reduced to a mean of 40.6 Nm from 58.0 Nm (p=0.0474)
Figure 45 – Mean tensile force of the muscles spanning the right knee during gait. Mean and standard deviation are shown for the control and immobilized knee trials.
Statistically significant changes to force in muscles spanning the right knee (Figure 45).

- The maximum force occurring in the right Vastus Lateralis between 0% and 25% of the gait cycle was reduced to a mean of 6.0 N from 172.8 N (p=0.0125)
- The maximum force occurring in the right Vastus Medialis between 0% and 25% of the gait cycle was reduced to a mean of 4.5 N from 111.0 N (p= 0.0183)
- The maximum force occurring in the right Vastus Intermedius between 0% and 25% of the gait cycle was reduced to a mean of 2.9 N from 69.5 N (p= 0.0128)
- The maximum force occurring in the right Sartorius between 40% and 70% of the gait cycle was reduced to a mean of 122.7 N from 178.9 N (p=0.0434)
- The maximum force occurring in the right Sartorius between 90% and 100% of the gait cycle was reduced to a mean of 1.9 N from 39.5 N (p=0.0013)
- The maximum force occurring in the right Biceps Femoris between 0% and 20% of the gait cycle was reduced to 208.7 N from 400.5 N (p<.0001)
- The maximum force occurring in the right Biceps Femoris between 40% and 55% of the gait cycle was reduced to null from 114.2 N (p<0.0001)
- The maximum force occurring in the right Biceps Femoris 3 between 90% and 100% of the gait cycle was reduced to 66.7 N from 229.1 N (p=0.0216)
- The maximum force occurring in the right Semitendinosus between 0% and 15% of the gait cycle was reduced to 85.3 N from 234.0 N (p=<.0001)
- The maximum force occurring in the right Semitendinosus between 25% and 45% of the gait cycle was reduced to null from 154.8 N (p=0.0047)
• The maximum force occurring in the right Semitendinosus between 90% and 100% of the gait cycle was reduced to 29.5 N from 138.1 N (p=0.0137)

• The maximum force occurring in the right Semimembranosus between 0% and 15% of the gait cycle was reduced to 108.8 N from 262.0 N (p<.0001)

• The maximum force occurring in the right Semimembranosus between 35% and 45% of the gait cycle was reduced to null from 201.8 N (p=0.0006)

• The maximum force occurring in the right Semimembranosus between 90% and 100% of the gait cycle was reduced to 35.4 N from 154.2 N (p=0.0148)

• The maximum force occurring in the right Gastrocnemius between 30% and 65% of the gait cycle was reduced to 1121.2 N from 1623.8 N (p=0.0093)
Figure 46 – Mean tensile force of the muscles spanning the left knee during gait. Mean and standard deviation are shown for the control and immobilized knee trials.
Statistically significant changes to force in muscles spanning the left knee (Figure 46).

- The maximum force occurring in the left Biceps Femoris between 0% and 20% of the gait cycle was reduced to 314.2 N from 371.6 N (p=0.0346)
- The maximum force occurring in the left Semimembranosus between 0% and 15% of the gait cycle was reduced to 185.6 N from 262.0 N (p=0.0318)
Discussion

The greatest number of significant changes to joint and muscle loading occurred in the immobilized (right) leg, with more changes occurring at the right knee than any other joint. No statistically significant changes were observed at the left ankle, and only two changes each were observed at the left knee and hip, all of which were reductions in magnitude. Only two joint loads increased in magnitude when the knee was immobilized – the maximum posterior force occurring at the right ankle, and the maximum internal rotation moment at the right hip. Two loads reversed direction – during the right stance phase of gait, the joint reaction force at the right hip became a posterior force rather than an anterior force, and as the subjects neared the Right Toe Off phase of gait, the axial rotation moment at the right knee remained an external rotation moment rather than reversing direction to peak in an internal rotation moment. The remainder of the statistically significant changes to joint and muscle loading were reductions in magnitude.

These results have positive implications for the concern that immobilized knee gait, such as that resulting from knee arthrodesis, induces damage to these joints. This damage and joint degradation has been asserted by a number of publications [5], [10], [11], [52], but thus far no data has been presented to support it. The present study finds that lower body joint loading, which has been linked to osteoarthritis [96], [97], is generally reduced as a result of rigid knee immobilization, failing to support the assertion that this immobilization induces damage to these joints. It is possible that damage to these joints may occur as a result of other factors, including loading rate or impact [98],
deviation from normal loading patterns, or a reduced range of motion resulting in load concentrations, but these were not investigated and would require further study.

It is likely that walking speed played a role in these reductions [99]. Subjects walked at a self-selected speed in the gait analysis study, and as demonstrated in the previous chapter, this resulted in a reduction in speed during the immobilized knee condition. Since speed was not a controlled variable, it is impossible to know the exact contribution to the reductions in joint and muscle loading – this is irrelevant to the aim of the current study, however, the purpose of which was to quantify and determine changes to joint and muscle loading due to knee immobilization. Since a reduction in walking speed occurs as a result of immobilization, and is likely to similarly occur in patients who undergo knee arthrodesis, it was important to incorporate this reduction in speed into the simulations.

Particularly notable among the changes induced by immobilization of the knee was the effect on quadriceps forces (Figure 45). Forces in the vastus lateralis, vastus intermedius, and vastus medialis muscles were effectively reduced to zero, while loading of the rectus femoris took on a dramatically altered pattern. Reduction of vasti forces is readily explained; the origin of each lies on the femur, and they all share insertion into the tibia via patellar ligament via the patella via the quadriceps tendon. With the femur and tibia fused, preempting any degree of knee extension, activation of these muscles contributes nothing to kinematics. The altered loading pattern of the rectus femoris, with an origin at the anterior inferior iliac spine, is a result of its increased contribution to hip flexion (as resistance to hip extension). Comparison to the hip flexion angle of Figure 28
in Chapter 6 is illustrative; rectus femoris force increases with eccentric contraction as the hip extends, peaking as the hip reaches its peak extension angle and begins to flex.

While this result makes sense mechanically, and is intuitively predictable when using the given musculoskeletal modeling parameters, it is unknown whether it is physiologically accurate. Synergistic recruitment of the vasti resulting from paired muscle innervation may result in varying levels of vasti interaction, in spite of the complete lack of functional benefit. Clinically, patients who undergo knee arthrodesis and then subsequent reversal demonstrate an extensive reduction in quadriceps muscle strength [12], [44], [45] consistent with muscular disuse atrophy, and supportive of the results of the present simulation.

Surface electromyography could provide some measure of muscle activation for comparison against these results; the use of surface electromyography was explored during the design of the gait study giving rise to the data used to drive these simulations, and it was collected from some subjects, but the data was not ultimately usable. Regardless, the muscle activation patterns of subjects who have been temporarily fitted with an immobilizing brace are likely to be different from those of patients who have undergone long-term knee fusion, making the relevance of such data questionable. One potential method of validating the predicted quadriceps activity is the use of surface electromyography to measure quadriceps activation during gait in patients who have undergone permanent knee arthrodesis, but no data of this type is presently available.

The present research has significant implications for the clinical decision making process regarding knee arthrodesis, as well as the development and testing of rigid knee
implants. Concern over subsequent damage to other joints resulting from knee arthrodesis may be overblown, a result of conservatives estimates due to a lack of data. These results support the reduction of the weight of this concern as a factor weighing against a decision to performing knee fusion. In as much as this factor has reduced the incidence of knee arthrodesis, as explored in Chapter 5, this work may serve to increase the number of knee arthrodesis procedures performed. Joint loading values during gait with an immobilized knee have been heretofore unquantified – this data may be used as input parameters for the testing of rigid knee implants by means of finite element analysis or benchtop mechanical testing. This may help prevent mechanical failure of rigid knee implants, as reported in literature, in future implant designs.

**Acknowledgements**

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CHAPTER EIGHT

DESIGN OF AN IMPLANTABLE DEVICE TO SATISFY THE PROPOSED TREATMENT MODEL

A surgical treatment model is designed as an alternative to knee arthrodesis, and preliminary development work is undertaken to assist in the licensing and clinical translation of said treatment model.

Abstract

Having identified severe knee dysfunction as an inadequately addressed condition in patients, a novel treatment model is proposed. The constraints of this model require that it provide a patient with a weakened or missing knee extensor mechanism the stability to ambulate independently, such as with knee arthrodesis, while allowing the patient to otherwise bend the knee. Design of the proposed treatment model occurred over the course of several years, included development of functional prototypes, and was guided by the regulatory requirements for the design of medical devices in the United States. Two patent applications have been filed with the United States Patent and Trademark Office for protection of the intellectual property generated from this work, and the Clemson University Research Foundation is actively seeking to license this work for clinical translation.
Present Need

Severe knee dysfunction can interfere with patient independence, quality of life, and mental health, and current treatment options often leave patients and surgeons to choose between poor alternatives. These alternatives, explored in detail in Chapter 4, require that patients have adequate remaining anatomy and strength for knee stability with a total knee replacement, or else provide complete stability at the expense of permanent knee immobilization. While existing total knee replacement designs provide varying levels of mechanical stability at the expense of natural knee kinematics, no designs compensate for extensor mechanism damage or weakness [100]. When this stability is required, the most viable treatment option, arthrodesis, eliminates all movement at the knee. The resulting loss of function and poor outcome measures relative to unaffected patients often conflict with patients’ expectations for surgery. Patients may strongly resist the selection of knee arthrodesis as treatment, in spite of the high risk and poor prospects of salvage total knee replacement. This results in an ethical dilemma for surgeons, who must weigh the benefits of arthrodesis against the low probability of success of salvage total knee replacement in this patient subset [8].

Initial collaboration with two practicing orthopedic surgeons, Frank Voss, M.D. of USC Medical School in Columbia, SC, and Kim Chillag, M.D. of the Moore Center for Orthopedics in Columbia, SC, resulted in the proposal of a theoretically superior alternative treatment that would provide both complete stability and an ability to flex the knee. Such a treatment could compensate for lost anatomy or strength during ambulation.
and standing activities, but could otherwise allow a patient to flex the knee so as to minimize interference with other activities of daily living.

The initial proposal, by Kim Chillag, M.D., took the form of a total knee replacement that could be locked in full extension to provide the stability necessary to walk, but that could otherwise be unlocked to allow the patient to flex the knee. This initial concept utilized a “sliding lock pin” which would reside fully within the femoral component during knee flexion, and which could, with the assistance of gravity, slide down into a recess within the tibial component when the user fully extended their knee (Figure 47). This design would require that the patient lift their fully extended leg until the tibia was raised above the femur so that the pin could slide back into the femoral component with the assistance of gravity, in order to unlock and allow the patient to again flex the knee.

![Device Prototype](image)

**Figure 47 – Device Prototype – Preliminary drawing of a total knee replacement with a sliding lock pin, as proposed by Kim Chillag, M.D.**
**Design Controls**

While the initially proposed design embodied the core elements of the theoretically superior treatment alternative, practical limitations interfered with its viability, e.g. the physical capability of a patient with severe knee dysfunction to disengage the locking mechanism by lifting his fully extended leg above parallel with the ground. In addition to the core design requirements, a clinically viable alternative treatment must satisfy a number of additional elements, including requirements of the surgeons, patients, and the relevant regulatory authority. One can best account for this by using a structured design process. Federal regulations govern the design of medical devices in the United States, overseen by the Food and Drug Administration (FDA), and these regulations are located in Title 21 of the Code of Federal Regulations, Part 820, Subsection 30 - Design Controls. This subsection was used as a guide to assist this work throughout the design process.

Criteria for the physical and performance requirements of the desired design solution were developed in collaboration with the clinician partners, and while not formalized, were used as a set of Design Inputs [820.30(f)] (Table 12).
## Example Design Inputs

<table>
<thead>
<tr>
<th>Functional / Performance</th>
<th>Must enable patients with deficient or missing quadriceps mechanisms to walk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Should flex freely when a patient is sitting, lying down, or otherwise inactive.</td>
</tr>
<tr>
<td></td>
<td>Design should not require invasive interaction.</td>
</tr>
<tr>
<td>Similar Designs</td>
<td>Must provide stable interface suitable for bone-PMMA cement adhesion.</td>
</tr>
<tr>
<td></td>
<td>Must interface with variable length bone augments or intramedullary stems.</td>
</tr>
<tr>
<td></td>
<td>Design should be as durable as existing salvage total knee replacement designs.</td>
</tr>
<tr>
<td>Regulatory</td>
<td>The design should be manufactured from materials used in previously cleared or approved medical devices for use in the knee.</td>
</tr>
<tr>
<td>Output from Risk Management</td>
<td>Implant design should minimize the risk of failure of the locking mechanism during walking.</td>
</tr>
<tr>
<td></td>
<td>The device should remain locked until the patient takes specific action to unlock it. It cannot accidentally unlock while walking.</td>
</tr>
<tr>
<td></td>
<td>Implant geometry should prevent the locking mechanism from engaging when the device is not in full extension.</td>
</tr>
<tr>
<td>Other Essential Design Requirements</td>
<td>The design should interface with an existing modular total knee replacement platform to assist in translation/licensing.</td>
</tr>
</tbody>
</table>

*Table 12 – Design inputs for the proposed treatment model*
Design Review meetings, as prescribed by 21 CFR 820.30(e), were conducted periodically throughout the design process, and included our clinical partners. The purpose of these meetings was to ensure that all relevant design requirements were identified, that the proposed designs satisfied these requirements, and to prioritize further work. Design Review meetings were conducted on the follow dates:

- Tuesday, August 10, 2010
- Friday, September 24, 2010
- Wednesday, October 20, 2010
- Tuesday, November 9, 2010
- Friday, January 14, 2011
- Friday, April 1, 2011
- Friday, October 21, 2011
- Friday, January 13, 2012
- Friday, March 30, 2012
- Friday, April 27, 2012
- Friday, October 25, 2013
Prior Art Review

In addition to satisfying the design requirements, the commercial viability of any proposed device is highly dependent on the current intellectual property landscape. Any similarity of the developed work to existing intellectual property held by others may require license of said IP, and could prove to be an insurmountable barrier to commercialization. Ideally, the intellectual property of any proposed treatment method would also be protectable, providing value and an incentive to commercialization.

A diligent prior art review was conducted, and similarity to the desired treatment model was found in three general categories of technologies: external knee braces, prosthetic limbs (for transfemoral amputees), and implantable knee joint replacements. There was no more than a moderate degree of similarity between the proposed device and existing technology (Table 13).

The most relevant limitations on device design are those of total knee replacement designs, which can be found under US Patent Class 623, “Prosthesis (i.e. artificial body members), parts therof, or aids and accessories therefor”, within subclass “Implantable Prosthesis” (11.11) and subclass “Joint Bone” (18.11). Here, relevant subclasses include “With Magnet” (18.12) and “Knee Joint Bone (20.14). All categories within the 20.14 parent were searched, including “Constrained Joint” (Class 623/20.24), “Including an intermediate member” (20.28), “Movable” (20.29), and “Moveable Bearing” (20.33).
### Prior Art Review

<table>
<thead>
<tr>
<th>Description of Prior Art</th>
<th>Type</th>
<th>Degree of Similarity</th>
<th>Primary Differentiator(s) of Our Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgically Implantable Devices</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomical Motion Hinged Prosthesis / US 12/307,102</td>
<td>Patent App.</td>
<td>Low</td>
<td>One example of an industry standard hinge and rotating platform design. Other examples can be found in 623/20.24, 20.25, 20.28, 20.29. Our device locks in extension as an improvement upon arthrodesis, negating the purpose for the various changes/improvements to hinged/rotating designs.</td>
</tr>
<tr>
<td>Orthopaedic knee fusion apparatus / 5,108,398</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device does not assist in bone-to-bone fusion, but rather replaces the need for it.</td>
</tr>
<tr>
<td>Knee Arthrodesis Implant / US 13/061,415</td>
<td>Patent App.</td>
<td>Low</td>
<td>This device is one example of many that serve to permanently fuse the femur and tibia. Our device resembles a total knee replacement, providing knee flexion as desired. This prior art offers no advantages over a successful knee fusion.</td>
</tr>
<tr>
<td>The Stanmore Knee Arthrodesis Prosthesis / 2010</td>
<td>Journal Article</td>
<td>Moderate</td>
<td>This device is one that permanently fuse the knee, preventing any motion. Our device resembles a total knee replacement, providing knee flexion as desired. This prior art offers no advantages over a successful knee fusion.</td>
</tr>
<tr>
<td>Surgical Distraction Device / US 6,849,076</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Similarity: Our device will use an internal magnet in a knee implant, and will require an external magnetic field to actuate the locking mechanism. Differentiator: Everything else.</td>
</tr>
<tr>
<td><strong>Prosthetic Limbs for Transfemoral Amputees</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artificial knee / US 4,756,713</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device is surgically implanted, and the locking mechanism is distinct.</td>
</tr>
<tr>
<td>Above-Knee Prosthesis With Variable Resistance Knee Joint / US 10/707,732</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device is surgically implanted, and the locking mechanism is distinct.</td>
</tr>
<tr>
<td>Stabilized artificial knee mechanism / US 4,206,519</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device is surgically implanted, and the locking mechanism is distinct.</td>
</tr>
<tr>
<td><strong>External Knee Braces</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-Locking and Unlocking Pivot / US 2646793</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device is surgically implanted, and the locking mechanism is distinct.</td>
</tr>
<tr>
<td>Locking Knee Joint for Orthopaedic Brace / 3,826,251</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device is surgically implanted, and the locking mechanism is distinct.</td>
</tr>
<tr>
<td>Automatic locking orthotic knee device / 5,267,950</td>
<td>Issued Patent</td>
<td>Low</td>
<td>Our device is surgically implanted, and the locking mechanism is distinct.</td>
</tr>
</tbody>
</table>

*Table 13 – Existing intellectual property with a minimum of a low degree of similarity to the proposed treatment model.*
Intellectual property protection of all of the basic design elements is expired. One patent covering such attributes includes US Patent 3,934,272 “Knee Prosthesis,” 1976. This patent describes the most basic elements of a hinged/constrained knee replacement, “upper and lower metal” components to be fixed to the femur and tibia that are connected by a lateral axis pin.

Figure 48 - Exploded diagram of the invention described in US Patent 3,934,272 "Knee Prosthesis" 1976.
In addition to the basic elements of a hinged/constrained knee design, US Patent 4,262,368, “Rotating and Hinged Knee Prosthesis,” 1981 describes an implant that includes a rotating bearing that allows for internal/external rotation. In addition to the essential femoral and tibial components and a lateral axis pin constraining motion outside of the flexion/extension axis of the implant, this patent describes a proximal-distal pin and bushing that constrain motion outside of the internal-external rotation axis.

The results of this preliminary prior art review show that intellectual property protection the most basic design elements has expired, allowing a wide freedom to operate.
Prototyping and Preliminary Designs

The Frank H. Stelling and C. Dayton Riddle Orthopaedic Education and Research Laboratory, located within CUBEInC, was the primary base of operations for design of the proposed treatment model. Design of an alternative treatment was undertaken within the confines of the proposed design inputs, resulting in a number of competing alternative proposals. SolidWorks 3D modeling software was used to create and convey representations of the proposed device designs, and a ProJect SD 3000 (3D Systems, Rock Hill, SC) (Figure 51), located within CUBEInC, was used to create rapid prototypes for proof of concept. Several device designs were developed, each of which was intended to provide the beneficial stability of knee fusion without the drawbacks associated with a permanently fused knee. Several of these designs are described in detail below.

Figure 50 – Design work was based in the Frank H. Stelling and C. Dayton Riddle Orthopaedic Education and Research Laboratory at CUBEInC, in Greenville, South Carolina
Dropping Pin

This design, developed by Dr. Kim Chillag, was established prior to the collaborative research effort. It uses an internal locking pin and is assisted by gravity (Figure 47). The femoral and tibial components of this design have internal channels, which hold the pin, and can slide freely along the proximal/distal axis. When the user moves his leg to full extension, the pin may translate distally with the assistance of gravity, allowing the pin to reside within the femoral and tibial channels simultaneously. In this position, the pin prevents flexion of the joint. When the user wishes to resume flexion, he may raise his leg above parallel with the ground to allow gravity to assist the pin to fully return to the channel of the femoral component.


Cam Lock

The femoral component of this design has the curvature of a cam in the sagittal plane, allowing for complete freedom of rotation in flexion, a very tight fit in mid-flexion, and a stable fit in complete extension (Figure 52). There are internal springs which compress as the hinge component of the design rises vertically. As the femoral component (cam) rotates, the variable distances of the articulating surface from the hinge axis causes the component to rise and fall.

In order to move from flexion to extension, the user must overcome the force of internal springs. The distance from the hinge axis to the articular surface increases as the device moves into midflexion, causing spring compression. As the device continues to move into full extension, the distance from the hinge to the articulating surface decreases, and spring tension is relieved. In addition to the lower energy state of the spring, the increased congruency between the femoral and tibial components (flat on flat) assists in maintaining full extension. In order to flex the knee, sufficient rotational force must be applied to overcome spring tension to return the device to flexion.

Figure 52 – Device Prototypes - Cam-Lock design utilizing variable flexion radius and spring
**Proximal-Distal Magnet**

This design is based on a typical hinged knee device, but utilizes magnets to keep the femoral and tibial components in contact in full extension. Magnets fully embedded in the femoral component line up with magnets embedded within the tibial component when the device is rotated into full extension. This generates continuous attractive force that serves to pulls the femoral and tibial components together. This results in some degree of compression of the conforming articular surfaces, and flexion is countered by magnetic attraction. In order the flex the knee, the patient must apply sufficient flexion force, which may be supplied by an external brace.

![Device Prototypes – Rapid Prototype of the Proximal-Distal Magnet design](image)

**Medial-Lateral Magnet**

This design is also based on a typical hinged knee device, but utilizes magnets to keep the femoral and tibial components in full extension. Four magnets are embedded in
the femoral and tibial component, two in each, in such a way as to be lined up when the
device rotation is at full extension. The magnets are rigidly attached to their respective
knee components. The four magnets are aligned in a single axis when in full extension,
where the device maintains the most stable position within the magnetic field. The lowest
energy state of the device is reached when in full extension, allowing the device to resist
flexion during stiff gait walking. When the user wishes to flex the device, force sufficient
to overcome the magnetic field is applied.

![Device Prototypes](image)

*Figure 54 – Device Prototypes – Rapid prototype of the Medial-Lateral Magnet design*

**Pushbutton Latch**

Once the user moves this knee design into full extension it mechanically locks,
requiring actuation of a pushbutton to release the device back into flexion. A spring-
loaded latch rests in the center of the tibial component, between the femoral condyles. As
the femoral component moves into extension, an angled surface pushes the latch back,
compressing the spring. In full extension, the latch reaches a recessed area of the femoral
component, engaging and locking it in place. A bumper on the tibial component prevents hyperextension. A spring-loaded pushbutton on the side of the femoral component is actuated by the user by pushing down on the skin in the area over the button, disengaging the latch and allowing the user to rotate the device. When implanted, the user would actuate the device by pushing down on the skin over the area of the button.

![Figure 55 – Device Prototypes – Rapid prototype of the Pushbutton Latch design](image)

**Magnetic Latch**

The Magnetic Latch Design is based on hinged total knee replacement designs, incorporating a latch mechanism within the femoral component, anterior to the standard hinge. The anterior latch consists of two separate cylindrical “locks”, which lie fully within a recessed “femoral lock housing” when deactivated. Magnets are embedded internally within the “locks,” and the polarities are aligned in axis such that the “locks” have a tendency to be drawn together. The “hinge device” lies between the femoral
condyles and partially covers the “femoral lock housing”, preventing the “locks” from moving beyond the recess of the “femoral lock housing” in the femoral component. When the knee is rotated to full extension, the locks line up with a matching “hinge lock recess” within the “hinge device.” This prevents the device from locking in place unless the user has aligned the knee in extension.

The device may be locked in extension by briefly passing a specially designed two-sided magnetic key (Figure 57) within close proximity to both sides of the knee (Figure 60). This handheld key contains specifically oriented magnets, and its magnetic field serves to actuate the internal locking mechanism of the implant system, which contains several fully sealed magnets of its own. Once the “locks” are drawn together on either side of the “hinge lock recess bumper”, attraction due to the magnetic field will maintain their proximity and the implant will remain locked in extension until the
handheld key is reapplied in its reversed polarity orientation (performed by simply turning the key over), allowing a patient to walk with the rigid knee with the functional equivalence of an arthrodesis. Because the knee system has two internal magnetic levers, the locking mechanism requires simultaneous application of a magnetic field to both the medial and lateral sides of the knee. This may be accomplished with the handheld key, thus preventing accidental disengagement from unknowingly standing near a strong magnetic field.

![Rendering of the Engage Key](image)

Figure 57 – Rendering of the Engage Key. Magnets are embedded within the cylindrical endpieces

**Design Decision Matrix**

The ability of each proposed design concept to satisfy Design Input criteria was evaluated, scored, and weighted in order to select a single design for further development work.
### Functional / Performance

- **Must enable patients with deficient or missing quadriceps mechanisms to walk**: 15%
- **Should flex freely when a patient is sitting, lying down, or otherwise inactive.**: 15%
- **Design should not require invasive interaction.**: 10%

### Similar Designs

- **Must provide stable interface suitable for bone-PMMA cement adhesion.**: 5%
- **Must interface with variable length bone augments or intramedullary stems.**: 5%
- **Design should be as durable as existing salvage total knee replacement designs.**: 5%

### Regulatory

- **Should be manufactured from materials used in predicate knee implant designs**: 10%
- **Should minimize risk of failure of locking mechanism during walking.**: 10%
- **Device should remain locked until specific action taken to unlock it. It cannot accidentally unlock while walking.**: 10%
- **Implant geometry should prevent the locking mechanism from engaging when the device is not in full extension.**: 10%
- **The design should interface with an existing modular total knee replacement platform to assist in translation/licensing.**: 5%

### Output from Risk Management

- **Total Weighting Factor**: 100%

### Other Essential Requirements

- **Ranking**
Final Model Development

The Magnetic Latch design, subsequently named “The Engage,” best satisfied all input criteria. Continued design work has resulted in iterative improvements on this basic design (Figure 58, Figure 56, Figure 59).

Figure 58 – Photo rendering of the Engage design
Figure 59 – Prototype of the Engage design as implanted in SawBones bone analog

Figure 60 – Photograph of the Engage Key in use, as it would be used to unlock the device
With the Engage, a patient may sit comfortably with a flexible knee. This enables sitting in close-quarter spaces, such as a plane or the front seat of a car, and performing otherwise difficult or impossible activities, such as tying one’s shoes. When standing or walking is desired, a patient extends his leg while sitting and passes the handheld key over the knee to lock the device (Figure 61). A video demonstration of these activities may be found at: http://www.youtube.com/watch?v=OgxpPxNkgGw&

![Figure 61 – Demonstration of use: 1) Patient sits comfortably; 2) Patient extends right knee and prepares to use key; 3) Patient passes key over the implant, locking it in extension; 4) Patient ambulates with rigid-knee gait; 5) Patient sits, unlocks the device with key in order to sit comfortably again](image)

The use of magnets implanted within orthopedic knee joint replacement devices is not novel, but predicate devices have not applied this concept to rigid knee immobilization [101], [102]. This should facilitate regulatory clearance or approval of the Engage without infringing on existing intellectual property. One such predicate device, cleared by the FDA through the 510(k) process (K09218), contains an internally sealed magnet used to drive a screw mechanism when an external magnetic field is applied, providing a non-invasive post-surgical method of lengthening the femoral shaft of the implant.
In support of full scale manufacturing, manufacturing cost estimates were developed (Table 15). Initial functional prototypes were manufactured through Medcast, Inc. (C/O Tom Myers, 596 East 200 North, Warsaw, Indiana 46582, Telephone: (574) 269-6142, tom@medcast.com, www.medcast.com) and Machining and Technical Services (MTS) of Clemson University (C/O Jeff Holliday, Riggs Hall, Clemson, South Carolina, 29634, Telephone: (864) 656-3202, jhli@clemson.edu, www.clemson.edu/ces/research/mts/).
## Estimated Manufacturing Costs

<table>
<thead>
<tr>
<th>Individual Assembly Components</th>
<th>Material</th>
<th>Manufacturing Operations</th>
<th>Initial Tooling &amp; Setup ($)</th>
<th>Marginal Unit ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Component</td>
<td>CoCrMo</td>
<td>Lost wax investment cast¹</td>
<td>≈$15,000</td>
<td>≈$200</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Milling²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laser etch (Lot, Part, Unique ID #s)²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shot peening²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polishing²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial Tray</td>
<td>CoCrMo</td>
<td>Lost wax investment casting¹</td>
<td>≈$15,000</td>
<td>≈$150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Milling²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laser etch (Lot, Part, Unique ID #s)²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shot peening²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tibial Poly</td>
<td>Moderately Crosslinked UHMWPE</td>
<td>Mill²</td>
<td>≈$200</td>
<td>≈$100</td>
</tr>
<tr>
<td>Axle</td>
<td>316L SS</td>
<td>Lathe²</td>
<td>≈$200</td>
<td>≈$50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laser etch (Lot, Part, Unique ID #s)²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polishing²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passivation²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bushings (x4)</td>
<td>Moderately Crosslinked UHMWPE</td>
<td>Milling²</td>
<td>≈$200</td>
<td>≈$50</td>
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<tr>
<td>Yoke</td>
<td>316L SS</td>
<td>Milling²</td>
<td>≈$400</td>
<td>≈$100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polishing²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passivation²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locking Mechanism (Multiple Components)</td>
<td>316L SS, NdFeB</td>
<td>Lathe²</td>
<td>≈$500</td>
<td>≈$100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assembly²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polishing²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laser etch (Lot, Part, Unique ID #s)²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passivation²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional Operations (Not applicable to prototypes)</td>
<td>Cleaning²</td>
<td>N/A</td>
<td>≈$7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Packaging¹</td>
<td>≈$20,000</td>
<td>≈$15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Labeling³</td>
<td>≈$10,000</td>
<td>≈$4</td>
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<tr>
<td></td>
<td>Sterilization (&amp; 5 year Validation)⁴</td>
<td>≈$30,000</td>
<td>≈$10</td>
<td></td>
</tr>
</tbody>
</table>

### Total Initial Setup and Marginal Unit Costs

≈ $91,500 ≈ $776

### Per Unit Cost

| 10 qty. | $3,926 ea. |
| 100 qty. | $1,691 ea. |
| 1,000 qty. | $868 ea. |
| 10,000 qty. | $785 ea. |

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Intellectual Property Protection

The above design work was presented to the Clemson University Research Foundation (CURF). Upon review, CURF approved funding for the pursuit of intellectual property protection. Myers Bigel Sibley & Sajovec, P.A. (4140 Parklake Ave, Suite 600, Raleigh, NC 27612, Telephone: (919) 854-1400, Fax: (919) 854-1401, www.myersbigel.com) was selected as the representative law firm, and a provisional patent application was filed on July 17, 2012 (Lockable Knee Implants and Related Methods, U.S. Provisional Patent Application 61/672,352). The provisional patent application was subsequently converted to two full patent applications on July 17, 2013, additionally incorporating the use in other joints of the body:

Figure 62 – First two figures of Utility Patent, “Lockable Knee Implants and Related Methods”

Commercial Outreach

A number of commercial outreach activities were undertaken in support of external licensing of the intellectual property generated as part of this work.
April 6, 2011 Preliminary discussion of the technology and the potential for collaboration was initiated with Carlos Sanchez of Stryker Orthopaedics (Mahwah, NJ)

September 26, 2012 Kevin Cook of Zimmer Orthopaedics was contacted by email.

November 16, 2012 Mutual NDAs were signed with Biomet (Warsaw, IN), and the technology was presented by teleconference. Biomet requested an update after completion of the research studies proposed as a part of this body of work.

December 5, 2012 Commercialization of the Engage through the formation of a startup company was proposed by Eric M. Lucas at the LaunchPad SC competition. The proposal received second place.

July 9, 2013 License of the intellectual property was proposed to John Vinciguerra of DJO Surgical during a visit to Clemson University. Mr. Vinciguerra requested an update after feedback from a previously submitted grant application.

July 29, 2013 The Engage was presented to an audience at CUBEInC put on by Michael Gara.

November 15, 2013 The Engage was presented during the Elevator Pitch Competition of SC BIO annual meeting in Charleston, South Carolina.

January 30, 2014 The work was presented by teleconference to the management team of DJO Surgical.
February 20, 2014    The Engage was presented to a visiting group of investors from Net Scientific at CUBEInC.

The current status of commercialization efforts is positive, but confidential, and may be out of date at the time of publication of this document. Lisa Perpall, of the Clemson University Research Foundation, recommends the following statement: “We are in tentative talks with a prospective licensee, which happens to be a global orthopedic OEM, so we are very hopeful we may soon have a partner in commercialization to bring this technology to market.”

Acknowledgements

The following people are gratefully acknowledged for their assistance in this work: Lisa Perpall, M.S., M.B.A., and Jan Comfort, M.L.S.
CHAPTER NINE
DISCUSSION

In which the preceding body of research is discussed.

Surgical treatment options are limited in patients whose knee dysfunction preempts salvage by means of total knee replacement. While total knee replacement designs with varying degrees of mechanical stability have been developed to compensate for anatomic deficiencies, no such designs compensate for a missing or severely compromised knee extensor mechanism. Knee arthrodesis may salvage the limb and provide the stability necessary to ambulate independently, but the resulting inability to bend the knee affects gait biomechanics and can cause restrictive functional problems. These limitations contribute to the undesirability of knee arthrodesis among patients and surgeons alike [8]. In spite of these limitations, however, it is apparent from the large number of recently published case reports that the procedure is still the most clinically appropriate treatment in many cases.

It is proposed that an alternative treatment could provide these patients with increased function over the current standard of care. Such a treatment could incorporate aspects of existing approaches to provide patients with maximum stability while minimizing functional limitations. The inclusion criteria for this approach can be defined as dysfunction of the knee with contraindication for existing total knee replacement designs. This includes, but is not limited to, patients who currently undergo knee
arthrodesis. In spite of the number of published case reports, however, the total number of affected patients has not been previously quantified, and thus the need for such an alternative treatment is unknown.

In Chapter 5, this dissertation establishes the overall incidence of knee arthrodesis in the United States over the past two decades, and thus a measure of the need for an alternative treatment. The Nationwide Inpatient Sample, the largest all-payer inpatient database in the United States, was acquired to facilitate estimates of this patient subset. A significant portion of the time and effort for this work went into the creation of a custom database analysis tool, programmed using SAS (Cary, NC, USA). This tool allowed for custom database searches by ICD-9-CM procedural code, and performed appropriate statistical analysis on the queried data. The results of this work show that in spite of the severe functional limitations and undesirability of the procedure, its incidence averaged over 1,000 cases annually. And while the total number of knee arthrodesis cases has not risen with the increased incidence of total knee replacement, it has also not seen a significant decline, suggesting that increased awareness and improvements in current treatment alternatives are not sufficient to address the significant number of affected patients. The age and method of reimbursement of this patient group indicates a high incidence of Social Security Disability, which may, in turn, suggest that existing treatment methods have been unable to restore these patients to sufficient function to participate in the workforce. Knee arthrodesis procedures are concentrated in teaching hospitals and in urban areas, suggesting that these patients are increasingly driven to seek out surgeons outside of their local area, and most likely a result of a selection for or
referrals to orthopedic surgeons who specialize in knee reconstruction. This same concentration may also serve to facilitate targeting of this patient subset, both in the dissemination of knowledge of a novel treatment and the physical outlays required for such a treatment.

These results demonstrate a compelling opportunity for the proposed alternative treatment model. One of the primary benefits of knee arthrodesis is joint stability, enabling patients to ambulate independently. Fusing the knee, however, necessarily affects the biomechanics of gait, and the temporary stability of the proposed treatment model would induce biomechanical changes similar or equivalent to those of knee arthrodesis treatment. Knee arthrodesis itself is contraindicated in patients with contralateral hip arthritis or replacement, and it has been suggested that knee arthrodesis may induce pain in other joints and the spine. In spite of these clinical concerns, the changes to gait kinematics and kinetics induced by knee arthrodesis have not been directly explored. The importance of understanding the changes to gait kinematics and kinetics induced by knee immobilization is discussed in Chapter 4.

In Chapter 6, these gait changes are simulated and quantified by studying the gait of normal, healthy subjects with an artificially immobilized knee. In order to account for this potential limitation, the work of Chapter 6 was conducted over the course of an extended period of knee immobilization, and the effects of increased acclimation time was also studied. This work suggests that allowing a subject to acclimate to an immobilized knee for a minimum of 0.25 miles of walking is not significantly different from acclimation over 24+ hours. It is possible that longer term immobilization induces
additional changes, but ethical considerations precluded such study. An analysis of the
gait changes induced by knee immobilization shows that gait changes primarily result in
order to assist ground clearance of the immobilized limb and to minimize excess energy
expenditures. Complete quantification of the specific changes in joint angle, net joint
moment, and net joint reaction force are provided, and will assist in the development of
future hypotheses regarding the effects of knee arthrodesis. The increase in reaction
forces at the contralateral hip may be of particular consequence, as it has been suggested
that this joint is associated with early induced arthritis after knee arthrodesis. The
complete characterization of rigid knee gait is also important for the design and testing of
an implantable device that would be subjected to these gait changes, such as the proposed
treatment model.

One significant limitation of gait analysis and the resulting calculations of net
joint moment and net reaction force, however, is the neglect of musculature. This
approach underestimates joint loading, and does not provide a picture of the muscular
changes that are induced by rigid knee immobilization. A musculoskeletal model was
developed and used, in conjunction with motion capture data from the previous gait
analysis study, to run simulations comparing normal and immobilized knee gait. A
complete characterization of joint forces, joint moments, and muscle forces is provided in
Chapter 7. These results showed that while the loading patterns were sometimes altered,
there was generally a reduction in the peak magnitude of joint forces, joint moments, and
muscle forces. Of particular note was the near-complete reduction of quadriceps forces.
Aside from the rectus femoris, which spans the hip and can serve as a hip flexor, the
vastus medialis, vastus intermedius, and vastus lateralis do not functionally contribute when the knee is rigidly immobilized. This is an important consideration for the estimation of joint loading at the knee, and provides insight into muscular disuse atrophy after knee arthrodesis. The full characterization of loading patterns provided in Chapter 7 can be used in the development and testing of existing and future orthopedic implants subjected to such conditions, driving computational, wear, or mechanical testing conditions.

Design of an alternative treatment model occurred with the assistance of the practicing clinical collaborators, and occurred in parallel with the preceding research studies. This design process was guided by the requirements of medical device development regulations in the United States, as outlined in 21 CFR 820.30, facilitating translation of the device to clinical use. The proposed design is a variant of a total knee replacement, satisfying the material, functional, regulatory, and risk requirements of such designs. The novelty of the proposed treatment lies in the engagement of a temporary locking mechanism, which is actuated by means of the application of an external magnetic field. This actuation method is not novel, having been used in orthopedic knee joint replacement applications that have been cleared for market by the FDA through the less stringent 510(k) process. This locking mechanism compensates for a lost or weakened quadriceps extensor mechanism, maintaining the knee in extension to enable a patient to stand or ambulate independently with the functional equivalence of knee arthrodesis. Unlike arthrodesis, this locking mechanism can be disengaged to facilitate knee bending. Applications for protection of the intellectual property created out of this
work have been filed, and are assigned to Clemson University. The inventors have engaged industry members in support of the license of said intellectual property.

The preceding body of work represents the identification and elimination of gaps in knowledge in diverse areas relating to knee dysfunction and arthrodesis, through which the common thread is support for a proposed device design. These advances call attention to the previously unrecognized significance of the clinical need, and provide insight into the biomechanical effects of knee immobilization (as in knee arthrodesis). In addition to the scientific and clinical value of the individual research components, the synergism of this work provides a cohesive package supporting translation of the proposed treatment model to clinical and commercial use. Components of this work are critical to many commercialization processes, including market analysis, market strategy, and design control, and the intellectual property generated from this work enables industry-University partnership through licensing. In advancing knowledge in these areas, this work also creates opportunities for further study, and recommendations for building upon it are made in the next chapter.
CHAPTER TEN
RECOMMENDATIONS FOR FUTURE WORK

In which recommendations are made for subsequent researchers to build upon the results of this body of work.

The focus of this work is severe knee dysfunction and its treatment. The research methods utilized within the work are varied, but interrelated, and were necessary to build and defend a robust case for an alternative treatment model. This collection of work forms a robust and cohesive dissertation, containing the elements necessary to achieve its stated objectives. With that said, there are a number of opportunities to further development or build upon the work contained within.

The total number of patients undergoing knee arthrodesis in the United States was estimated in Chapter 5, using the Nationwide Inpatient Sample. This patient subpopulation had never been quantified before, and in spite of the detailed characterizations provided within this work, these results provides fertile ground for further analysis. The underlying etiologic reasons for undergoing knee arthrodesis are diverse, as discussed in Chapter 4, and include the failure of total knee replacements. The author was intrigued by the fact that the number of knee arthrodesis procedures remained relatively constant, in spite of a significant increase in the number of total knee replacement surgeries over the same time period. Further study into the reasons for undergoing knee arthrodesis may provide insight into the question of why the number of
knee arthrodesis procedures has not changed over time. Longitudinal analysis using the Nationwide Inpatient Sample, however, is impossible, as identifying patient information is stripped from the data, and each record represents a single discharge. A patient hospitalized twice will show up as two different records, with no possible way to connect them. One reason given for undergoing knee arthrodesis is infection, and one possible approach using the Nationwide Inpatient Sample is to document the number of procedures performed with an associated diagnosis of infection[47]. This requires, however, that one assumes that the presence of infection is always the direct cause of failure and the reason for surgery. Another promising approach, though one that was not open to the author, is to supplement the present national estimates with longitudinal patient data from a different data source, such as the registry of a large scale research institute [28].

Normal, healthy subjects with a rigidly immobilized knee were used as a proxy for patients with knee arthrodesis in Chapter 5. This approach has precedents in the literature, and it provided reliable control trials for direct comparison. While the present work showed that short term immobilization (after walking 0.25 miles) was not significantly different from longer term immobilization (24+ hours), there is no evidence that this approach effectively simulates gait after immobilization over a much longer term, as would be the case in patients with an actual knee arthrodesis. In spite of the confounding factors involved, a future study of patients with an actual arthrodesis may be considered. The number and dispersion of such patients, in addition to exclusion criteria resulting from varying etiologies, however, may make such a study difficult. The design
of such a study would require a reliable control group, utilizing age or otherwise matched control variables. The author suggests that such a study also collect surface electromyography data, particularly monitoring the activity of the vastus lateralis, vastus intermedius (if plausible), vastus medialis, and rectus femoris. This data can then be compared against the estimation of muscle activity in Chapter 7.

If those estimations are accurate, they serve as a potential source of difference between short and long term knee immobilization. When the knee is rigidly immobilized, the computational model estimated that quadriceps muscle forces drop to near-zero, with the exception of the rectus femoris, which spans the hip and acts as a hip flexor. It is likely that over the long term, such as in a patient with a permanent knee arthrodesis, the quadriceps muscles would atrophy due to functional disuse. We used Dual-energy Xray Absorptiometry to characterize the lean muscle mass, among other things, of the subjects in Chapter 6. This technique could similarly be used in patients with a permanent knee arthrodesis, allowing for a comparison of the lean muscle mass of the thigh in the operated vs. non-operated legs. It may be hypothesized that differences in lean muscle mass are a result of atrophy due to functional disuse.

As has been mentioned previously in this work, several authors of articles in clinical journals have asserted a link between knee arthrodesis and pain and arthritis in other joints of the lower body. While this link has been suggested or hypothesized, no studies have established or even explored either correlation or causation. The muscle and joint loading patterns established by the computational modeling of Chapter 7 suggest a potential source of such a link, and provide a unique opportunity for further investigation.
One possible method to establish correlation would be a longitudinal clinical study, documenting radiographic evidence for arthritis in other joints at the time of knee fusion and for a period of subsequent years. It would be more difficult to establish causation clinically, but the results of Chapter 7 the use of similar musculoskeletal modeling techniques may provide evidence for such a link.

Failure Mode and Effects Analysis (FMEA) entails the use of methods to preemptively detect causes of failure. One such method is the use of finite element analysis techniques, and they have seen extensive adoption in design and reliability studies. Meaningful output from FEA studies is dependent on meaningful and accurate assumptions, however, such as an accurate estimation of the loading conditions of an orthopedic implant. Utilization of FEA to test any implantable, rigid-knee orthopedic device, including the proposed treatment method of Chapter 8, is made possible through the reporting of loading patterns provided in Chapter 7. The author recommends that future work utilize this technique to predict potential causes of failure of the proposed treatment model, and to thus assist in the refinement of design parameters. This recommendation has already, in fact, been taken; this work is currently being performed as the focus of the Master’s thesis of a current graduate student, John P. O’Donnell.

Given the purpose of the preceding research, the investigation and proposal of clinical treatment models, it is not surprising that the methods utilized are diverse. Inpatient database analysis, motion capture, human subject testing, computational modeling, and FDA guided design and development techniques were required to achieve the stated objective. As the preceding dissertation shows, this research successfully
accomplishes its stated aims. In accomplishing these aims, however, the previously
uninvestigated research areas broached by this work have demonstrated the potential for
future work, and the techniques employed leave fertile ground for subsequent researchers.
The author has documented several of his approaches in “Standard Operating Procedures”
and has, in some cases, created automated programs to assist in this work; It is his hope
that future researchers will continue to build upon the foundation laid in this work. The
author and his collaborators have also secured intellectual property on the development
work. This dissertation provides strong support for the licensing and translation of this
intellectual property.
APPENDIX A – ADDITIONAL DATA FROM THE NATIONWIDE INPATIENT SAMPLE

Data from the Nationwide Inpatient Sample that hasn’t been developed far enough to merit an individual chapter.

The SAS program developed in Chapter 5 to query and analyze the Nationwide Inpatient Sample, documented in the Appendix B, was used to procure additional data on orthopedic knee joint procedures for comparison against knee arthrodesis.

![Number of Procedures Performed in United States](image-url)
While the relative number of primary and revision total knee replacement procedures has grown since 1993, no such increase has occurred with knee arthrodesis.
Aside from a dramatic reduction in the length of stay for all procedures occurring between 1993 and 1997, this measure has not continued to decrease for knee arthrodesis in subsequent years.

The cost of all procedures has risen in the United States over the past two decades. These costs have increased at a greater rate for revision total knee replacement and knee arthrodesis.
A greater percentage of revision total knee replacements than primary total knee replacements are performed in metropolitan areas. An even greater percentage of knee arthrodesis procedures are performed in metropolitan areas.
The increasing complexity of revision total knee replacement and knee arthrodesis, as compared to primary total knee replacement, is reflected in the greater number of procedures performed at teaching hospitals.

Prior to 2005, a single ICD-9-CM Procedural code (Revision TKR – Not Otherwise Specified) was used to classify any and all revision total knee replacements. In that year, new codes were introduced to allow for a more detailed description of the revision work, i.e. whether only some or all of the previously implanted components were replaced.
The number of diagnoses of knee stiffness has increased over the past two decades.
TKR by age/gender trends (reproduction of previous publications, but required for further breakdown)
APPENDIX B – SAS CODE FOR ANALYZING THE NATIONWIDE INPATIENT SAMPLE

1 – MasterNISCode.sas

/******************************************************************
******  Statistical analysis - Nationwide Inpatient Sample *****
******  Eric Montgomery Lucas, 2013-2014                     *****
************************************************
**************************
/*/ This code will output analysis to Excel files in "E:\NIS Studies"*/

/*/ What is the ICD-9-CM code you are interested in? */
%LET FilterCode = 8154;

/*/ Is that a procedural code (PRCODE) or diagnostic code (DXCODE)? */
%LET SEARCHPARAM = PRCODE;

/*/ Give your study a short nickname, less than 8 characters long. */
%LET StudyName = TKR8154;

/*/ What are your desired age cutoffs? First group is 0 to one BELOW Agebin1. */
%LET Agebin1 = 55; /* This age starts the second group. */
%LET Agebin2 = 60; /* This age starts the third group. */
%LET Agebin3 = 65; /* This age starts the fourth group. */
%LET Agebin4 = 70; /* This age starts the fifth group. */
%LET Agebin5 = 75; /* The sixth group includes everyone this age and older. */

/*/ What year would you like to start your search? */
%LET StartYear = 1993;

/*/ What year would you like to end your search? */
%LET EndYear = 1995;

/*/ Do you want to further break down output by a domain? "No"=0; "Yes"=1 */
%LET ByDomain = 1;

/*/ If so, which domain do you want to add? Gender is "FEMALE" */
%LET DomainValue = Female;

******************************************************************************
******************************************************************************
**********   Mess with the code below at your own risk...   **********
******************************************************************************
******************************************************************************
/*/ The code below automatically sets the directory containing the data & SAS files. */

X "cd
""%substr(%sysget(SAS_EXECFILEPATH),1,%eval(%length(%sysget(SAS_EXECFILEPATH))-%length(%sysget(SAS_EXECFILENAME))))"

/* Imports census data to make appropriate estimates. */
%INCLUDE "2-ImportCensusData.sas"

/* Big ol' Macro to run my data */
%macro DataProcessing;
   %do i=&StartYear %to &EndYear;
      %INCLUDE "3-PrepareNISData.sas"
      %INCLUDE "4-GenerateOutput.sas"
      %INCLUDE "4-GenerateOutput xDomain.sas"
      %INCLUDE "5-ProcessData.sas"
   %end;
%mend DataProcessing;
%DataProcessing;

%INCLUDE "6-PoissonAnalysis.sas"

ods tagsets.excelxp
   file="E:\NIS Studies\&studyname._info_general.xls"
   style=minimal
   options ( Orientation = 'landscape'
            FitToPage = 'yes'
            Pages_FitWidth = '1'
            Pages_FitHeight = '100' );
   title "&Studyname Information on Demographics"
   proc print data=Yearstest;
   run;
ods tagsets.excelxp close;
run;
/* Import US Census data broken down by age, gender. */
PROC IMPORT datafile="CensusYearAgeGender.csv"
out=Census
dbms=csv
replace;
getnames=yes;
RUN;

/* Creates a new variable to describe which age group each age is in. */
DATA CensusBinned;
  set Census;
  AGEBIN = 0;
  IF (.< AGE < &AgeBin1.) THEN AgeBin = 1;
  IF (&Agebin1. <= AGE < &AgeBin2.) THEN AGEBIN = 2;
  IF (&Agebin2. <= AGE < &Agebin3.) THEN AGEBIN = 3;
  IF (&Agebin3. <= AGE < &Agebin4.) THEN AGEBIN = 4;
  IF (&Agebin4. <= AGE < &Agebin5.) THEN AGEBIN = 5;
  IF (AGE >= &Agebin5.) THEN AGEBIN = 6;
RUN;

/* Sorts the data to prepare for summing it. */
PROC SORT;
  by year AGEBIN;

/* Sums the appropriate age groups and puts the total into a new variable. */
PROC MEANS NOPRINT;
  by year AGEBIN;
  var N MaleN FemaleN;
  output out=CensusN sum=AgeBinSum MaleNSum FemaleNSum;
Run;

DATA YearsTest;
  set CensusN;
Run;
DATA YearsTestMale;
  Set YearsTest;
  Female=0;
Run;
DATA YearsTestFemale;
  Set YearsTest;
  Female=1;
Run;
DATA YearsTest;
  Set YearsTestMale YearsTestFemale;
Run;

PROC SORT DATA=YearsTest ;
  BY YEAR AGEBIN FEMALE ;
RUN;
/* Prepare a year if NIS data for analysis. */
LIBNAME NIS&i "E:\NIS Data\&i\";
Run;

DATA NIS &StudyName. &i;
SET NIS&i.\NIS_trends_supplemental_&i.;
RETAIN DISCHGS 1;
RETAIN YEAR &i;
&StudyName = 0;
/*PR1&StudyName = 0;
IF PR1="&FilterCode"
THEN PR1&StudyName = 1; */
IF pr1="&FilterCode" OR
pr2="&FilterCode" OR
pr3="&FilterCode" OR
pr3="&FilterCode" OR
pr4="&FilterCode" OR
pr5="&FilterCode" OR
pr6="&FilterCode" OR
pr7="&FilterCode" OR
pr8="&FilterCode" OR
pr9="&FilterCode" OR
pr10="&FilterCode" OR
pr11="&FilterCode" OR
pr12="&FilterCode" OR
pr13="&FilterCode" OR
pr14="&FilterCode" OR
pr15="&FilterCode"
THEN &StudyName = 1;
AGEBIN = 0;
IF (< AGE < &AgeBin1 ) THEN AGEBIN = 1;
IF (&Agebin1 <= AGE < &Agebin2 ) THEN AGEBIN = 2;
IF (&Agebin2 <= AGE < &Agebin3 ) THEN AGEBIN = 3;
IF (&Agebin3 <= AGE < &Agebin4 ) THEN AGEBIN = 4;
IF (&Agebin4 <= AGE < &Agebin5 ) THEN AGEBIN = 5;
IF (AGE >= &Agebin5 ) THEN AGEBIN = 6;

/* Includes formatting files to make data from the NIS readable. */
%INCLUDE "E:\NIS Studies\Sas Code\HCUP_FORMATS.sas";
%INCLUDE "E:\NIS Studies\Sas Code\I9_Formats.sas";

PROC FORMAT;
VALUE AGEBIN
0="Missing"
1="0 to &Agebin1 minus 1"
2="&Agebin1 to &Agebin2 minus 1"
3="&Agebin2 to &Agebin3 minus 1"
4="&Agebin3 to &Agebin4 minus 1"
5="&Agebin4 to &Agebin5 minus 1"
6="&Agebin5 and up";
RUN;
4-GenerateOutput.sas

/* Run the data analysis and create a PDF for each year. */

ODS TAGSETS.EXCELXP
    file="E:\NIS Studies\&studyname._CountData_&i.Total.xls"
    STYLE=statistical
    OPTIONS ( Orientation = 'landscape'
    FitToPage = 'yes'
    Pages_FitWidth = '1'
    Pages_FitHeight = '100' );
    Title "&Studyname Information &i.";

PROC SURVEYMEANS MISSING SUM MEAN STDERR;
    WEIGHT discwt ;
    CLASS
        agebin
        FEMALE
        died
        pay1
        elective
        hosp_teach
        hosp_locteach
        hosp_location
        hosp_region;
    CLUSTER hospid ;
    STRATA NIS_stratum ;
    VAR
        dischgs
        /*PR1&StudyName*/
        agebin
        died
        pay1
        elective
        hosp_teach
        hosp_locteach
        hosp_location
        hosp_region
        NPR
        LOS
        totchg ;
    DOMAIN &StudyName.;
RUN;

ods tagsets.excelxp close;
4-GenerateOutput xDomain.sas

/* Run the data analysis and create a PDF for each year. */

ODS TAGSETS.EXCELXP
    file="E:\NIS Studies\&studyname._CountData_&i.GenderAge.xls"
    STYLE=minimal
    OPTIONS ( Orientation = 'landscape'
      FitToPage = 'yes'
      Pages_FitWidth = '1'
      Pages_FitHeight = '100' )
    Title "&Studyname Information &i.";

PROC SURVEYMEANS MISSING SUM MEAN STDERR;
    WEIGHT discwt ;
    CLASS
      agebin
      FEMALE
      died
      pay1
      elective
      hosp_teach
      hosp_locteach
      hosp_location
      hosp_region;
    CLUSTER hospid ;
    STRATA NIS_stratum ;
    VAR
      dischgs
      /*PR1&StudyName*/
      agebin
      died
      pay1
      elective
      hosp_teach
      hosp_locteach
      hosp_location
      hosp_region
      NPR
      LOS
      totchg ;
    DOMAIN &Studyname.*FEMALE;
RUN;

ods tagsets.excelxp close;
5-ProcessData.sas

/* Delete all observations that don't satisfy the searched code. */
DATA NIS_&StudyName._&i;
    SET NIS_&StudyName._&i;
    IF &StudyName = 1;
/* Prepare each dataset for a Poisson analysis. */
PROC SORT;
    BY YEAR AGEBIN FEMALE ;
title1 "Set with desired data from all years.";
RUN;
/* Delete gender values that are not 0 or 1 (Male or Female)*/
Data NIS_&StudyName._&i ;
    Set NIS_&StudyName._&i ;
    IF Female ^= 1 AND Female ^= 0 THEN delete ;
Run;
/* Output a dataset with the weighted counts for each year */
PROC MEANS DATA=NIS_&StudyName._&i NOPRINT ;
    by YEAR AGEBIN FEMALE;
    VAR DISCWT;
    OUTPUT out=a&i sum=countwt;
RUN;
/* Sort the dataset to be merged */
PROC SORT DATA=a&i ;
    BY YEAR AGEBIN FEMALE ;
RUN;
/* Merge the datasets into a single dataset 'YearsTest' to be read and
 analyzed */
Data YearsTest ;
    Set YearsTest ;
    Merge YearsTest a&i ;
    By Year Agebin Female ;
Run;
/* Add variable DemographicN so that the male and female counts can be
 analyzed */
Data YearsTest ;
    Set YearsTest ;
    IF Female = 0 THEN DemographicN = MaleNSum ;
    IF Female = 1 THEN DemographicN = FemaleNSum ;
Run;
/* Create a new variable 'CountMil' so that the data can be read in the
 poisson analysis (sig figs) */
Data YearsTest ;
    Set YearsTest ;
    Count = countwt*1 ;
    CountMil = count * 1000000 ;
Run;
/* Format the table 'YearsTest' in this order for easy comparison */
Data YearsTest ; /*(Drop = countwt); */
    Set YearsTest ;
    Format Year Agebin Female _FREQ_ AgeBinSum DemographicN Count CountMil ;
Run;
/* Prep data for Poisson Analysis */
Data Yearstest;
  SET Yearstest;
  ln = log(DemographicN);
Run;

/* Poisson Analysis */
PROC GENMOD DATA=Yearstest ;
  class Agebin Female Year;
  model CountMil = Female Agebin Year / dist = poisson
    link = log
    offset = ln
    Type1
    Type3;
  estimate "Rate: Agebin=1 Sex= male" intercept 1 Agebin 0 0 0 0
    0 Female 1 0;
  estimate "Rate: Agebin=2 Sex=male" intercept 1 Agebin 0 1 0 0
    0 Female 1 0;
  estimate "Rate: Agebin=3 Sex=male" intercept 1 Agebin 0 0 1 0
    0 Female 1 0;
  estimate "Rate: Agebin=4 Sex=male" intercept 1 Agebin 0 0 0 1
    0 Female 1 0;
  estimate "Rate: Agebin=5 Sex=male" intercept 1 Agebin 0 0 0 0
    1 Female 1 0;
  estimate "Rate: Agebin=6 Sex=male" intercept 1 Agebin 0 0 0 0
    1 Female 1 0;
  estimate "Rate: Agebin=1 Sex=female" intercept 1 Agebin 0 0 0 0
    0 0 0 1 Female 0 1;
  estimate "Rate: Agebin=2 Sex=female" intercept 1 Agebin 0 0 0 1
    0 0 0 0 Female 0 1;
  estimate "Rate: Agebin=3 Sex=female" intercept 1 Agebin 0 0 0 0
    1 0 0 0 Female 0 1;
  estimate "Rate: Agebin=4 Sex=female" intercept 1 Agebin 0 0 0 0
    0 1 0 0 Female 0 1;
  estimate "Rate: Agebin=5 Sex=female" intercept 1 Agebin 0 0 0 0
    0 0 1 0 Female 0 1;
  estimate "Rate: Agebin=6 Sex=female" intercept 1 Agebin 0 0 0 0
    0 0 0 1 Female 0 1;
  estimate "1994 from 1993 Rate Ratio" year -1 1 0 0 0 0 0 0 0 0 0
    0 0 0 0 0 0 0 0 0;
  estimate "1995 from 1993 Rate Ratio" year -1 0 1 0 0 0 0 0 0 0 0
    0 0 0 0 0 0 0 0 0;
  estimate "1996 from 1993 Rate Ratio" year -1 0 0 1 0 0 0 0 0 0 0
    0 0 0 0 0 0 0 0 0; /*
  estimate "male/female Rate Ratio" Female 1 -1;
  estimate "female/male Rate Ratio" Female -1 1;"
estimate "Agebin (&Agebin1. to one year less than &Agebin2.)/(0 to one year less than &Agebin1. ) Rate Ratio" agebin -1 1 0 0 0 0;
estimate "Agebin (&Agebin2. to one year less than &Agebin3.)/(0 to one year less than &Agebin1. ) Rate Ratio" agebin -1 0 1 0 0 0;
estimate "Agebin (&Agebin3. to one year less than &Agebin4.)/(0 to one year less than &Agebin1. ) Rate Ratio" agebin -1 0 0 1 0 0;
estimate "Agebin (&Agebin4. to one year less than &Agebin5.)/(0 to one year less than &Agebin1. ) Rate Ratio" agebin -1 0 0 0 1 0;
estimate "Agebin (&Agebin5. and up)/(0 to one year less than &Agebin1. ) Rate Ratio" agebin -1 0 0 0 0 1;

lsmeans agebin / diff exp cl;
lsmeans Female / diff exp cl;
lsmeans year / diff exp cl;

output out=poissonoutput xbeta=xb stdxbeta=std;

run;
APPENDIX C – SAS CODE FOR ANALYZING KINEMATIC AND KINETIC VALUES OF INTEREST

1 – BraceGait Master SAS Code.sas

/******************** Running statistics on gait analysis data.  ********************
*******************************************************************************

/* The code below allows you to select which values to examine (From File#3) */
%LET StartNumber = 1 ;
%LET EndNumber = 70 ;

/* The code below automatically sets the directory containing the data & SAS files. */
X "cd "%substr(%sysget(SAS_EXECFILEPATH),1,%eval(%length(%sysget(SAS_EXECFILENAME)))-%length(%sysget(SAS_EXECFILENAME)))"";
/* If the above doesn’t work, you will have to comment it out and copy the directory below. */
/* X "cd C:\Users\LUCAS8\Dropbox\Clemson\Lucas Shared\2 Gait Analysis\Data\SAS Code"; */

/* Import the data files and then combines them into one database. Print the contents. */
%INCLUDE "2 - ImportAndMergeData.sas";

/* Identify specific point of interest */
%INCLUDE "3 - Identify Points of Interest.sas";

/* Data Analysis Step */
%INCLUDE "4 - Data Analysis.sas";
/**Import the three data files and then combine them into one database.*/
proc import datafile="DataX.csv"
   out=DataX
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="DataY.csv"
   out=DataY
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="DataZ.csv"
   out=DataZ
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="DataPelvicCGxz.csv"
   out=PelvicCGxy
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="DataForcesMomentsX.csv"
   out=DataMomentsX
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="DataForcesMomentsY.csv"
   out=DataMomentsY
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="DataForcesMomentsZ.csv"
   out=DataMomentsZ
dbms=csv
   replace;
   getnames=yes;
run;
/***** Combine the above datasets. *****/
data GaitData;
   set DataX DataY DataZ PelvicCGxy DataMomentsX DataMomentsY DataMomentsZ ;
run;

Data GaitData;
   set GaitData;
   TRIALBIN = "A";
   if TRIAL="C1" then TRIALBIN="C" ;
   if TRIAL="B1" then TRIALBIN="B" ;
   if TRIAL="B2" then TRIALBIN="B" ;
   if TRIAL="B3" then TRIALBIN="B" ;
run;

/***** Copies the data to a new database and *****
***** prints its contents for verification. *****/
data a;
   set GaitData;
run;
PROC contents;
   title1 'Data Contents';
3 - Identify Points of Interest.sas

******************************************************************************
*Identify specific point of interest*
******************************************************************************

%LET JointInfo1 = PelvicCGRight ;
%LET JointInfo2 = PelvicCGLeft ;
%LET JointInfo3 = PelvicCGRange ;
%LET JointInfo4 = PelvicZLeftSwing ;
%LET JointInfo5 = PelvicZRightSwing ;
%LET JointInfo6 = PelvicZAAfterLHS ;
%LET JointInfo7 = PelvicZAAfterRHS ;
%LET JointInfo8 = PelvicRotationCCW ;
%LET JointInfo9 = PelvicRotationCW ;
%LET JointInfo10 = PelvicObliquityLTO ;
%LET JointInfo11 = PelvicObliquityLeftSwing ;
%LET JointInfo12 = PelvicObliquityRTO ;
%LET JointInfo13 = PelvicObliquityRightSwing ;
%LET JointInfo14 = PelvicTiltLTO ;
%LET JointInfo15 = PelvicTiltPeakRTO ;
%LET JointInfo16 = PelvicMeanTiltRightSwing ;
%LET JointInfo17 = HipExtensionStart ;
%LET JointInfo18 = HipFlexionStart ;
%LET JointInfo19 = HipAdductionMean ;
%LET JointInfo20 = HipAdductionFirstTO ;
%LET JointInfo21 = HipAdductionSecTO ;
%LET JointInfo22 = HipAddMeanSLimbSup ;
%LET JointInfo23 = HipRotationMean ;
%LET JointInfo24 = HipRotMean ;
%LET JointInfo25 = KneeFlexionTO ;
%LET JointInfo26 = KneeFlexionSwing ;
%LET JointInfo27 = KneeAdductionMax ;
%LET JointInfo28 = KneeAdductionMin ;
%LET JointInfo29 = KneeRotMin ;
%LET JointInfo30 = AnkleFlexionTO ;
%LET JointInfo31 = AnkleFlexionContraTO ;
%LET JointInfo32 = AnkleMaxInversion ;
%LET JointInfo33 = AnkleMeanInversion ;
%LET JointInfo34 = AnkleMaxAdduction ;
%LET JointInfo35 = AnkleAdductionHS ;
%LET JointInfo36 = AnkleAddCTO ;
%LET JointInfo37 = HipExtensionMoment ;
%LET JointInfo38 = HipFlexionMoment ;
%LET JointInfo39 = KneeFlexionMoment ;
%LET JointInfo40 = KneeExtensionMoment ;
%LET JointInfo41 = AnklePlantarMom ;
%LET JointInfo42 = AnkleDorsiMom ;
%LET JointInfo43 = HipAddMom1;
%LET JointInfo44 = HipAddMom2;
%LET JointInfo45 = KneeAbdMom1;
%LET JointInfo46 = KneeAbdMom2;
%LET JointInfo47 = AnkleInvMom;
%LET JointInfo48 = AnkleEvMom;
%LET JointInfo49 = HipIntRotMom;
%LET JointInfo50 = HipExtRotMom;
%LET JointInfo51 = KneeIntRotMom;
%LET JointInfo52 = KneeExtRotMom;
%LET JointInfo53 = MeanFFAdductionMom;

%LET JointInfo54 = HipForceXStart;
%LET JointInfo55 = HipForceXTO;
%LET JointInfo56 = HipForceXSS;
%LET JointInfo57 = HipForceXHS;
%LET JointInfo58 = KneeForceXTO;
%LET JointInfo59 = KneeForceXHS;
%LET JointInfo60 = AnkleForceXTO;
%LET JointInfo61 = AnkleForceXHS;
%LET JointInfo62 = HipForceYTO;
%LET JointInfo63 = HipForceYSS;
%LET JointInfo64 = HipForceYHS;
%LET JointInfo65 = KneeForceYTO;
%LET JointInfo66 = AnkleForceYTO;
%LET JointInfo67 = AnkleForceYHS;
%LET JointInfo68 = HipForceZTO;
%LET JointInfo69 = HipForceZSS;
%LET JointInfo70 = HipForceZHS;
%LET JointInfo71 = KneeForceZTO;
%LET JointInfo72 = KneeForceZSS;
%LET JointInfo73 = KneeForceZHS;
%LET JointInfo74 = AnkleForceZTO;
%LET JointInfo75 = AnkleForceZSS;
%LET JointInfo76 = AnkleForceZHS;
4 - Data Analysis.sas

%macro JointAnalysis;
  %do i=&StartNumber. %to &EndNumber.;
  /* Reference out to each of the Joint Info Files. */
  %INCLUDE "&&JOINTINFO&i...sas" ;
  Run;
  /* And here begins the analysis, which is run on each Joint Info File. */
  DATA B;
  set GaitData;
  if joint="&SetJoint." and plane="&SetPlane." ;
  if gaitcycle < &StartMargin or gaitcycle > &StopMargin then
    delete;
  PROC SORT;
    by subject joint side plane trial repetition;
  %MACRO MinMaxOrOther;
    %if &FindType = MINIMUM %then
      %do;
        PROC MEANS NOPRINT;
        by subject joint side plane trial repetition;
        var degrees;
        output out=c min=targetdegree
        minid(Degrees(gaitcycle))=CycleDegMinMax ;
        %put Type used: MINIMUM ;
      %end
    %else %if &FindType = MAXIMUM %then
      %do;
        PROC MEANS NOPRINT;
        by subject joint side plane trial repetition;
        var degrees;
        output out=c max=targetdegree
        maxid(Degrees(gaitcycle))=CycleDegMinMax ;
        %put Type used: MAXIMUM ;
      %end
    %else %if &FindType = MEAN %then
      %do;
        PROC MEANS NOPRINT;
        by subject joint side plane trial repetition;
        var degrees;
        output out=c mean=targetdegree;
        %put Type used: MEAN ;
      %end
    %else %if &FindType = RANGE %then
      %do;
        PROC MEANS NOPRINT;
        by subject joint side plane trial repetition;
        var degrees;
        output out=c range=targetdegree ;
      %end
%put Type used: MAXIMUM ;
%end;
%else %put &FindType Something messed up. Look through your work and try again. ;
%MEND MinMaxOrOther;
%MMinMaxOrOther;

*PROC PRINT;

%Macro PelvisOrOther;
%if &SetJoint = Pelvis OR &SetJoint = PelvisCG %then %do;
/* Does this if pelvis (because "Side" messes it up.) */
/*proc freq;
   by subject;
   tables trial/norow nocol nopercent;
proc freq;
   tables trial/norow nocol nopercent;
   tables trial*subject/norow nocol nopercent;
   tables subject/norow nocol nopercent;
proc sort;
   by side;
proc freq;
   by side;
   tables subject*trial/norow nocol nopercent;*/
proc sort data=c;
   by joint plane;

title1 "&Description. (&FindType. DEGREES between &StartMargin. and &StopMargin. )"
proc glimmix nobound data=c;
   *plots=residualpanel; /* Max, Min, or Mean Degrees */
by joint plane;
class subject trial ;
model targetdegree = trial ;
random subject subject*trial ;
lsmeans trial /diff lines;
output out=res1 residual=rtargetdegree;
ods select lsmeans;
ods trace on;
ods show;
proc univariate plot normal data=res1;
   var rtargetdegree;
ods select 'Tests for Normality';
ods trace on;
ods show;
proc glm data=res1;
   class trial;
model rtargetdegree=trial;
   means trial/hovtest=levene;
ods select "Levene's HoV Test";
ods trace on;
ods show;

RUN; QUIT;

title1 "&Description. (% Gait Cycle where &FindType. between &StartMargin. and &StopMargin. occurs.)";
proc glimmix nobound data=c;
    *plots=residualpanel; /* % Gait Cycle where above occurs */
    by joint plane;
    class subject trial;
    model CycleDegMinMax = trial;
    random subject subject*trial;
    lsmeans trial /diff lines;
    output out=res2 residual=rtargetdegree;
        ods select lsmeans;
        ods trace on;
        ods show;
    proc univariate plot normal data=res2;
        var rtargetdegree;
        ods select 'Tests for Normality';
        ods trace on;
        ods show;
    proc glm data=res2;
        class trial;
        model rtargetdegree=trial;
        means trial/hovtest=levene;
        ods select "Levene's HoV Test";
        ods trace on;
        ods show;
    RUN; QUIT;
    %put Joint: Pelvis ;
%end;
%else /* Everything except pelvis. */
    /*proc freq; by subject;
    tables trial*side/norow nocol nopercent;*/
    proc freq;
        tables trial*side/norow nocol nopercent;
        tables trial*subject/norow nocol nopercent;
        tables subject*side/norow nocol nopercent;
    proc sort; by side;
        proc freq; by side;
        tables subject*trial/norow nocol nopercent;*/
    proc sort;
        by joint plane;
### Degrees

```r
title1 "&Description. (&FindType. DEGREES between &StartMargin. and &StopMargin. )";
proc glimmix nobound data=c ;
   *plots=residualpanel;       /* Max, Min, or Mean
by joint plane;
class subject trial side;
model targetdegree = trial side trial*side;
random subject subject*trial subject*trial*side;
lsmeans trial side trial*side/diff lines;
output out=res3 residual=rtargetdegree;
   ods select lsmeans;
   ods trace on;
   ods show;
data res3 ;
   set res3;
   trialside=trial||side;
proc univariate plot normal data=res3 ;
   var rtargetdegree;
      ods select 'Tests for Normality';
      ods trace on;
      ods show;
proc glm data=res3 ;
   class trialside;
   model rtargetdegree=trialside;
   means trialside/hovtest=levene;
      ods select "Levene's HoV Test";
      ods trace on;
      ods show;
RUN; QUIT;
```

### Above occurs

```r
title1 "&Description. (% Gait Cycle where &FindType. between &StartMargin. and &StopMargin. occurs.)";
proc glimmix nobound data=c;
   *plots=residualpanel;       /* % Gait Cycle where
by joint plane;
class subject trial side;
model CycleDegMinMax = trial side trial*side;
random subject subject*trial subject*trial*side;
lsmeans trial side trial*side/diff lines;
output out=res4 residual=rtargetdegree;
   ods select lsmeans;
   ods trace on;
   ods show;
data res4;
   set res4;
   trialside=trial||side;
proc univariate plot normal data=res4;
   var rtargetdegree;
      ods select 'Tests for Normality';
      ods trace on;
      ods show;
proc glm data=res4;
```
class trialside;
model rtargetdegree=trialsid;
means trialside/hovtest=levene;
   ods select "Levene's HoV Test";
   ods trace on;
   ods show;
RUN; QUIT;

%put Joint: Not Pelvis ;
%end;
%MEND PelvisOrOther;
%PelvisOrOther;

%end;
%mend JointAnalysis;
%JointAnalysis;
Below is just one example of the 60+ Joint Info files used to examine particular points of interest. Each file took the same format, but the Description, StartMargin, Stop Margin, FindType, SetJoint, SetPlane, and SetSide values differed.

**PelvicCGRight.sas**

```sas
/* Identify a specific point of interest */
%LET Description = Pelvic Sway Right ;
/* Describe point of interest */
%LET StartMargin = 1 ;
/* Start looking at this % gait cycle */
%LET StopMargin = 55 ;
/* Stop looking at this % gait cycle */
%LET FindType = MINIMUM ;
/* All Caps MINIMUM, MAXIMUM, or RANGE */
%LET SetJoint = PelvisCG ;
/* Which joint is of interest */
%LET SetPlane = x ;
/* Which plane is of interest */
```
APPENDIX D – SAS CODE FOR ANALYZING JOINT AND MUSCLE LOADING

1 – Stat Analysis Master Program.sas

/***********************************************************
****  Running statistical analysis on AnyBody data.  *****/
/*******************************************************************/

/* Which points of interest would you like to analyze? Enter the first
and last numbers, and this program will analyze them along with every
value in between. You need to look in the third include file (#3) in
order to get the correct numbers. */
%LET StartValue = 1;
%LET EndValue = 1;

/* The code below automatically sets the directory containing the data
& SAS files. */
X "cd 
""%substr(%sysget(SAS_EXECFILEPATH),1,%eval(%length(%sysget(SAS_EXECFILEPATH))-%length(%sysget(SAS_EXECFILENAME))))""
/* If the above doesn't work, you will have to comment it out and copy
the directory below. */
/* X "cd C:\Users\LUCAS8\Dropbox\Clemson\Lucas Shared\2 Gait
Analysis\Data\SAS Code"; */

/* Import the data files and then combines them into one database.
Print the contents. */
%INCLUDE "2 - Import And Merge Data.sas";

/* Identify specific point of interest */
%INCLUDE "3 - Identify Points of Interest.sas";

/* Data Analysis Step */
%INCLUDE "4 - Data Analysis.sas";
2 – Import and Merge Data.sas

/*Import the three data files and then combine them into one. */

proc import datafile="S05SAScontrol.csv"
   out=S05Control
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="S05SASbraceright.csv"
   out=S05BraceRight
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="S05SASbraceleft.csv"
   out=S05BraceLeft
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="S06SAScontrolright.csv"
   out=S06ControlRight
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="S06SASbraceright.csv"
   out=S06BraceRight
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="S06SASbraceleft.csv"
   out=S06BraceLeft
dbms=csv
   replace;
   getnames=yes;
run;

proc import datafile="S08SAScontrolright.csv"
   out=S08ControlRight
dbms=csv
   replace;
   getnames=yes;
run;
proc import datafile="S08SAScontrolleft.csv"
      out=S08ControlLeft
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S08SASbraceright.csv"
      out=S08BraceRight
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S08SASbraceleft.csv"
      out=S08BraceLeft
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S09SAScontrolright.csv"
      out=S09ControlRight
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S09SAScontrolleft.csv"
      out=S09ControlLeft
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S09SASbraceright.csv"
      out=S09BraceRight
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S09SASbraceleft.csv"
      out=S09BraceLeft
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S10SAScontrolright.csv"
      out=S10ControlRight
      dbms=csv
      replace;
      getnames=yes;
run;

proc import datafile="S10SAScontrolleft.csv"
  out=S10ControlLeft
dbms=csv
replace;
getnames=yes;
run;

proc import datafile="S10SASbraceright.csv"
  out=S10BraceRight
dbms=csv
replace;
getnames=yes;
run;

proc import datafile="S10SASbraceleft.csv"
  out=S10BraceLeft
dbms=csv
replace;
getnames=yes;
run;

proc import datafile="AllSubjectLeftMuscle.csv"
  out=LeftMuscle
dbms=csv
replace;
getnames=yes;
run;

proc import datafile="AllSubjectRightMuscle.csv"
  out=RightMuscle
dbms=csv
replace;
getnames=yes;
run;

/*** Combine the above datasets. *****/
data AnyBody;
  set S05Control
  S05BraceRight
  S05BraceLeft
  S06ControlRight
  S06BraceRight
  S06BraceLeft
  S08ControlRight
  S08ControlLeft
  S08BraceRight
  S08BraceLeft
  S09ControlRight
  S09ControlLeft
  S09BraceRight
  S09BraceLeft
  S10ControlRight
$10ControlLeft
$10BraceRight
$10BraceLeft
LeftMuscle
RightMuscle;
run;

/***** Copies the data to a new database and *****
***** prints its contents for verification. *****/
data a;
  set AnyBody;
Run;
PROC contents;
  title1 'Data Contents';
3 – Identify Points of Interest.sas

/************************************
*Identify specific point of interest*
************************************/

%LET Info1 = 1RightAnkleForceAP ;
%LET Info2 = 2RightAnkleMomentSE1 ;
%LET Info3 = 3RightAnkleMomentSE2 ;
%LET Info4 = 4RightAnkleMomentAxial1 ;
%LET Info5 = 5RightAnkleMomentAxial2 ;
%LET Info6 = 6RightKneeForcePD1 ;
%LET Info7 = 7RightKneeForcePD2 ;
%LET Info8 = 8RightKneeForcePD3 ;
%LET Info9 = 9RightKneeForceML1 ;
%LET Info10 = 10RightKneeForceML2 ;
%LET Info11 = 11RightKneeForceML3 ;
%LET Info12 = 12RightKneeForceAP1 ;
%LET Info13 = 13RightKneeForceAP2 ;
%LET Info14 = 14RightKneeMomentF1 ;
%LET Info15 = 15RightKneeMomentF2 ;
%LET Info16 = 16RightKneeMomentAb1 ;
%LET Info17 = 17RightKneeMomentAb2 ;
%LET Info18 = 18RightKneeMomentAxial1 ;
%LET Info19 = 19RightKneeMomentAxial2 ;
%LET Info20 = 20RightKneeMomentAxial3 ;
%LET Info21 = 21RightKneeMomentAxial4 ;
%LET Info22 = 22RightHipForcePD1 ;
%LET Info23 = 23RightHipForcePD2 ;
%LET Info24 = 24RightHipForceML1 ;
%LET Info25 = 25RightHipForceML2 ;
%LET Info26 = 26RightHipForceML3 ;
%LET Info27 = 27RightHipForceAP1 ;
%LET Info28 = 28RightHipForceAP2 ;
%LET Info29 = 29RightHipForceAP3 ;
%LET Info30 = 30RightHipMomentAb1 ;
%LET Info31 = 31RightHipMomentAb2 ;
%LET Info32 = 32RightHipMomentEx ;
%LET Info33 = 33LeftAnkleForceAP ;
%LET Info34 = 34LeftKneeMomentSE1 ;
%LET Info35 = 35LeftKneeMomentSE2 ;
%LET Info36 = 36LeftKneeMomentAxial1 ;
%LET Info37 = 37LeftKneeMomentAxial2 ;
%LET Info38 = 38LeftKneeForcePD1 ;
%LET Info39 = 39LeftKneeForcePD2 ;
%LET Info40 = 40LeftKneeForceML1 ;
%LET Info41 = 41LeftKneeForceML2 ;
%LET Info42 = 42LeftKneeForceML3 ;
%LET Info43 = 43LeftKneeForceAP1 ;
%LET Info44 = 44LeftKneeForceAP2 ;
%LET Info45 = 45LeftKneeMomentF1 ;
%LET Info46 = 46LeftKneeMomentF2 ;
%LET Info47 = 47LeftKneeMomentAb1 ;
%LET Info48 = 48LeftKneeMomentAb2 ;
%LET Info49 = 49LeftKneeMomentAxial1 ;
%LET Info50 = 50LeftKneeMomentAxial2 ;
%LET Info51 = 51LeftKneeMomentAxial3 ;
%LET Info52 = 52LeftKneeMomentAxial4 ;
%LET Info53 = 53LeftHipForcePD1 ;
%LET Info54 = 54LeftHipForcePD2 ;
%LET Info55 = 55LeftHipForceML1 ;
%LET Info56 = 56LeftHipForceML2 ;
%LET Info57 = 57LeftHipForceML3 ;
%LET Info58 = 58LeftHipForceAP1 ;
%LET Info59 = 59LeftHipForceAP2 ;
%LET Info60 = 60LeftHipForceAP3 ;
%LET Info61 = 61LeftHipMomentAb1 ;
%LET Info62 = 62LeftHipMomentAb2 ;
%LET Info63 = 63LeftHipMomentEx ;
%LET Info64 = 64LeftHipMomentEx2 ;
%LET Info65 = 65LeftHipMomentEx3 ;
%LET Info66 = 66MuscleRectusFemoris ;
%LET Info67 = 67MuscleVastusLateralis ;
%LET Info68 = 68MuscleVastusMedialis ;
%LET Info69 = 69MuscleVastusIntermedius ;
%LET Info70 = 70MuscleSartorius1 ;
%LET Info71 = 71MuscleSartorius2 ;
%LET Info72 = 72MuscleBicepsFemoris1 ;
%LET Info73 = 73MuscleBicepsFemoris2 ;
%LET Info74 = 74MuscleBicepsFemoris3 ;
%LET Info75 = 75MuscleSemitendinosus1 ;
%LET Info76 = 76MuscleSemitendinosus2 ;
%LET Info77 = 77MuscleSemitendinosus3 ;
%LET Info78 = 78MuscleSemimembranosus1 ;
%LET Info79 = 79MuscleSemimembranosus2 ;
%LET Info80 = 80MuscleSemimembranosus3 ;
%LET Info81 = 81MuscleGastrocnemius ;
%LET Info82 = 82MuscleSoleus ;
3 – Data Analysis.sas

%macro JointAnalysis;
  %do i=&StartValue. %to &EndValue.;

  /* Reference out to each of the Joint Info Files. */
  %INCLUDE "Points of Interest\&INFO\&&INFO&i...sas" ;
  Run;

  /* And here begins the analysis, which is run on each Joint Info File. */
  DATA B;
    set AnyBody;
    if joint = "&SetJoint." and plane = "&SetPlane.";
    if gaitcycle < &StartMargin or gaitcycle > &StopMargin then delete;
  PROC SORT;
    by subject joint side plane trial repetition;
  Run;

  /* Define and run a macro that determines whether we are searching 
   for a Minimum, Maximum, Mean, or Range. It pulls this information 
   for each point of interest file. */
  %MACRO MinMaxOrOther;
    %if &FindType = MINIMUM %then %do;
      PROC MEANS NOPRINT;
      by subject joint side plane trial repetition;
      var Value;
      output out=c min=targetdegree
      minid(Value(gaitcycle))=CycleDegMinMax ;
      %put Type used: MINIMUM ;
    %end;
    %else %if &FindType = MAXIMUM %then %do;
      PROC MEAN S NOPRINT;
      by subject joint side plane trial repetition;
      var Value;
      output out=c max=targetdegree
      maxid(Value(gaitcycle))=CycleDegMinMax ;
      %put Type used: MAXIMUM ;
    %end;
    %else %if &FindType = MEAN %then %do;
      PROC MEANS NOPRINT;
      by subject joint side plane trial repetition;
      var Value;
      output out=c mean=targetdegree;
      %put Type used: MEAN ;
    %end;
    %else %if &FindType = RANGE %then %do;

200
**PROC MEANS NOPRINT;**

by subject joint side plane trial repetition;
var Value;
output out=c range=targetdegree ;
%put Type used: MAXIMUM ;
%end;
%else %put &FindType Something messed up. Look through your work and try again.;
%MEND MinMaxOrOther;
%MinMaxOrOther;

*PROC PRINT;

%MACRO OneOrBothSides;
%if &SetSide = Right OR &SetSide = Left
%then %do;

/* Delete all observations from opposite side. */
DATA C ;
set C;
if Side ^= "&SetSide." then delete;
Run;

/* Does this because some of the left and right values are inverted.
This only compares one side against itself. */
/* And here begins the analysis, which is run on each Joint Info File. */

proc freq;
by subject;
tables trial/norow nocol nopercent;
proc freq;
tables trial/norow nocol nopercent;
tables trial*subject/norow nocol nopercent;
tables subject/norow nocol nopercent;
proc sort;
by side;
proc freq;
by side;
tables subject*trial/norow nocol nopercent;

%end;
/*PROC PRINT;*/

proc glimmix nobound data=c;
*plots=residualpanel; /* Max, Min, or Mean Value */
by joint plane;
class subject trial ;
model targetdegree = trial ;
random subject subject*trial ;
lsmeans trial /diff lines;
output out=res1 residual=rtargetdegree;
/*
ods select lsmeans;
ods trace on;
ods show;
*/
proc sort;
  by joint plane subject trial;
proc means noprint;
  by joint plane subject trial;
  var rtargetdegree;
  output out=res11 mean=rtargetdegree;
proc univariate plot normal data=res11;
  var rtargetdegree;
  /*
    ods select 'Tests for Normality';
    ods trace on;
    ods show;
  */
proc glm data=res11;
  class trial;
  model rtargetdegree=trial;
  means trial/hovtest=levene;
  /*
    ods select "Levene's HoV Test";
    ods trace on;
    ods show;
  */
RUN; QUIT;

**Description. (% Gait Cycle where &FindType. between &StartMargin. and &StopMargin. occurs.)**

 We NEXT look at the % of the gait cycle where the Maximum/Minimum occurs.
 If we are looking at a Mean or Range, this code will error out but that's okay.
 *********************************************************************/
proc glimmix nobound data=c;
  *plots=residualpanel;  /* % Gait Cycle where above occurs */
  by joint plane;
  class subject trial ;
  model CycleDegMinMax = trial;
  random subject subject*trial;
  lsmeans trial /diff lines;
  output out=res2 residual=rCycleDegMinMax;
  /*
    ods select lsmeans;
    ods trace on;
    ods show;
  */
proc sort;
  by joint plane subject trial;
proc means noprint;
  by joint plane subject trial;
  var rCycleDegMinMax;
  output out=res22 mean=rCycleDegMinMax;
proc univariate plot normal data=res22;
  by joint plane;
  var rCycleDegMinMax;
  /*
   ods select 'Tests for Normality';
   ods trace on;
   ods show;
  */
proc glm data=res22;
  by joint plane;
  class trial;
  model rCycleDegMinMax=trial;
  means trial/hovtest=lev;
  /*
   ods select "Levene's HoV Test";
   ods trace on;
   ods show;
  */
RUN; QUIT;
%put No comparison of sides (Left/Right) ;
%end;
%else %do;
  /* Left and Right sides together. */
  /*proc freq; by subject;
   tables trial*side/norow nocol nopercent;
  proc freq;
   tables trial*side/norow nocol nopercent;
   tables trial*subject/norow nocol nopercent;
   tables subject*side/norow nocol nopercent;
  proc sort; by side;
   proc freq; by side;
   tables subject*trial/norow nocol nopercent;
  */
  proc sort; by joint ;
  title1 "&Description. (&FindType. Value between &StartMargin. and &StopMargin. )";
  /***************************************************************************/
  We FIRST look at the Maximum/Minimum/Range with the following code.
  ***************************************************************************/
proc glimmix nobound data=c ;
  *plots=residualpanel; /* Max, Min, or Mean Value */
by joint plane;
class subject trial side;
model targetdegree = trial side trial*side;
random subject subject\*trial subject\*trial\*side;
lsmeans trial side trial\*side/diff lines;
output out=res3 residual=rtargetdegree;

/*
ods select lsmeans;
ods trace on;
ods show;
*/

proc sort;
by joint plane subject trial side;
proc means noprint;
by joint plane subject trial side;
var rtargetdegree;
output out=res33 mean=rtargetdegree;
data res33 ;
set res33;
trialside = trial||side;
proc univariate plot normal data=res33 ;
by joint plane;
var rtargetdegree;
/*
ods select 'Tests for Normality';
ods trace on;
ods show;
*/
proc glm data=res33 ;
by joint plane;
class trialside;
model rtargetdegree=trialsid;
means trialside/hovtest=levene;
/*
ods select "Levene's HoV Test";
ods trace on;
ods show;
*/
RUN; QUIT;

title1 "&Description. (% Gait Cycle where &FindType. between &StartMargin. and &StopMargin. occurs.);";
/****************************
*******************************
We NEXT look at the % of the gait cycle where the Maximum/Minimum occurs.
If we are looking at a Mean or Range, this code will error out but that's okay.
*******************************************************************************/
proc glimmix nobound data=c;
*plots=residualpanel; /* % Gait Cycle where above occurs */
by joint plane;
class subject trial side;
model CycleDegMinMax = trial side trial*side;
random subject subject\*trial subject\*trial\*side;
lsmeans trial side trial\*side/diff lines;
output out=res4 residual=rCycleDegMinMax;
/*
ods select lsmeans;
ods trace on;
ods show;
*/
proc sort;
  by joint plane subject trial side;
proc means noprint;
  by joint plane subject trial side;
  var rCycleDegMinMax;
  output out=res44 mean=rCycleDegMinMax;
data res44;
  set res44;
  trialside = trial||side;
proc univariate plot normal data=res44;
  by joint plane;
  var rCycleDegMinMax;
  ods select 'Tests for Normality';
  ods trace on;
  ods show;
*/
proc glm data=res44;
  by joint plane;
  class trialside;
  model rCycleDegMinMax=trialside;
  means trialside/hovtest=levene;
  ods select "Levene's HoV Test";
  ods trace on;
  ods show;
*/
RUN; QUIT;

%put Comparison of Left vs. Right Included ;
%MEND OneOrBothSides;
%MEND OneOrBothSides;
%MEND JointAnalysis;
%MEND JointAnalysis;
Below is just one example of the 43+ Point of Interest files used to examine particular values of interest. Each file took the same format, but the Description, StartMargin, Stop Margin, FindType, SetJoint, SetPlane, and SetSide values differed.

**LeftAnkleMomentAxial1.sas**

```
/*************************************************
***** Identify a specific point of interest *****
*************************************************/

/* Describe point of interest. */
%LET Description = LeftAnkleMomentAxial1 ;

/* Start looking at this % gait cycle */
%LET StartMargin = 40 ;

/* Stop looking at this % gait cycle */
%LET StopMargin = 60 ;

/* All Caps MINIMUM, MAXIMUM, or RANGE */
%LET FindType = MINIMUM ;

/* Which joint is of interest */
%LET SetJoint = Anklemom ;

/* Which plane is of interest */
%LET SetPlane = z ;

/* Which side is of interest */
%LET SetSide = Both ;
```
REFERENCES


