WHEN AND WHAT TO STIMULATE?

AN EVALUATION OF A CUSTOM FUNCTIONAL ELECTRICAL STIMULATION SYSTEM AND ITS NEUROPROSTHETIC EFFECT ON GAIT IN CHILDREN WITH CEREBRAL PALSY

by

Nicole Zahradka

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biomechanics and Movement Science

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ABSTRACT

Atypical gait patterns are commonly observed in children with cerebral palsy (CP), a neuromuscular disorder affecting the development of movement and posture and impacting approximately 764,000 people in the United States. Resulting from the absence of one or more of the components that make up a typical gait cycle, gait patterns in CP have been characterized by atypical lower extremity kinematics. Surgical and non-surgical interventions are used to treat these gait deviations. Surgical interventions produce improvements in function that are modest at best and may result in iatrogenic crouch gait while more conservative interventions (non-surgical) have successfully improved spatiotemporal deviations but have not shown changes in kinematics. Walking interventions using functional electrical stimulation (FES) have demonstrated improvements in spatiotemporal, kinematic, and kinetic parameters. Current FES systems, however, are limited in flexibility and number of muscle groups capable of being targeted with FES; potentially limiting gait improvements attainable with use of FES. The overall goal of this dissertation was to develop a FES system, programmable with individualized stimulation algorithms, to assess the feasibility of using it as a neural orthosis during walking in children with CP.

In Aim 1, we successfully developed a FES system and systematically quantified its system performance to validate the system as an accurate device for assisting gait before implementing it in a patient population. By combining commercially available devices and custom software, we have developed a closed-loop FES system, capable of detecting 7 phases of gait and stimulating 10 muscle groups while walking. The FES

system was validated in 7 typically developing children, during treadmill walking at self-selected speed, by comparing the FES system's gait phase detection and delivery of stimulation to the desired timing derived from the 'gold standard' (motion capture system). Overall root mean square errors (RMSEs) of average gait phase detection and duration were 7.23 ± 2.38% and 4.58 ± 2.68% of the gait cycle, respectively. Modifications were made to the stimulation trigger to account for system delays in gait phase detection, resulting in the actual FES output to the desired stimulation timing having an average difference of 0.67 ± 4.25% of the gait cycle. The FES system accurately delivered stimulation, and our ability to detect all 7 phases of gait number of gait phases detected provided independent control over the delivery of stimulation. This development allowed the flexibility for the physical therapist to choose the muscle groups targeted with FES when using the system as a neuroprosthetic device.

In Aim 2, we effectively deployed the FES system as a wearable device during walking in subjects with CP in which immediate effects were made to joint angles when muscle groups were stimulated during FES-assisted walking. To evaluate the immediate changes created during FES-assisted walking, six children with CP donned our custom FES system and walked on a treadmill at their self-selected speeds. Kinematic data were collected for walking conditions without FES and with FES applied using individualized stimulation programs. The results demonstrated that targeting major muscle groups during FES-assisted walking changed the lower extremity kinematics; responses to FES varied between subjects.

This dissertation work illustrates the importance of improving existing FES devices and contributes to the evidence supporting positive kinematic changes produced during FES-assisted interventions in CP.

Chapter 1

INTRODUCTION

1.1 Background and Significance

Cerebral Palsy (CP) is a group of disorders affecting the development of movement and posture, attributed to non-progressive disturbances to the developing fetal or infant brain[1]. CP is the most prevalent childhood neuromotor diagnosis with an estimate of 764,000 people having CP and approximately 10,000 new cases in the US each year[2]. The CDC estimates that approximately 3.3 of every 1,000 children in the US between the age of 3 and 10 are diagnosed with CP. The estimated lifetime economic costs for a person with CP exceeds that of the average individual by $921,000 (2003 dollars), of which, lifetime direct medical costs for individuals with CP are estimated to be approximately 1.2 billion dollars[3]. Spastic CP, the most common classification of CP, has a prevalence of 70-81%[4,5] and is characterized by clinical and functional impairments of decreased passive joint range of motion, increased muscle spasticity/tone, impaired coordination, decreased muscle strength, and diminished ability to ambulate without assistance or assistive devices[6–8].

The general trend of CP is a downward spiral of progressive loss of function[9], which negatively impacts all three components of the WHO ICF model of disability (i.e., body function and structure, activity, and participation) and ultimately the quality of life.

CP is a particularly challenging disorder because although the lesion to the brain is non-progressive, the musculoskeletal impairments and functional limitations associated with CP are progressive. Gross motor function in individuals with CP is

commonly categorized using the Gross Motor Function Classification System (GMFCS)[10]; grouping individuals into 5 different levels of gross motor function based on voluntary movement with a focus on sitting, walking, and wheeled mobility[11]. GMFCS levels I-III are associated with ambulatory individuals; individuals classified as GMFCS levels I-II do not require assistive devices when walking, while level III individuals use rolling walkers or crutches. GMFCS level IV is associated with individuals who are not capable of walking without assistance, typically relying on powered mobility, and GMFCS level V is associated with non-ambulatory individuals who are transported in a wheelchair in all settings. GMFCS levels are associated with different motor development[12] curves and functional abilities[13]. Individuals with CP peak at lower levels of gross motor function than their typically developing peers (Figure 1.1) and, depending on the GMFCS level their motor skill levels may decline during adolescence [12,14]. With health-related quality of life in children with physical disabilities already significantly lower than typically developing children[15], this functional decline is extremely problematic because quality of life domains, such as function, participation, and physical health, are also associated with GMFCS functional level[16]. Therefore, functional decline may contribute a further decrease in health-related quality of life in individuals with CP.

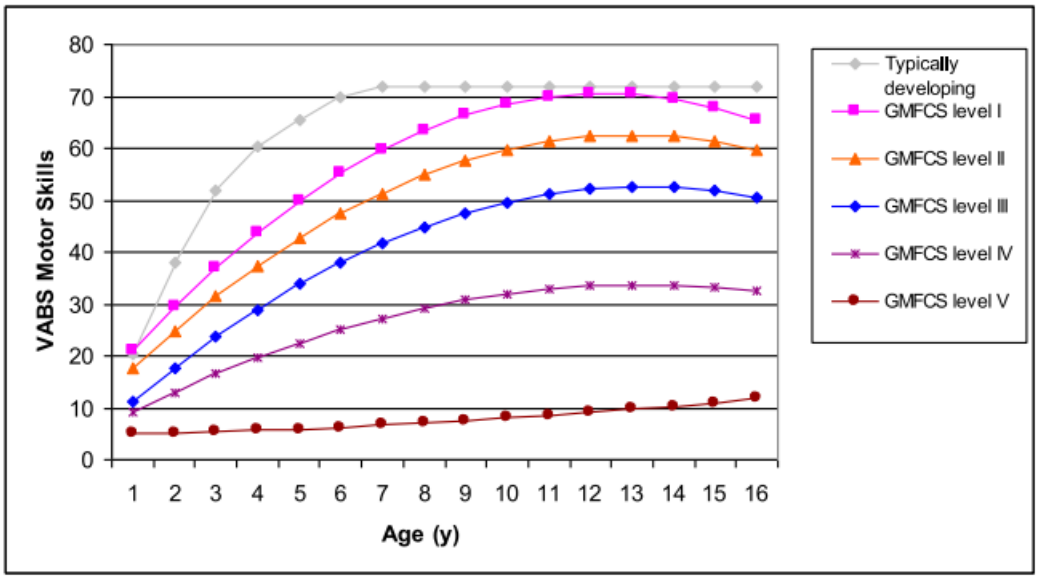

Figure 1.1: A model of the association between the scores of the Vineland Adaptive Behavior Scales (VABS) and age based on each level of the Gross Motor Function Classification System (GMFCS). The model of developmental trajectories of mobility performance suggests the onset of decline in function begins during adolescence[12].

The risk of further decline in function, occurring as most children with CP become less independent with functional mobility as they age[17–22], leads to diminished participation in physical activity[23]. It is suggested that greater physical activity requirements[24,25] are needed in children with disabilities in order to prevent or delay the decline in function and the secondary conditions that can result from inactivity[26] such as greater musculoskeletal and cardiovascular impairments[27,2823]. Additionally, as adults, the secondary complications associated with a sedentary lifestyle significantly impacts the quality of life of individuals with physical disability; resulting in higher mortality rates that are primarily attributed to cardiovascular disease[29–34].

The normal progression of CP is for a progressive loss of walking function.

Walking function, characterized by spatiotemporal and kinematic parameters, in individuals with CP declines through adolescence and into adulthood[22]. In typical gait, a successful gait cycle is comprised of five components: (1) stability in stance, (2) clearance of the foot in swing, (3) appropriate pre-positioning of the foot in swing, (4) adequate step length, and (5) conservation of energy[35]. The absence of one or more of these components, often observed in CP gait[35–37], results in inefficient walking and increased energy expenditure[38–40]. The energy cost of walking significantly differs between each GMFCS level; with higher metabolic demands associated with higher GMFCS levels[40].

Deviations from typical gait, resulting in inefficient walking, are observed in the hip, knee, and ankle angles; most often observed in the sagittal plane where the majority of motion occurs during walking[35,41]. One missing component of successful typical gait, commonly observed in CP, is a lack of toe clearance during swing period; individuals tend to trip and fall due to reduced and delayed peak knee flexion angle[22,42]. Atypical kinematics, such as lack of toe clearance, are the secondary impairments associated with the primary impairments[35], such as muscle weakness or spasticity, in CP. The deviations observed in joint kinematics can be used to identify potential underlying impairments[36,37] for each individual. Gait patterns, resulting from these factors, have been classified by common postural patterns exhibited in this population[43–48]. The hip, knee, and ankle angles, in the sagittal plane, are used to define four common patterns in individuals with spastic diplegia: equinus, jump gait, apparent equinus, and crouch

gait[49]. These gait patterns range in severity and the number of joints that are affected by underlying impairments. Equinus is observed in the most functional walkers[17] and is associated with deviations solely at the ankle; the ankle is in excessive plantarflexion. Commonly observed changes with age result in jump gait, defined by excessive plantarflexion at the ankle and flexion at the knee and hip during early stance, and apparent equinus, defined by excessive flexion at the knee and hip throughout the stance period[43]. Gait deviations typically culminate in crouch gait[43], which is associated with excessive flexion at the hip and knee and excessive dorsiflexion at the ankle[44].

Primary impairments, along with compensatory strategies, contribute to the vicious cycle of deterioration of walking function in individuals with CP.

Compensatory strategies, observed as alterations in gait kinematics, are products of underlying impairments associated with central neurological lesions. In CP, these underlying impairments include muscle weakness, impaired selective control, and spasticity[35,37]. The abnormal behavior of the key muscle groups (gluteus maximus, quadriceps, hamstrings, dorsiflexors, and plantarflexors)[41] that control movement in the sagittal plane, such as stability and forward progression during gait, contribute to muscle and bony abnormalities that lead to the decline of walking function observed in CP. For example, spasticity of the hamstrings and plantarflexors have been attributed to excessive knee flexion[50] and toe walking[36,37], respectively, while weak dorsiflexors contribute to toe clearance problems during mid-swing[36]. Previous work has reported deviations from typical phasic activity and co-contraction of several of the key muscle groups, such as the tibialis anterior, soleus, vastus lateralis, and hamstrings, during gait in CP[46,51–53]. More specifically, the quadriceps and semitendinosus were found to be active for over 75% of the gait cycle[54]; with quadriceps firing for almost twice as long

as the corresponding muscles in the typically developing population[53]. The increased activity of the quadriceps suggests the presence of spasticity or improper limb positioning requiring extended muscle activity for support. The interplay between the underlying impairments and compensatory strategies creates a perpetuating cycle where the limb is in a position that reduces the muscle's ability to produce the desired movement and when the desired movement is not produced, the limb cannot advance to the proper position[55] for the muscle to provide the necessary force; typically resulting in the absence of one or more of the five components of successful typical gait. The decline in function over time, without intervention, indicates that even small improvements are important[17].

Surgical interventions to correct musculoskeletal deformity and muscle spasticity exacerbate muscle weakness and may result in iatrogenic crouch gait.

Surgery, used as an intervention to treat gait deviations and associated musculoskeletal complications, potentially exacerbates the declining function[47] and health in CP. Wide spread adoption of single event multiple level orthopedic surgery (i.e., combined procedures including muscle tendon lengthening, tendon transfer, rotational osteotomy, femur shortening, stabilization of the hip and foot) has replaced multiple event single level approaches[56–60]. Although multilevel approaches reduce the total number of surgeries an individual may experience, they are associated with forced periods of prolonged immobility which have detrimental effects on strength and mobility and increase the odds of developing crouch gait[47]. Additionally, procedures such as tendon lengthening for contractures and dorsal rhizotomy for abnormal muscle spasticity and tone exacerbate mobility loss by putting muscles at unfavorable lengths for generating force by unmasking underlying muscle weakness[61–65]. Muscle lengthening, specifically lengthening of the heel cord, in young children is one of the

most common causes of crouch gait[43,50]. Muscles associated with the surgical interventions are weakened[8,17–21,35,47,66], recovery of pre-surgical function is lengthy (1-2 years) and in spite of painful and arduous rehabilitation, improvements in function are generally equivocal or modest at best, even when skeletal alignment is improved[57,67–69].

Conservative interventions used to improve gait function in CP are effective.

Conservative interventions (i.e., non-surgical) provide potential opportunities to avoid or delay surgical intervention for the correction of bony deformities[70] that contribute to gait deviations in CP. Although conservative interventions do not address existing skeletal deformities, they are able to target factors[71] contributing to the development of bony deformities and the loss of gait and mobility function[72–75]. Interventions targeting primary impairments, such as muscle weakness and spasticity, assume improvement in impairments will carry over to walking function in CP. The positive relationship existing between muscle strength and walking ability[76,77] led to strength training interventions with the hypothesis that increasing strength will result in increased walking function. Previous work shows this relationship to be valid[71,77–80]; however, Damiano et al. reported that increases in muscle strength were not found to produce large improvements in gait[81]. Other interventions target functional deviations with the assumption that focusing on improving the function will lead to reduced impairments. These walking interventions focus on kinematic and spatiotemporal variables to achieve goals of reducing gait deviations[72,73,82]. Previous studies have succeeded in reducing spatiotemporal deviations with the use of supported treadmill exercise[72,73] and robotic-assisted walking[74,75] but have not reported kinematic changes.

FES targets impairment and function to improve walking in CP.

Approaches of improving gait in children with CP by either reducing physical impairments or activity based training have shown some success; however, therapies combining the two approaches have a greater opportunity to improve overall gait by targeting both underlying causes of gait deviations and the task of walking. Functional electrical stimulation is the application of electrical stimulation to generate functional movements such as standing[83–85], walking[86–88], and grasping[89,90] in individuals with upper motor neuron lesions. Previous studies have set the foundation for using FES during gait in children with CP by demonstrating that FES assistance during a functional activity (ambulation) can produce changes in walking towards more typical patterns[91,92]. FES-assisted walking has improved both underlying impairments and functional outcomes, such as muscle size[93], spatiotemporal parameters[93–95], passive range of motion[94], kinematics[96–98], and kinetics[98]. Specific kinematic and spatiotemporal improvements seen in gait, with FES assistance, include improved ankle and knee angles, cadence, step length, and walking velocity[91,94,97–99]. Of note, when FES was used to augment traditional orthopedic surgery, FES subjects showed improvements in a more timely manner with improved walking function at 4 months and fewer ablative surgeries than the surgical only group; which did not show improved walking function until 12 months[94]. Thus, FES-assisted gait may be beneficial before significant contracture formation occurs to reduce incidence of surgery or to reduce the amount of multilevel surgery, and to promote earlier return to function, which could lower the overall cost to treat progressive musculoskeletal consequences of CP. These positive changes in impairment and function provide incentive to continue advancing and refining assistive devices to increase the success rate of achieving more typical gait.

Increased control in FES systems is necessary for accurate timing of stimulation delivery during walking in CP.

To elicit restorative walking patterns, several FES systems implement finite-state controllers to trigger stimulation. Finite-state controlled FES systems incorporate a level of accuracy exhibited in closed-loop controllers while maintaining the clinically-friendly setup associated with open-looped control. This type of controller, technically a closed-looped control because of the feedback component, uses preset sequences of stimulation[100] that are triggered when specific conditions are met and require minimal sensors to acquire feedback from the subject.

Technologies such as force sensing resistors, accelerometers, and micro-electromechanical system devices are increasingly used in research based and commercial devices for detecting gait events, measuring activity, quantifying spatiotemporal variables of gait, and for tracking and analyzing gait kinematics. These external sensors can provide feedback on different parameters during the gait cycle[101] and can be used to trigger the stimulation. Some commercially available FES systems that take advantage of such technologies are the Odstock Dropped Foot Stimulator systems (Biomedical Engineering and Medical Physics, Salisbury, UK), WalkAide System (Innovative Neurotronics, Reno, NV, USA), and Ness L300® Plus (Bioness Inc, Valencia, CA, USA). Designed with only one or two stimulation channels, these FES systems utilize force sensing resistors (Odstock Dropped Foot Stimulator and Ness L300® Plus) or tilt sensors (WalkAide) to provide limited, but sufficient, differentiation of the gait cycle to trigger the delivery of stimulation at appropriate times.

During a gait cycle, there are seven distinct phases of gait: four phases during stance period and three phases during swing period[102]. FES systems that utilize gait events as feedback to the controller typically have limited timing control because they are not capable of detecting all seven phases of gait. FES systems with the most basic

gait detection can distinguish between stance and swing periods[103]. An increased number of gait phases can be detected in FES systems that use force sensing resistors[93–97,99,104,105] or a combination[106] of force sensing resistors and gyroscopes to differentiate between the four phases in stance period and between stance and swing periods, but have not demonstrated the capability of differentiating between the three phases during swing period. Additionally, accurate placement of force sensing resistors can be difficult in subjects with gait pathologies. With the timing of the delivery of stimulation playing a crucial role in FES interventions[107–109], the capability of detecting all seven phases of gait is needed to provide the amount of control necessary to deliver stimulation in a manner that is representative of typical muscle firing patterns.

Furthermore, custom FES systems have been designed to investigate FES interventions while walking[94,97,110] but system performance and the accuracy of stimulation timing is rarely reported. Pappas and colleagues reported the reliability to detect 4 gait phases to be within 90ms when their gait phase detection system[106] (GPDS) was compared to phase detection by motion capture, while reporting the capacity of the combined GPDS and FES system to alter ankle trajectories[110]. Senanayake and colleagues validated their GPDS, against average gait phase duration differences derived from the literature to be within 80ms, and alluded to the ability to implement this system as a trigger for accurately timed delivery of stimulation[111] Methods of evaluating custom FES systems have not assessed the actual timing of stimulation signals; such testing is necessary to verify system performance and the accuracy in delivery of stimulation to ensure that augmentations during FES interventions are created as a result of the application of stimulation at the targeted times in the gait cycle.

Motion analysis allows us to quantify the immediate effects of customized FES programs during FES-assisted gait.

CP has many presentations of gait deviations and 3D motion capture provides a method to quantify and compare these differences to typical gait. Baseline measurements are used to assess the improvements that occur during FES interventions. Studies have shown that the joint where kinematic improvements occur is influenced by the muscle groups targeted with FES during walking. For example, stimulation to the gastrocnemius only[92], gastrocnemius and tibialis anterior[92,99], or dorsiflexors only[96,97,99,112,113] promoted positive changes at the ankle and stimulation to the quadriceps[96,114] improved the knee flexion angle. However, there is a lack of evidence of the effect of targeting proximal muscles during FES-assisted gait[115]. Previous work by van der Linden et al. began evaluating the orthotic effects of FES to the dorsiflexors and quadriceps in children with CP[96]. Both conditions produced statistically significant effects in the Gillett Gait Index (GGI), a measure of the deviation of 'overall' gait pattern from typical and stimulation of the dorsiflexors produced statistically significant improvements in the swing and foot-floor angle. Utilizing a custom FES system that expands the number of gait phases and consequently muscle groups that can be targeted to include proximal and distal muscles may allow more gait deviations to be addressed during walking with individualized stimulation programs; potentially creating larger improvements in lower extremity kinematics. Quantifying the changes made to the lower extremity kinematics, with the use of FES, provides a measure of the neuroprosthetic effect of stimulation. When the use of FES produces joint angles that are more similar to typically developing individuals, the individuals with CP are demonstrating more typical walking patterns during FES-assisted walking; alluding to lower energy expenditure[116] and more efficient gait[38,117].

Interventions for CP need further development to reverse the general trend for loss of function. We propose an innovative, physiologically based FES intervention with scientific-based methodology to produce neuroprosthetic reduction of gait deviations in CP.

Innovative approaches are needed to enhance functional ability and activity for individuals with CP. Implementing these innovative and progressive interventions into clinical practice has the potential to improve function, participation, and quality of life of many children and adolescents as they enter adulthood. The overall goal of this line of research is to prevent the typical downward spiral of walking function of individuals with CP that occurs from adolescence into adulthood; and potentially to reduce the need for surgical interventions that exacerbate weakness, have long recovery times and may or may not enhance gait function.

1.2 Specific Aims and Hypotheses:

Cerebral Palsy (CP) is a non-progressive disorder caused by a lesion of the fetal or infant brain that results in muscle weakness, spasticity, and other motor impairments. There are several common pathologic gait patterns of CP affecting the kinematics at the hip, knee, and ankle and these are exacerbated by lower extremity weakness and progressive loss of joint motion as individual's age. Functional electrical stimulation (FES), used as a neuroprosthetic device, improves walking abilities in individuals with CP but its use is typically confined to one or two muscle groups. Further improvements may be seen if multiple muscle groups could be stimulated to correct gait deviations and attain a more typical walking pattern. While individuals with CP have demonstrated changes in gait with FES, this study population is highly heterogeneous and not all individuals may benefit from the same targeted muscle groups with FES. Evaluating the effect of individualized stimulation programs may contribute to successful implementation of FES in therapeutic settings. The overall goal of the proposed work is

to determine the effectiveness of a FES system, capable of targeting 10 muscles during walking, to improve gait parameters in children with CP.

Aim 1: Develop a multichannel functional electrical stimulation (FES) system capable of stimulating 10 lower extremity muscles during a gait cycle.

Gait analysis literature and normative data from empirical gait analysis will be used to derive stimulation programs for appropriate activation timing of the gluteal, hamstring, quadriceps, plantarflexor, and dorsiflexor muscle groups to emulate a typical gait cycle. Then, sensor data will be used to identify individual gait events and trigger FES for the appropriate timing pattern of muscle groups during a gait cycle. Gait event detection determined by the sensor data verses gait event detection using traditional 3D gait analysis (gold standard) will be compared. Actual FES output will be compared to the desired stimulation algorithm output during treadmill walking of seven typically developing children to validate the FES system. The following hypotheses will be investigated:

Hypothesis 1.1: The average difference in timing of gait event detection and duration determined between the sensor system and motion capture system will have a root mean square error of 5% or less of the gait cycle.

Hypothesis 1.2: The average difference in timing of delivery of the actual stimulation and desired timing of stimulation will be equal to or less than the average onset variability of gait phases.

Aim 2: Evaluate changes in the lower extremity kinematics in children and adolescents with spastic diplegic CP as a result of individualized stimulation programs.

Individualized stimulation programs will be created by a group of physical therapists, derived to target the subject's gait deviations, and include options to (1) target multiple muscle groups, such as the gluteals, hamstrings, quadriceps, dorsiflexors, and/or plantarflexors, and (2) deliver stimulation during different phases of gait. The individual's stimulation program will be applied as the participant walks on a treadmill at their comfortable walking speed. The hip, knee, and ankle angles will be calculated and compared between the no stimulation and stimulation conditions.

Hypothesis 2.1: The custom FES system can be used during walking in subjects with CP.

Hypothesis 2.2: FES will have immediate effects to the sagittal hip, knee, and ankle angles when muscle groups are stimulated using individualized stimulation programs during FES-assisted walking.

Chapter 2

THE DEVELOPMENT AND VALIDATION OF A CUSTOM MULTICHANNEL FUNCTIONAL ELECTRICAL STIMULATION SYSTEM FOR THE DELIVERY OF STIMULATION DURING WALKING

2.1 Abstract

Walking interventions using functional electrical stimulation (FES) simultaneously target the underlying causes of gait deviations and the task of walking itself. Evidence supports the benefits of using FES to improve walking ability in individuals with gait deviations, however, these systems are typically confined to one or two muscle groups and may not allow the customization of muscle groups needed to address the individual's additional gait deviations. To incorporate more muscle groups into an FES system, greater control over the timing of the delivery of stimulation was needed to apply appropriately timed stimulation to the additional muscle groups. Our system, consisting of communication between inertial measurement units (IMUs) and stimulators (Hasomed® RehaStim), was capable of detecting all 7 phases of gait which yielded greater refinement in feedback and control and enabled stimulation to 10 channels associated with 5 muscle groups, bilaterally.

Gait phase detection (used as the FES system control) and the timing of the delivery of stimulation were compared to the desired timing determined by the motion capture system during walking in seven typically developing children. Although gait phase detection in the FES system did not meet the required time difference established in Hypothesis 1.1, i.e., a root mean square error of 5% or less of the gait cycle, the compensations made to the stimulation trigger timing produced on/off times of the

stimulation signals that met the requirements established in Hypothesis 1.2. The FES system accurately delivered stimulation and can be used as a device for assisting gait in populations with pathologic gait.

2.2 Introduction

Functional electrical stimulation (FES) is the application of electrical stimulation to generate functional movements such as standing[83–85], walking[86–88], and grasping[89,90] in individuals with upper motor neuron lesions. FES systems are used as neuroprosthetic devices[118] in rehabilitative settings and the delivery of stimulation relies on open-loop or closed-loop controllers. While adaptive closed-loop control is the ideal controller for FES systems because of the capability to modulate stimulation parameters to achieve desired movements, a stable closed-loop feedback system has not been developed[100,119]. In addition, the sensors required to provide this amount of feedback are cumbersome and time consuming to attach and remove[100]; therefore, open-loop controlled FES systems are typically used in clinical settings. Open-loop controlled FES systems are usually easy to don/doff but provide less accurate movement control because of the reliance on user input to trigger the delivery of stimulation[120]. The Parastep I (Sigmedics, Inc., Fairborn, OH, USA) and RehaStim (Hasomed Inc., Germany) are two examples of commercially available FES systems utilizing open-looped controllers. Both systems require the user to push a button to activate the stimulation and once the program is initiated, the stimulation parameters, such as timing, cannot be modified.

Finite-state controlled FES systems may provide an intermediate solution in controls by incorporating a level of accuracy exhibited in closed-loop controllers while utilizing a minimized number of sensors to maintain the clinically-friendly setup associated with open-looped control. This type of controller, technically a closed-looped control because of the feedback component, uses preset sequences of stimulation[100] that are triggered when specific conditions are met and require minimal sensors to acquire feedback from the subject.

FES systems have been utilized in walking interventions in children with cerebral palsy (CP) to restore movement during gait[91,92,95–97,114,121]. To elicit restorative walking patterns, several FES systems implement finite-state controllers to trigger stimulation and utilize external sensors to provide feedback on different parameters during the gait cycle[101]. Technologies such as force sensing resistors, accelerometers, and micro-electromechanical system devices are increasingly gaining popularity and are used in research-based and commercial devices for detecting gait events, measuring activity, quantifying spatiotemporal variables of gait, and for tracking and analyzing gait kinematics. Some commercially available FES systems that take advantage of such technologies are the Odstock Dropped Foot Stimulator systems (Biomedical Engineering and Medical Physics, Salisbury, UK), Respond II Select (Medtronic Inc., Minneapolis, MN, USA), and Ness L300® Plus (Bioness Inc, Valencia, CA, USA). These devices use sensors to detect different events during the gait cycle which is used to control the delivery of stimulation.

The use of different gait phases as finite states for a controlled FES system (feedback for triggering stimulation) has been studied in the literature. During a gait cycle, there are seven distinct phases of gait: four phases during stance period and three phases during swing period[102]. FES systems that utilize gait events as the feedback to the controller typically have limited timing control because they are not capable of detecting all seven phases. FES systems with the most basic gait detection methods can distinguish between stance and swing periods[103]. A greater number of phases during the stance period can be detected by FES systems that utilize force sensing resistors[93,95–97,99,104,105,121], or a combination of force sensing resistors and gyroscopes[110], however, these systems are not capable of differentiating between the three phases during swing period. Accurate placement of force sensing resistors can be difficult in subjects with

gait pathologies and may be susceptible to mechanical failure during long term use[122]. With the timing of the delivery of stimulation playing a crucial role in FES interventions[107–109], the capability of detecting all seven phases of gait is needed to provide the amount of control necessary to deliver stimulation in a manner that is representative of typical muscle firing patterns.

Custom FES systems[97,110,121] have been designed to investigate FES interventions while walking; however, system performance and the accuracy of the timing of stimulation delivery are rarely reported. Pappas and colleagues reported the reliability to detect 4 gait phases to be within 90ms when their gait phase detection system[106] (GPDS) was compared to phase detection by motion capture, while reporting the capacity of the combined GPDS and FES system to alter ankle trajectories[110]. Senanayake and colleagues validated their GPDS, against average gait phase duration differences derived from the literature to be within 80ms, and alluded to the ability to implement this system as a trigger for accurately timed delivery of stimulation[111]. Methods of evaluating custom FES systems have not assessed the actual timing of stimulation signals; such testing is necessary to verify system performance and the accuracy in delivery of stimulation to ensure that augmentations during FES interventions are created as a result of the application of stimulation at the targeted times in the gait cycle. Reporting system performance and validation techniques of FES systems will provide the foundation and protocol for fellow investigators when assessing their custom FES systems.

We have designed a sensor system capable of gait phase detection, using commercially available Inertial Measurement Units (Opal^{TM}, APDM, Portland, OR, USA) for near real-time gait event detection during treadmill walking. Our system has evolved from a unilateral wireless shoe sensor system, composed of 6 force sensing

resistors (FSRs) and 2 Opals, to a bilateral sensor system, composed of 2 Opals. The custom FES system allows communication between the sensor system and commercially available stimulators (RehaStim, Hasomed Inc., Germany) yielding near real-time feedback and enabling stimulation of 10 muscle groups during walking. The bilateral configuration represented the minimal data set to assess system performance.

The purpose of Aim 1 is to evaluate the (1) near real-time performance of the gait phase detection of the sensor system when compared to post-processed gait phase detection determined by instrumented motion capture, which is considered the 'gold standard' for gait analysis, and (2) timing of delivery of actual stimulation when compared to the desired stimulation timing determined by the motion capture data, in typically developing (TD) children and a child with CP, when using the closed-loop FES system during walking.

2.3 Methods

The custom FES system was designed with criteria to (1) provide greater control over the stimulation trigger by detecting all 7 phases of gait, (2) allow the physical therapist to choose the number of stimulation channels used, and (3) support manually programmed stimulation parameters individualized for each subject, muscle group, and gait phase. The criteria were established to provide the flexibility necessary for the optimization of stimulation in an effort to reduce gait abnormalities during walking in individual's with CP. Before the FES system was used in children with CP, gait phase detection, gait phase duration, and stimulation timing were validated against the motion capture data to minimize the FES system as a potential source of error when used to as a neuroprosthetic device during ambulation. After the FES system was validated in

typically developing individuals, it was trialed in 1 subject with CP as a proof of concept to verify the feasibility of using the FES system during walking in children with CP.

2.3.1 Experimental Protocol

Seven typically developing (TD) children (5 Females, 12.4 ± 2.15 years old) and one child with CP (Male, 16 years old) were recruited locally and IRB approved parental consent and child assent documents were obtained prior to subject participation. Prior to the gait analysis, each subject's self-selected walking speed was determined over ground with the 10 Meter Walk Test (MWT)[123] and height and weight were collected. Subject's self-selected walking speed was used to set the treadmill speed; however, if the subject identified that the self-selected speed felt too fast on the treadmill, the treadmill speed was adjusted based on subject feedback. The subject donned the sensor system (described in section 2.3.2.1) while walking on a split-belt, instrumented treadmill (Bertec, Columbus, OH, USA). After a treadmill-walking accommodation period[124], a 30 second walking trial was collected. Kinematic and kinetic data were captured using an 8-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA, USA) and two force plates (Bertec, Columbus, OH, USA), respectively.

2.3.2 Components of the multichannel FES system

2.3.2.1 Gait Phase Detection (GPD) of the sensor system

The sensor system[125], consisting of two IMUs (Opal^{TM}, APDM, Portland, OR, USA), detected different events of gait, associated with the onset of different gait phases, using gyroscope data that were wirelessly streamed into custom software (LabVIEW, National Instruments, Austin, TX, USA). The IMUs were placed on the lateral shanks near the ankles; ipsilateral and contralateral shank angular velocity were

used to detect 7 phases of gait: loading response (LR), mid-stance (Mst), terminal stance (Tst), pre-swing (PSw), initial swing (ISw), mid-swing (MSw), and terminal swing (TSw). The distinct pattern[126] of the medio-lateral (Z-axis) shank angular velocity, from the gyroscope signal, consists of three positive peaks during the stance period followed by a deep negative peak during the swing period (Figure 2.1) and was used as the primary input for gait phase detection. Gait phases were differentiated based on a set of pre-defined rules, as indicated in Table 2.1.

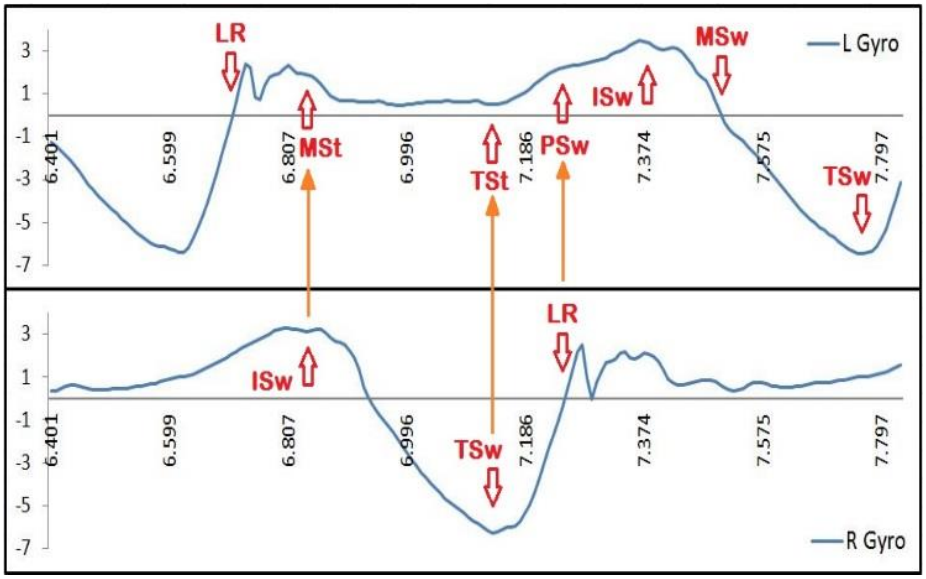

Figure 2.1: Red arrows indicate gait phase detection based on distinct characteristics of the left (top) and right (bottom) gyroscope signals. Orange arrows illustrate the use of contralateral (right gyroscope) information for detection of mid-stance (MSt), terminal stance (TSt) and pre-swing (PSw) on the ipsilateral side (left).

Table 2.1: Gyroscope characteristics used to determine gait phases. *LR* Loading response, *Mst* Mid-stance, *Tst* Terminal stance, *PSw* Pre-swing, *ISw* Initial swing, *MSw* Mid-swing, *TSw* Terminal swing.

Gait Phase	Gyroscope Characteristics
LR	Zero crossing[103] (positive direction)
Mst	Contralateral 3rd peak
Tst	Contralateral Valley[102]
PSw	Contralateral zero crossing[102] (positive direction)
ISw	3rd peak[127]
MSw	Zero crossing (negative direction)
TSw	Valley[101]

2.3.2.2 Functional Electrical Stimulation (FES) System

A multichannel surface FES system was designed by incorporating two IMUs (Opal™, APDM, Portland, OR, USA), two stimulators (RehaStim, Hasomed Inc., Germany), and a LabVIEW based GPD software capable of communicating with the stimulators. The software used gait phase information to control stimulation timing based on typical muscle activity during self-selected walking[128] for the 7 phases of gait (Table 2.2). The delivery of stimulation was simulated and recorded as five analog channels, bilaterally, associated with key muscle groups, including the plantarflexors, dorsiflexors, quadriceps, hamstrings, and gluteals.

Table 2.2: Stimulation program based on typical muscle firing patterns during gait[128]. Black boxes illustrate when the muscle groups were stimulated during the gait cycle. *LR* Loading response, *Mst* Mid-stance, *Tst* Terminal stance, *PSw* Pre-swing, *ISw* Initial swing, *MSw* Mid-swing, *TSw* Terminal swing.

	STANCE PERIOD				SWING PERIOD		
Gait Phase	LR	Mst	Tst	PSw	ISw	MSw	TSw
Plantarflexors		■	■	■			
Dorsiflexors	■			■	■	■	■
Quadriceps	■	■		■			■
Hamstrings	■					■	■
Gluteals	■	■					■

2.3.3 Data Analysis

2.3.3.1 Validation of Gait Phase Detection and Duration

Onset of the 7 gait phases (LR (HS), Mst, Tst, PSw (TO), ISw, MSw, TSw) were detected two ways: (1) gait phase detection based on sensor data (Table 2.1) and (2) gait phase detection based on motion capture kinetic and kinematic data (Table 2.3). The onsets of LR (Heel Strike (HS)) and ISw (Toe Off (TO)) were detected using kinetics data. The timing of these events were determined using a threshold of 20N: identifying frames when force signal in the vertical direction exceeded and fell below the threshold, with a frame width of 8 frames, were associated with HS and TO, respectively. The other phases (Mst, Tst, PSw, MSw, and TSw) were detected using characteristics defined in the kinematic data. Detection and duration of each of the 7 gait phases were compared between the sensor and motion capture systems. Differences in gait phase detection and gait phase duration were quantified using root mean square error (RMSE). The average and standard error for each gait phase were reported to describe the differences in detection and duration between the sensor and the motion capture based systems.

Table 2.3: Kinematic and kinetic definitions used for gait phase detection in the motion capture system. *LR* Loading response, *Mst* Mid-stance, *Tst* Terminal stance, *PSw* Pre-swing, *ISw* Initial swing, *MSw* Mid-swing, *TSw* Terminal swing.

Gait Phase	Kinematic Definitions
LR	Heel Strike[102] (HS)
Mst	Contralateral Toe Off[102]
Tst	Contralateral Maximum Shank Angular Velocity[102]
PSw	Contralateral Heel Strike[102]
ISw	Toe Off (TO)[102]
MSw	Maximum Knee Angle[102]
TSw	Maximum Shank Angular Velocity[101]

2.3.3.2 Validation of the Delivery of Stimulation

The schematic in Figure 2.2 illustrates the two systems that generated the stimulation signals compared to validate the timing of the delivery of stimulation. While the participants walked on a treadmill at a comfortable speed, the FES system generated a stimulation signal (stimulation output) that was simultaneously collected, through analog channels, with the kinematic and kinetic data from the motion capture system. An amplitude threshold method was implemented to determine onset/offset of the stimulation signals for each stride and normalized to the gait cycle. The on events were averaged for each percent of the gait cycle and an average "on" event was determined if $\geq$ 50% of the strides were on at each percent of the gait cycle. The resulting "on" events were compared to the desired stimulation timing detected by the motion capture system (DESIRED: MOCAP). The differences in the on/off timing of the actual stimulation signal delivery and desired stimulation timing, as a percentage of the gait cycle, were compared to the average variance of onset detection for the 7 phases of gait.

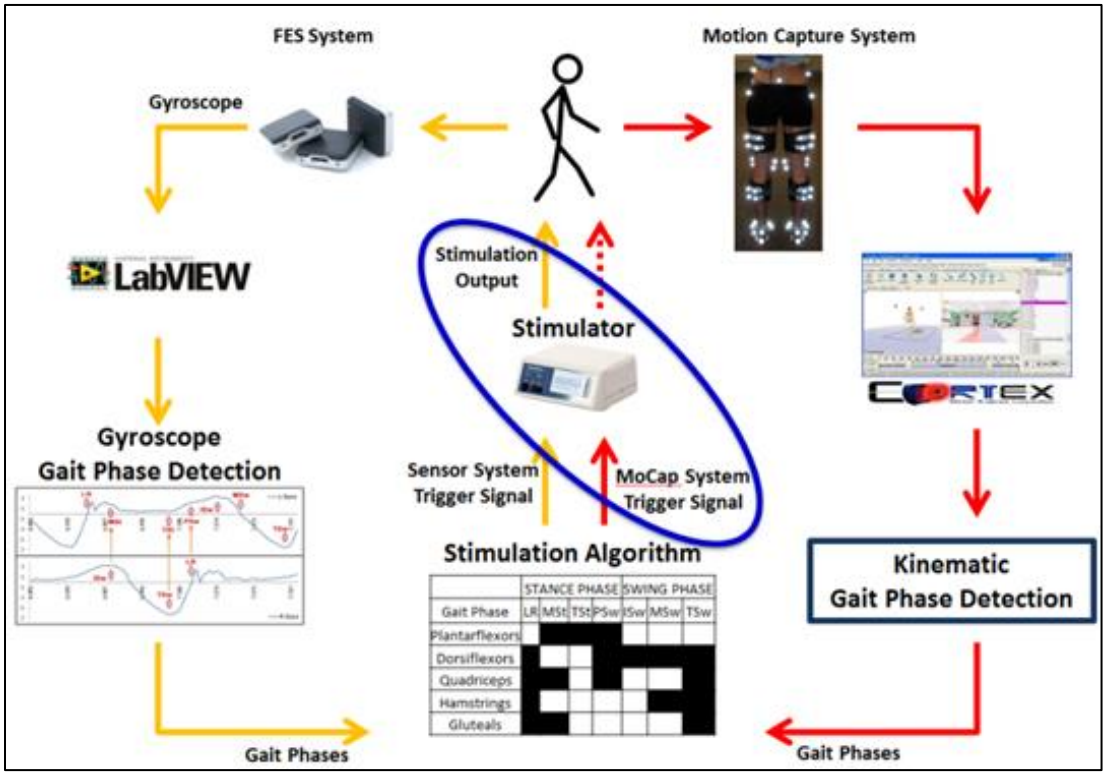

Figure 2.2: Schematic of the comparison between the actual stimulation output of the FES system (yellow arrows) to the desired stimulation timing based upon trigger signals derived from analysis of motion capture data (red arrows). The blue circle indicates comparison of actual stimulation output to desired stimulation timing.

2.3.4 Development of the FES System's Stimulation Trigger

There were three iterations of the FES system software to adjust the timing of the stimulation trigger to generate stimulation signals that most closely matched the desired stimulation timing based on the motion capture data. The original trigger method used the current gait phase to trigger the desired muscle group(s) associated with the phase detected (i.e. when LR was detected, the muscle groups active during LR were triggered (Table 2.2)). During pilot testing, the original triggering method produced stimulation signals that were delayed when compared to DESIRED: MOCAP, occurring

between 2-15% of the gait cycle after the desired stimulation timing. The delayed signals were due to detection delays in the GPD of the sensor system and a lag created by the stimulator's required time for communicating with the LabVIEW software and generation of stimulation pulses (Figure 2.3).

Therefore, the second trigger method implemented was a pre-trigger strategy; stimulation was triggered in advance by using the currently detected phase to trigger the stimulation channels associated with the muscle groups active in the following phase (i.e., plantarflexors are active during Mst, using the pre-trigger strategy, this muscle group was triggered by detection of LR) (Table 2.2). The results from the pre-trigger method showed that the on/off times of the stimulation signal occurred prior to the DESIRED: MOCAP (Figure 2.3). The differences in onset times ranged from 2-17% of the gait cycle and were dependent on the GPD delay. With the implementation of the pre-trigger strategy for stimulation, the greater the delay in gait phase detection, the smaller the difference between the stimulation signal and DESIRED: MOCAP.

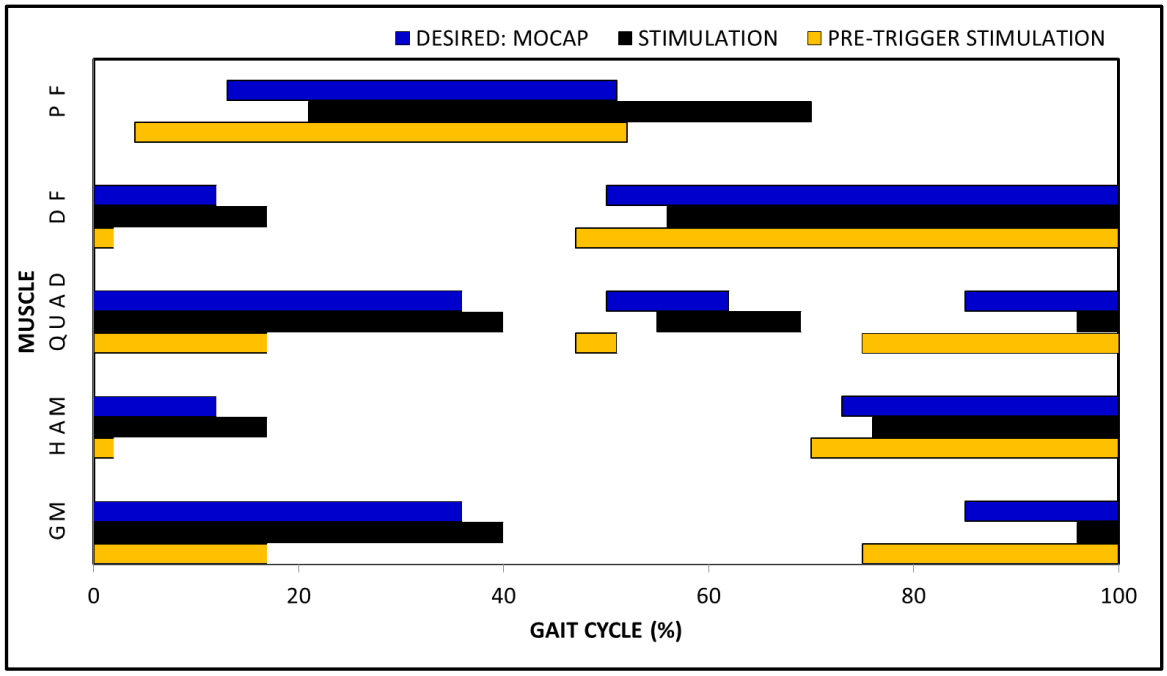

Figure 2.3: Comparison of On/Off timing of the desired stimulation timing based on motion capture data (DESIRED: MOCAP), the delivery of actual stimulation recorded as an analog signal (STIMULATION), and the delivery of actual stimulation recorded as an analog signal when the pre-trigger strategy was implemented (PRE-TRIGGER STIMULATION).

The third, and final, trigger method tested was a time delay trigger method and used a similar strategy to the pre-trigger method. The stimulation was triggered a phase in advance as before, however, a delay time was included before delivery of the stimulation trigger. The delay time was phase dependent and equal to a percentage of the average duration of the previous phase in which stimulus delivery was desired (Figure 2.4). For each subject, several gait cycles were collected, prior to the start of stimulation, to calculate average gait phase durations. Five different percent delays were evaluated to determine the delay that produced the most accurate trigger for the stimulation when compared to the desired stimulation timing in the TD group. Three different percent delays were evaluated in a similar manner for 1 subject with CP. The

% DELAY represents the time corresponding to the % of the duration of the *previous* gait phase used to pre-trigger stimulation. In the TD group, the delays consisted of 0% DELAY (representing the pre-trigger method), 25% DELAY, 50% DELAY, 75% DELAY, and 100% DELAY (representing the original trigger method). In the subject with CP, the delays consisted of 0% DELAY, 50% DELAY, and 75% DELAY. The timing of the stimulation signals generated from each of the % DELAYs were compared to the desired stimulation timing using the methods outlined in 2.3.3.2.

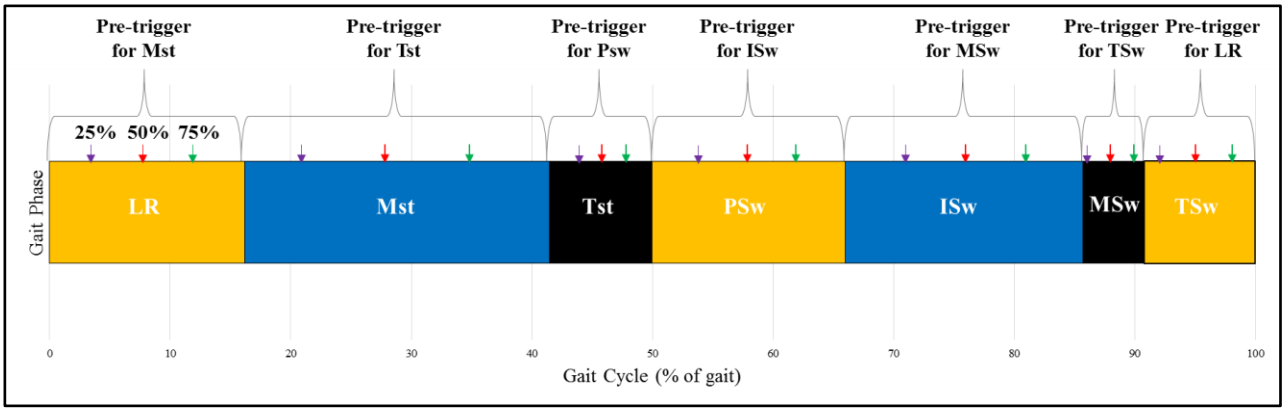

Figure 2.4: An example of the gait phase detection and trigger timing, as a percentage of the gait cycle, for one subject. Purple, red and green arrows illustrate the timing of the 25%, 50%, and 75% DELAY triggers, respectively, for each gait phase. A time delay was added to the detection of the gait phase to trigger stimulation for the following phase. The delays were based on gait phase duration: 25% delay sent a trigger a quarter of the way through the gait phase, 50% delay sent a trigger halfway through the gait phase, and 75% delay sent a trigger three quarters of the way through the gait phase. The same percent delay method was used for all phases. *25%* 25% DELAY trigger, *50%* 50% DELAY trigger, *75%* 75% DELAY trigger, *LR* Loading response, *Mst* Mid-stance, *Tst* Terminal stance, *PSw* Pre-swing, *ISw* Initial swing, *MSw* Mid-swing, *TSw* Terminal swing.

2.4 Results

2.4.1 Gait Phase Detection and Duration during walking in typically developing children

The average and standard errors were calculated for the time differences in gait phase detection and duration between those determined by the sensor system and analysis of 'gold standard' motion capture system data (Figure 2.5). Time differences of gait phase detection and duration varied by phase. Average differences in detection ranged from 18 ms to 100 ms. Gait event detection RMSEs were less than 71 ms for LR, Mst, PSw, ISw, and MSw. However, the RMSEs were 97.90 ms and 104.64 ms for Tst and TSw, respectively. MSw had the most similar onset times to the motion capture system (RMSE=35.17 ms). The average RMSE in detection time between the sensor and motion capture systems was 72.28 ms. Gait phase duration differences ranged from -60.67 ms to 82.09 ms (RMSE=41.30-86.55 ms). The phases with the smallest and largest difference in duration between that determined by the sensor and motion capture systems were LR and MSw, respectively. The average phase duration RMSE between the sensor and motion capture systems was 45.79 ms.

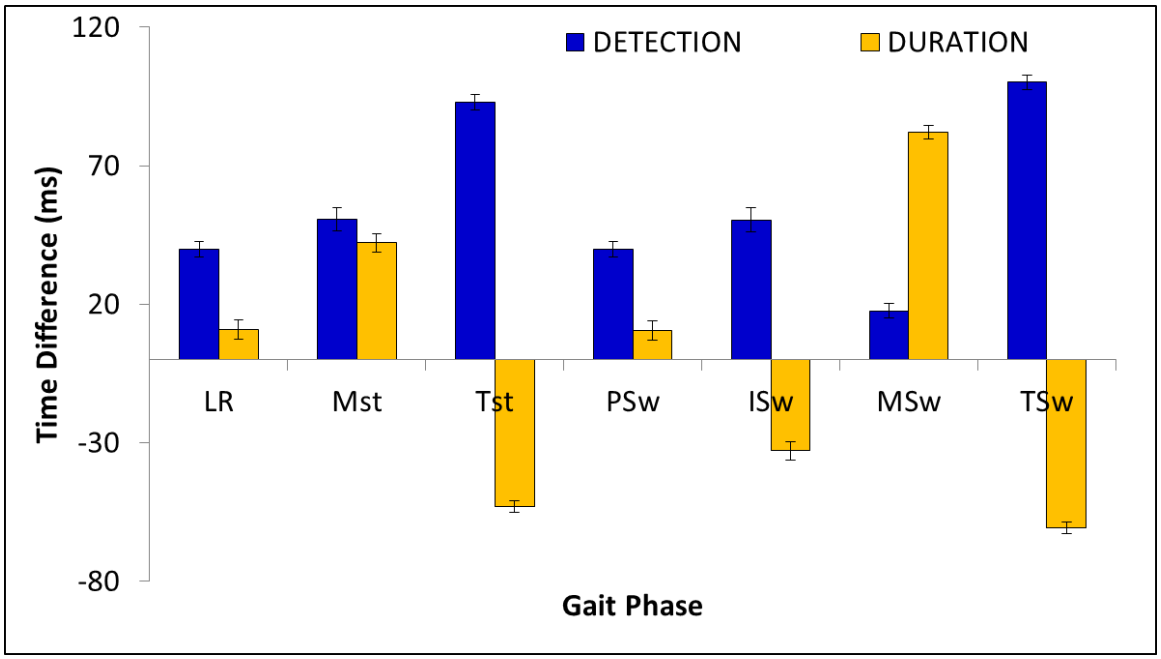

Figure 2.5: Average time difference (ms) of gait phase detection and duration between the sensor and motion capture systems during walking in typically developing children. Positive values indicate sensor system delays.

When comparing the differences in phase detection based on percentages of the gait cycle, 1% of the gait cycle is associated with approximately 10 ms (gait cycle duration= 1 second). The average sensor system detection delay was ~1.8% of the gait cycle; the overall gait cycle RMSE, between the sensor and motion capture systems, was 22.84 ms (~2% of the gait cycle). The average (±STD) RMSE of gait phase detection and duration, as a percentage of gait, between the sensor and motion capture systems were 7.23 ± 2.38% and 4.58 ± 2.68% of the gait cycle, respectively (Table 2.4).

Table 2.4: Gait phase detection and duration RMSEs (% of the gait cycle) between sensor and motion capture systems during walking in typically developing children.

GAIT PHASE	LR	Mst	Tst	PSw	ISw	MSw	TSw
DETECTION	5.19	7.00	9.79	5.20	7.06	3.57	10.46
DURATION	4.13	5.72	5.82	4.28	5.15	8.65	6.51

2.4.2 Gait Phase Detection and Duration during walking in 1 subject with CP

Time differences of gait phase detection and duration also varied by phase during walking in 1 subject with CP. The average and standard error of time differences in gait phase detection and duration between the sensor system and motion capture system data are shown in Figure 2.6. Average differences in detection ranged from -79 ms to 139 ms. Gait event detection RMSEs ranged from 67 ms (LR) to 151 ms (MSw). The average RMSE in detection time between the sensor and motion capture systems was 94.60 ms. Gait phase duration differences ranged from -218 ms to 117 ms (RMSE=52.38-225.53 ms). The phases with the smallest and largest difference in duration between that determined by the sensor and motion capture systems were PSw

and ISw, respectively. The average RMSE in phase duration between the sensor and motion capture systems was 123.86 ms.

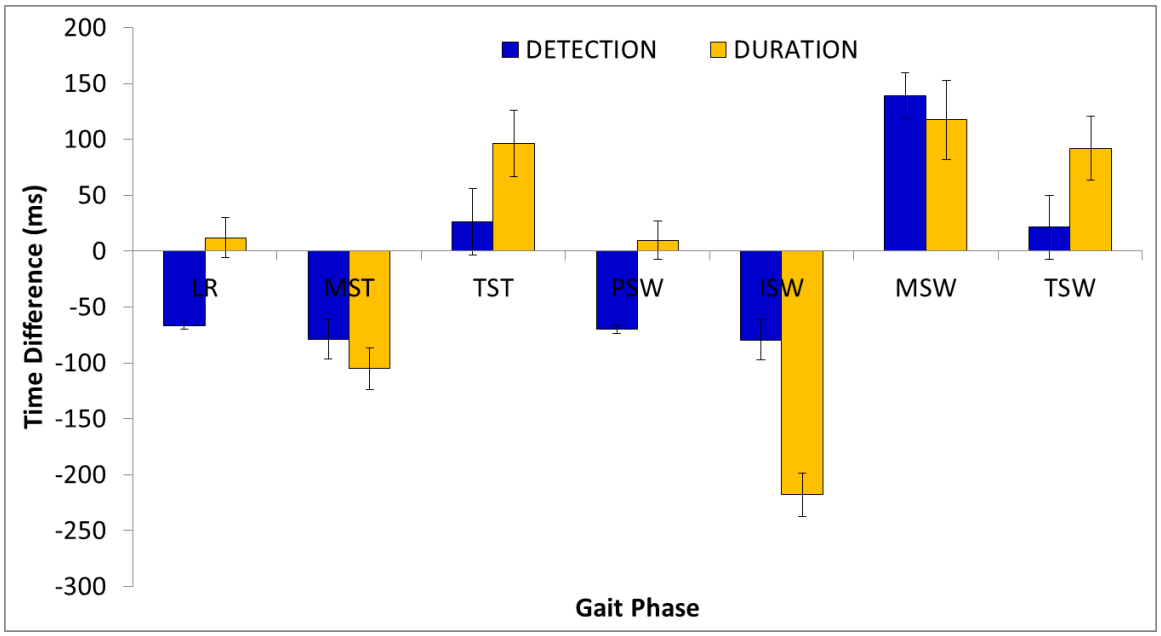

Figure 2.6: Average time difference (ms) of gait phase detection and duration between the sensor and motion capture systems during walking in 1 subject with CP. Positive values indicate sensor system delays.

When comparing the differences in phase detection based on percentages of the gait cycle, 1% of the gait cycle is associated with approximately 14 ms (gait cycle duration= 1.4 seconds). The average (±STD) RMSE of gait phase detection and duration, as a percentage of gait, between the sensor and motion capture systems were 6.76 ± 1.98% and 8.85 ± 4.28% of the gait cycle, respectively (Table 2.5).

Table 2.5: Gait phase detection and duration RMSEs (% of the gait cycle) between sensor and motion capture systems during walking in 1 subject with CP.

GAIT PHASE	LR	Mst	Tst	PSw	ISw	MSw	TSw
DETECTION	4.82	6.76	6.65	5.05	6.82	10.84	6.37
DURATION	3.88	8.53	9.39	3.74	16.11	11.29	8.98

2.4.3 Stimulation Delivery Validation in typically developing children

Stimulation signals, produced by the FES system, were evaluated for five time delay conditions added to the pre-trigger signal. The delay conditions were 0% DELAY, 25% DELAY, 50% DELAY, and 75% DELAY, and 100% DELAY and the delay time for each phase was calculated based on the individual's average gait phase duration. Average (±STD) phase durations varied between the gait phases (Table 2.6); therefore different gait phases had different associated delay times. The average pre-trigger time for each gait phase, based upon the pre-trigger % DELAY strategy, is outlined in Table 2.7. The longer % DELAYS were associated with shorter pre-trigger times. For example, the 0% DELAY trigger signal was applied 144.95 ms before Mst while the 75% DELAY trigger was applied 36.24 ms before Mst.

Table 2.6: Average (±STD) gait phase durations (ms) during walking in typically developing children. Each individual's phase duration was used to calculate the time delay as a percentage of each gait phase.

Gait Phase	Average (± STD) Duration (ms)
LR	144.95 ± 41.28
Mst	308.96 ± 41.51
Tst	90.91 ± 22.83
PSw	144.16 ± 42.34
ISw	87.15 ± 35.84
MSw	221.64 ± 29.66
TSw	90.98 ± 22.47

Table 2.7: Average pre-trigger time (ms) prior to the desired phase at which the stimulation timing was desired in typically developing individuals.

	Time (ms) prior to the desired phase at which stimulation trigger was delivered				
Desired Gait Phase	0% DELAY	25% DELAY	50% DELAY	75% DELAY	100% DELAY
LR	90.98	68.24	45.49	22.75	0
Mst	144.95	108.71	72.47	36.24	0
Tst	308.96	231.72	154.48	77.24	0
PSw	90.91	68.18	45.46	22.73	0
ISw	144.16	108.12	72.08	36.04	0
MSw	87.15	65.36	43.57	21.79	0
TSw	221.64	166.23	110.82	55.41	0

Figure 2.7 illustrates the on/off timing of the five time delay conditions compared to the desired stimulation timing for each of the five muscle groups. The 0% DELAY and 100% DELAY were included to represent the pre-trigger and original trigger, respectively. Similarly to the pre-trigger and original trigger, the 0% DELAY and 100% DELAY produced stimulation signals that were, on average, 8.6% of the gait cycle earlier and 7.3% of the gait cycle later than the desired stimulation timing, respectively. The difference between the stimulation signal and desired stimulation timing had ranges of 22% and 19% of the gait cycle for the 0% and 100% DELAY conditions, respectively.

The on/off timing of the stimulation signals were proportional to the time delays added to the pre-trigger. With a pre-trigger delay of 50% gait phase, the stimulation signals were closest to the desired stimulation timing. The average difference between the stimulation signals and desired stimulation timing was 0.7% of the gait cycle and had a range of 16% of the gait cycle; stimulation signals occurred 7% earlier and 9% later in the gait cycle than the desired stimulation time. With a pre-trigger delay of 25%

gait phase, the average timing difference was -4.3% of the gait cycle indicating that, on average, the stimulation signals occurred prior to the desired stimulation timing. The stimulation signals ranged from occurring 12% earlier to 6% later in the gait cycle than the desired stimulation time. A pre-trigger delay of 75% gait phase produced stimulation signals with an average timing difference of 1.3% of the gait cycle and a range of 19% of the gait cycle. For all delay conditions, the termination of stimulation to the TS muscle group occurred later than the desired stimulation timing; ranging from 2% to 16% of the gait cycle later than the desired stimulation time.

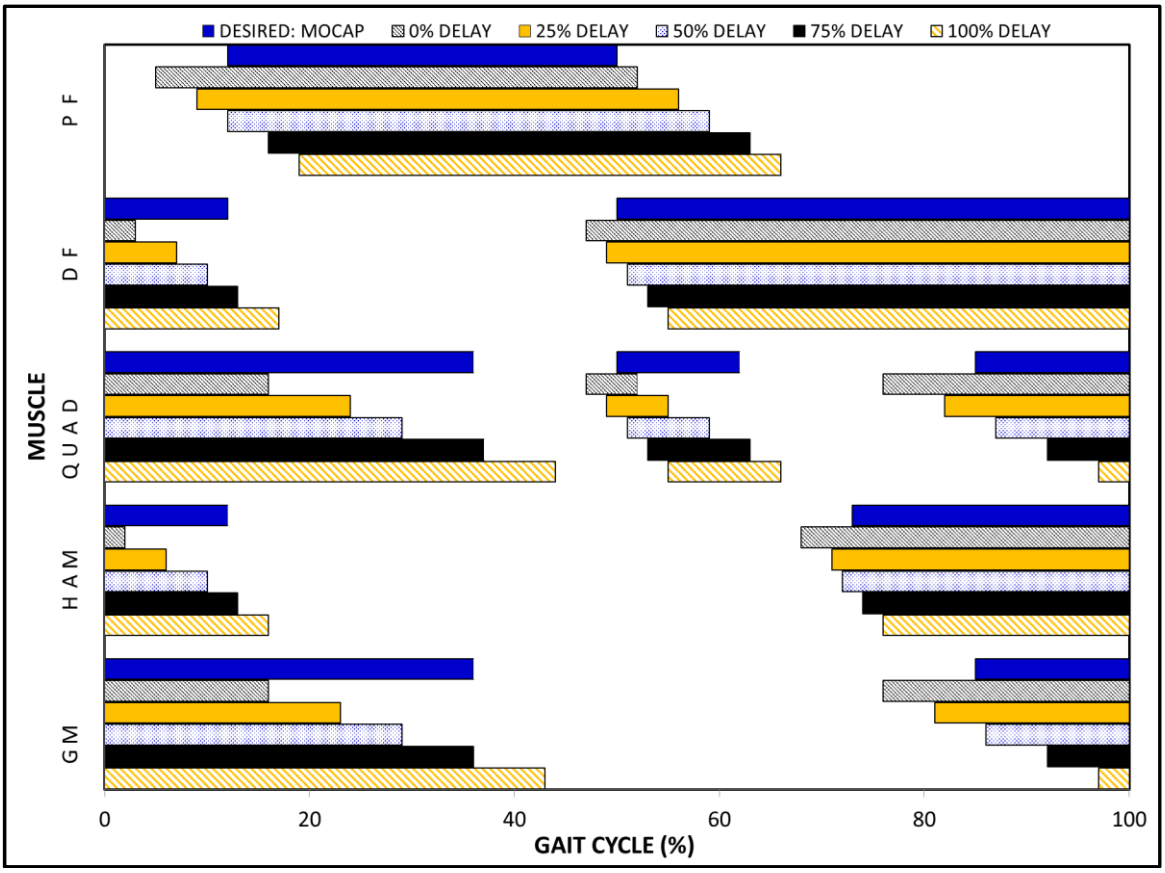

Figure 2.7: Comparison of the On/Off timing of the desired stimulation time based on motion capture data (DESIRED: MOCAP) and the delivery of stimulation, recorded as analog signals, when the percent delay method was used as the trigger. Five percent delays were evaluated: no delay added to the pre-trigger (0% DELAY), 25% delay added to the pre-trigger (25% DELAY), 50% delay added to the pre-trigger (50% DELAY), 75% delay added to the pre-trigger (75% DELAY), and 100% delay added to the pre-trigger (100% DELAY).

2.4.4 Stimulation Delivery Validation in 1 subject with CP

Stimulation signals, produced by the FES system, were evaluated for three time delay conditions added to the pre-trigger signal; 0% DELAY, 50% DELAY, and 75% DELAY. Similarly to the TD group, the delay time for each phase was calculated based on the individual's average gait phase duration. Average (±STD) phase duration varied

between the gait phases (Table 2.8); the longest phase was Mst (273.00 ± 60.05 ms) and the shortest phase was ISw (78.80 ± 62.09 ms). The average pre-trigger time for each gait phase, based upon the pre-trigger % DELAY strategy, is outlined in Table 2.9. Similarly to the TD group, smaller % DELAYS were associated with longer time differences between the trigger signal and the desired phase. For example, the 0% DELAY trigger signal was applied 204.02 ms before Mst and the 75% DELAY trigger signal was applied 51.05 ms before Mst. A 75% DELAY trigger during walking in 1 subject with CP produced the most similar time differences between the trigger signal and the desired phase when compared to the 50% DELAY trigger during walking in the TD group that the other conditions tested.

Table 2.8: Average (±STD) gait phase durations (ms) during walking in 1 subject with CP. The individual's gait phase durations were used to calculate the time delay for each % DELAY condition.

Gait Phase	Average (± STD) Duration (ms)
LR	204.20 ± 46.39
Mst	273.00 ± 60.05
Tst	231.50 ± 89.57
PSw	204.10 ± 46.35
ISw	78.80 ± 62.09
MSw	212.89 ± 94.58
TSw	234.10 ± 87.29

Table 2.9: Average pre-trigger time (ms) prior to the desired phase at which the stimulation timing was desired in 1 subject with CP.

	Time (ms) prior to the desired phase at which stimulation trigger was delivered		
Desired Gait Phase	0% DELAY	50% DELAY	75% DELAY
LR	234.10	117.05	58.52
Mst	204.20	102.10	51.05
Tst	273.00	136.50	68.25
PSw	231.50	115.75	57.87
ISw	204.10	102.05	51.03
MSw	78.80	39.40	19.70
TSw	212.89	106.44	53.22

Figure 2.8 illustrates the on/off timing of the three time delay conditions compared to the desired stimulation timing for each of the five muscle groups. The 0% DELAY was included to represent the pre-trigger strategy. The 0% DELAY produced stimulation signals that were, on average, 13.5% of the gait cycle earlier than the desired timing. The difference between the stimulation signal and desired stimulation timing had a range of 19% of the gait cycle; with the termination of stimulation to the quadriceps having the largest difference in timing.

The on/off timing of the stimulation signals were proportional to the time delays added to the pre-trigger. With a pre-trigger delay of 75% gait phase, the stimulation signals were closest to the desired stimulation timing. The average difference between the stimulation signals and desired stimulation timing was 1.5% of the gait cycle and had a range of 7% of the gait cycle; stimulation signals occurred 5% earlier and 2% later in the gait cycle than the desired stimulation time. With a pre-trigger delay of 50% gait phase, the average timing difference was -6.2% of the gait cycle indicating that, on average, the stimulation signals occurred prior to the desired stimulation timing. The

stimulation signals ranged from occurring 10% to 2% earlier in the gait cycle than the desired stimulation time.

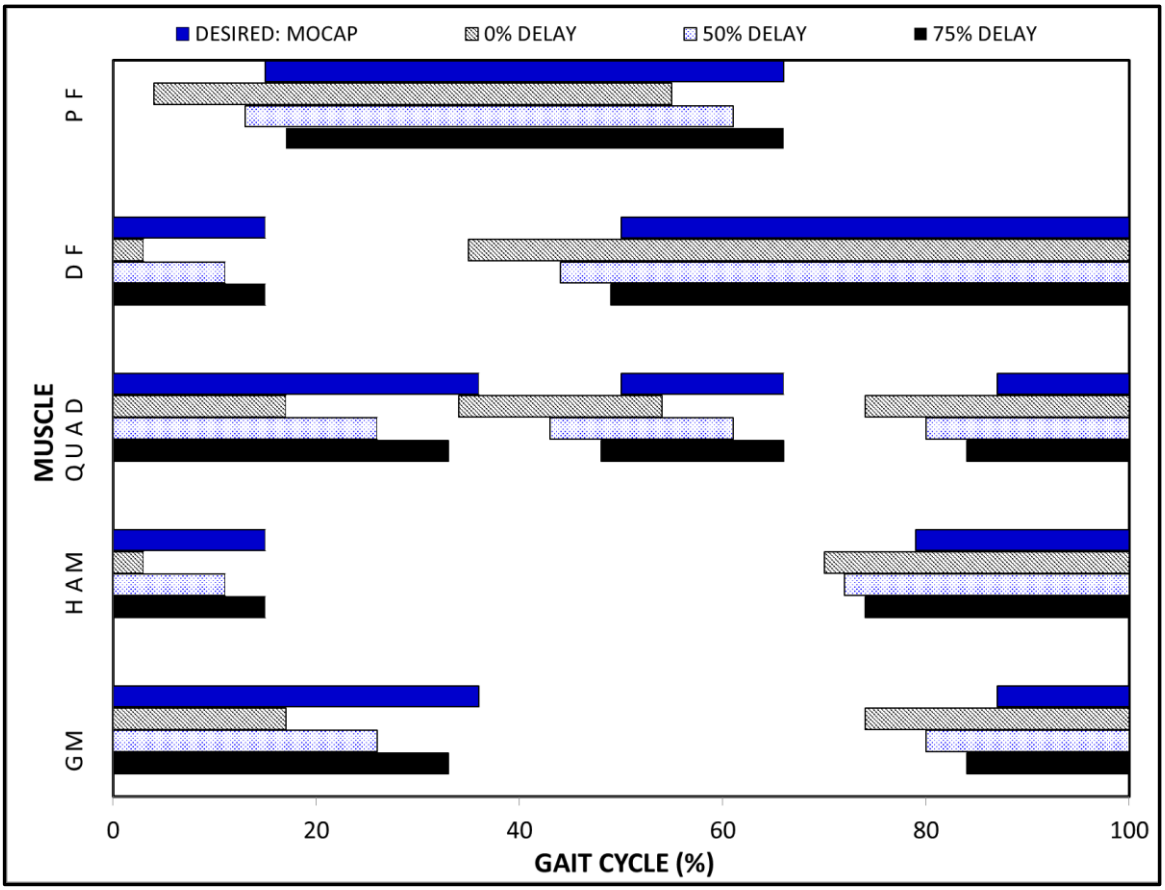

Figure 2.8: Comparison of the On/Off timing of the delivery of stimulation, recorded as an analog signal, when different delays were added to the pre-trigger method and the desired stimulation timing based on motion capture data (DESIRED: MOCAP) in one subject with CP. Three percent delays were evaluated: no delay added to the pre-trigger (0% DELAY), 50% delay added to the pre-trigger (50% DELAY), and 75% delay added to the pre-trigger (75% DELAY).

2.5 Discussion

A multichannel functional electrical stimulation (FES) system, capable of stimulating 10 lower extremity muscle groups during a gait cycle, was successfully developed in Aim 1 and consisted of two wireless sensors, two 6-channel stimulators, and custom software. The FES system was designed with a level of increased control over the delivery of stimulation and programmable stimulation parameters for each subject, muscle group, and gait phase. Additionally, offline adjustments can be made to the muscle groups targeted with stimulation, stimulation parameters, and timing strategies providing flexibility in the features of the FES system necessary to customize stimulation based on the variations in gait deviation and to compensate for muscle fatigue. This system has more adaptive features than most of the commercially available devices that are typically limited to improving one type of gait deviation (i.e. Odstock Drop Foot stimulator, WalkAide, and Bioness can only correct for foot drop during swing).

The gait phase detection (GPD) portion of the FES system software was capable of detecting all seven phases of gait from the gyroscope signal, streamed from the sensors worn on both shanks, during walking in typically developing individuals and 1 individual with CP. Time differences of gait phase detection and duration between the sensor system and the 'gold standard' varied by phase. Some of these differences may be attributed to variations in phase definition between the two systems and synchronization between motion capture PC and computer used for sensor system. Average gait phase detection and duration RMSEs of 5% of the gait cycle or less during walking in TD individuals were established, a priori, as the threshold of acceptable differences between the sensor and motion capture systems. The benchmark RMSE was not met for gait phase detection; the average detection RMSE was 7.23 ± 2.38% of the

gait cycle (approximately 72 ms). However, our system's gait phase detection had better performance than other systems reported in the literature[106,129–131]; Pappas and colleagues reported an average difference in gait phase detection of 90 ms[106]. The FES system had an average gait phase duration RMSE of 4.58 ± 2.68% of gait cycle which met the benchmark measure.

Several iterations of the sensor system were necessary to reduce gait phase detection delays to a minimal level. Gait phase detection relied on signals streamed from commercially available sensors (Opal^{TM}, APDM, Portland, OR, USA) with specifications suggesting wireless data transmission delays on the order of 10-75 ms (manufacturer literature)[132]. In an effort to compensate for transmission delays and other system delays, the sensor system evolved from a unilateral wireless shoe sensor system, composed of 6 force sensing resistors (FSRs) and 2 Opal, to a bilateral sensor system, composed of 2 Opals using only gyroscope signals. By reducing the number of input signals (hardware evolution), using contralateral events to define some of the gait phases, and gyroscope signal analysis software modifications, we were able to create a more mechanically robust system with reduced differences in gait detection and duration when compared to the motion capture system, reduce the setup time, and have less sensor placement sensitivity.

Previous FES systems had limited stimulation capabilities due to the technology used for determining gait phases. Most systems in the literature that relied solely on FSRs[95–97,104,105,121,133] or tilt sensors[93,134] to control stimulation timing demonstrated diminished number of gait phases detected, dependent on the number of FSRs used or if a tilt sensor was used instead of FSRs, and restricted the timing of the delivery of stimulation. This insufficient feedback control may have restricted the muscle groups capable of being activated based on the feasibility of the FES system to trigger the

stimulation appropriately. Our system's ability to detect all 7 gait phases allows more appropriate timing of stimulation to as many as 5 muscle groups, bilaterally, governed only by the number of channels available on the stimulator.

Additional FES system improvements were investigated to compensate for the inherent sensor system delays and reduce the differences between the stimulation timing (DESIRED: MOCAP) and the delivery of stimulation including the evaluation of different percent delays added to the pre-trigger signal. In typically developing individuals, gait phase detection with a 50% DELAY compensation was determined as the most accurate finite-state controller to trigger FES and produce appropriately timed stimulation signals to the gluteal, hamstring, quadriceps, plantarflexor, and dorsiflexor muscle groups during a typical gait cycle. In order for the finite-state controller to be considered sufficient, the average difference in timing of the actual stimulation output and desired stimulation timing of stimulation needed to be equal to or less than the average gait phase onset variability during walking of the TD group. The average gait phase onset variability, determined by gait phase detection from motion capture data, was 3.86 ± 0.70% of the gait cycle. When actual stimulation output was compared to the desired stimulation timing, there was an average difference of 0.67 ± 4.25% of the gait cycle; illustrating that there was less variability, on average, in the timing of the delivery of stimulation than the onset of the gait phases. The timing of stimulation delivered by the FES system met the benchmark measures in performance. Although the system goal was not achieved for the gait phase detection, the stimulation results demonstrated that the trigger designed to compensate for the delays was successful and the timing of the stimulation was within our criteria.

After the validation of the FES system in typically developing individuals, the FES system was piloted in one adolescent with CP to verify the timing of the delivery

of stimulation prior to investigating the effects of applying the FES system during walking. Results indicated that a different pre-trigger delay than the one determined for the TD group (50% DELAY) was needed. A 75% DELAY added to the pre-trigger produced stimulation signals that better matched the desired stimulation timing (Figure 2.8). The 75% DELAY during walking in the individual with CP created similar time differences between the trigger signal and the desired gait phase to the 50% DELAY during walking in typically developing individuals. The need for an increased pre-trigger delay may be attributed to slower walking speed resulting in longer gait phase durations and gait cycles exhibited by the individual with CP compared to TD. The average gait cycle in the TD group and the individual with CP was ~1 sec and ~1.4 sec, respectively. Based on the slower walking speeds reported in individuals with CP[135], a 75% DELAY will be utilized to trigger the stimulation during walking individuals with CP in Aim 2.

The system performance of the FES system contributes to the evidence that finite-state control is a viable method for triggering stimulation and the accuracy of the stimulation timing is likely greater than open-loop systems. The rigorous evaluation of system performance of gait phase detection and delivery stimulation signals, in typically developing individuals, illustrates the importance of validating the FES system to reduce the potential of the system as a source of error when used as a device to assist gait in patient populations. Reporting system performance provides researchers with a foundation when developing their custom FES systems and will, hopefully, encourage more standardization when reporting on FES system capabilities.

One of the limitations of the FES system is the timing delay in the delivery of stimulation resulting in the application of a pre-trigger compensation algorithm. Sources of timing delay include latencies associated with wireless streaming of IMU data (~10-

75 ms: manufacturer literature)[132], system timing indeterminacies associated with USB communication protocol (as high as 55 ms)[136], and windows operating system not operating at a real-time capacity. A second limitation of the FES system is the controller used to trigger stimulation. The use of a finite-state controller cannot provide the level of feedback necessary for real-time modulation of stimulation parameters to compensate for muscle fatigue. With the capability of offline adjustments, however, the system allows for modifications that help to address muscle fatigue. For example, the use of variable frequency trains known to preserve force in FES applications[107] may be implemented; this feature is not currently available in commercial systems. Furthermore, stimulation pulse duration and current amplitude can be manually adjusted to account for declining gait function associated with fatigue. Even with declines in walking function, the system's gait phase detection is robust enough to detect distinct gait phases for FES to proceed. There are potential mobility limitations with the use of a tethered FES system. The participants are limited to treadmill walking or donning the cumbersome stimulators during overground ambulation. There is also the risk of tripping on the electrode cables and their length limits where stimulators can be placed.

One experimental limitation of Aim 1 is the evaluation of the FES system solely during treadmill walking. Although gait phase detection successfully differentiated between the 7 phases of gait when subjects walked at constant speeds on the treadmill, the system's performance in different environments such as overground walking is unknown. Further evaluation of the system's performance during overground walking or perturbations to the limb while walking may provide more insight into the robustness of the system's gait phase detection. An additional experimental limitation was the synchronization method between the motion capture PC and the computer used for GPD. To compare gait phase detection between the two systems, we used a trigger

signal from the computer used for GPD to initiate recording in the motion capture PC. This method of synchronization may have led to delays in the start of the motion capture recording; therefore, gait phase detection delays may be greater than the delays reported. However, the signals and desired stimulation timing compared for the validation of the delivery of stimulation were both collected in the motion capture computer; therefore, we are confident that the time differences between the actual stimulation output and desired stimulation timing are an accurate representation of the delays that exist in stimulation delivery of the FES system.

2.6 Conclusion

The goal of Aim 1 was to evaluate the sensor system used for finite control to a custom FES system and validate the timing of delivery of stimulation when compared to gait phase detection determined by the motion analysis data. The sensor system was reasonably accurate in detecting gait phases and the software compensations ensured the delivery of stimulation was accurate when compared to the motion capture system. Investigation of the FES system in patient populations is needed prior to implementing the system to verify that it produces similar results to that in typically developing children.

Chapter 3

EVALUATION OF FUNCTIONAL ELECTRICAL STIMULATION-INDUCED LOWER EXTREMITY KINEMATIC CHANGES RESULTING FROM INDIVIDUALIZED STIMULATION PROGRAMS DURING WALKING: A CASE-SERIES STUDY IN 6 CHILDREN WITH CEREBRAL PALSY

3.1 Abstract

Walking interventions using functional electrical stimulation (FES) have demonstrated benefits to gait such as decreased deviations in spatiotemporal, kinematic, and kinetic parameters. Previous studies that utilized commercially available FES systems were typically confined to 1 or 2 muscle groups, such as the dorsiflexors and plantarflexors, and limited the amount of individualization of the stimulation program. Increased options, such as muscle group targeted, timing, and level of stimulation, is needed to address subject specific gait deviations and responses. We aimed to demonstrate that our FES system, designed with more options for the physical therapists to choose from, can be used in individuals with CP and that customized stimulation strategies change multiple joint kinematics during walking.

Six children with CP donned the FES system, developed in Aim 1, and walked on a treadmill at self-selected speed while kinematic data were collected during walking without FES and with individualized FES programs developed by the physical therapists. Overall joint angle measures, at the hips, knees, and ankles in the sagittal plane, demonstrated that stimulation during walking produces alterations to the joints; responses varied between individuals. Individualized stimulation programs were successfully deployed during walking in all 6 individuals with CP and lower extremity

kinematics were modified. FES systems with increased customization options provide the therapists with a device that allowed them to prescribe stimulation programs that better matched the individual's deviation than a one size fits all device and may increase the effectiveness of FES as an intervention to improve gait in individuals with CP.

3.2 Introduction

Cerebral Palsy (CP) is a non-progressive disorder caused by a lesion of the fetal or infant brain that results in muscle weakness, spasticity, and other motor impairments. CP is the most prevalent childhood neuromotor diagnosis with an estimate of 764,000 people having CP and approximately 10,000 new cases in the US each year[2]. Spastic CP, the most common classification of CP having a prevalence of 70-81%[4,5], is characterized by clinical and functional impairments of decreased passive joint range of motion, increased muscle spasticity/tone, impaired coordination, decreased muscle strength, and diminished ability to ambulate without assistance or assistive devices[6–8].

The normal progression of CP is for a progressive loss of walking function characterized by spatiotemporal and kinematic parameters; most children become less independent with functional mobility as they enter their teenage years and adulthood[14,17,19,21,22,137]. Contributing factors to this deterioration are muscle weakness, caused by a lack of muscle strength gains commensurate with gains in body size and weight[66], and the presence of spasticity. These underlying factors result in the absence of one or more of the components that comprise a successful typical gait cycle[35], often observed in CP gait[35–37], and lead to inefficient walking and increased energy expenditure[38–40]. Deviations from typical gait are observed in the hip, knee, and ankle angles and pathologic gait patterns of CP, associated with these deviations, have been classified by reoccurring postural patterns observed in this population[43,44,46]. Four common gait patterns seen in individuals with spastic diplegia are: equinus, jump gait, apparent equinus, and crouch gait[44]; defined by the kinematics at the hip, knee, and

ankle angles in the sagittal plane. These gait patterns range in severity, with equinus observed in the most functional walkers[17], and follow commonly observed changes with age, typically culminating in crouch gait[43].

Approaches of improving gait in children with CP by utilizing functional electrical stimulation (FES) to reduce gait deviations target both the underlying causes of gait deviations, such as physical impairments, and the task of walking. Previous studies have set the foundation for using FES during gait in children with CP by demonstrating that FES assistance does produce changes in walking towards more typical patterns[91,92]. FES-assisted walking has improved both underlying impairments and functional outcomes, such as muscle size[93], spatiotemporal parameters[93–95], passive range of motion[94], kinematics[96–98], and kinetics[98]. Specific kinematic and spatiotemporal improvements seen in gait, with FES assistance, include improved ankle and knee angles, cadence, step length, and walking velocity[91,94,97–99]. Studies have shown that the joint where kinematic improvements occur is influenced by the muscle groups targeted with stimulation; stimulation to the gastrocnemius[92] only, dorsiflexors[96,97,99,112,113] only, or gastrocnemius and tibialis anterior[92,99] promoted changes at the ankle while stimulation to the quadriceps[96,114] improved knee flexion angle. However, assessing the effects of an FES strategy during walking in children with CP has been difficult due to the heterogeneity of the study population[115,138].

A one size FES program does not fit all individuals with CP; improvements are influenced by the variation of gait patterns observed in CP gait[139] and subject specific responses to FES[96,140]. To address the variability in subjects with CP, it is necessary to

have stimulation programs that can be custom tailored to the individual. Increased options are needed such as the ability to target more muscle groups, flexibility to target different combinations of muscle groups, and increased control over the timing of the delivery of stimulation than the systems that are commercially available. Systems such as the Odstock Dropped Foot Stimulator systems (Biomedical Engineering and Medical Physics, Salisbury, UK), Respond II Select (Medtronic Inc., Minneapolis, MN, USA), and Ness L300® Plus (Bioness Inc, Valencia, CA, USA) are typically confined to the stimulation of 1 to 2 muscle groups and there is a lack of available systems that are able to address multiple joints during walking.

A custom FES system, designed with increased gait phase detection capability and the flexibility to deliver stimulation to 12 channels during walking, was developed to address limitations of the commercially available FES systems. Our FES system, comprised of two inertial measurement units (Opal™, APDM, Portland, OR, USA) and two stimulators (RehaStim, Hasomed Inc., Germany), used gyroscope signals to detect all 7 phases of gait[125] which provided finite state control over the timing of the delivery of stimulation. Utilizing the characteristics of the gyroscope signal allowed increased gait phase detection, compared to foot sensitive resistors[93,95–97,99,104,105,121], by differentiating between the three different phases of the swing period. This finite state control system facilitated stimulation delivery control based on the subject's gait phase. Additionally, the use of two stimulators allowed stimulation of up to 12 muscle groups during FES-assisted walking. The added channels provided the ability to test a series of stimulation patterns; individually programed to target subject specific gait deviations.

This case series demonstrates that (1) our FES system can be used in individuals with CP and (2) the flexibility of our FES system allows the stimulation strategy to be tailored to change multiple joint kinematics during walking in individuals with CP.

3.3 Methods

The custom FES system was worn during walking in six children with CP (4 Male, 14 ± 2 years old). Individualized stimulation programs were determined prior to the data collection and implemented during treadmill walking at a comfortable speed. The effects of FES-assisted walking on lower extremity kinematics were evaluated.

3.3.1 Experimental Protocol

Subjects were recruited through an outpatient CP clinic and local referral sources. Additional means, such as advertisements and recruitment flyers, were approved by the Institutional Review Board and administration and distributed to other contacts. Parental consent and child assent were obtained prior to subject participation.

3.3.1.1 Subject Screening

All individuals with CP were screened by a physical therapist and an orthopedic surgeon. Individuals were screened for study eligibility, based on the inclusion and exclusion criteria (Table 3.1), and symptomatic or known pulmonary and cardiac disease using guidelines from the Asthma Control Test and the American Heart Association.

Table 3.1: Eligibility criteria for Functional Electrical Stimulation (FES) walking study participation.

Inclusion	Exclusion
• Age 10-18 • The diagnosis of spastic diplegic CP • Levels I-III GMFCS classification • Sufficient covering of the femoral head in the acetabulum (MIGR%<40%) • Exhibit typical gait deviations characterized in CP (i.e. crouch, equinus, jump gait) • Achieve at least 0° of dorsiflexion during passive ROM in physical exam • Visuoperceptual skills and cognitive/ communication skills to follow multiple step commands for attending to exercise and data collection • Seizure-free or well controlled seizures and no other neurological or musculoskeletal diagnoses such as dystonia, severe scoliosis, or hip instability • Willingness to participate in testing and training sessions at Shriners Hospitals for Children as prescribed by the study • Ability to communicate pain or discomfort with testing and training procedures • Ability to obtain Parental/guardian consent and child assent/consent	• Diagnosis of athetoid or ataxic CP • Significant scoliosis with primary curve > 40° • Spinal fusions extending into the pelvis • Severe tactile hypersensitivity • Joint instability or dislocation in the lower extremities • Lower extremity surgery or fractures in the past year • Botulinum toxin injections in the LE muscles within the past 6 months • Implanted medical device contraindicated with the application of FES • Severe spasticity of the leg muscles (i.e. A score of 4 on the Modified Ashworth Scale) • Uncharacteristic lower extremity joint pain during walking • History of pulmonary disease limiting exercise tolerance (Asthma Control Test screen) or history of known cardiac disease (American Heart Association screen). • Severely limited range of joint motion/ irreversible muscle contractures, i.e.> 10° knee flexion, >15° hip flexion contractures • Pregnancy

3.3.2 FES System Options

The custom FES system was designed with a number of features that allowed therapists to tailor the stimulation program to the individual. The system provided flexibility to choose the muscle groups targeted with stimulation; options included the

gluteals, hamstrings, quadriceps, dorsiflexors, and/or plantarflexors. For each muscle group, the therapist was able to choose the phase(s) of gait the muscle group was active such as Loading Response, Midstance, Terminal Stance, Preswing, Initial Swing, Midswing, and Terminal Swing. The timing of the delivery of stimulation was controlled by the onset of each of the 7 phases of gait; therefore, the stimulation was able to be applied during 1 or multiple gait phases. The stimulator current was programmable for each muscle group and the stimulation pulse duration was programmable for each muscle group and each phase of gait the muscle group was activated. These settings were adjustable during FES-assisted walking.

3.3.2.1 Individualized Stimulation Program

A customized stimulation program was created for each participant and was derived from the individual's gait deviations. A group of physical therapists, experienced in identifying gait deviations seen in CP, used visual inspection of frontal and sagittal videos of the individual walking (approximately 10 steps) to identify the individual's gait deviations. The targeted muscle groups, timing and level of stimulation needed to improve the individual's gait were determined based on clinical judgment (Table 3.2). Consensus was reached when there was agreement on the gait deviations exhibited, the muscles to target, the timing and level of stimulation needed.

Functional levels of stimulation were associated with concentric muscle contractions and used to produce a vigorous movements. Reduced levels of stimulation were associated with eccentric actions and used to provide control to the limb when that targeted muscle group was lengthened. For each participant, stimulation current amplitudes and pulse durations needed to attain a functional level contraction for each muscle group was established based on the goal associated with the muscle group

(Appendix A). The pulse duration for reduced level stimulation was set to 50% of the pulse duration used during the functional level stimulation. The percentage method was used to maintain consistency when setting the pulse duration for reduced level stimulation. Another percentage that was piloted was 25% of the functional level pulse duration. Both the 25% and 50% were trialed and did not restrict the movement and based on visual observation, the 50% provided greater assistance and was therefore chosen. All settings were recorded and incorporated into the individualized stimulation parameters that was applied during treadmill walking (Appendix B).

Table 3.2: For each participant, the group of physical therapists determined the muscle groups, gait phases, and level of stimulation needed to improve gait deviations. ***F*** indicated the muscle group and gait phase when a functional level of stimulation was applied and ***R*** indicated the muscle group and gait phase when a reduced level of stimulation was applied. *LR* Loading response, *Mst* Mid-stance, *Tst* Terminal stance, *PSw* Pre-swing, *ISw* Initial swing, *MSw* Mid-swing, *TSw* Terminal swing

		Case					
Muscle Group	Gait Phase	1	2	3	4	5	6
Plantarflexors	Mst		R		R	F	
	Tst		F		F	F	F
	PSw	F	F	F	F	F	F
Dorsiflexors	LR						F
	PSw						F
	Isw	F	F	F	F	F	F
	MSw	F	F	F	F	F	F
	TSw	F	F	F	F	F	F
Quadriceps	LR		R		R	F	F
	Mst		F		F	F	
	PSw		R				
	MSw						F
	TSw	F		F			F
Hamstrings	Tst		F				
Gluteals	LR		F				F
	Mst	F	R	F	F		F
	Tst	F	R	F	F		F
	TSw		R				

3.3.2.2 Data Collection

Gait phases were visually inspected while walking to verify that all seven phases of gait were detected and the individualized gyroscope signal thresholds were determined while the subject walked on the treadmill. The subject's anthropometric measures, such as height and weight, were recorded and used during data processing for normalization of kinetics and kinematics. Self-selected walking speed was determined over ground with the 10 MWT[123]. A comfortable speed was established, based on

subject feedback, if self-selected speed was too fast on the treadmill. Electrodes for delivery of electrical stimulation were placed on the muscle groups that were included in the individualized stimulation program, bilaterally, based on Robinson and Snyder-Mackler placement protocol[141], and stimulation was delivered to ensure appropriate electrode placement. Following placement, the individualized stimulation intensities were determined for each muscle group, based on the protocol described in the section 3.3.1.2.1. If stimulation thresholding was done on the day prior to the gait analysis, marks were made on the legs to identify the corners of each electrode, which served as a guide for placement the following day, and stimulation intensities were rechecked.

3.3.2.3 Gait Analysis

Subjects donned the FES system, consisting of inertial measurement units (Opal^{TM}, APDM, Portland, OR, USA) worn on both shanks and the electrodes, while walking on a treadmill. If the subject typically wore orthotics or used an assistive device while walking, he/she was not permitted to wear/use these during the data collection but had the option to hold the side handrails, on the treadmill, for support. A non-weight bearing harness was used for safety. After a treadmill-walking accommodation period[124], a 30-second walking trial was collected while the subject walked at a comfortable speed with no stimulation to establish baseline kinematic measures. A required seated rest of 5 minutes separated each of the walking trials. The individualized stimulation condition was applied while the subject walked on the treadmill at his/her comfortable speed. The subject walked with stimulation for 30 seconds prior to the start of the data collection to adjust to the stimulation. Following the 30 seconds to acclimate to the stimulation, data were collected in a similar manner to the no stimulation trial. An additional no stimulation walking trial was collected at the end of the data collection.

Kinematic data were captured for all trials using a Motion Analysis camera system (Motion Analysis Corporation, Santa Rosa, CA, USA).

3.3.3 Data Analysis

Kinematic data were processed in Visual 3D (C-Motion Inc., Germantown, MD, USA) and the last five consecutive right and left gait cycles, with valid kinematic and gait phase detection data, were used for the analysis. Average joint angles, calculated as a percentage of gait, were determined for the no stimulation (NO STIM) and stimulation (STIM) conditions. The variability, defined as one standard deviation from the mean, of the hip, knee, and ankle angles during the no stimulation condition was determined at each percent of the gait cycle for each subject. Kinematic data collected from a group of typically developing (TD) children who participated in another aim of the study were used to form the reference data set. The joint angles were plotted for the stimulation, no stimulation, and TD data as a percent of the gait cycle. Periods of improvement during the stimulation condition were considered to be a joint angle that exceeded the variability of the no stimulation condition and changed in the direction of the TD joint angle.

3.4 Results

Six children with CP, who had different levels of functional mobility and gait deviations while walking (Table 3.3), participated in the study to determine the feasibility of walking with individualized stimulation programs and the effects observed in the lower extremity kinematics.

Table 3.3: Characteristics of participants. *(B)* bilateral use

Case	Age	Sex	GMFCS	Height (m)	Weight (kg)	Self-selected Speed (m/s)	Treadmill speed (m/s)	Assistive Device	Braces
1	15	M	III	1.67	32.13	0.77	0.60	(B) lofstrand crutches	-
2	16	M	III	1.70	60.06	0.83	0.80	(B) lofstrand crutches	(B) AFO
3	18	M	II	1.70	61.97	0.98	0.90	-	-
4	12	M	II	1.52	42.60	1.07	0.75	-	-
5	12	F	III	1.31	31.60	0.60	0.45	Posterior and Anterior Walkers	-
6	13	F	II	1.44	42.53	0.90	0.80	-	-

The group of physical therapists used subject specific gait deviations and changes in gait variables necessary to produce more typical walking to establish the goals of the stimulation program. Table 3.4 outlines the goals associated with each subject's stimulation program and if the goal was achieved during FES-assisted walking. The goals aimed to improve several parameters of gait; however, only the goals associated with sagittal plane kinematics were evaluated. The joint angles during the no stimulation and stimulation conditions were compared to determine the effectiveness of the stimulation program in achieving the sagittal plane kinematic goals. Improvements varied between subjects. Reducing knee flexion during stance, however, was achieved with several stimulation programs. There was increased knee extension during loading response and midstance in 4 and 5 out of 6 subjects, respectively.

Joint angle plots illustrate the magnitude and periods of the change in the lower extremity kinematics during FES-assisted walking at the ankle, knee, and hip when compared to the no stimulation condition for each of the 6 subjects (Appendix C). During FES-assisted walking, improvements in lower extremity kinematics were typically observed during the beginning of the stance period or the end of the swing period. Reduced hip flexion angles were observed at the beginning of the stance period for Cases 2, 3, and 6; stimulation created increased hip flexion during the swing period in Cases 1, 3, 4, 5, and 6 (Figure C.3). Knee angles were improved during loading response and midstance in Cases 1, 3, 5, and 6 and during midstance in Case 2. Knee flexion was also reduced during terminal swing in Cases 1, 5, and 6 (Figure C.2). Ankle angles were improved during loading response and midstance in Cases 3, 5, and 6; during initial swing, ankle angles were also more typical bilaterally in Case 1, on the left side in Case 4, and on the right side in Case 5 (Figure C.1).

Individualized stimulation programs created changes in the lower extremity kinematics of six individuals with CP and a reduction in knee flexion angle during the beginning of the stance phase was an improvement observed in multiple individuals.

Table 3.4: The group of physical therapists established important modifications in gait to improve walking in the participants. Goals for each subject were determined based on their gait deviations. Changes in lower extremity kinematics were used to determine if each goal of the sagittal plane kinematics was achieved during FES-assisted walking. Additional goals, such as kinetic improvements, were included in the stimulation programs but the outcomes were not determined. √: goal for the subject. +: walking with stimulation created an improvement in the joint angle and the goal was achieved; 0: the stimulation did not change the subject's joint angle and the goal was not achieved; -: walking with stimulation created a joint angle that was more deviated than the no stimulation condition and the goal was not achieved. In some cases, the left and right sides responded differently, therefore, 2 symbols are listed. The left symbol corresponded to the response of the left side and the right symbol corresponded to the response of the right side. *N/A* not applicable, *LR* Loading response, *Mst* Mid-stance, *Tst* Terminal stance, *PSw* Pre-swing, *ISw* Initial swing, *MSw* Mid-swing, *TSw* Terminal swing

Goal		*Case*											
		1		2		3		4		5		6	
Sagittal Kinematic	Gait Phase	Desired	Achieved	Desired	Achieved	Desired	Achieved	Desired	Achieved	Desired	Achieved	Desired	Achieved
Increased Hip Extension during Stance	LR		0|-				0|+				+|-		+
	Mst	√	0			√	0			√	+|-	√	+
	Tst		-				0				0|-		0
Increased Knee Extension during Stance	LR		+		-		+		-		+		+
	Mst	√	+	√	+	√	+	√	-	√	+	√	+
	Tst		+|0		-|+		+		0|+		+|0		0
Increased Knee Flexion at end of Stance	PSw			√	0|+								
Increased Knee Extension at end of Swing	TSw					√	-					√	+|0
Increased Dorsiflexion during Swing	ISw		+		-		-		-|0		-		0
	MSw	√	+	√	-	√	-	√	-|+	√	-	√	-
	TSw		+		-|0		-		+		-		-|0
Additional													
Increased push-off power		√	N/A	√	N/A	√	N/A	√	N/A	√	N/A	√	N/A
Assist in forward leg progression during stance period				√	N/A								
Increased Hip External Rotation during Stance				√	N/A			√	N/A				
Increased Stability during Stance						√	N/A			√	N/A		

3.5 Discussion

The FES system was deployed as a wearable device during walking in subjects with CP. The different phases of gait were detectable and used to trigger stimulation to the targeted muscle groups prescribed for each individual. The different stimulation programs created for each subject illustrates the variation in the gait of individuals with CP and the muscle groups deemed by the group of therapists to best address these deviations. When given the option, the therapists chose proximal muscle groups, such as the gluteals and the quadriceps, as well as the plantarflexors and dorsiflexors, which are more commonly targeted with FES, to correct gait deviations. Commercially available systems, such as the WalkAide System (Innovative Neurotronics, Reno, NV, USA) and Odstock Dropped Foot Stimulator systems (Biomedical Engineering and Medical Physics, Salisbury, UK), are designed with only one or two stimulation channels; limiting the gait deviations that can be addressed with FES. The hamstring muscle group was also an available option; however, it was only included in the stimulation program for Case 2. Targeting the hamstrings to promote trailing limb angle were suggested as secondary strategies in Cases 1, 3, 5, and 6 but not used because, based on visual observation, stimulation to this muscle group during the swing period typically restricted the leg from forward progression. With the flexibility to pick and choose the muscle groups to target and test, the custom FES system successfully provided more options for the therapist to customize the stimulation program.

Additionally, the system's ability to detect 7 phases of gait increased the timing control of the delivery of stimulation and provided therapists with the option to turn stimulation on/off during different phases of the swing period. FES systems in the literature had not been able to distinguish the different gait phases that occur during swing; limiting the FES system's capability of controlling stimulation during this

period. For previous studies targeting only the plantarflexors and/or dorsiflexors[95,104,112], less distinction of the gait phases was needed to provide sufficient timing control. However, when additional muscle groups, such as proximal muscles, were added to the option of targeted muscle groups, greater control was necessary for the therapist to prescribe appropriate timing of stimulation. The group of therapists utilized this feature of the custom FES system when determining the timing of the gluteals and quadriceps for the individualized stimulation programs. Stimulation to these muscle groups was initiated later in the swing period during the midswing or terminal swing phases.

Another feature that was utilized when designing the stimulation program for Cases 2 and 4 was the ability to deliver different levels of stimulation to the same muscle group during different times of the gait cycle. This provided the level needed to create a functional movement as well as the level needed to assist in controlling the limb without restricting the movement. For example, in both Cases 2 and 4, a functional level of stimulation to the plantarflexors was used during Tst and PSw to promote pushoff while a reduced level of stimulation was used during Mst to assist in controlling the progression of the shank over the foot without restricting the motion. Only two levels of stimulation for each muscle group were used for this study, however, for each muscle the FES system supported the programming of different pulse durations for each phase of gait. The current is also programmable for each muscle group. These FES system features gave the therapists the opportunity to adjust the stimulation programs based on the individual's gait deviations as well as the subject's response to FES.

Six individualized FES programs, with unique sets of goals, were able to be prescribed by the group of therapists. The FES programs were tailored to each of the subject's gait deviations and adjustments were made based on the subject's response to the stimulation when trialed during walking. For example, in Case 3, the quadriceps had

to be removed from his prescribed stimulation program even though it would address some of his gait deviations because targeting this muscle group caused the subject's knees to lock out. Adjustments to the prescribed stimulation program was based on visual observation of the immediate responses to FES and there was no prior training with the FES system. The application of FES during walking was a novel task for all subjects.

All participants were able to walk with the FES system and tolerate stimulation that targeted multiple muscle groups. However, time was required to adjust to walking with the FES system. The participants' movements initially appeared robotic but over a brief acclimation period of 30 seconds became more natural. All six cases demonstrated immediate effects were made to the hip, knee, and ankle angles when muscle groups were targeted during FES-assisted walking. Attainment of the goals associated with the stimulation programs and joint angle plots illustrated that improvements varied between subjects and that different portions of the gait cycle were effected when using FES.

Although each subject exhibited different gait deviations and responses to FES, two subjects (Case 5 and Case 6) had similar stimulation program goals and showed achievement of the goals during similar portions of the gait cycle. During FES-assisted walking, increased hip extension was achieved bilaterally in Case 6 and on the left side in Case 5, increased bilateral knee extension was achieved in both subjects, and although neither subject achieved the goal of increased dorsiflexion during swing, both subjects demonstrated more typical ankle angle.

The subject in Case 5 was the most limited walker out of the six participants and gait phase detection was difficult when walking without FES. However, when FES was applied the seven phases of gait were clearly detected based on visual observation. She showed large improvements in her knee and ankle angles when walking with FES; there

was a >20° reduction in knee flexion angle at initial contact. On the left side, there was increased hip and knee extension and ankle plantarflexion during loading response and midstance which suggested that she was in a more supported position. Extension in the left leg also provided the opportunity for clearance of the right foot during swing. Similar improvements were seen in the right knee angle and ankle angles; the right ankle demonstrated typical angles during midstance.

The subject in Case 6 had high level walking function; she did not require assistive devices and it took her a very short time to adjust to walking with the stimulation. Of note, by the end of the minute trial her walking was so smooth that it wasn't obvious the stimulation was being applied until the system was turned off and her gait deviations returned. She demonstrated bilateral improvements in hip and knee flexion angles as well as a decrease in ankle dorsiflexion during loading response and midstance. Similar to Case 5, this suggested that her ipsilateral limb was more supported during the stance period and the increased extension provided more room for foot clearance on the contralateral side. The improvements in Cases 5 and 6 demonstrated that individuals with different levels of ability may benefit from FES-assisted walking when it is designed for the individual's needs.

Similar improvements were produced in knee angle in Cases 1, 5, and 6, when compared to the literature, even though targeting the quadriceps was prescribed at different times in the gait cycle. In the literature, improvements in knee angle during initial contact and midstance were used to quantify the changes created when stimulating the quadriceps during walking. Van der Linden et al. reported reduced knee flexion at initial contact in 2 out of the 4 participants when the quadriceps were stimulated from initial contact through loading response[96]. In the case study by Khamis et al., the subject showed increased knee maximal extension at mid-stance when the

quadriceps were stimulated from initial contact to pre-swing[114]. The knee angle plots illustrated that increased knee extension was achieved towards the end of terminal swing and maintained through midstance, similar to the literature, in Cases 1, 5, and 6. However, the timing of the delivery of stimulation to the quadriceps varied between the 3 subjects. In Case 1, stimulation was applied only during TSw; in Case 5, stimulation was applied from LR through Mst; and in Case 6, stimulation was applied from MSw through LR. Achieving similar improvements in knee angle with variations in the timing of the delivery of stimulation to the quadriceps suggests that tailoring the stimulation program to the individual is necessary to account for the differences in gait deviations and subject responses that cannot be addressed with a one size fits all program.

Conversely, in Case 4 the subject did not have a positive response to his prescribed stimulation program. The subject had a high level walking function and tolerated the FES; however, there was minimal improvement in his joint angles. Joint angles illustrate that, at best, there was no improvement, and at worst, the use of FES increased joint angle deviation compared to typical gait. When FES was applied, he continued to walk but in a more crouched posture; represented in the increased flexion in the hip and knee angle, bilaterally. Additional training with FES may have alleviated the subject's immediate reponse to crouch.

For all six participants, the FES system was programed with individualized stimulation programs that targeted a unique combination of muscle groups and gait phases based on the goals hypothesized to improve the subject's gait. The FES system was able to be used as a wearable device during walking and FES-assisted walking promoted immediate kinematic changes in individuals with CP.

Although the FES system was developed and deployed to individualize the dosing and timing of FES during walking, there were several limitations in Aim 2. The

protocol to determine the optimal muscle combination and stimulation parameters is an iterative process; kinematic outcomes may improve with multiple thresholding sessions to identify the ideal parameters for each muscle group. Additionally, multiple thresholding sessions would provide more feedback to the physical therapists for modifying the stimulation program; potentially enhancing the individualized algorithm. Kinematic outcomes may show more improvements with different stimulation parameters. Although changes were created in the joint angles, some of these changes were exaggerated, i.e. some cases showed hyperextension at the knee during mid-stance and/or excessive plantarflexion during the swing period. Different stimulation parameters have the potential to resolve 'overshooting' the targeted joint angles (TD).

The timing of the delivery of stimulation was a factor that may have contributed to reduced improvements in kinematics. The current FES system was designed to allow the therapists to alter the timing of FES based on each gait phase; the therapists were not able to set additional delays for specific muscles. However, the sophistication of the system allows for future customization of variable phase delays which can be trialed to determine if the timing of the stimulation was influencing the magnitude of the kinematic changes.

The variables used to assess the benefits of different stimulation conditions when walking with FES were chosen based on the method used to define gait patterns in CP. The sagittal hip, knee, and ankle angles are used to identify different gait patterns; therefore, the hip, knee, and ankle angles were evaluated with the assumption that improved joint angles would result in improved gait. Although the kinematics illustrated the changes created with the use of FES, corresponding kinetic and spatiotemporal parameters would provide more insight into understanding why kinematic changes occurred and may demonstrate additional improvements in gait. Furthermore, the

combination of the kinematic and kinetic data would help demonstrate the advantages of using FES to achieve proper limb positioning.

Another limitation was the limited amount of practice the participants received. FES-assisted walking was an unfamiliar task and subjects were given a brief acclimation period of 30 seconds to capture the immediate novel effects of FES. Some of the subjects reacted to the FES and changed their walking patterns instead of letting the system enhance their steps. Longer acclimation periods and repeat sessions to fine tune the FES may create greater changes toward typical, however, learning then becomes an issue with assessment. With additional practice, it may become difficult to differentiate the changes created by FES and the changes created from learning. This aim is part of a larger study where the FES system is used in a walking intervention; assessing the kinematics while walking, with and without stimulation, at the end of training may provide more insight into the neuroprosthetic effects produced when using the FES system during walking.

In general, there is a paradigm shift in the way FES systems are being utilized. These systems are not only being used as neuroprosthetic devices but also implemented into exercise and learning paradigms to promote functional carry over. Further development of the FES system may contribute to greater improvements in kinematics during walking and should focus on the additional customization to the timing of the delivery of stimulation. The use of joint angle feedback may enable real-time modifications to stimulation parameters to compensate for gait deviations resulting from muscle fatigue during FES walking training programs. Additionally, replacement of the stimulators with a wireless system will create a tether-free FES system that can easily be used in different environments.

3.6 Conclusion

The FES system was effectively used during walking in individuals with CP and the lower extremity kinematics were altered when stimulation was applied during FES-assisted walking. The features of the FES system provided therapists with the flexibility and more options, such as proximal muscle groups, to generate subject specific stimulation patterns based on the subject's gait deviations. The ability to easily modify the muscle groups targeted, current and pulse duration of the stimulation signal, and timing of the stimulation allowed further customization during testing to account for the subject's response to FES. All subjects tolerated stimulation to multiple muscle groups during walking and the changes in joint kinematics varied between individuals. Additional practice walking with the FES system may produce further improvements in the kinematics. Future FES-assisted walking interventions should consider prescribing custom tailored stimulation algorithms to address the individual's gait deviations in an effort to produce more typical gait.

Chapter 4

CONCLUSIONS

Functional electrical stimulation, when used as a neuroprosthetic device during walking, has facilitated immediate gait improvements in children with cerebral palsy[91,93,95–97,99,121,133]; however, evidence of the benefits associated with targeting multiple muscle groups, including proximal muscles, were limited[115]. Existing FES systems[95,96,99,104,112,114,142], typically confined to one or two muscle groups, did not provide sufficient timing control over the delivery of stimulation or number of stimulation channels necessary to carry out an investigation of multiple muscle group stimulation during ambulation. The overall goals of this dissertation, accomplished in Aims 1 and 2, were to develop an FES system with increased resolution and flexibility to target individual or multiple muscle groups with stimulation and to utilize this device during walking in individuals with CP to assess feasibility of generating and implementing individualized stimulation programs and its effects on lower extremity kinematics.

The multichannel FES system, capable of stimulating 10 lower extremity muscles during the gait cycle, was successfully developed by combining a sensor system that provided increased finite-state control over the delivery of stimulation with two 6-channel stimulators. The greater level of differentiation of the gait cycle in the sensor system, compared to the literature[103,106], allowed for more timing control over the trigger to the stimulators; resolving potential timing issues when incorporating proximal muscles of the lower extremity into the stimulation algorithm. Gait phase detection and

duration of the sensor system were validated against the desired timing derived from the 'gold standard' and demonstrated that the sensor system was reasonably accurate. The system met the requirements established in Hypothesis 1.1 for average gait duration RMSE; however, the average gait detection RMSE was close to, but did not meet, the benchmark measure. Compensations made to the timing of the stimulation trigger accounted for the gait detection RMSE difference that exceeded Hypothesis 1.1.

Delivery of stimulation was most accurate when a compensation of 50% delay was added to the pre-trigger; the benchmark measure in Hypothesis 1.2 was satisfied. Additionally, the FES system had the flexibility to stimulate different combinations of muscle groups which allowed us to address novel questions regarding FES-assisted walking. The FES system supported manual modulation of the stimulation level by allowing distinct stimulation parameters to be programed for each individual, muscle group, and gait phase. This modulation produced stimulation levels that were more representative of typical muscle activity[128] than constant levels of stimulation. The validation of gait phase detection and timing of the delivery of stimulation demonstrated that the FES system can accurately be used as a device for assisting gait.

In Aim 2, the FES system was successfully deployed during walking in individuals with CP and the system was able to detect different phases of gait and trigger stimulation to the muscle groups prescribed by the group of physical therapists, accomplishing Hypothesis 2.1. The prescribed stimulation programs were created to reduce subject specific gait deviations by identifying the muscle groups to stimulate, the gait phases to apply stimulation, and the level of stimulation needed to achieve the goals associated with typical walking. When given the option to target proximal muscle groups, such as the gluteals and the quadriceps, as well as the plantarflexors and dorsiflexors, the therapists chose to add the proximal muscle groups to the stimulation

programs to improve more gait deviations; addressing a limitation of the commercially available FES systems. The custom FES system also provided the therapists with more control over the timing of the delivery of stimulation, allowing them to turn the stimulation on/off at each phase of gait, and the ability to program the pulse duration for each muscle group and gait phase. With the flexibility to pick and choose the stimulation settings, the custom FES system successfully provided more options for the therapist to customize the stimulation program.

All participants were able to walk with the FES system and tolerate stimulation that targeted multiple muscle groups. However, time was required to adjust to walking with the FES system. The participants' movements initially appeared robotic but over a brief acclimation period of 30 seconds became more natural. Hypothesis 2.2, stating that FES will have immediate effects to the sagittal hip, knee, and ankle angles when muscle groups are stimulated using individualized stimulation programs during FES-assisted walking was found to be true; all six cases demonstrated immediate changes were made to portions of the hip, knee, and ankle angles. Attainment of the goals associated with the stimulation programs, however, were not always achieved and joint angle plots illustrated that improvements varied between subjects and that different portions of the gait cycle were effected when using FES.

Although a greater number of study participants are needed to formulate general conclusions about the effects of utilizing individualized FES programs to improve lower extremity kinematics during walking, the case series in Aim 2 provided examples of some of the potential benefits of customized FES programs. One example was the ability to achieve similar improvements in knee angle with variations in the timing of the delivery of stimulation to the quadriceps; suggesting that tailoring the stimulation program to the individual is necessary to account for the differences in gait deviations

and subject responses that cannot be addressed with a one size fits all program. Additionally, individuals with different levels of ability may benefit from FES-assisted walking when it is designed for the individuals' needs, such as in the improvements observed in Cases 5 and 6. Overall, the FES system was able to be used in a population with atypical gait and individualized stimulation programs were able to correct some of the gait deviations observed in the individuals with CP.

This dissertation work contributes to FES walking and CP intervention efforts by demonstrating benefits of utilizing a FES system with the flexibility to customize the stimulation program to the individual's needs and the changes observed in kinematics when individualized stimulation programs are used during FES-assisted walking; additional analyses that would further strength these results are: (1) evaluation of the lower extremity kinematics during walking with individualized stimulation programs compared to a standardized stimulation program, (2) kinetic parameters, and (3) spatiotemporal parameters. These measures would provide more insight into the changes that occur when muscle groups are stimulated during walking and the benefits of customized stimulation programs.

Further development of the FES system may contribute to greater improvements in kinematics during walking and should focus on increasing control over the modulation in stimulation parameters. The current system allows different stimulation parameters to be manually programmed for each muscle group and gait phase; however, exaggerated movements were observed in some of the walkers with the use of stimulation. The use of joint angle feedback to modulate stimulation may reduce overcorrection. Monitoring joint angles may also enable real-time modifications to stimulation parameters to compensate for gait deviations resulting from muscle fatigue. Additionally, replacement of the stimulators with a wireless system will create a tether-

free FES system that can easily be used in different environments. The current FES system is also adaptable; the system control (sensor system) is independent of the stimulators, therefore researchers can add more stimulators to increase the number of channels and still utilize the sensor system to trigger stimulation accordingly.

Additional investigations that can utilize the current FES system are the effects of targeting other combinations of muscle groups that were not included in the current study, such as the plantarflexors and dorsiflexors, and the effects of individual or multiple muscle group stimulation. Moreover, the individualized approach used in Aim 2 may aid in the development of FES-assisted walking interventions in CP that produce greater improvements than the interventions that standardize the muscle groups targeted.

Although this preliminary study shows that the majority of subjects (5 out of 6) have immediate lower extremity kinematic benefits during FES-assisted walking, collecting clinical measures, in conjunction to the gait analysis in a larger population, may provide more insight into the muscle groups that produce the greatest benefits when targeted. The addition of clinical measures can also be used to investigate if there are characteristics that will indicate whether a subject will have a positive response to walking with FES or not. Additionally, the development and evaluation of a FES walking training intervention can demonstrate if FES is capable of creating neurotherapeutic changes in children with CP; with the potential for a clinically deployable FES-assisted walking training regimen. Lastly, combining neuroimaging techniques, such as fNIRS, with FES-assisted walking or an FES-assisted walking training protocol can provide insight into the changes occurring in cortical activity with the use of FES. Moreover, a better understanding of the way that FES facilitates

functional improvements in children with CP will help direct research and interventions in an effort to improve overall quality of life in these individuals.

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Appendix A

STIMULATION THRESHOLDING

Stimulation thresholding refers to the process used to determine subject specific stimulator settings needed to produce a functional response for each muscle. A charge-balanced bi-phasic waveform was used for stimulation. Stimulation frequency was set at 40 Hz.

Baseline Stimulation Parameters

First, the subject specific stimulation amplitude and pulse duration needed to produce a motor threshold response for each muscle group included in the individualized stimulation program was determined. These settings established the 'baseline' stimulation parameters which were fine-tuned by determining the parameters needed to produce the functional response. The stimulation amplitude was initially set to 30 mA and the pulse duration needed to produce a response was determined by ramping up the pulse duration until a response was observed at each muscle while the subject was standing in a neutral position with weight distributed equally between two feet.

If the pulse duration reached 250 microseconds (μs) without a muscle response being observed, the stimulation amplitude was increased by 10 mA and pulse duration was reevaluated. These steps were repeated until the stimulation amplitudes and pulse durations (less than 250 microseconds) that produce a muscle response at each of the muscle groups included in the individualized stimulation program, bilaterally, were determined. The reason the amplitude was increased before the maximum pulse

duration capabilities of the stimulator were met was to ensure that the pulse duration did not reach maximum when fine tuning during the following steps of stimulation thresholding.

Fine Tuned Stimulation Parameters

The stimulation amplitude and pulse duration, determined during baseline stimulation thresholding, were set as the initial value for determining the necessary pulse duration needed to create a concentric muscle contraction and functional movement in the leg. The functional level stimulation settings were established for each muscle group included in the individualized stimulation program based on the goal associated with the position and joint (Figure A.1). The stimulation thresholding flow chart (Figure A.1) indicates: the general position the subject was evaluated in, the joint that was observed when thresholding, the muscle group that was targeted, a secondary position (if indicated), and the goal of the stimulus; which was used to determine the current amplitude and pulse duration. The physical therapist used clinical judgment to decide if the overall goals were met. The general positions the subject stood in were: (1) standing, defined as a neutral standing position unless a secondary position was identified, and (2) single leg standing, defined as a stable standing position on the leg that was not being evaluated while the opposite leg was non-weight bearing. Stimulation thresholding was performed, for the muscle groups of interest, from the left to the right of the flow chart, in standing and followed by single leg standing, for the (1) hip, (2) knee, and (3) ankle on the right side followed by the left side. If subjects were not able to achieve a stable single leg standing position, a side lying position was used when evaluating pulse duration. The pulse duration was increased, in small increments (~5 μs), until the goal associated with the muscle group was achieved or the subject's maximum tolerance was reached. If the subject was not able to tolerate any level of

stimulation and still wanted to participate, numbing cream (EMLA cream) was available to apply to the skin at the location of the electrodes for electrical stimulation. If numbing cream (EMLA cream) was not able to provide enough relief to the subject, the muscle group was excluded from all stimulation conditions. If a pulse duration of 500 microseconds did not achieve the goal associated with the muscle group, outlined in Figure A.1, the amplitude was raised by 10 mA and the pulse duration level was reevaluated. The amplitude continued to be raised by 10 mA and the pulse duration continued to be reevaluated until the functional movement was achieved.

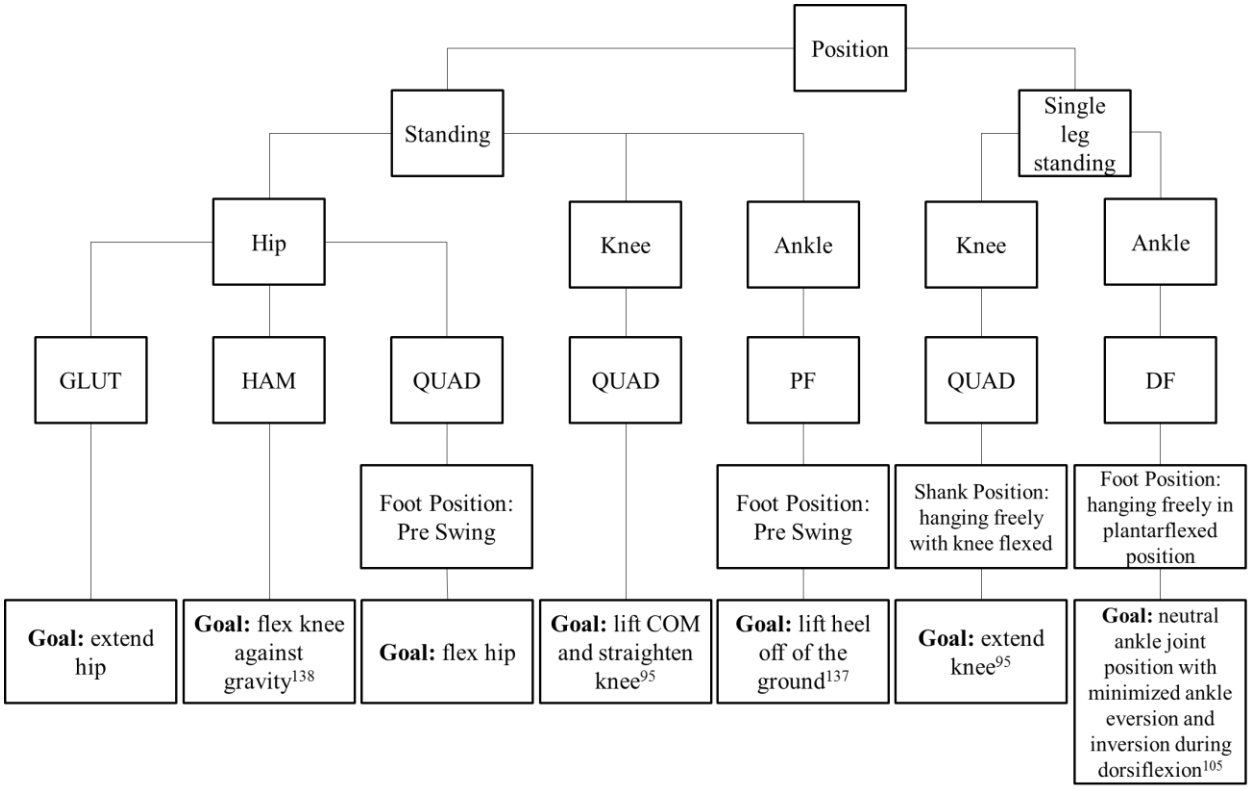

Figure A.1: The stimulation thresholding flow chart indicates the position the lower extremity joints were tested in, the muscle groups associated with each joint, and the goal associated with the position/joint/muscle group. These were the criteria used to set the stimulation pulse duration. A secondary position was noted for some of the joints and muscle groups to position the limb correctly for specific phases of the gait cycle. *PF* Plantarflexors[143], *DF* Dorsiflexors[107], *QUAD* Quadriceps[96], *HAM* Hamstrings[144], *GLUT* Gluteals, *COM* center of mass.

For the quadriceps, three different stimulation thresholds were outlined in Figure A.1, however flexion at the hip was unattainable with stimulation to the quadriceps when the foot was placed in pre-swing position for all subjects. This finding was not surprising because the psoas major and iliacus muscles are too deep to be comfortably reached with transcutaneous electrodes. Although a portion of the electrode was on the

distal rectus femoris, we did not try to preferentially recruit the rectus femoris separate from the remaining quadriceps. The values for the quadriceps associated with meeting the goals of (1) lifting the COM and straightening the knee, and (2) extending the knee were incorporated into the software for the associated gait phases (i.e. the pulse duration that creates a lift in the COM and straightens the knee was used during the mid-stance phase of gait).

Appendix B

INDIVIDUALIZED STIMULATION PROGRAMS

B.1 Case 1

Based on the frontal and sagittal videos, the stimulation program for case 1 was designed to increase push-off power, increase toe clearance during swing period, gain more hip and knee extension during stance period, and help progress the leg forward during stance period. However, the stimulation program was adjusted during the data collection because the subject demonstrated restrictions to leg progression when initial stimulation program was applied. Modifications included applying stimulation to the plantarflexors only during PSw instead of Mst through PSw, excluding the hamstrings from the stimulation program, and activating the quadriceps during TSw instead of LR through Mst (Table B.1).

Table B.1: **S**timulation program for subject in case 1. Red boxes illustrate the gait phases when functional levels of stimulation were applied to the muscle group. The current (mA) was programmed for each muscle group and the pulse duration (μs) was programmed for each muscle group and gait phase. The left and right sides were programmed separately. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

	Case 1								
	Pulse Duration (μs)								**Current (mA)**
	Gait Phase	LR	Mst	Tst	PSw	Isw	MSw	TSw	
Muscle Group	**Side**								
Plantarflexors	Left				250				45
	Right				250				50
Dorsiflexors	Left					250	250	250	50
	Right					250	250	250	55
Quadriceps	Left							405	65
	Right							470	55
Hamstrings	Left								
	Right								
Gluteals	Left		385	385					80
	Right		405	405					90

B.2 Case 2

For case 2, the stimulation program focused on achieving more (1) push-off power (targeting the plantarflexors during stance period), (2) toe clearance during swing period, (3) external rotation at the hip (targeting the gluteals from TSw to Tst), (4) knee extension during stance period, (5) knee flexion during end of stance period (targeting hamstrings from Tst to PSw), and (6) progression of the leg in the forward direction during the end of stance period (Table B.2). A secondary strategy to stimulate the quadriceps from PSw to ISw, to aid in leg progression during the end of stance period, was tested and used. Assessment of the stimulation program indicated that no changes needed to be made and the subject's legs were able to progress through the gait cycle.

Table B.2: **S**timulation program for subject in case 2. Red boxes illustrate the gait phases when functional levels of stimulation were applied to the muscle group. Blue boxes illustrate when reduced levels of stimulation were applied to the muscle group. The reduced levels of stimulation corresponded to 50% of the pulse duration used during functional level stimulation. The current (mA) was programmed for each muscle group and the pulse duration (μs) was programmed for each muscle group and gait phase. The left and right sides were programmed separately. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

	Case 2								
		Pulse Duration (μs)							**Current (mA)**
	Gait Phase	LR	Mst	Tst	PSw	Isw	MSw	TSw	
Muscle Group	**Side**								
Plantarflexors	Left		106	201	201				50
	Right		106	213	213				50
Dorsiflexors	Left					180	180	180	50
	Right					203	203	203	50
Quadriceps	Left	106	211		106				40
	Right	104	208		104				40
Hamstrings	Left			162					40
	Right			210					40
Gluteals	Left	204	102	102				102	50
	Right	252	126	126				126	40

B.3 Case 3

The stimulation program (Table B.3), developed for case 3, targeted the gluteals and quadriceps from Mst to PSw to increase extension at the hip and knee, respectively, during stance period. Additionally, the goal of targeting the gluteals during this time in the gait cycle was to increase stability. The quadriceps were targeted from TSw (functional level) to Mst (reduced level) to aid in leg extension at the end of swing period. The dorsiflexors were active from ISw to LR to increase toe clearance during swing period and the plantarflexors were active from Mst (reduced level) to ISw to increase push-off power. A secondary strategy to target the hamstrings during swing period, in an attempt to improve training limb angle, was suggested but not used. During testing, modifications were made to original stimulation program because the subject showed adverse effects to stimulation of the quadriceps during the stance period of gait. Stimulation to the quadriceps caused his legs to lock in extension, therefore, the quadriceps were only activated during TSw. The plantarflexors were also modified to being active only during PSw.

Table B.3**:** Stimulation program for subject in case 3. Red boxes illustrate the gait phases when functional levels of stimulation were applied to the muscle group. The current (mA) was programmed for each muscle group and the pulse duration (μs) was programmed for each muscle group and gait phase. The left and right sides were programmed separately. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

	Case 3								
	Pulse Duration (μs)								**Current (mA)**
	Gait Phase	LR	Mst	Tst	PSw	Isw	MSw	TSw	
Muscle Group	**Side**								
Plantarflexors	Left				275				35
	Right				250				35
Dorsiflexors	Left					285	285	285	50
	Right					240	240	240	55
Quadriceps	Left							300	55
	Right							275	60
Hamstrings	Left								
	Right								
Gluteals	Left		365	365					90
	Right		285	285					75

B.4 Case 4

Subject 4's stimulation program (Table B.4) consisted of stimulation to the (1) gluteals to target hip external rotation from Mst to PSw, (2) plantarflexors for more push-off power at Mst, using a reduced level of stimulation, which continued during Tst to ISw at a functional level of stimulation, and (3) dorsiflexors, to increase toe clearance, from ISw to LR. If cuing to unlock the left knee was successful, it was suggested that stimulation to the quadriceps may be needed to increase knee extension from LR to Mst; this strategy was implemented. The secondary strategy of stimulating the quadriceps during TSw was not used.

Table B.4: Stimulation program for subject in case 4. Red boxes illustrate the gait phases when functional levels of stimulation were applied to the muscle group. Blue boxes illustrate when reduced levels of stimulation were applied to the muscle group. The reduced levels of stimulation corresponded to 50% of the pulse duration used during functional level stimulation. The current (mA) was programmed for each muscle group and the pulse duration (μs) was programmed for each muscle group and gait phase. The left and right sides were programmed separately. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

	Case 4								
		Pulse Duration (μs)							**Current (mA)**
	Gait Phase	LR	Mst	Tst	PSw	Isw	MSw	TSw	
Muscle Group	**Side**								
Plantarflexors	Left		165	330	330				35
	Right		155	310	310				35
Dorsiflexors	Left					180	180	180	40
	Right					200	200	200	35
Quadriceps	Left	125	250						40
	Right	170	340						40
Hamstrings	Left								
	Right								
Gluteals	Left		300	300					60
	Right		340	340					55

B.5 Case 5

For subject 5, the stimulation program activated the gluteals and quadriceps from LR to Tst to promote extension at the hip and knee. Another goal of activating the gluteals during this time in the gait cycle was to increase stability during weight bearing. Activation of the dorsiflexors from ISw to LR was used to increase toe clearance; the subject dragged her toes a lot. Lastly, activation of the plantarflexors from Mst to ISw was to increase push-off power. Secondary strategies that were recommended were to use (1) a reduced level of stimulation for the dorsiflexors during PSw, (2) reduced level of stimulation for the quadriceps during Mst, and to activate (3) hamstrings to assist knee flexion during swing period, and (4) quadriceps during push-off to provide a stronger lever arm. The secondary strategies were not used. The gluteal muscle group was removed from the stimulation program because subject 5 was not able to tolerate walking with stimulation targeting the gluteals, even with the use of EMLA cream (Table B.5).

Table B.5: Stimulation program for subject in case 5. Red boxes illustrate the gait phases when functional levels of stimulation were applied to the muscle group. The current (mA) was programmed for each muscle group and the pulse duration (μs) was programmed for each muscle group and gait phase. The left and right sides were programmed separately. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

	Case 5								
	Pulse Duration (μs)								**Current (mA)**
	Gait Phase	LR	Mst	Tst	PSw	Isw	MSw	TSw	
Muscle Group	**Side**								
Plantarflexors	Left		230	230	230				30
	Right		325	325	325				35
Dorsiflexors	Left					302	302	302	35
	Right					310	310	310	30
Quadriceps	Left	350	350						35
	Right	350	350						35
Hamstrings	Left								
	Right								
Gluteals	Left								

B.6 Case 6

For subject 6, the stimulation program activated the gluteals from LR to Tst to promote extension at the hip during stance period. The quadriceps were targeted from MSw to Mst for more extension at the knee during the end of swing period and pre-position the leg better for weight bearing. Activation of the dorsiflexors from PSw to Mst was to increase toe clearance and promote heel strike at initial contact; the subject dragged her toes and typically contacted the ground with the mid/fore foot. Activation of the plantarflexors from Tst to ISw was to increase push-off power. The stimulation program is outlined in Table B.6. Secondary strategies that were recommended were to stimulate (1) gluteals through PSw, (2) quadriceps through Mst at a reduced level, (3) quadriceps during push-off to give a stronger lever arm, (4) dorsiflexors during PSw at a reduced level, and (5) hamstrings during PSw to promote trailing limb angle. The secondary strategies were not used.

Modifications were made to the pulse duration of the quadriceps to achieve more extension at the knee; pulse duration was set to 300 μs.

Table B.6: Stimulation program for subject in case 6. Red boxes illustrate the gait phases when functional levels of stimulation were applied to the muscle group. The current (mA) was programmed for each muscle group and the pulse duration (μs) was programmed for each muscle group and gait phase. The left and right sides were programmed separately. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

	Case 6								
	Pulse Duration (μs)								**Current (mA)**
	Gait Phase	LR	Mst	Tst	PSw	ISw	MSw	TSw	
Muscle Group	**Side**								
Plantarflexors	Left			250	250				50
	Right			300	300				35
Dorsiflexors	Left	292			292	292	292	292	50
	Right	225			225	225	225	225	40
Quadriceps	Left	250					250	250	40
	Right	250					250	250	40
Hamstrings	Left								
	Right								
Gluteals	Left	320	320	320					60
	Right	250	250	250					60

Appendix C

LOWER EXTREMITY KINEMATICS

C.1 Average ankle angles during walking with and without FES

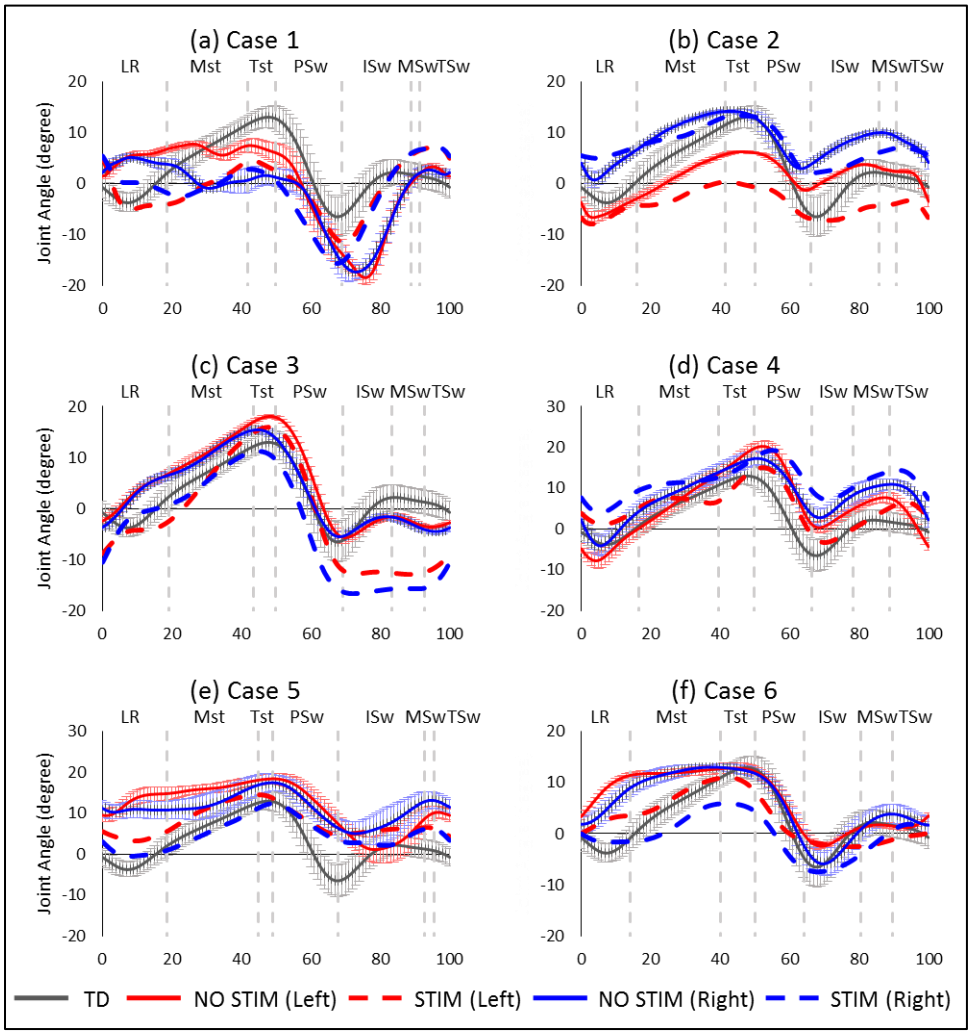

Figure C.1: Left and right average (±STD) ankle angles during the no stimulation condition (NO STIM) were compared to the left and right average ankle angles during walking with the stimulation program (STIM) for each subject. The ankle angles on the left side during NO STIM and STIM walking are represented by the red solid and dashed lines, respectively. The ankle angles on the right side during NO STIM and STIM walking are represented by the blue solid and dashed lines, respectively. The average (±STD) ankle angle of typically developing children, graphed in grey, were used as reference joint angles to determine if the stimulation program produced an improvement in the ankle angle. The grey vertical lines indicate the different phases of the gait cycle for each subject. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

C.2 Average knee angles during walking with and without FES

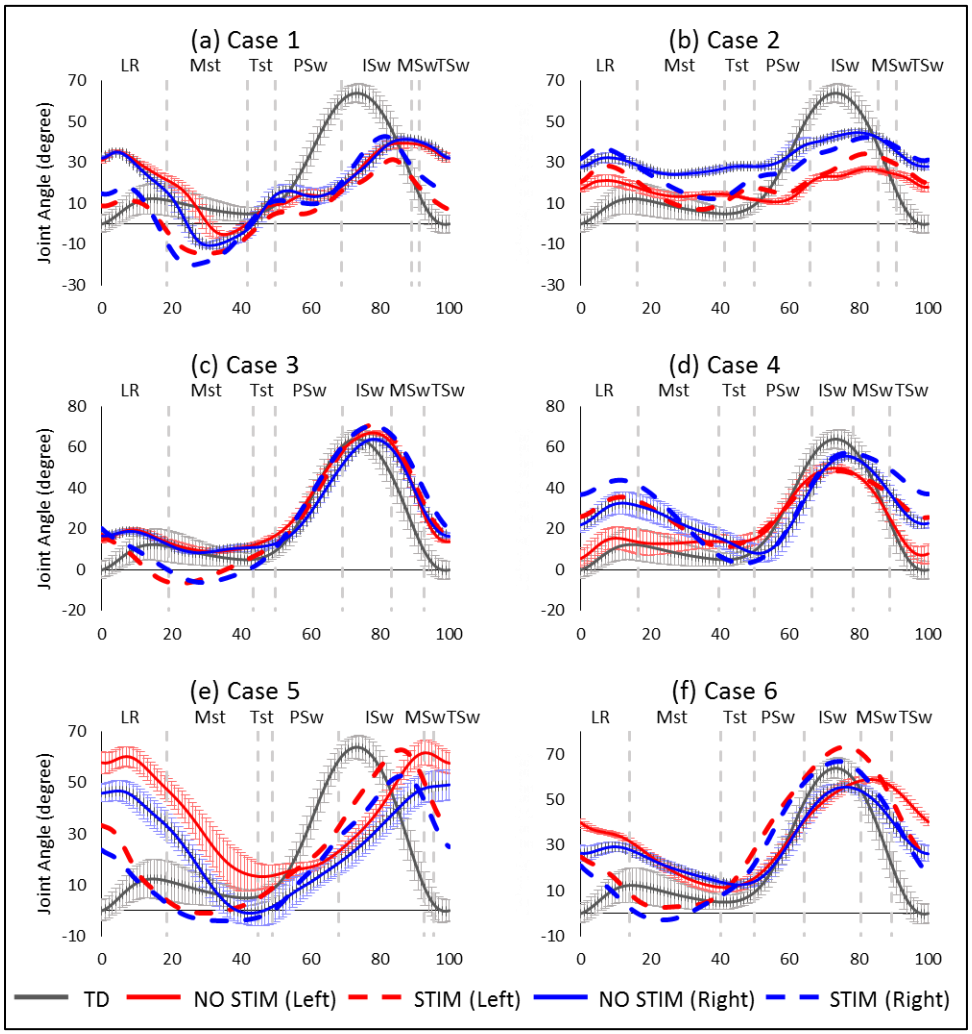

Figure C.2: Left and right average (±STD) knee angles during the no stimulation condition (NO STIM) were compared to the left and right average knee angles during walking with the stimulation program (STIM) for each subject. The knee angles on the left side during NO STIM and STIM walking are represented by the red solid and dashed lines, respectively. The knee angles on the right side during NO STIM and STIM walking are represented by the blue solid and dashed lines, respectively. The average (±STD) knee angle of typically developing children, graphed in grey, were used as reference joint angles to determine if the stimulation program produced an improvement in the knee angle. The grey vertical lines indicate the different phases of the gait cycle for each subject. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

C.3 Average hip angles during walking with and without FES

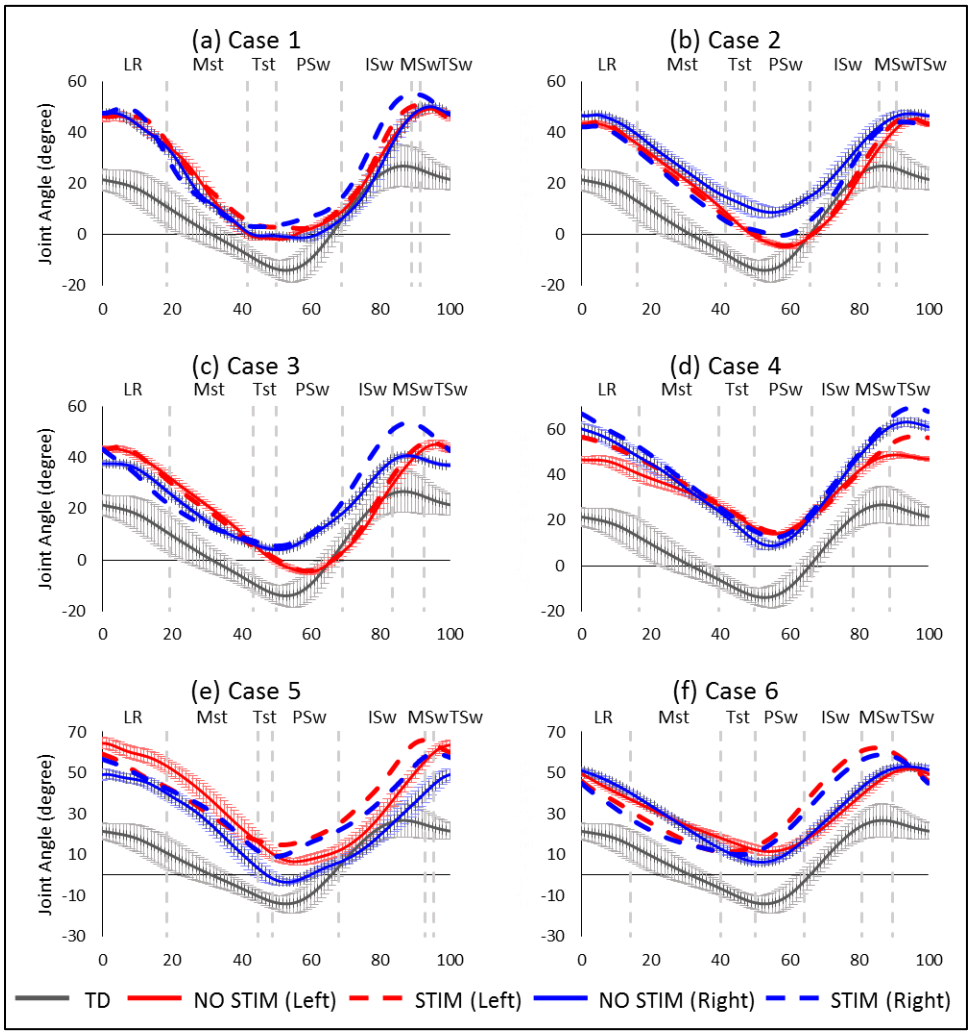

Figure C.3: Left and right average (±STD) hip angles during the no stimulation condition (NO STIM) were compared to the left and right average hip angles during walking with the stimulation program (STIM) for each subject. The hip angles on the left side during NO STIM and STIM walking are represented by the red solid and dashed lines, respectively. The hip angles on the right side during NO STIM and STIM walking are represented by the blue solid and dashed lines, respectively. The average (±STD) hip angle of typically developing children, graphed in grey, were used as reference joint angles to determine if the stimulation program produced an improvement in the hip angle. The grey vertical lines indicate the different phases of the gait cycle for each subject. *LR* Loading response *Mst* Mid-stance *Tst* Terminal stance *PSw* Pre-swing *ISw* Initial swing *MSw* Mid-swing *TSw* Terminal swing.

Appendix D

INSTITUTIONAL REVIEW BOARD

UNIVERSITY OF DELAWARE
RESEARCH OFFICE

210 Hullihen Hall
University of Delaware
Newark, Delaware 19716-1551
Ph: 302/831-2136
Fax: 302/831-2828

DATE: March 1, 2016

TO: Samuel Lee, PT, PhD
FROM: University of Delaware IRB

STUDY TITLE: [422073-5] Functional Electrical Stimulation to Improve Crouch Gait in Cerebral Palsy

SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: March 1, 2016
EXPIRATION DATE: February 26, 2017
REVIEW TYPE: Administrative Review

Temple is the the IRB of record

Thank you for your submission of Continuing Review/Progress Report materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Administrative Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.