MUSCLE ACTIVITY IN
UPPER EXTREMITY AMPUTEES

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ABSTRACT

Purpose – Three interdependent studies designed as preliminary investigations of phantom and prosthetic limb control in upper extremity amputees. The purpose was to (1) compare muscle activation patterns of the phantom limb to anatomically expected patterns (2) compare muscle activation patterns of the phantom limb and those used to control a prosthesis (3) compare the use of upper arm muscle activity in phantom limb movements between users of different types of prosthetic devices. These studies aimed to expand the understanding of the role of the peripheral nervous system in movements of phantom and prosthetic limbs.

Methods – Fifteen participants with varying levels of upper extremity amputations participated. Kinesiologic EMG (surface/fine wire) was utilized to examine residual limb muscle activation patterns during movements of the phantom and prosthesis. A series of phantom movements based on level of amputation were executed. After completing phantom limb movements participants donned their prosthesis and completed movements of the device. Muscles were considered active when the threshold of activity exceeded two standard deviations above rest trial. Visual analysis of EMG activity and goodness of fit Pearson Chi-Square tests were used to examine frequency occurrences in muscle activation patterns.

Results –The majority of muscle activation patterns for the completion of phantom limb movements, regardless of the level of amputation, varied from anatomically expected muscle activation patterns. The majority of participants also used different muscle activation patterns to control similar movements of the phantom limb and prosthetic device. Finally, muscle activation patterns to control the movement of a phantom hand were different based on the type of device participants used, with body-powered prosthetic users activating muscles of the upper arm more frequently than myoelectric prosthetic users.

Significance – This dissertation was a preliminary study into novel theories regarding phantom and prosthetic control. Results emphasize a dire need for future research to explore the injury response of the PNS, how this impacts phantom limb experiences, how these changes impact or is impacted by the CNS, and how to utilize the body's natural response to injury to enhance control and function of prosthetic devices.

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DEDICATION

This dissertation is dedicated to everyone living with limb loss, especially those who personally participated in my research. Without the many individuals who volunteered not only their time, but also their experiences, this project could not have been completed. Thank you for your time, your knowledge, your stories, the friendships, and most importantly your immense support. I sincerely hope that this dissertation expands the field of research to provide you with the advancements that you all so highly deserve. The connections formed throughout my years of research have enhanced my life in more ways than I ever imagined. Thank you again for your interest in research and your support in me.

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LIST OF ABBREVIATIONS

PLS – Phantom Limb Sensation

PLP – Phantom Limb Pain

PLC – Phantom Limb Control

CNS – Central Nervous System

PNS – Peripheral Nervous System

UMN – Upper Motor Neuron

LMN – Lower Motor Neuron

PMR – Preferential Motor Re-innervation

DMN – Direct Muscular Neurotinization

TMR – Targeted Muscle Re-innervation

GLOSSARY OF TERMS

Axon – or nerve fiber, long slender projection of a neuron that conducts action potentials to muscles (Javed & Lui, 2019)

Direct Muscle Neurotinization (DMN) – denervated muscles lose neuromuscular junctions, causing the entire muscle to become sensitive to acetylcholine (ACh), allowing nerves to re-innervate the muscle at any location (G. Brunelli & Monini, 1985)

Endoneurial Tube – layer of delicate connective tissue around the myelinated sheath of each myelinated nerve fiber in the peripheral nervous system (Peters, Palay, & Webster, 1991)

Lower Motor Neuron (LMN) – located within the PNS, connects the CNS to the muscles required for movement (Javed & Lui, 2019)

Motor Control - initiation and direction of purposeful and voluntary movements (Roller, Lazaro, Byl, & Umpherd, 2013)

Motor Learning - internal process of obtaining new motor skills, through practice and incorporation, resulting in the automaticity of a desired movement (Nieuwboer, Rochester, Müncks, & Swinnen, 2009)

Motor Skill - coordinated muscle movements (Haibach, Reid, & Collier, 2017)

Phantom Limb - the sensation that the amputated or missing limb is still present (Herta Flor et al., 1998)

Phantom Limb Control (PLC) - purposeful, directed, and intentional movements completed by at least a portion of the limb that is no longer physically present (Brodie, Whyte, & Niven, 2007)

Preferential Motor Re-innervation (PMR) - growing motor axon terminals preferentially re-innervate motor branches while sensory axons favor sensory branches (Brushart, 1988)

Regeneration – after injury re-growing axon terminals find their original endoneurial tubes and reconnect with their original end organ (Fawcett & Keynes, 1990)

Re-innervation – after injury re-growing axon terminals enter incorrect endoneurial tubes and are guided to inappropriate end organs (Brushart, 1988)

Schwann Cell – cells within the peripheral nervous system that produce the myelin sheath around neuronal axons (Navarro et al., 2005)

Targeted Muscle Re-innervation (TMR) –the transferring of remaining arm nerves to the chest, or other biomechanically irrelevant muscles, after amputation, to enhance prosthesis control (T A Kuiken, Dumanian, Lipschutz, Miller, & Stubblefield, 2004)

Upper Motor Neuron (UMN) – located within the CNS, transmit impulses from the cortex to the spinal cord where they synapse with LMNs (Javed & Lui, 2019)

Wallerian Degeneration - the removal and recycling of debris produced after injury to a nerve (Fawcett & Keynes, 1990)

CHAPTER 1: INTRODUCTION

Canada has reported more than 200,000 people currently living with amputation in the country, while the United States reports more than 2.8 million citizens with amputation ("Disability Tax Credit for Amputees: What makes you eligible?," 2017). In the United States alone 185,000 amputations occur each year (Kozak & Owings, 1998). Due to diseases, traumas, and congenital abnormalities, the number of amputations is predicted to double by 2050 (Ziegler-Graham, MacKenzie, Ephraim, Travison, & Brookmeyer, 2008).

Amputation, the loss, removal, or incomplete formation of part or all of an extremity, cause changes to occur within both the peripheral nervous system (PNS) and the central nervous system (CNS) (Herta Flor, 2002). The concurring changes, within both areas of the nervous system, can result in the perception of a phantom limb. Phantom limb sensation (PLS) is the phenomena experienced by a person with an amputation that the amputated or missing limb is still present (Herta Flor, 2002; Herta Flor et al., 1998). PLS is occasionally accompanied by pain felt within the phantom limb, know as phantom limb pain (PLP). PLP can be an excruciating pain, that hinders the quality of life of a person with an amputation, and therefore has been at the forefront of phantom phenomena research (Birbaumer et al., 1997; Carlen, Wall, Nadvorna, & Steinbach, 1978; H. Flor et al., 1995; H Flor et al., 1996; Jensen, Krebs, Nielsen, & Rasmussen, 1983; Estelle Raffin, Richard, Giraux, & Reilly, 2016; Weeks, Anderson-Barnes, & Tsao, 2010). PLP has been frequently correlated to extensive changes that occur within the brain, known as cortical reorganization, that occur immediately after amputation and may persist over time (Herta Flor, Nikolajsen, & Staehelin Jensen, 2006; Mercier, Reilly, Vargas, Aballea, & Sirigu, 2006; Ramachandran & Hirstein, 1998; Yao, Chen, Kuiken, Carmona, & Dewald, 2015). The PNS is also affected after an amputation with the injured axons eventually sprouting new ends that attempt to establish new connections (Herta Flor, 2002). The inability of these new axons to establish new connections may drive, or maintain, increased cortical reorganization and therefore an increase in PLP; this theory has been investigated minimally, utilizing only computer models (Spitzer, Böhler, Weisbrod, & Kischka, 1995). Great debate still remains over whether PLP is caused/maintained by a bottom-up, PNS driven, or top-down, CNS driven, mechanism (Makin, Scholz, Henderson Slater, Johansen-Berg, & Tracey, 2015; Ossipov, Dussor, & Porreca, 2010; Sherman, Sherman, & Parker, 1984).

The least studied component of the phantom limb phenomena is the general ability of an amputee to control the movement of the phantom limb, termed phantom limb control (PLC) (Brodie et al., 2007). Many amputees report being able to open and close the hand, wiggle the fingers and toes, and control movement of the phantom limb, as if the anatomical limb was still

present. Electromyography (EMG) studies have identified that PLC is more than just imagining a movement. During movements of the phantom limb muscles within the remaining portion of the limb (residual limb) contract to execute the movement (E. Raffin, Mattout, Reilly, & Giraux, 2012). In trans-humeral amputees, the muscles used to move the phantom were different than those expected to move the anatomical hand (K. Reilly, Mercier, Schieber, & Sirigu, 2006). Phantom movements have been negatively correlated to both PLP and changes within the CNS, implying that the PNS may play a larger role in facilitating PLC (Gagné, Reilly, Hétu, & Mercier, 2009; Osumi et al., 2015). Unfortunately the role of the PNS and its impact on muscle activation for motor control (the initiation and direction of purposeful and voluntary movements) (Roller et al., 2013) of a phantom limb has been understudied in people with amputation.

The goal of this dissertation is to focus on the changes that occur within the PNS, specifically changes in muscle activation patterns, in people with upper extremity amputation, changes that have previously been an under investigated component to the phenomena of phantom limbs. Changes within the PNS due to amputation, in addition to changes within the CNS, may play a large role in PLC and deserve to be studied with the same rigor as changes within the CNS and PLP. This dissertation offers new potential mechanisms that could have a significant impact on control of the movement of a phantom limb; the following preliminary studies are at the forefront of this research.

Control over a phantom limb does not provide an individual with an amputation any functional capabilities. Therefore, after the amputation many individuals are prescribed a prosthetic device that is intended to assist in restoring functional abilities. To utilize these devices, individuals must learn how to generate muscle contractions of the residual limb to control movements of the terminal device (hook or hand) of the prosthesis. Prosthetic devices are typically body-powered or myoelectric (Chadwell, Kenney, Thies, Galpin, & Head, 2016). A Body-powered prosthesis utilizes a cable and is supported by a harness to link proximal body movement to distal prosthetic movement (E. Biddiss & Chau, 2007). For example, with a voluntary opening device, the terminal device is most typically opened when scapula (through protraction) and/or upper body movement generates tension on the cable. The terminal device closes (via elastic bands) when tension on the cable is eliminated. A myoelectric prosthesis relies on sensors within the prosthetic socket to pick up and amplify electrical activity generated from specific muscles within the residual limb to control the terminal device. A myoelectric prosthesis can provide the user with more degrees-of-freedom in movement than a body-powered prosthetic device including, rotation of the wrist, and different grasp patterns.

Regardless of the type of device prescribed, users must learn the skill of control through patterns of muscle activity that may not have previously been used to move an intact limb. This learned skill takes time and much practice, thus, many individuals become frustrated and more than 30% reject their prescribed upper extremity prostheses. The primary reasons for upper extremity prosthetic rejection involve a lack of intuitiveness for usage and minimal dexterity, resulting in a prosthesis that drastically differs from natural hand movements (E. A. Biddiss &

Chau, 2007). Currently, no research has been conducted on the comparison of muscle activity for PLC and prosthesis control or if learning to control a prosthetic device impacts PLC.

The following series of studies were designed to provide the field with foundational research exploring the role of the PNS in PLC and control of prosthetic devices. The theoretical frameworks discussed next are new potential theories that may interact with mechanisms of the CNS and are utilized to drive further research regarding the role of the PNS in phantom limbs. This dissertation is comprised of three specific studies:

Study 1: To compare muscle activation patterns of the phantom hand/arm to documented muscle activation patterns of an anatomical limb during like movements in multiple levels of amputation.

Study 2: To compare muscle activation patterns of the phantom hand/arm to muscle activation patterns used to control the terminal device of a prescribed prosthesis.

Study 3: To compare whether users of body-powered prosthetic devices will have more muscles of the upper arm unexpectedly active during movements of the phantom hand/wrist than myoelectric prosthetic users.

1.1 Theoretical Frameworks

1.1.1 Study 1

Study 1 will identify whether different muscle activity patterns are utilized to control the phantom hand/arm compared to expected muscle activity patterns used to control an anatomically intact limb in multiple levels of amputation. The hypothesis is that people with all levels of upper extremity amputation will utilize muscle activity patterns different from expected muscle activity patterns used to control an anatomically intact limb. Previous research investigating muscle activation patterns of the residual limb to control phantom movements has focused on changes in muscle activation patterns of trans-humeral participants; stating that trans-radial amputees maintain their anatomical muscle activity and that shoulder disarticulation amputees are not capable of phantom movements (Gagné et al., 2009; K. Reilly et al., 2006) This study aims to expound on previous research and determine if individuals, with all levels of amputation, are able to control their phantom limb using muscles other than those anatomically expected. The potential theoretical framework of peripheral motor nerve re-innervation into denervated muscles, after peripheral nerve injury, and during congenital limb loss was used as support for this hypothesis. This study enrolled fifteen people with varying levels of upper extremity amputation.

Peripheral motor nerves innervate muscles of the extremities. When a movement signal is initiated in the brain it traverses to the spinal cord and then into a specific peripheral motor nerve, causing muscle contraction (Javed & Lui, 2019; Navarro, 2009). A single motor nerve innervates multiple muscle fibers through many terminal axon branches. The muscle fibers innervated by a single motor nerve are known as a motor unit. Fine movements require activation

of small motor units with few muscle fibers while larger movements require activation of large motor units with many muscle fibers (Heckman & Enoka, 2012). Muscles cannot contract, or facilitate movements, without innervation of a motor nerve. Limb amputation severs motor nerves at the level of the distal terminal axon branches, or the entire proximal axons which disrupts the innervation of muscles at the site of amputation known as denervation. Denervation may occur to the entire muscle or parts of the muscle, remaining within the residual limb, depending on the location of amputation and where the nerve was cut. When a denervation injury occurs within the PNS, efferent signals from the motor cortex of the brain do not produce targeted muscle contraction (Navarro, 2009). The motor cortex is arranged into a somatotopic map, known as a homunculus, that corresponds to the different anatomical areas of the body and muscles responsible for movement (Marieb, 2015; Penfield & Boldrey, 1937). Areas of the motor cortex that represent the target muscles become electrically silent after denervation (Navarro, 2009). To compensate for the inability to activate targeted muscles, inhibitory factors, that typically block activity in the areas neighboring the denervated muscle representation, are eliminated (Rossini et al., 1994; Wall, Xu, & Wang, 2002). Within hours of injury, the denervated muscle representation diminishes as the neighboring area representation enlarges and stimulation thresholds decrease. This is known as cortical reorganization (P. Chen, Goldberg, Kolb, Lanser, & Benowitz, 2002). Examples of such compensation mechanisms within the CNS are seen through stimulation of the cortical hand region that elicits movement in the shoulder, trunk, or face (Navarro, 2009). Such cortical reorganization may be part of the explanation for the phantom phenomena to occur immediately after surgery. However studies have identified a longer term negative correlation between PLC and cortical reorganization, implying the possibility of another, slower, repair process overtaking control of the movement of the phantom limb. This PNS repair process may eventually become the dominant process for PLC and contribute to the reversal of the initial cortical reorganization. Unfortunately, such studies have not investigated differences in PLC over time since amputation, and therefore there is no data providing a time line for such shifts. The average time since amputation as documented in three previous studies investigating the relationship between cortical reorganization, PLP and PLC was 15.45 years. Only five total participants were within three years since amputation (Gagné et al., 2009; Karl, Birbaumer, Lutzenberger, Cohen, & Flor, 2001; Estelle Raffin et al., 2016). Multiple studies have found a correlation between the functional motor activity of regenerated, and re-innervated, peripheral motor nerves and a reversal of cortical reorganization, allowing cortical representations to return to their original locations, although the process may take up to 3 months after initial injury to begin seeing results (Giraux, Sirigu, Schneider, & Dubernard, 2001; Todd A Kuiken et al., 2007; Röricht et al., 2001).

Regeneration and/or re-innervation, the physiological repair that occurs with nerve lesions, is under studied and may contribute to control of phantom limb movement, and reversal of cortical reorganization. With injury, the PNS initiates a repair process that facilitates axon regrowth of peripheral motor nerves (Yiu & He, 2006). The injured axon begins to grow new terminal axons that penetrate the area of injury in an attempt to regenerate and find its original

target end muscle (Fawcett & Keynes, 1990; Kingham & Terenghi, 2006; Robinson, 2000; W. Sulaiman & Gordon, 2013). New terminal axons attempt regeneration within a few hours of injury (Fawcett & Keynes, 1990) and within 24-36 hours the sprouting regenerating axons penetrate the area of injury (Robinson, 2000). When access to original target end muscles is inhibited, sprouting terminal axons may innervate target destinations near the site of injury they did not formerly supply, termed re-innervation (Brushart, 1990; Navarro, 2009; W. Sulaiman & Gordon, 2013). With amputation, including congenital absence of a limb, complete regeneration is not entirely possible since some (or all) target end muscles are no longer present, however remaining muscles may have also lost some (or all) of their innervation allowing them to accept new axonal growth.

It is theorized that peripheral nerve re-innervation may elicit contractions of anatomically unexpected muscles to control movement of a phantom limb. This theory is supported by a newly developed secondary surgical procedure for people with amputation, called *Targeted Muscle Re-innervation* (TMR). TMR surgically manipulates the biological repair process of re-innervation. Surgeons purposefully denervate a muscle, such as pectoralis major, then implant the distal end of a peripheral mixed nerve (motor and sensory fibers) that formerly supplied an upper extremity muscle (Cheesborough, Smith, Kuiken, & Dumanian, 2015). TMR was developed specifically to enable upper extremity amputees to control a prosthetic device through natural muscle contractions. After TMR patients are able to contract re-innervated residual muscles to control the function of myoelectric prosthetic devices. Patients are able to operate multiple functions of the device and even simultaneously operate different components (such as the elbow and hand (Todd A. Kuiken et al., 2009).

Individuals with congenital limb loss almost never report pain in the phantom limb, and do not present with cortical reorganization (Herta Flor et al., 1998; Wilkins, McGrath, Finley, & Katz, 1998). The presence of non-painful PLS and PLC is not well understood in congenital amputees. In 1962 Simmel reported that individuals with congenital limb loss do not experience PLS (Simmel, 1962). This was refuted by Poeck (Poeck, 1969), but further investigation remained dormant until the 1990's after which multiple researchers reported that congenital amputees indeed have phantom experiences (Brugger, Kollias, Müri, et al., 2000; Collins et al., 2017; Funk, Shiffrar, & Brugger, 2005; Lacroix, Melzack, Smith, & Mitchell, 1992; Melzack, Israel, Lacroix, & Schultz, 1997; Price, 2006; Ramachandran, 1993; Ramachandran & Hirstein, 1998; K. T. Reilly & Sirigu, 2008; Saadah & Melzack, 1994). Unfortunately, questions regarding the mechanism behind PLS remain unanswered. The ability to move a phantom limb is experienced by many amputees, both traumatic and congenital (Brodie et al., 2007), and provides the foundation for the exploration of the theory that regeneration and re-innervation of peripheral nerves to new end muscles occurs after amputation or in the presence of congenital limb absence leading to enhanced PLC, with diminished PLP and cortical reorganization.

1.1.2 Study 2 & 3 Theoretical Framework

Study 2 will identify if different muscle activity patterns are utilized to control the phantom hand/arm from muscle activity patterns used to control the terminal device of a prosthesis. The hypothesis is that different muscles will be utilized to control the prosthesis from the phantom hand/arm. The theoretical framework of motor learning was used to support this hypothesis. This study enrolled fourteen people with various levels of upper extremity amputation who had been prescribed either a myoelectric or body-powered prosthesis.

Study 3 will explore if use of a prosthetic limb impacts muscle activation patterns used to control a phantom hand/arm. The hypothesis is that body-powered device users will have more muscles of the upper arm unexpectedly active during movements of the phantom hand/wrist than myoelectric prosthetic users. The theoretical framework of motor learning was used to support this hypothesis. This study enrolled eleven people with below elbow amputations, 6 who use a myoelectric prosthesis and 5 who use a body-powered prosthesis. Only people with below elbow amputations were recruited for this study due to the similarities in prosthetic design for this level of amputation.

Initiation and completion of purposeful, voluntary movements involves the complex coordination of intricate skills to facilitate motor control (Roller et al., 2013; Shumway-Cook & Woollacott, 2001). Motor skills are developed through maturation, practice, and are influenced by genetic factors, anatomical and neurophysical traits (Haibach et al., 2017). Variability in motor skills results from motivation to solve problems encountered within the environment, which facilitates learning (Gibson & Pick, 2000) yet, developed motor skills such as reaching and grasping are uniform among individuals and acquired in a successive manner over time (Haibach et al., 2017; Zoia et al., 2013). Motor learning is the internal process of obtaining new motor skills, through practice and incorporation, resulting in the automaticity of desired movements (Nieuwboer et al., 2009). As motor learning occurs, the motor skill is transformed from a general performance experience to a construct stored within the brain. With much practice the skill is consolidated and retained in memory so that the motor control process can be recalled at will (Dudai, Karni, & Born, 2015). PLC may result from the reacquisition of developed movement skills (reaching/grasping) through original processes after injury, known as recovery of function (Shumway-Cook & Woollacott, 2001), whereas the ability to control the movement of an artificial limb (prosthesis) requires extensive practice and motor learning. Motor learning is required to achieve automatic function of the terminal device and is not always achieved by upper extremity amputees. Although PLC does not provide the amputee with a functional result or visual/tactile confirmation of the movement, the innate representation of the motor developed skill may not completely disappear, resulting in persistence of motor control (Gallagher, Butterworth, Lew, & Cole, 1998). The second and third studies of this dissertation are being completed as preliminary studies that hope to expand the field of knowledge regarding the differences in PLC and prosthetic control. Results obtained from these studies have the

potential to initiate further studies into motor learned skills versus motor developed skills and the impact of motor learning on similarly executed motor developed skills.

1.2 Summary

These three interdependent studies, discussed as separate chapters within this document, aim to expand the field of knowledge regarding the ability to control the movement of both a phantom and a prosthetic limb in people with upper extremity amputation. This dissertation focuses solely on results obtained from the residual limb and PNS; PLP and changes within the CNS were not measured and therefore only minimally discussed in the following literature. Results from these studies may expand interest into further studies of the biological response of the PNS to amputation, the difference between PLC and control of prosthetic devices, and the impact of prosthetic control on PLC. There is a strong potential for these results to not only open the field to further research but also influence future surgical procedures, and prosthetic design.

CHAPTER 2: LITERATURE REVIEW

2.1 Amputation:

2.1.1 Demographics/Cause:

A study published in 2008 reported the prevalence of upper extremity limb loss at roughly 8% of all people living with amputation (Ziegler-Graham et al., 2008). Unlike lower extremity amputations, which are typically caused by disease related complications; upper extremity amputations are typically due to trauma. Two-thirds of upper extremity amputations are due to traumatic events, adolescent to young adults (under 45 years of age) make up most of this number (Barmparas et al., 2010; Ziegler-Graham et al., 2008). An inquiry into the National Trauma Databank in the United States from 2000 to 2004 found that 41.1% of all traumatic major limb amputations resulted in the loss of the upper extremity (Barmparas et al., 2010). Congenital absence of a limb occurs between 3.5 and 7.1 per 10,000 live births, depending on the location of the study (Ephraim, Dillingham, Sector, Pezzin, & MacKenzie, 2003).

2.1.2 Surgical Techniques:

The surgical process of amputation is removal of the distal portion of an extremity and requires the severance of all structures at the specified site. Disarticulation amputations occur at a joint and do not require severing of a bone. Level of amputation is determined by multiple factors including tissue viability, potential prosthetic fit, tissue coverage and padding of the end of the residual limb (Ovadia & Askari, 2015). Anterior and posterior soft tissue skin flaps are necessary for closures of the amputation site; when adequate coverage is not available, higher levels of amputation are required (Adams & Lakra, 2019; Ovadia & Askari, 2015). To pad the residual limb, surgeons may choose myoplasty or myodesis techniques. Myoplasty is the suturing of muscles, typically agonist and antagonist, to one another so that muscles pad the end of the limb. Myodesis, a more challenging surgical technique, sutures muscle directly to the bone (Ovadia & Askari, 2015).

Various surgical techniques are utilized to prevent the formation of neuroma after amputation. Traction neurectomy, the process of adding traction to a nerve before severing and allowing the proximal severed end to retract away from the site of amputation into more viable soft tissue beds, is currently the most utilized procedure at the time of amputation (Adams & Lakra, 2019; Bowen, Wee, Kalik, & Valerio, 2017; Ovadia & Askari, 2015). Forming a loop between two severed nerves or burying the ends of severed nerves into nearby muscles are two alternative methods to prevent neuroma. Burying severed nerves into remaining muscles has been shown to diminish neuroma formation more than traction neurectomy, however it currently remains a less utilized technique (Dellon & Mackinnon, 1986; Dellon, MacKinnon, & Pestronk, 1984; Ducic, Mesbahi, Attinger, & Graw, 2008; Pet, Ko, Friedly, & Smith, 2015).

A fourth, newer process, called targeted nerve implantation (TNI) eliminated neuroma

formation in 92% of patients when completed during primary amputation surgery, and in 87% of patients after a secondary surgery to treat existing neuroma (Pet, Ko, Friedly, Mourad, & Smith, 2014).The TNI procedure denervates a portion of an expendable healthy muscle by isolating and dividing a terminal branch of a motor nerve. The motor junction is identified and the proximal major nerve axon of the nerve severed due to amputation is implanted into the denervated muscle. The theory behind TNI is that the regenerating terminal nerve branches of the nerve severed due to amputation will enter the motor junction and branch out in an organized fashion rather than creating a neuroma (Pet et al., 2014). Targeted muscle re-innervation, specifically focused on re-innervating nerves in amputees, has also been shown to be effective at reducing the occurrence of neuroma formation and neuropathic pain (Dumanian et al., 2019; Valerio et al., 2019).

2.1.3 Congenital Limb Loss:

Congenital amputations occur when an individual is born without a limb (amelia), this includes individuals born with only a portion of the limb (phocomelia). Congenital amputation may be caused by failure of a limb to form or amputation of a formed limb in utero. Failure of a limb to form properly is typically the result of viruses, chemicals, or genetic factors whereas amputation of a formed limb in utero is frequently caused by amniotic band syndrome (Gold, Westgate, & Holmes, 2011). Amputation of a limb in utero would be most similar to traumatic amputation experienced later in life, whereas processes for failure of a limb to form may be very different.

How the PNS of CNS is affected by congenital amputation is not well understood, as most studies on phantom phenomena in congenital amputation are descriptive in nature. However, some theories have been developed around the idea of an innate body schema that is ingrained in all humans. A neural framework that outlines body representations and innate movements required for life would continue to function regardless of the physical presence of a limb (Gallagher et al., 1998; Price, 2006). The original belief that congenital amputees could not present with phantom limbs has been refuted, although the presence of phantom limbs remains low (Brugger, Kollias, Müri, et al., 2000; Collins et al., 2017; Funk et al., 2005; Lacroix et al., 1992; Melzack et al., 1997; Price, 2006; Ramachandran, 1993; Ramachandran & Hirstein, 1998; K. T. Reilly & Sirigu, 2008; Saadah & Melzack, 1994). Previous researches postulated that phantom limbs in congenital amputees may be due to learning behaviors from intact limbs, this however does not explain the presence of phantom limbs in individuals with bilateral, or quadrilateral congenital amputations (Brugger, Kollias, Muri, et al., 2000; Price, 2006). Phantom limbs therefore, may be constructs developed because of an ingrained neural body framework. Within this representation are innate motor schemas, required for human survival (eg: reaching/grasping for feeding, walking for movement) (Gallagher et al., 1998). All humans (barring any genetic malfunctions) develop these vital skills in the same manner (motor developed skills). When this innate functional system is disrupted by congenital or traumatic amputation the missing limb may be represented in the schema within the brain and thus

experienced as a phantom (Bolognini, Olgiati, Maravita, Ferraro, & Fregni, 2013; Brugger, Kollias, Muri, et al., 2000; Gallagher et al., 1998; Makin et al., 2015). For example, after amputation many amputees forget the limb is no longer there and attempt to use it, the missing limb continues to function within an innate movement pattern required for human survival. Innate movements do not require visual conformation or reinforcement to complete. Further support can be found in the work of Brugger, who found that transcranial magnetic stimulation over the motor cortex responsible for the amputated limb can produce movements of the phantom limb, even in congenital amputees with no reported PLC (Brugger, Kollias, Muri, et al., 2000)

However, without tactile or visual reinforcement it is possible that the neural representation may deteriorate, although it may not be completely eliminated. The phantom limb may disappear due to cortical reorganization, such as with the diminished stimulation threshold of neighboring areas that are receiving reinforcement (Gallagher et al., 1998; Navarro, 2009), or different mechanisms of action in utero. Such cortical reorganization may occur more efficiently in utero, rather than later in life. This reorganizational shift may explain why some congenital amputees do not experience a phantom. If the neural framework efficiently reorganizes itself, especially in utero, the phantom may not be as strongly expressed. The mechanisms responsible for neural reorganization in utero may be more efficient and may be different than that occurring within adults, explaining the contrast between phantom experiences in congenital vs traumatic amputees. Further research is needed on the ability to reactivate the innate representation of a limb in congenital amputees, which may be done by simply asking them to complete movements.

2.1.4 Phantom Limbs:

Between 60% and 80% of all upper extremity amputees, and at least 18% of congenital upper extremity amputees, experience phantom limb sensation (PLS), which is an awareness of the presence of their amputated limb (Collins et al., 2017; Herta Flor, 2002; Herta Flor et al., 1998). PLS includes the feeling of all non-painful sensations of the phantom limb (Abramson & Feibel, 1981; Bouffard, Vincent, Boulianne, Lajoie, & Mercier, 2012). These sensations can include the general awareness of the presence of the limb, limb position sense, temperature, and sensory sensations (Hunter, Katz, & Davis, 2003). The majority of amputees with PLS (over 80%) experience pain associated with PLS termed phantom limb pain (PLP) (Ephraim, Wegener, MacKenzie, Dillingham, & Pezzin, 2005; Herta Flor, 2002; Herta Flor et al., 1998; Kooijman, Dijkstra, Geertzen, Elzinga, & Van Der Schans, n.d.; Nikolajsen & Christensen, 2015; Ramachandran, Stewart, & Rogers-Ramachandran, 1992). PLP has the characteristics of neuropathic pain including patient reported sensations of electric shock, burning, throbbing, cramping, tingling, and stabbing (H. Flor et al., 1995; Montoya et al., 1997; Ramachandran & Hirstein, 1998). Painful sensations range in severity from mild symptoms requiring no intervention to severe symptoms requiring medical treatment with strong neuropathic and opioid medications.

PLP has been negatively correlated with the ability of an amputee to control the movement of the phantom limb known as phantom limb control (PLC) (Osumi et al., 2015). PLC is the purposeful, direct, and intentional execution of movement of a phantom limb (Brodie et al., 2007; E. Raffin et al., 2012). Raffin et al. used functional MRI to show that phantom limb movements and imagined movement of a limb activate distinct areas of the cerebral cortex. During executed phantom limb movements the primary motor and sensory cortices were active, however during imagined movements these areas showed no activity. During imagined movements the inferior and superior parietal lobes were active, while they were not active during executed movements (E. Raffin et al., 2012). To further investigate differences between phantom limb movement and imagined movements, Raffin et al. (2012) used electromyography (EMG) to record muscle activity in residual limb muscles and corresponding muscles of the intact limb (Estelle Raffin, Giraux, & Reilly, 2012). Participants included four trans-radial and ten trans-humeral amputees. They found an absence of muscle activity in both arms during the execution of the imagined movement task. They also found a significant increase, above baseline, in muscle activity during the execution of phantom movements within the residual limb, even though no direct movement of the residual limb was required (Estelle Raffin et al., 2012).

PLC is more than imagining a movement; it requires significant muscle activity of the muscles of the residual limb (Gagné et al., 2009; E. Raffin et al., 2012; Estelle Raffin et al., 2012; K. Reilly et al., 2006). In 2006 Reilly et al. studied seven people with upper extremity amputation who reported being able to voluntarily move their phantom limb (PLC). Subjects moved their phantom limb at the same pace and in the same range of motion as their intact limb, while muscle activity was recorded. They found that residual limb muscles were active during movements of the phantom limb. Patterns of muscle activity remained the same over time, with distinct muscle activity patterns for different movements. Interestingly, muscle activity patterns varied among participants during the execution of the same movement. Results from this study indicate that amputees are not producing random contractions of residual limb muscles when asked to move their phantom limb but rather purposeful, specific motor controlled movements with differing patterns of muscle activity (K. Reilly et al., 2006).

2.2 Motor Control/Motor Learning:

Execution of a voluntary movement skill (motor control) is a complex process that begins within the CNS. The decision to initiate a movement and the plan to execute movement begins within the prefrontal cortex. The prefrontal cortex projects to the motor cortex to deliver the planned movement request (Mushiake, Saito, Sakamoto, Itoyama, & Tanji, 2006) The primary motor cortex, located in the frontal lobe along the precentral gyrus, is largely responsible for generating neural impulses for the execution of movement (Marieb, 2015). The primary motor cortex contains a motor homunculus, a map within the brain illustrating areas dedicated to processing motor signals for different anatomical areas of the body (Marieb, 2015; Penfield & Boldrey, 1937). The amount of cortex assigned to a particular body part represents the amount of motor control necessary. For example, the hands require extensive fine motor movements,

therefore they are largely represented within the motor cortex (Penfield & Boldrey, 1937; Schott, 1993). Motor control begins with an action potential in the cell body of an upper motor neuron (UMN) located within the primary motor cortex. The signal descends to the brain stem, where it then crosses to the contralateral side as it travels through the corticospinal tract. Once within the spinal cord, the UMNs synapse with lower motor neurons (LMN) in the ventral horn of the spinal cord. There are no synapses within the corticospinal tract; all UMNs synapse with LMNs in the spinal cord. LMNs send axons out through ventral roots, where they become spinal nerves (Javed & Lui, 2019). Spinal nerves, responsible for the initiation of movement of the upper extremity, merge together in a complex network known as the brachial plexus (Blair, Rapoport, Sostman, & Blair, 1987). The brachial plexus receives contributions from nerve roots C5 to T1, all responsible for movement of the upper extremities. Intricate branching forms three trunks, six divisions, three cords, and terminates into five main peripheral motor nerves: median, radial, ulnar, musculocutaneous, and axillary (Orebaugh & Williams, 2009). Typically, although some variations exist, the median nerve innervates most muscles of the anterior forearm; the radial nerve innervates all muscles in the posterior portions of the arm and forearm; the ulnar nerve innervates hand and finger flexors; the musculocutaneous nerve innervates muscles of the anterior compartment of the arm; and the axillary nerve innervates some of the muscles of the shoulder (Moore, Agur, & Dalley, 2015). Once an impulse travels from the CNS through the spinal cord to the peripheral nerves, it synapses at a neuromuscular junction, where the signal is transmitted to the muscle fibers. The motor neuron releases acetylcholine (Ach), which binds to receptors on the membrane of the muscle fiber initiating the process of contraction (Levitan & Kaczmarek, 2015). As the UMNs and LMNs are executing the movement, multiple areas of the brain are receiving information regarding the accuracy of the movement; the basal ganglia and cerebellum are largely involved in this process (Aoki et al., 2019; Popa, Streng, Hewitt, & Ebner, 2016). For example, if the cerebellum identifies that motor corrections are needed information is sent to the motor cortex allowing the motor areas to correct the activity of the UMNs and LMNs. As movements are repeated and completed successfully they become smooth and precise, this motor learning is due to the strengthening of synapses within the cerebellum. The cerebellum then regulates and stores learned movements for future execution (Popa, Streng, Hewitt, & Ebner, 2016).

Voluntary movement involves intricate motor control processes carried out by specific patterns of muscle activation. Motor skills result from the coordination of these muscle activation patterns into systematic and purposeful movements. Developed motor skills, such as reaching and grasping, progress quickly over the first three months of life without the need for practice (Haibach et al., 2017). As individuals grow and mature, they encounter problems within the environment that facilitate the need for further skills acquired through motor learning (Gibson & Pick, 2000). Motor learning involves identification of an end goal and development of a motor plan to facilitate movement. Successful execution of the motor plan results in response programming, the brains ability to program sequences of muscle activity related to the response. Unsuccessful executions result in adaptation, an attempt to diminish performance errors and

increase effective movements. Adaptation occurs through various attempts at completing a task or overcoming an obstacle (Roller et al., 2013). Through practice and experience, functional muscle activity patterns are developed into high-level motor programs for generating movements (Schmidt, 1976; Scott Kelso, Tuller, & Harris, 1983).

Three stages of motor learning, described by Haibach et al., occur before motor control becomes automatic, advancement from one stage to the next takes extensive practice and time. The first stage is the *cognitive stage* characterized by slow, inconsistent, and inefficient movements. Much thought is required to complete the movement with specific attention applied to understanding how body parts should move to accomplish the goal. Cognitive activity is essential, and movements are carried out consciously; the skill must be understood before execution is possible. Many trials and errors occur in this stage. The second stage is the *associate stage,* where movements are more fluid, reliable and efficient. This stage involves a mixture of consciously executed movements with some occasional automaticity. Less thought is required to complete the movement, which becomes more refined through practice. The final stage of motor learning is the *autonomous stage*. Movements no longer require high levels of cognitive activity and are executed more automatically. Movements are accurate and consistently efficient (Haibach et al., 2017). Motor learning is accomplished when there is a relatively permanent change in the capability of the person to perform the learned task (Gibson & Pick, 2000; Newell, 1991; Roller et al., 2013).

2.2.1 Motor Control of Phantom Limbs:

The muscles used by trans-humeral amputees to move a phantom limb differ from that of an anatomically intact limb (Gagné et al., 2009; K. Reilly et al., 2006). Very few reports are available that investigate the occurrence of anatomically unexpected muscles completing phantom limb movements in multiple levels of amputation. This dissertation will attempt to enhance the knowledge regarding muscle activity to control phantom limbs in all levels of upper extremity amputation. When an amputation occurs, or a limb is not fully formed, based on the level of amputation, the residual limb often retains the origin of some muscles, but the insertion is often absent or lost. Remaining muscles contract when moving a phantom limb even through the execution of movements for which the muscles may not have been anatomically responsible (Gagné et al., 2009; K. Reilly et al., 2006). Reilly et al. (2006) examined muscle activity patterns of bilateral upper extremities during movements of hand opening/closing, wrist flexion/extension, and finger abduction/adduction in unilateral upper extremity amputees. They found muscle activity during fine movements of the phantom hand in proximal muscles (biceps, triceps, deltoid, brachialis) in four trans-humeral amputees. Interestingly, they found muscles within the residual forearm of three trans-radial amputees were active in accordance with anatomically expected activity. Only one high-level (shoulder disarticulation) upper extremity amputee was included in the investigation. This individual presented with an immobile, frozen phantom limb, drawing the researchers to conclude that high-level amputees cannot have sufficient motor neurons remaining to move a phantom limb. Co-contractions, with a reliable

pattern of activity, were identified in residual limb muscles (pectoralis major, latissimus dorsi, trapezius) that would not be responsible for producing anatomical movements of the hand in the shoulder disarticulation patient (K. Reilly et al., 2006). The statement that shoulder disarticulate amputees do not have sufficient motor neurons to control phantom limb movements based on a single observation is unscientific. Clinical experience with multiple shoulder disarticulate patients who report control over a phantom limb warrants further investigation of immobile phantom limbs.

Gagne further examined muscle activity in the biceps, triceps, and deltoids of the residual and intact limbs of eight additional trans-humeral amputees and found muscle activity patterns were consistent for the same requested phantom movements over time but varied among movements and participants (Gagné et al., 2009). These findings support previous findings that residual limb muscles are active during movement of the phantom limb (Gagné et al., 2009; K. Reilly et al., 2006). The 2009 publication did not report muscle activity patterns within the residual limb of trans-radial amputees during phantom limb movements; yet they report maintenance of their anatomic muscle activity patterns, per their previous findings in three participants in the 2006 publication (Gagné et al., 2009).

Collectively, the results of these studies show that amputees consistently use specific patterns of muscle activity to control movements of a phantom limb. However, the patterns of muscle activity for each executed phantom movement differ among participants (Gagné et al., 2009; K. Reilly et al., 2006). Furthermore, these reports reveal that not every amputee uses the same patterns of muscle activity to complete phantom movements. A potential theory for such results may be that mechanisms of peripheral nerve repair after amputation or the impact of motor learning to control a prosthetic device are contributing to muscle activation patterns during phantom limb movements.

2.2.2. Motor Learning and Prosthetic Rejection:

Regardless of the type of prosthetic device prescribed, functional control requires motor learning (Alcaide-Aguirre, Morgenroth, & Ferris, 2013; Bouwsema, van der Sluis, & Bongers, 2010; Dromerick et al., 2008). Not all upper extremity amputees become proficient with their devices, with more than 30% of upper extremity amputees rejecting their prescribed prosthetic device (E. A. Biddiss & Chau, 2007). Rejection is largely due to frustration with extensive motor learning; for example, complicated muscle activity patterns are required to control the terminal device (E. A. Biddiss & Chau, 2007; Bouffard et al., 2012; Bouwsema et al., 2010).

In addition to difficulty with motor learning, rejection of the prosthesis may be due to discrepancies between muscles used to control movements of the phantom limb and muscles used to control the prosthetic device. In 2012 Bouffard et al. reported on interactions between PLC and the functional use of prostheses in trans-radial amputees. Twelve prosthesis users (three new and nine long-time users) completed multiple questionnaires and one-on-one interviews. Eight participants used body-powered prosthetic devices, and four utilized myoelectric devices.

Roughly 75% were capable of moving their phantom limb (PLC). Body-powered prosthesis users reported that PLC did not influence device control, while three of the myoelectric users stated PLC did influence the use of their prosthesis. This discrepancy may be explained by the control mechanism of each device. Terminal device control of a body-powered prostheses is created by shoulder and trunk movement as opposed to muscle contraction within the distal residual limb. The one participant, who reported PLC made using the myoelectric prosthesis more of a challenge, exhibited a disagreement between opening and closing the phantom hand and opening and closing the terminal device (Bouffard et al., 2012). Myoelectric prosthetic sensor placement is typically located over agonist/antagonist muscles where the best electrical activity can be captured, which may differ from muscles used to control the anatomic hand and/or phantom limb movements. Identification of specific muscles an individual amputee utilizes to control their phantom limb and utilization of the same muscles to control the prosthetic device may enhance user functionality if a disconnect does in fact exist.

2.3 Peripheral Nervous System:

The efferent motor fibers of the PNS originate as lower motor neurons within the ventral horn of the spinal cord (Javed & Lui, 2019). Efferent motor neurons directly innervate skeletal muscles through peripheral nerves that terminate in neuromuscular junctions within end muscles (Javed & Lui, 2019; Navarro, 2009). Nerve fibers within peripheral nerves are bundled together into fascicles by connective tissue and supported by three protective sheaths: the epineurium (outermost layer), the perineurium (middle layer), and the endoneurium (located between nerve fibers within a fascicle) (Peters et al., 1991). The endoneurium provides structure and support for gene regulation (Juliano & Haskill, 1993). Collagen fibers pack around each nerve fiber forming a wall of endoneurial tubes (Navarro et al., 2005; Peters et al., 1991). Within each endoneurial tube resides a terminal axon of a motor neuron and its accompanying Schwann Cells (Navarro et al., 2005).

Schwann Cells are critical for the function and survival of neurons within the PNS. In 1997 Riethmacher and team created mice that lacked ErbB3, an enzyme that controls the growth and development of Schwann Cells. They reported that peripheral nerves began to develop properly within the spinal cord; however shortly after the initiation of development, the nerves underwent degeneration. Results from this study show that Schwann Cells are not required for the initial creation of peripheral nerves, but are essential to survival of peripheral nerves (Riethmacher et al., 1997).

Schwann Cells are responsible for myelinating axons of peripheral nerves, providing directional guidance of the neurons and eliminating cellular debris when necessary (Bhatheja & Field, 2006). Myelin is a fatty layer that insulates an axon and assists in increasing the conduction rates of the neurons. Myelinating Schwann Cells form a single myelin sheath by wrapping around a large diameter motor axon (Bhatheja & Field, 2006; Salzer & Zalc, 2016). Along the axon more Schwann Cells wrap around, creating more myelin sheaths. The space between each myelin sheath is known as a node of Ranvier (Bhatheja & Field, 2006; Salzer &

Zalc, 2016). Myelination is critical for quick conduction of neural impulses and assurance that the signal is not lost before reaching the terminal muscle for contraction.

2.3.1 Peripheral Nervous System Injury Response:

When injury occurs to the peripheral nerves, the axons respond through physiologic changes required for survival and regrowth (Navarro, 2009). A 2006 study utilized DNA array technology to investigate the regulation of genes after peripheral nerve injury (Bosse, Hasenpusch-Theil, Küry, & Müller, 2006). Findings from this study showed that 192 genes participated in significant regulation in response to injury, roughly two-thirds were down-regulated (diminished) (Bosse et al., 2006). Down-regulation was mostly seen in genes encoding transmitter-related proteins and up-regulation (increases) within growth associated proteins, implying the ability of surviving neurons to switch from a transmitting state to a regenerative state (Bosse et al., 2006; Navarro, 2009). Schwann Cells specifically down-regulate the expression of proteins required for myelination and cell-adhesion, which initiates die back degeneration, destroying the myelin sheaths and producing debris. Within an hour of injury, die back degeneration occurs at the proximal end of the injured nerve until it reaches a viable node of Ranvier. This degeneration allows the injured axon to begin sprouting new terminal branches (W. Sulaiman & Gordon, 2013).

To remove and recycle the debris created by degenerating axons, Schwann Cells up-regulate pro-inflammatory cytokines, interleukin-1 and monocyte chemoattractant protein-1, which recruit macrophages to the injury site (O. Sulaiman, Boyd, & Gordon, 2005). Macrophages participate in Wallerian Degeneration, which removes and recycles the debris, preparing the environment for regrowth (Fawcett & Keynes, 1990). Macrophages work to remove growth inhibitory factors at the injury site and encourage the proliferation of Schwann Cells (Fawcett & Keynes, 1990; W. Sulaiman & Gordon, 2013).

Shortly after injury, new terminal axons begin to sprout from the proximal axon (Fawcett & Keynes, 1990; McQuarrie, 1985). A study published in 1985 utilized transmission electron microscopy to investigate the time of sprouting from an injured axon. Photos taken through a microscope looking at viable nodes of Ranvier, after die back degeneration, showed sprout formation in 9% of nerves tested after nine hours, and 33% had axonal sprouting after 27 hours (McQuarrie, 1985). A single axon may produce several terminal axon sprouts, which attempt to grow back toward their targets (Fawcett & Keynes, 1990; W. Sulaiman & Gordon, 2013).

2.3.1.1 Regeneration*:*

After peripheral nerve injury, the goal of the proximal axon is to regenerate, or find their original endoneurial tubes and innervate its original muscle (Fawcett & Keynes, 1990; Kingham & Terenghi, 2006; W. Sulaiman & Gordon, 2013). With crush injuries regeneration is typically successful, the endoneurial tubes are still intact allowing the new terminal axon to be contained and follow their original tube directly back to their target muscle (Fawcett & Keynes, 1990). Cut injuries (axotomy), which occur with amputation, disrupt the endoneurial tubes, causing

Schwann Cells at the distal axon injury site to proliferate and form new columns, known as bands of Bungner. Bands of Bungner attempt to guide the regenerating axons back to their endoneurial tubes and their target muscle (Kingham & Terenghi, 2006). For regeneration to occur, the new axon terminal must find their original target muscle (W. Sulaiman & Gordon, 2013). In a 2009 study, Hoke harvested distal nerves after axotomy to investigate the proteins released by Schwann Cells to guide the new terminal axons toward their targets. Results implied that Schwann Cells enhance the environment to support regeneration of the new axons to their original targets through the release of neurotrophic factors such as: glial cell line-derived neurotrophic factor (GDNF), and nerve growth factor (NGF) (Hoke & Mi, 2009).

2.3.1.2. Re-Innervation:

Cut injuries enhance the chance that new axonal terminals will be guided to different muscles (Fawcett & Keynes, 1990). Re-innervation occurs when new terminal axonal sprouts innervate target destinations that they did not formerly supply (Brushart, 1990; Navarro, 2009; W. Sulaiman & Gordon, 2013). Different axonal terminals from the same axon can enter different muscles that the nerve previously did not supply (W. Sulaiman & Gordon, 2013). Re-innervation can lead to functional muscle activation, although inappropriate patterns of firing can be seen if the muscle innervated typically produced differing actions from the re-innervated nerve (Brushart, 1990; Gordon, Stein, & Thomas, 1986; Navarro, 2009; W. Sulaiman & Gordon, 2013).

In a study published in 1986, Gordon et al. surgically re-innervated muscles with antagonistic function by crossing the tibial and common peroneal nerve in the lower extremity of cats. Crossing the nerves produced misdirection of the motor neurons to new muscles with antagonistic function of their original target muscles. In anatomically normal cats, there is alternating flexor and extensor activity throughout the step cycle, with ipsilateral flexor and extensor activity 180 degrees out of phase with flexor and extensor activity of the contralateral limb. Results from the re-innervation of antagonistic muscles showed muscle activity within the ipsilateral flexor in phase with the contralateral flexor. The re-innervated flexor presented a typical muscle activity pattern for an extensor. These results showed that flexor muscles, re-innervated by antagonist nerves, activate according to the normal muscle activity patterns of the antagonist nerves that now supply them. The re-innervated extensor continued to signal muscles based on its original anatomical purpose in addition to the antagonist muscle signal. Further examination of the surgical procedure found that 33% of the terminal axons of the tibial nerve returned to their original target muscle (Gordon et al., 1986). These findings imply that the extensor muscle was receiving impulses from both the original tibial nerve and the re-innervated common peroneal nerve, with activity in both phases of the cyclic motion.

2.3.1.3 Preferential Motor Re-Innervation:

The physiological cause of re-innervation is due to topographic changes to nerve bundles after axotomy, resulting in random growth of sprouting axon terminals and misrouting (Navarro, 2009). Misrouting is not a random occurrence; growing motor axon terminals preferentially re-

innervate motor branches, termed Preferential Motor Re-innervation (PMR) (Abdullah, O'Daly, Vyas, Rohde, & Brushart, 2013; Brushart, 1988, 1990, 1993; R. D. Madison, Robinson, & Chadaram, 2007; Roger D Madison, Archibald, Lacin, & Krarup, 1999). Motor branches innervating sensory organs, such as the skin, result in failure to establish motor outcomes. PMR was coined in a 1988 study that investigated the preference of severed terminal motor axons to re-innervate the motor specific branch of the femoral nerve in rats. A proximal location of the femoral nerve, where motor and sensory axons intermingle, was chosen so after axotomy the regenerating axons would have access to both muscular and sensory branches at the bifurcation of the nerve. Half of the animals had their distal and proximal ends aligned, and half had the distal end rotated 90 degrees to determine if alignment impacted direction of innervation. Eight weeks after axotomy, either the motor or sensory neurons were labeled, sections of each branch were mounted, and a blinded researcher counted the number of labeled neurons in each branch. In all groups more motor neurons were found within the motor branch than the sensory branch; rotation of the distal ends played no role in the outcome of re-innervation specificity (Brushart, 1988).

Additional studies have confirmed the presence of PMR through retrograde tracing techniques (Al-Majed, Neumann, Brushart, & Gordon, 2000; Franz, Rutishauser, & Rafuse, 2005) and electrophysiological techniques in both rats and primates (R D Madison, Archibald, Lacin, & Krarup, 1999). Debate still ensues regarding the process of PMR. Although Brushart's study could not identify the cause, they hypothesized three potential options: *Neurotropism* (Schwann cells release diffusible factors that drive growth and guide the growing axons); *Specific Recognition* (axons sample different endoneurial tubes and choose those with specific qualities); or *Neurotrophism* (axons enter tubes randomly but only survive within tubes that lead to muscle contact) (Brushart, 1988). Support for neurotropism was established through studies that reported terminal axons entering motor-specific endoneurial tubes even without end muscle contact (Brushart, 1993; Redett et al., 2005). A 2009 study supported neurotrophism by harvesting distal nerves after axotomy. This study reported up-regulation of pleiotrophin, a neurotrophic factor found in muscle. During development pleiotrophin is highly expressed, however expression is diminished in adult muscle unless the muscle becomes denervated. This finding implies that pleiotrophin is a target-specific factor that assists in survival of motor axons in new muscle after injury (Hoke & Mi, 2009). The most recent study on the mechanisms of PMR concludes that PMR is a complex phenomenon that involves input from proximal factors, endoneurial pathways, end target muscles, and a general supportive growth environment (Abdullah et al., 2013).

2.3.1.4 Muscular Re-innervation:

Muscles, in addition to nerves, exhibit adaptive repair characteristics after injury. Katz and Miledi (1964) split the Sartorius muscle of frogs into two pieces, a pelvic section with no motor innervation (denervated) and a tibial portion with motor innervation. After denervation the pelvic segment did not respond to nerve stimulation. The pelvic section of muscle became 100 to

1,000 times more sensitive to ACh than corresponding segments of a control muscle. Re-innervation of the pelvic portion could then be obtained by surgically implanting the Sartorius nerve in to the denervated muscle due to increased ACh sensitivity. The innervated tibial section also became slightly more sensitive to ACh, specifically in the area near the injury site (Katz & Miledi, 1964). These results showed that injury to muscles has similar effects to denervation; both remove the neural control of ACh sensitivity along muscle fibers. Katz and Miledi furthered the understanding of AChs role in re-innervation.

In 1995 Kuiken, Childress, and Rymer investigated the recovery of muscle after grafting a motor neurons onto denervated rat skeletal muscle. The researchers hypothesized that "hyper-reinnervation", grafting a large amount of neurons, of a denervated muscle would enhance the possibility of new terminal axons re-innervating muscle fibers, resulting in functional recovery. Results of this study found that hyper-reinnervation improved muscle to recovery after injury. The mass availability of motor neurons ensured an adequate number of motor neurons to re-innervate the muscle. The researchers concluded that such findings may be applicable to amputees, who experience muscle denervation, and that grafting of the residual peripheral nerves may enhance the recovery process and allow patients to utilize the newly innervated muscle functionally (Kuiken, Childress, & Rymer, 1995).

Wu and Kaas (2000) investigated the natural biological occurrence of muscular re-innervation in primates with upper-extremity amputation (the only study to investigate peripheral nerve re-innervation in amputees). First they determined the typical motor neuron organization within primates through retrograde tracers, that label motor neurons, injected into muscles. They established in control primates that: (1) motor neurons are located within the ventral horn of the spinal cord, (2) motor neurons form longitudinal columns, (3) motor neurons innervating the upper limbs are found in the lateral motor neuron pool of the ventral horn, (4) motor neurons for the upper arm are located in the ventromedial portion of the lateral motor neuron pool at C4-C8 levels, (5) motor neurons for the distal arm are located in the dorsolateral portion of the lateral motor neuron pool at the levels of C6-T2, and (6) small hand muscles are located in the extreme dorsolateral portion at the levels of C8-T2. Three primates with long-time unilateral amputation, at the shoulder level, were then investigated. The same tracers were injected into the intact limb, at the distal arm and shoulder level, resulting in similar findings to those in control subjects. Tracers injected into the shoulder muscles only, on the intact side, showed labeled neurons in the ventromedial portion of the lateral motor neuron pool above the level of C6. Tracers injected into the shoulder muscles of the amputated limb showed the same extent of labels as the entire intact limb, labeled neurons in both the dorsolateral and ventromedial portion of the lateral motor neuron pool, implying that nearly all motor neurons survived the amputation process. Muscles of the shoulder were hyper-innervated, innervated by both their expected nerve and re-innervated nerves of the distal arm. Results from this study provide evidence of motor nerves that previously controlled the amputated limb re-innervating new muscle targets of the residual limb. It was hypothesized that these results were due to damage of the proximal muscles during

amputation, causing partial denervation, allowing foreign nerves to establish new functional connections (Wu & Kaas, 2000).

2.3.1.5 Surgical Procedures

Direct Muscular Neurotization (DMN) and Targeted Muscle Re-innervation (TMR) involves implantation of a nerve directly into a muscle. DMN involves dividing the end of a nerve into multiple fascicles and implanting the fascicles directly into the endomysium, the sheath of connective tissue around a fascicle, in a denervated muscle allowing the formation of new neuromuscular junctions (G. Brunelli & Monini, 1985). Damage to a nerve initiates Wallerian degeneration and the removal of a damaged axon and neuromuscular junction distal to the injury. The microenvironment then alters to support axonal regeneration with ACh receptors spread over the muscle. Functional recovery has occurred as early as one month after implantation (G. A. Brunelli, 2005). The results from DMN are being further manipulated in TMR to allow upper extremity amputees to intuitively control a prosthetic limb.

TMR artificially initiates the neural repair mechanism by reassigning nerves that once transmitted signals to the anatomic hand/arm to other muscles and interfacing a prosthesis with the newly innervated muscles. This process allows people who are upper extremity amputees to control prosthetic devices by executing normal motor commands. The first successful TMR procedure was reported in 2004. Residual arm nerves, nerves responsible for executing upper extremity movement (Blair et al., 1987), were re-innervated into the pectoralis major of a person with a shoulder disarticulation amputation, since its functional capabilities were lost with the removal of the insertion site on the humerus (T A Kuiken et al., 2004). The pectoralis major was divided into three sections, the clavicular head, and upper and lower segments of the sternal head, after denervating each section by severing the original innervation. The musculocutaneous nerve was sutured to the clavicular head, the median nerve to the upper segment of the sternal head, and the radial nerve to the lower segment. The ulnar nerve was sutured to pectoralis minor, however re-innervation was unsuccessful. For recovery the participant was encouraged to move his phantom limb naturally. The amount of signal generated by each muscle was proportional to the amount of response by the prosthetic device, and strong co-contractions enabled switching between operations of the terminal device to control multiple degrees of freedom. Even with TMR, amputees must learn to control the strength of a muscle contraction and differentiate co-contraction patterns to switch between device modes if more than 2 degrees of freedom are utilized (T A Kuiken et al., 2004). However, TMR gives prosthetic control a natural feeling, since participants are able to learn how to control the prosthetic device by activating the same motor commands used to control the movement of their phantom limb, due to successful re-innervation of the distal peripheral motor nerves to intact proximal muscles.

2.4 Literature Review Summary:

An amputation of an upper extremity limb initiates adaptive physiologic repair mechanisms within the peripheral motor nerves and residual limb muscles. Residual muscles and nerves are biochemically altered to assist the repair by facilitating a growth environment that

supports regeneration/re-innervation. Regeneration and/or re-innervation may play a large role in an amputee's ability to control movement of his/her phantom limb after recovery of the PNS. Proximal muscles, of trans-humeral amputees, that do not typically control fine motor movements have shown activity when completing such movements of the phantom limb. However, more than 30% of upper extremity amputees fail to successfully learn how to intuitively control their prescribed prosthetic devices, leading to rejection. Rejection may be due to a disconnect between the muscle activity utilized to control the phantom limb and the muscle activity required to control the device. Surgically induced re-innervation procedures are being performed to specifically re-program muscles of the chest and upper arm to facilitate signals from the residual nerves to allow for intuitive control of a prosthetic devices through control of the phantom limb.

2.5 Study Hypotheses:

Individuals with upper extremity amputation experience physiological changes within the PNS and residual limb. The majority of upper extremity amputees are capable of controlling a phantom limb, and many reject their prescribed prosthetic device. This dissertation was designed to explore novel, preliminary, theories that may aid in explaining the ability of an amputee to control the movement of their phantom limb. PLC may be, in part, facilitated by the physiological repair mechanisms initiated by the PNS, suggesting that anatomically unexpected muscles will be used to control a phantom limb. It is possible that the biological repair of severed peripheral nerves leads to intuitive recovery of motor developed skills to control the phantom limb, whereas extensive motor learning is required to control a prosthetic device, resulting in control conflicts. Typical prosthetic devices are designed to be controlled by specific movements. For example, myoelectric prostheses are generally controlled by contraction of large flexor and extensor muscles. Body-powered devices are controlled by movements of the upper arm and trunk (E. Biddiss & Chau, 2007). The anatomical muscles required for hand/wrist/elbow movements are not necessarily targeted for control over these devices. Finally, it is possible that motor learning, required for the use of a prosthesis, may impact similar movements of the phantom limb. For example, a trans-radial amputee may be required to learn to utilize contractions of the shoulder to control the terminal device of the prosthesis, this learning may become incorporated into movements of the phantom limb. Based on these novel theories (peripheral nerve re-innervation/recovered motor developed skills/motor learning), the hypotheses put forward by this dissertation are (1) different muscle activation patterns than anatomically expected will be utilized to complete phantom limb movements (a potentially recovered motor developed skill), (2) different muscle activation patterns will be utilized for control over a prosthetic device (a motor learned skill), and (3) body-powered prosthetic users will utilize muscle activity of the upper arm to control movement of their phantom hand/wrist, whereas myoelectric users will not.

The following studies aim to: compare muscle activation patterns of all levels of phantom limbs to anatomically known muscle activation patterns (chapter 4), compare muscle activation

patterns of phantom limb movements to muscle activation patterns used to control prosthetic devices (chapter 5), and compare upper arm muscle activation to control movement of the phantom hand/wrist based on type of prescribed prosthesis (chapter 6). Identifying which muscles each amputee is using for PLC may allow for improved design of prosthetic devices that use the same muscles, making control of prosthetic devices more intuitive. Additionally, results from these studies may lead to new/more informed surgical procedures for amputations.

CHAPTER 3: METHODS

All three studies were completed in a one-time visit. A total of 15 participants were recruited and each participant completed the entire process (with the exception of subject 3 who did not utilize a functional prosthesis). The following chapter describes the participants, the experimental protocol, and the process for data recording and analyses. Each individual chapter then describes the components specific to the study it represents.

3.1 Participants

Fifteen individuals with upper extremity amputation participated in this dissertation project. All fifteen participants were utilized for study 1, fourteen were included for study two, and eleven with below elbow amputations were included for study three. In total, two individuals with wrist disarticulations, ten individuals with trans-radial amputations, two individuals with trans-humeral amputations, and one individual with a shoulder disarticulation participated. The average age of participants was 49.4±15 years with 21±17 years since amputation. None of the participants had undergone targeted muscle re-innervation. Characteristics collected from each participant are outlined in Table 3.1. Participants were recruited through informational pamphlets and flyers at support groups, amputee clinics in Saskatoon and Regina, and the National Amputee Coalition Conference of America. Data was collected in the School of Rehabilitation Sciences at the University of Saskatchewan, in the Physical Therapy department at Wascana Rehabilitation Centre, and in San Antonio, TX at the 2019 National Amputee Coalition Conference of America. The Research Ethics Board at the University of Saskatchewan, Saskatoon, SK, approved all study procedures. Each participant was provided with and signed informed consent prior to completing the study.

Table 3.1: Participant Characteristics

Subject Number	Age	Sex	Time Since Amputation (years)	Side	Level	Cause	Prosthetic Type	Terminal Device	Usage (Hrs/Day)	PLC Over Time	PLC on Pro Usage
1	85	M	1	Left	Trans-Humeral	Trauma	Body Powered	Hook	4-6	Intensified	No Role
2	41	F	41	Left	Trans-Radial	Congenital	Myoelectric	Hand	0-2	Remained	No Role
3	47	F	41	Right	Trans-Radial	Trauma	Not Functional	N/A	N/A	Remained	N/A
4	55	M	17	Right	Trans-Radial	Trauma	Body Powered	Hook	8+	Intensified	Makes Easier
5	50	F	28	Left	Wrist Disartic.	Trauma	Myoelectric	Hook	0-2	Intensified	Makes Easier
6	57	F	1	Right	Shoulder Disartic.	Disease	Myoelectric	Hand	4-6	Intensified	No Role
7	57	F	57	Left	Trans-Radial	Congenital	Myoelectric	Hook	8+	Remained	No Role
8	30	F	30	Left	Trans-Radial	Congenital	Myoelectric	Hand	8+	Remained	No Role
9	54	M	5	Left	Trans-Humeral	Trauma	Body Powered	Hook	8+	Remained	No Role
10	31	M	31	Right	Trans-Radial	Congenital	Myoelectric	Hand	8+	Remained	No Role
11	27	F	3	Left	Trans-Radial	Disease	Myoelectric	Hand	8+	Remained	Makes Easier
12	44	M	28	Left	Trans-Radial	Trauma	Body Powered	Hook	8+	Faded	No Role
13	37	M	13	Left	Wrist Disartic	Trauma	Body Powered	Hook	0-2	Intensified	Makes Easier
14	69	M	16	Left	Trans-Radial	Trauma	Body Powered	Hook	8+	Remained	No Role
15	57	M	3	Left	Trans-Radial	Trauma	Body Powered	Hook	8+	Intensified	No Role

[1] Data collected from participants: white = utilized for all three studies, blue = utilized for studies 1 and 2, red = utilized for study 1.

3.2. Experimental Protocol

After completing informed consent, participants were asked a series of questions designed to gain information regarding their background and experience with PLC. Following questionnaires, participants sat at an adjustable plinth for electrode placement. Kinesiologic EMG, fine wire and surface electrodes, were used to examine muscle activity within the residual limb during movements of the phantom hand/arm and terminal device of the prosthesis. Fine wire electrodes enabled targeting of small, deep, or less accessible, and specific muscles, especially those residing within the prosthetic socket, with precision that is not available with the use of surface electrodes. Surface electrodes were utilized only for large, superficial, easily accessible muscles that resided outside of the prosthetic socket. Table 3.2 visually depicts which type of electrode was utilized for each muscle based on level of amputation and socket design.

Table 3.2: Type of Electrode Used

Muscles	FDP	EDC	Pronator Teres	Supinator	Biceps Brachii	Triceps	Anterior Deltoid	Pectoralis Major	Trapezius
Subjects									
1					FW	FW	Surface	Surface	
2	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
3	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
4	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
5	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
6							FW	Surface	Surface
7	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
8	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
9					FW	FW	Surface	Surface	
10	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
11	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
12	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
13	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
14	FW	FW	FW	FW	Surface	Surface	Surface	Surface	
15	FW	FW	FW	FW	Surface	Surface	Surface	Surface	

[1]FW = Fine wire, FDP – flexor digitorum profundus, EDC – extensor digitorum communis

Target muscles varied depending on the level of amputation, including: flexor digitorum profundus (FDP), extensor digitorum communis (EDC), pronator teres, supinator, bicep brachii, triceps, anterior deltoid, and pectoralis major. In the shoulder-disarticulation participant, trapezius was targeted since biceps and triceps were not available. The expected muscle activation patterns of anatomically intact muscles are based on prior literature of muscle activation during movements of the arm in able bodied people with intact limbs. FDP is a major flexor of the digits and a secondary wrist flexor (M. E. Johanson, James, & Skinner, 1998; M. Elise Johanson et al., 1990; Levangie & Norkin, 2005). EDC is a major finger extensor and wrist extensor that does not cause radial or ulnar deviation (M. Elise Johanson et al., 1990; Levangie & Norkin, 2005; Schieber & Thach, 1985). Supinator is the only muscle active during slow-paced supination of the forearm, however biceps brachii is also active during fast-paced supination of the forearm and when the elbow is flexed during supination (Karen, Richard, James, J, & Thomas, 2006). Supinator is responsible for supinating the forearm and plays no role in flexing or extending the elbow joint (Moore, Dalley, & Agur, 2013). Pronator teres activates during pronation of the forearm when the arm is in a neutral position (Karen et al., 2006; Sergio & Ostry, 1995). However, pronator teres is a weak elbow flexor and therefore may be active during elbow flexion (Logan, 2006; Thepaut-Mathieu & Maton, 1985). Biceps brachii is the major elbow flexor, assisted by brachioradialis and brachialis (neither targeted in this study) in the upper arm and by pronator teres, flexor carpi radialis (not targeted in this study) and extensor carpi radialis (not targeted in this study) (Larson, 1969; Logan, 2006). The triceps are the major muscles responsible for elbow extension; they are assisted by the much smaller anconeus (not targeted in this study) (Levangie & Norkin, 2005; Logan, 2006). Anterior deltoid and pectoralis major are prime shoulder moving muscles responsible for flexion, internal rotation and adduction, and flexion and rotation respectively (Buneo, Soechting, & Flanders, 1994; Flanders, 1991)

A licensed clinician with 30 years of fine wire EMG experience placed the electrodes. Prior to electrode placement the skin was cleaned with alcohol and Nuprep gel. To identify and confirm the location of each muscle, anatomical landmarks and palpation of the residual limb during different attempted movements was conducted in addition to visual inspection of the EMG signal (Perotto & Delagi, 2011). *The Anatomical Guide for the Electromyographer 5th Edition,* was utilized for standardized technique for electrode placement. For the placement of a fine wire electrode into EDC, the examiner grasped the upper third of the forearm with their thumb placed on the subjects ulna and third digit placed on the subjects radius. The second digit bisected the thumb and third digit and the electrode was placed in the muscle identified by the tip of the second digit at a depth of one-half inch. For the placement of the FDP electrode, the examiner placed her fifth digit on the olecranon, with the remaining digits along the ulna. The electrode was placed in the muscle identified by the tip of the second digit on the ulnar side of the arm. The electrode for pronator teres was placed two finger widths distal to the point where the medial epicondyle and biceps tendon cross. The electrode for supinator was placed radial to the lowest portion of the biceps tendon, through EDC. When fire wires were needed for biceps

brachii they were inserted into the muscular portion of the middle of the upper anterior arm. The triceps electrode was placed into the lateral head, posterior to the deltoid insertion. The electrode for the anterior deltoid was placed three finger widths inferior to the acromion (Perotto & Delagi, 2011). Table 3.3 depicts targeted muscles in each subject. Once all electrodes were placed, a resting trial was performed, and then participants were asked to complete a series of movements with their phantom hand/arm. Surface and fine wire EMG data were collected at 2000 Hz using a 16-channel system (MA416, Motion Lab Systems, Inc., Baton Rouge, LA, USA; input impedance=31KΩ, common mode rejection ratio=100 dB at 40 Hz, bandpass filter 10–1000 Hz). Surface electrode signals were amplified to a setting of 2 gain (4000) resulting in a maximum input signal of ± 2.8 mV. Fine wire electrode signals remained at 0 gain (350) resulting in a maximum input signal of ± 18.0 mV.

Table 3.3: Muscles Targeted Based on Level of Amputation

Sub #	FDP	EDC	Pronator Teres	Supinator	Biceps Brachii	Triceps	Ant. Deltoid	Pec Major	Traps
1-TH									
2- TR									
3- TR									
4- TR									
5- WD									
6- SD									
7- TR									
8-TR									
9-TH									
10-TR									
11- TR									
12- TR									
13- WD									
14- TR									
15- TR									

[1] TR – trans-radial, TH – trans-humeral, WD – wrist disarticulation, SD – shoulder disarticulation, FDP – flexor digitorum profundus, EDC – extensor digitorum communis, Traps – trapezius.

[2]Green = muscles targeted

All fifteen participants completed all movements of the phantom hand/arm and, based on level of amputation, movements of the residual limb. Participants were instructed to sit comfortably and rest their forearms, or Humerus for trans-humeral amputees, on the plinth in front of them, mimicking the intact hand/arm position with their phantom limb. The palms were placed in a neutral position facing each other as the start position for all movements of the forearm. All movements, including finger flexion/extension (hand open and closing), wrist flexion/extension, forearm supination/pronation, elbow flexion, and elbow extension, were demonstrated by the examiner to ensure the participants understood each movement (Table 3.4). To begin data collection, participants sat quietly in the start position to record a 30 second rest trial. Movement trials were then initiated with finger flexion/extension by asking the participant to open and close their phantom hand briefly holding the extreme of available motion (fully opened or closed). Participants then returned to the rest position with the forearm (or Humerus) supported and performed wrist flexion/extension, holding the extreme of available motion (fully flexed or extended). Participants returned to the rest position and then performed forearm supination/pronation by rotating the palms to the ceiling then to the table. They were asked to hold the extreme of available motion (fully supinated or pronated). Elbow flexion and extension were captured as independent movements by placing the participant in a gravity resisted muscle testing position facilitating a concentric muscle contraction when performing the desired movement. For elbow flexion, participants were given the option of sitting away from the table or standing up, with arms relaxed at their sides. They were then asked to maintain relaxed hands as they curled their arms up toward the shoulder, holding the extreme of this position before returning to the rest position. To complete elbow extension participants were asked to stand, lean forward by bending their hips so their torso was horizontal and their upper arms were held in line with the torso allowing their elbows to bend to 90 degrees. In this position, the participant then extended their elbows, holding the extreme of the available motion before returning to the rest position. Table 3.4 outlines the order of movements completed by each participant and the active muscle during each movement in an anatomically intact limb based on previously described studies. Target muscles were chosen as they represent the primary contributors to the selected movement, although other muscles may function as secondary contributors (Table 3.4). None of the target muscles are normally expected to be active in any other movements. FDP was chosen for its active role in finger and wrist flexion. EDC was chosen for its active role in finger and wrist extension. Pronator teres was chosen for its active role in pronation of the forearm. Supinator was chosen for its active role in supination of the forearm. Biceps were chosen for their active role in elbow flexion and supination of the forearm. Triceps were chosen for their active role in elbow extension. Anterior deltoid, pectoralis major, and trapezius were chosen for their active roles in shoulder rolling.

Table 3.4: Order of Movements and Anatomically Expected Muscle Activations

Movement Task	Expected Muscle Activity in an Anatomically Intact Limb
Finger Flexion (Close hand)	**FDP*[1]** FDS[2]
Finger Extension (Open hand)	**EDC*** EDM, EPL, EPB, EI
Wrist Flexion	**FDP*** FDS, FCU, FCR, PL
Wrist Extension	**EDC*** ECRL, ECRB, ECU, EDM, EPL, EPB, EI, APL
Wrist Pronation	**PT*** PQ,
Wrist Supination	**S*** **Biceps***
Elbow Flexion	**Biceps*** Brachialis, Brachioradialis, **PT*,** FCR, ECR
Elbow Extension	**Triceps*** Anconeus,
Forward Shoulder Roll	**Anterior deltoid*** **Pectoralis major*** Coracobrachialis, Latissimus Dorsi **Trapezius** [3]

[1]Movements requested and anatomically known muscles responsible for the movement in an intact limb. * Indicates a study specific target muscle.

[2]Non-bolded muscles are additional anatomically expected muscles for each movement, however they were not targeted in this study.

[3]Trapezius became a target muscle in one participant.

[4]FDP = flexor digitorum profundus, FDS = flexor digitorum superficialis, EDC = extensor digitorum communis, EDM = extensor digitorum minimi, EPL/B – extensor pollicus longus/brevis EI = extensor indicis, FCU = flexor carpi ulnaris, FCR = flexor carpi radialis, PL = palmaris longus, ECRL/B = extensor carpi radialis longus/brevis, ECU = extensor carpi ulnaris, APL = abductor pollicus longus, PT = pronator teres, PQ = prontator quadratus, S = supinator

Prior to initiation of each movement a member of the research team demonstrated the movement. Participants were instructed to complete 10 self-paced movement cycles, however a one-minute time limit was placed on each trial. Three trials were completed for each movement. For every movement the participant was asked to move the phantom hand/arm and the intact hand/arm simultaneously at the same pace and through the same range of motion. Specifically participants were instructed to use the intact limb as a visual representation of the movement that the phantom limb was completing. By having simultaneous movement the research team was able to "visualize" the phantom movements. All participants were required to start in the standardized rest position, then cycle through each phase of a movement, such as from flexion to extension. A separate step voltage channel was synchronously recorded and manually triggered by the researcher to delineate phases of the participant's movement cycles.

Once all required movements of the phantom hand/arm and residual limb were completed each participant was asked to don their prosthesis (with the exception of Subject 3 who did not utilize a functioning prosthesis). Once the prosthesis was on, the participants then completed three trials of 10 cycles of each movement that the prosthesis was capable of conducting. Movements included opening/closing of the terminal device.

3.2.1 Data Processing

All data processing was completed using Matlab 9.6 (R2019a, The Mathworks Inc., Natick, MA). Raw EMG signals were high-pass filtered at 30 Hz to eliminate heart rate contamination (Drake & Callaghan, 2006; K. Reilly et al., 2006). These data were then full-wave rectified and linear enveloped using a dual-pass fourth-order low-pass Butterworth filter at 4 Hz (Ho, Cudlip, Ribeiro, & Dickerson, 2019).

Each movement was normalized to 100% of a cycle using the step voltage events manually triggered by the researcher during data collection from observing the intact limb. A full cycle included both components of the movement such as flexion/extension or supination/pronation, except for the isolated movements of elbow flexion and extension that included the movement and return to rest. Mean activation levels were calculated by ensemble averaging within-participant cycles from trigger "on" and trigger "off" phases. Mean activation data were then compared to a threshold value to determine is muscles were active or not. Muscles were identified as active when mean activation data exceeded two standard deviations above a rest trial (Konrad, 2005; Roberts & Gabaldón, 2008).

Similar to other kinesiologic EMG studies the results presented are descriptive in manner, focusing on explaining the coordination and interactions of each muscle identified for individual participants during different movements (Soderberg & Knutson, 2000). This study specifically investigated muscle activity (on) and muscle inactivity (off), rather than the amplitude of the signal due to inability of gaining baseline maximum voluntary contraction levels. Descriptive statistics were used to describe the variables. Additionally, nonparametric, goodness of fit Pearson Chi-Square tests were used to examine frequency of occurrence for categorical variables

throughout the dissertation. Although multiple movements were completed by the same participant, and CNS factors could be similarly involved in each movement, each specific movement was analyzed as an independent movement. Previous research has shown that amputees make separate phantom movements utilizing different muscle activation patterns for each movement (K. Reilly et al., 2006), therefore each movement was analyzed independently. No previous literature has explored the statistical significance of muscle activation during phantom limb movements, therefore the expected frequencies were compared based on chance frequencies (e.g. 50/50 for a "yes" vs. "no" categorization for the occurrence of muscle activity) and the analysis was designed to determine if the frequency of occurrence was different than chance alone. Rejecting the null hypothesis suggests that the occurrence being tested was not random chance. Significance level was set at $P<.05$. Data were analyzed using IBM SPSS Statistics. Methods utilized to determine individual goals of each study are outlined within the following separate chapters.

CHAPTER 4: MUSCLE ACTIVATION PATTERNS DURING PHANTOM LIMB CONTROL IN UPPER EXTREMITY AMPUTEES

4.1 Introduction

People with upper extremity amputation experience the sensation of the presence of the missing limb, known as a phantom limb (Herta Flor, 2002; Herta Flor et al., 1998). Directed, purposeful, and intentional movements of a phantom limb are known as phantom limb control (PLC) (Brodie et al., 2007). PLC presents in traumatic or disease-related amputations (>80%) and congenital limb loss (>18%), necessitating muscle activity within the remaining residual limb to execute movements (Collins et al., 2017; Herta Flor, 2002; Herta Flor et al., 1998; Estelle Raffin et al., 2012). Studies have shown that proximal muscles of the residual limb, in trans-humeral amputees, produce muscle activity during fine motor movements of the phantom hand, movements those muscles would not complete in an anatomically intact limb (Gagné et al., 2009; K. Reilly et al., 2006). These studies hypothesized that level of amputation plays a vital role in the muscle activation patterns required to execute movement of a phantom limb. They found in three trans-radial amputees that muscle activity was similar to that expected for the movement of an anatomically intact limb (K. Reilly et al., 2006). They also postulated that high-level amputations result in inadequate motor neurons to execute movement of a phantom limb (K. Reilly et al., 2006). The current study operates on the theory that PLC may largely be due to the Peripheral Nervous Systems (PNS) physiological repair response to injury, and therefore, impacts muscle activation patterns at all levels of amputation.

With amputation, or congenital absence of a limb, re-growing or newly developing axon terminals are not necessarily capable of connecting with their anatomically expected target muscle, causing the possibility of nerves re-innervating unexpected target destinations (Navarro, 2009; W. Sulaiman & Gordon, 2013). It may be possible that re-innervation of motor nerves, to denervated or injured muscles, facilitates the execution of motor commands to unexpected muscles used to control the movement of a phantom limb. Re-innervation is currently being surgically manipulated in order to specifically target muscles of the trunk to enhance control of prosthetic devices by making the required movements more intuitive (T A Kuiken et al., 2004). To investigate the potential of this theory, kinesiologic electromyography (EMG) was used to record specific muscle activity within the residual limb, in amputees with varying levels of amputation, while completing movements of the phantom hand/arm. The hypothesis was that people with all levels of upper extremity amputation would have muscle

activity used to control a phantom limb, and these muscle activity patterns will differ from expected muscle activity patterns used to control an anatomically intact limb.

4.2 Methods

4.2.1 Participants

All fifteen individuals enrolled in the dissertation project participated in this specific study (Chapter 3). The average age of participants was 49.4± 15 years with 21± 17 years since amputation. Characteristics collected from each participant are outlined in Table 3.1.

4.2.2. Experimental Protocol and Analysis

To complete this specific study all fifteen participants completed the methods outlined in Chapter 3. Data was taken from EMG recordings during phantom limb movements. No prosthesis was required for this study and data from prosthetic movements was not analyzed.

There are multiple descriptors of muscle activation patterns. Anatomically expected activity is the pattern of activation for individual muscles, that has been identified by previous research, based on movements executed. Variations of these patterns are considered unexpected and include; anatomically inappropriate activity, abnormal co-contractions, prolonged activity, early onset of activity, and delayed onset of activity. Anatomically inappropriate activity occurs when a muscle (or muscles) not expected to contract during a specific movement is active, without activity of the expected muscle. For example muscle activity within only the anterior deltoid, or activity in anterior deltoid and biceps, during finger movements would be unexpected, and categorized as an anatomically inappropriate activation (Brunner & Romkes, 2008). Abnormal co-contractions of muscles involve the spread of muscle activity to include the expected muscle along with muscles that are not normally utilized for the completion of the movement, especially when antagonist muscles are active (Farmer et al., 1998). Prolonged activity occurs when a muscle remains active during the antagonist movement, or fails to stop activity in an appropriate manner before the start of the antagonist movement (Brunner & Romkes, 2008; Hallett, Shahani, & Young, 1975; Hore, Wild, & Diener, 1991). Early onset of activity occurs when a muscle becomes active before the start of the antagonist movement (Brunner & Romkes, 2008); and delayed onset of activity occurs when the muscle fails to activate at the initiation of the movement (Hore et al., 1991). Although all components of activity were investigated for each movement, abnormalities of EMG activity involving anatomically inappropriate activity, and abnormal co-contractions were required for the definition of unexpected muscle activation. Timing differences, although evaluated and discussed below, do not solely categorize the movement as being completed by unexpected muscle activation. Such differences could be due to anatomical differences between participants, or timing of trigger data collection, and therefore are not individually utilized for the definition of anatomically unexpected muscle activation.

The additional occurrence of no muscle activation detected was also investigated. No activation detected means that the muscles targeted with electrodes were silent during the requested movement. Electrode placement was chosen based on specific activity of each muscle in a requested movement. No activation detected could imply that muscles other than those anatomically expected and targeted by electrodes may be completing the requested movement, or that the participant was not capable of eliciting necessary muscle contractions to complete the movement.

To obtain the specific outcome measure of this study, muscle-activation patterns from each phantom movement were compared to expected behavior within anatomically intact limbs. Expected behavior is outlined in the above Table 3.4. Muscle activation patterns during each phase of a cycle were investigated, such as which muscles were "on" and "off" for hand opening, hand closing, wrist flexion, wrist extension, wrist supination, elbow flexion, and elbow extension. Muscles were determined to be "on" once the threshold of activity reached more than two standard deviations above the rest trial (Roberts & Gabaldón, 2008). Unexpected muscle activation patterns, varying from patterns determined by previous research in anatomically intact limbs (Buneo et al., 1994; M. E. Johanson et al., 1998; M. Elise Johanson et al., 1990; Karen et al., 2006; Larson, 1969; Levangie & Norkin, 2005; Moore et al., 2013; Schieber & Thach, 1985; Sergio & Ostry, 1995; Thepaut-Mathieu & Maton, 1985), during phantom limb movements, show that different muscles than anatomically expected are being utilized to complete movements, which potentially could be caused by re-innervation after PNS injury.

Muscle activation patterns were then grouped by overall findings and categorized by level of amputation. This allowed for the identification of unexpected muscle activation occurrences based on level of amputation. To investigate the hypothesis that people with all levels of upper extremity amputation would have muscle activity used to control a phantom limb, and these muscle activity patterns will differ from expected muscle activity patterns used to control an anatomically intact limb, goodness of fit Chi Square tests were conducted to determine if the frequency of occurrence was different than random. The first analysis involved determining if the frequency of muscle activation occurrences, in all levels of amputation, during phantom limb movements versus no muscle activation was different than random (50/50 chance).

The second analysis involved determining if the frequency of anatomically unexpected muscle activation patterns versus anatomically expected muscle activation patterns was different than random in participants who still have remaining muscle bellies of the muscles needed for hand control. For this analysis only participants who could potentially utilize an anatomically expected muscle activation pattern were included. For instance, a trans-humeral amputee, who does not have remaining muscle bellies from muscles used for hand control, would not have the chance to use anatomically expected muscles to open and close the phantom hand. Trans-humeral amputees are anticipated to utilize only unexpected muscles to complete phantom hand movements, therefore they were excluded from statistical analysis for those movements so that

we could identify if anatomically unexpected patterns were being utilized regardless of the chance for anatomically expected muscles to activate as expected. Statistical analysis was conducted solely to determine if the occurrence of unexpected muscle activity is greater than chance, not to determine the overall significance of unexpected muscle activity. Including movements with no chance of being completed by anatomically expected muscles would skew the results in favor of the hypothesis. To further explore the occurrence of unexpected muscle activation patterns, a Chi Square test was conducted to determine if the frequency of anatomically inappropriate or abnormal co-contractions differed from random chance.

4.3 Results

Fifteen participants completed six requested movements (finger flexion, finger extension, wrist flexion, wrist extension, forearm supination, forearm pronation) of a phantom forearm; three participants completed two additional movements (elbow flexion, elbow extension) of a phantom upper arm, for a total of 96 phantom movements completed by the collection of study participants. Analyzed EMG data was visually inspected for unexpected muscle activation, including anatomically inappropriate activity, abnormal co-contractions, and no activation, along with prolonged activity, early onset of activity, and delayed onset of activity. Results for each movement completed by each participant are visually depicted in Table 4.1.

Table 4.1: Complete Muscle Activation Categorizations Based on Phantom Limb Movements

Movements	Finger Flex	Finger Extend	Wrist Flex	Wrist Extend	Wrist Pro.	Wrist Sup.	Elbow Flex	Elbow Extend
Subjects								
1	Inappropriate	Inappropriate	Inappropriate	No Activation	Inappropriate, Pro	No Activation	Co	Co
2	Co w/A	No Activation	Inappropriate, A	No Activation	Inappropriate, A	Co, Early	No Phantom	No Phantom
3	Co w/A	Co w/A	Co w/A	Co, Delay	Inappropriate	Inappropriate	No Phantom	No Phantom
4	Co, Pro	Inappropriate A, Early	Expected	Expected	Inappropriate A	Expected	No Phantom	No Phantom
5	Expected	No Activation	No Activation	Co, Delay	Co w/A	Co w/A, Early	No Phantom	No Phantom
6	Inappropriate	No Activation	Inappropriate, Delay	No Activation	No Activation	Inappropriate, Delay	Inappropriate	Inappropriate
7	Co, Early	Expected	Co, Early	Expected	Inappropriate A	Co, Early	No Phantom	No Phantom
8	Inappropriate	No Activation	Inappropriate	Inappropriate, Delay	Expected	Expected	No Phantom	No Phantom
9	Inappropriate	No Activation	Inappropriate	No Activation	Inappropriate	Inappropriate, Early	Inappropriate	Co w/A,
10	Inappropriate, Pro	Inappropriate	Inappropriate, Pro	Inappropriate, Delay	Co w/A	Expected	No Phantom	No Phantom
11	Expected	Expected	No Activation	Co, Early	Co, Pro	Inappropriate	No Phantom	No Phantom
12	No Activation	No Activation	Inappropriate, Co	Inappropriate, Delay	Expected	Co	No Phantom	No Phantom
13	Co w/A, Pro	Co w/A, Early	Inappropriate, Co, Pro	Co, Early	Co, Pro	Co w/A, Early	No Phantom	No Phantom
14	Expected	Co	Co w/A	Co, Early	Inappropriate A	Co, Early	No Phantom	No Phantom
15	Co w/A, Pro	Co w/A, Early	Co	Co w/A, Early	Co	Co w/A, Early	No Phantom	No Phantom

[1]15 participants, 96 phantom limb movements, analyzed EMG data visually inspected for expected, anatomically inappropriate muscle activity, abnormal co-contractions, prolonged/early/delayed activity, and no activation for expected movements.

[2]Inapproprate – anatomically inappropriate activity, Co – abnormal co-contractions, A – antagonist muscle active, Pro – prolonged muscle activity, Early - early onset of activity, Delay – delayed onset of activity, No Activation– no activity during movement, No phantom – this movement did not require movement of a phantom limb

The data collected from each participant was then grouped by anatomically expected muscle activations, co-contractions of the anatomically expected muscle plus the addition of other muscles, anatomically inappropriate muscle activation and no activation. These groups were then categorized by level of amputation. Table 4.2 outlines the percent of phantom limb movements completed by anatomically expected, anatomically unexpected, and no muscle activation patterns based on level of amputation.

Table 4.2: Categories of Phantom Limb Movements Completed Based on Level of Amputation

	WD	TR	TH	SD
1.Anatomically Expected	8.3%	20%	0%	0%
2. Abnormal Co-contractions	66.7%	40%	18.8%	0%
3. Anatomically Inappropriate	8.3%	28.3%	62.5%	62.5%
4. No Activation	16.7%	11.7%	18.5%	37.5%

[1] Percent of phantom limb movements completed by (1) anatomically expected muscle activation patterns, (2) abnormal co-contractions, (3) anatomically inappropriate muscle activation patterns, (4) exhibiting no muscle activation.

[2]Abbreviations: WD – wrist disarticulation, TR – trans-radial, TH – trans-humeral, SD – shoulder disarticulation

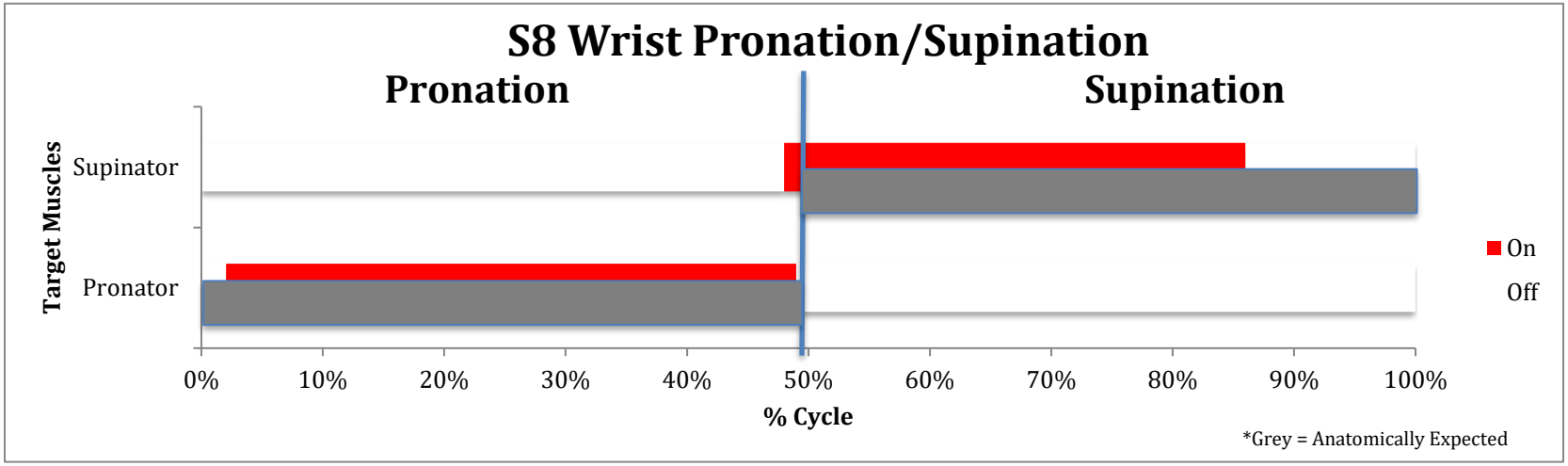
It was hypothesized that people with all levels of upper extremity amputation would have muscle activity within the residual limb used to control phantom limb movements. The absence of muscle activity within muscles targeted by electrodes could imply that a different muscle, not targeted in this study, was being utilized to complete the movement or that the participant was unable to successfully execute the phantom movement requested. Fifteen movements (15.6%) presented with no muscle activation within muscles targeted by electrodes. A chance alone occurrence would have resulted in 48 movements with no muscle activation detected and 48 movements with activation detected. The frequency of the occurrence of no muscle activations compared to muscle activity within the residual limb during phantom limb movements was different from chance alone, $\chi^2(1, N=96) = 45.375$, $p < .001$ The participant with a shoulder disarticulation presented with the highest percentage of movements (37.5%) with no muscle activation detected (Table 4.2). Target muscles for this participant were limited to anterior deltoid, pec major, and trapezius. Activity was observed within pec major for flexion of the phantom fingers, wrist and elbow in varying patterns for each movement. Activity within trapezius was observed for extension of the phantom elbow.

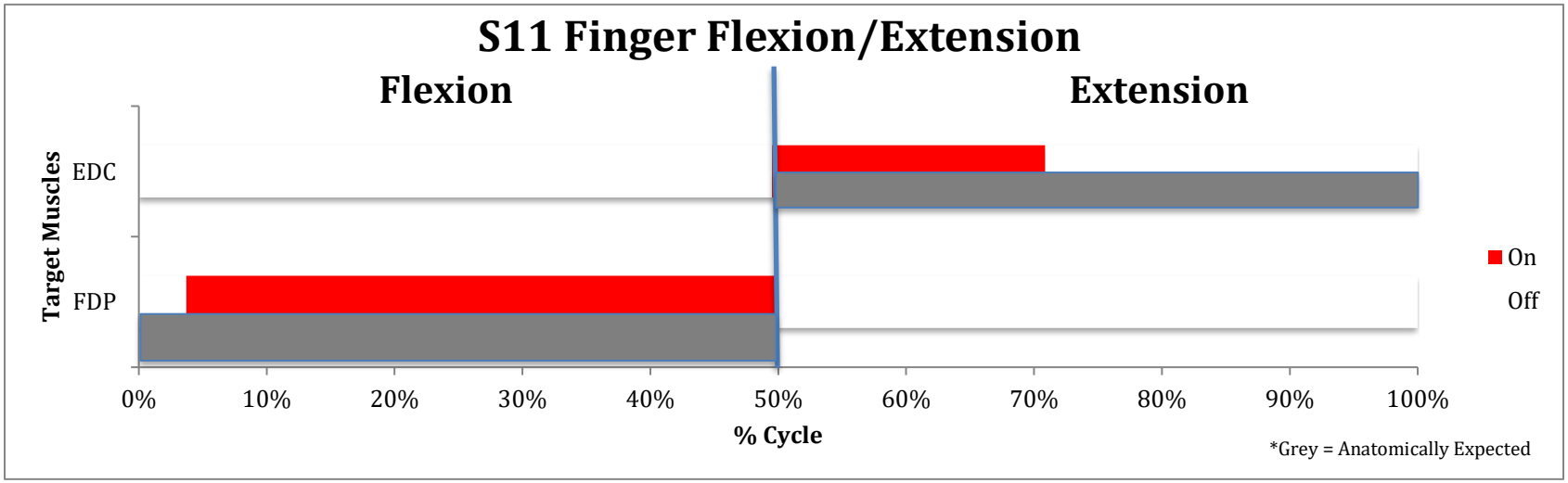
It was then hypothesized that muscle activity patterns used for PLC will differ from expected muscle activity patterns used to control an anatomically intact limb. The majority of muscle activation patterns for the completion of phantom limb movements, regardless of the level of amputation, varied from anatomically expected muscle activation patterns. Participants presented with contractions of the muscles, targeted by electrodes, within the residual limb during 81 movements. Only 13 of these 81 movements (16%) were completed by anatomically expected muscle activation patterns.

The thirteen expected muscle activation patterns for phantom limb movements (16%) were completed solely by contraction of anatomically expected muscles. To determine if the frequency of movements completed by anatomically expected muscle activation patterns compared to those utilizing unexpected muscle activation patterns differed from random chance, participants with no chance of using expected muscles were removed from the analysis. Participants with amputations above the elbow had a 0% chance of using anatomically expected muscles to control movements of the hand, wrist, and forearm, and therefore those movements were not included in the analysis. Additionally, the participant with a shoulder disarticulation was not able to use expected muscle activation patterns for any movement, and therefore was also excluded from this statistical analysis. For this analysis muscle activation patterns during 61 total movements were investigated. The expected frequency, based on chance alone, would be 30.5 unexpected and 30.5 expected muscle activation patterns. The frequency of the occurrence of anatomically expected muscle activation patterns compared to the occurrence of anatomically unexpected muscle activation patterns was different from chance alone, $\chi^2(1, N=61) = 20.082$, $p < .001$ Anatomically unexpected muscle activation patterns were seen at a frequency greater than chance compared to expected muscle activation patterns.

Participants with trans-radial amputations experienced the highest percentage (20%) of movements completed solely by anatomically expected muscle activation patterns. Only three

participants, for one complete cycle (two individual movements), paired appropriate agonist and antagonist muscle contractions in a reciprocal pattern of activation as expected in an anatomically intact limb. Figure 4.1 shows the six movements completed as anatomically expected. The rest of the anatomically expected muscle activation patterns occurred for only one-half of a complete cycle (one individual movement, such as for just flexion, or just extension). Figure 4.2 shows three examples of anatomically expected muscle contraction for half of a complete movement cycle.


S8 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Supinator
Pronator
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected


S11 Finger Flexion/Extension
Flexion
Extension
Target Muscles
EDC
FDP
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

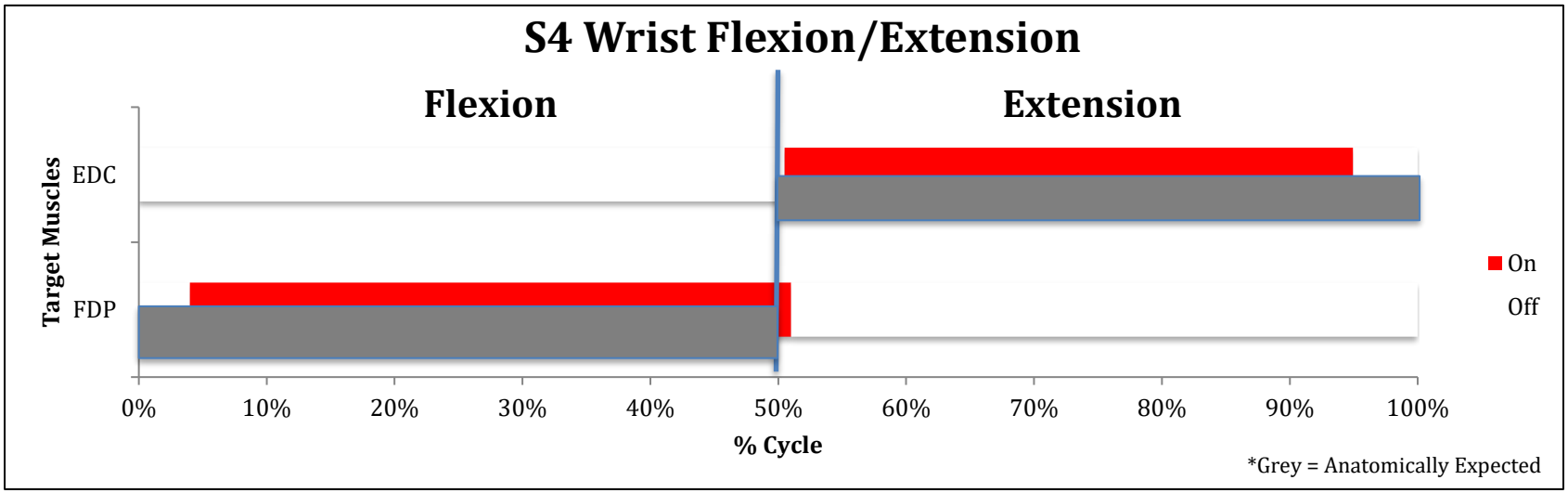
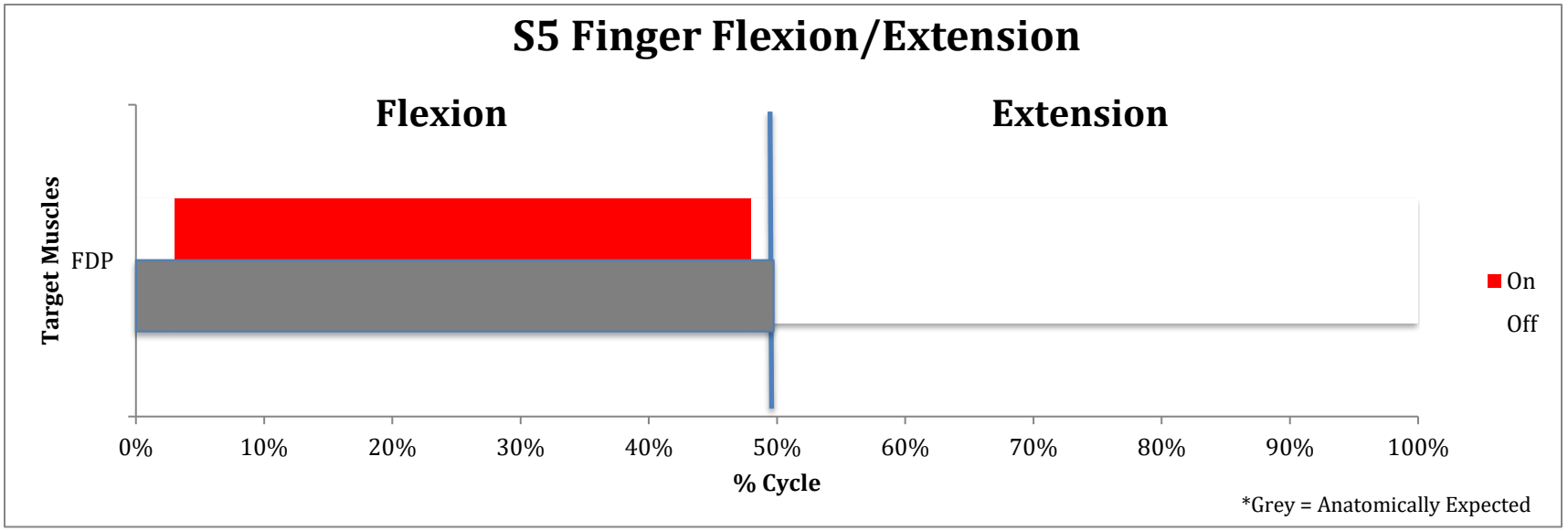
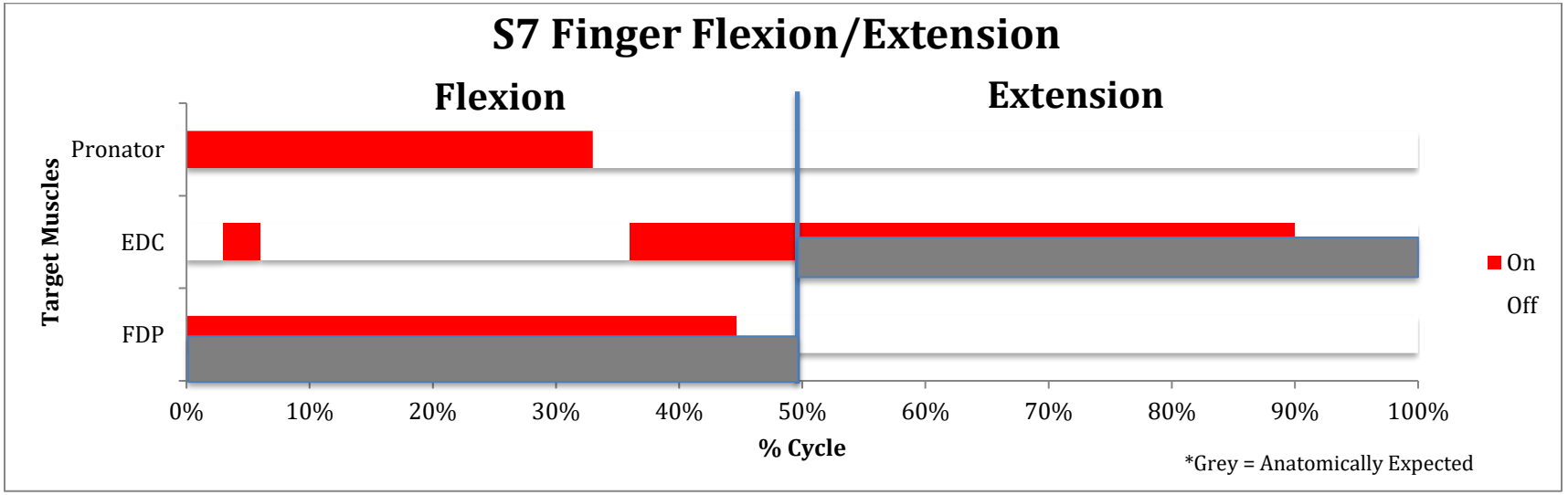


Figure 4.1: Anatomically Expected Muscle Activity, Complete Cycles

Three participants paired appropriate agonist and antagonist muscle activity in a reciprocal pattern of activation as expected in an anatomically intact limb. S8 = pronator for pronation and supinator for supination. S11 = pronator for pronation and supinator for supination. S4 =FDP for finger flexion and EDC for finger extension.


S5 Finger Flexion/Extension
Flexion
Extension
Target Muscles
FDP
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected


S7 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Pronator
EDC
FDP
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

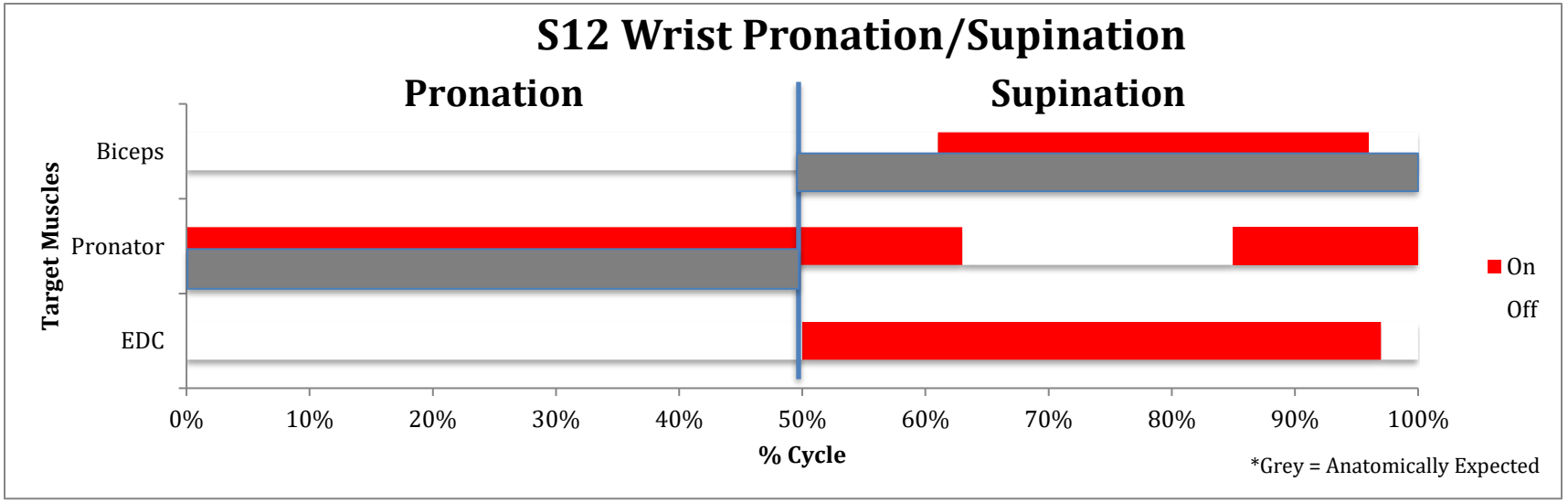


Figure 4.2: Anatomically Expected Muscle Activity, Half Cycles

Seven movements were completed by anatomically expected muscle activity for one-half of a complete movement cycle. S5=FDP for finger flexion. S7 = EDC for finger extension. S12 = pronator for pronation of the wrist.

When anatomically expected muscles were active for requested movements, they were typically accompanied by abnormal co-contractions of unexpected muscles, at times including the antagonist muscle. The role of each target muscle in completing a requested movement varies based on the level of amputation. Table 4.3 visually depicts the percent of movements completed by each unexpected target muscle based on muscles available for the completion of each movement.

Table 4.3 Percent of Participants Using an Unexpected Muscle for Phantom Limb Movements

A[3].

	Finger Flexion	Finger Extension	Wrist Flexion	Wrist Extension	Wrist Pronation	Wrist Supination
FDP	Expected	16.7%	Expected	0%	8.3%	8.3%
EDC	33.3%	Expected	16.7%	Expected	33.3%	66.7%
P	50%	16.7%	41.7%	33.3%	Expected	0%
S	16.7%	8.3%	8.3%	16.7%	33.3%	Expected
B	16.7%	0%	25%	8.3%	16.7%	Expected
T	16.7%	0%	16.7%	8.3%	8.3%	0%
D	0%	0%	0%	8.3%	0%	8.3%
PM	0%	0%	8.3%	8.3%	0%	0%

B[4].

	Finger Flexion	Finger Extension	Wrist Flexion	Wrist Extension	Wrist Pronation	Wrist Supination	Elbow Flexion	Elbow Extension
B	100%	50%	100%	0%	0%	0%	Expected	100%
T	0%	0%	0%	0%	100%	100%	0%	Expected
D	50%	0%	0%	0%	0%	0%	50%	50%
PM	0%	0%	0%	0%	0%	0%	50%	0%

C[5].

	Finger Flexion	Finger Extension	Wrist Flexion	Wrist Extension	Wrist Pronation	Wrist Supination	Elbow Flexion	Elbow Extension
D	0%	0%	0%	0%	0%	0%	0%	0%
PM	100%	0%	100%	0%	0%	100%	100%	0%
Trap	0%	0%	0%	0%	0%	0%	0%	100%

[1]Total percent of participants who produced muscle activity within target muscles during unexpected movements. Muscles that are anatomically expected to be active during a movement are identified by the word "Expected" in their cell.

[2]Abbreviations: FDP – flexor digitorum profundus, EDC – extensor digitorum communis, P – pronator, S – supinator, B – biceps, T – triceps, D – anterior deltoid, PM – pectoralis major, Trap – trapezius

[3]A. Twelve participants with amputations below the elbow completed phantom movements of finger flexion, finger extension, wrist flexion, wrist extension, wrist pronation, and wrist supination. All participants with amputations below the elbow presented with all target muscles.

[3]B.Two trans-humeral participants completed phantom movements of finger flexion, finger extension, wrist flexion, wrist extension, wrist pronation, wrist supination, elbow flexion and elbow extension. Trans-humeral participants presented with only target muscles of the upper arm.

[5]C. One participant with a shoulder disarticulation completed phantom movements of finger flexion, finger extension, wrist flexion, wrist extension, wrist pronation, wrist supination, elbow flexion and elbow extension. The shoulder disarticulation participant presented with access to anterior deltoid, pec major, and trapezius.

Pronator was active in all wrist extension movements completed by the participants with wrist disarticulation, however it was only active in 30% of wrist extension movements in participants with trans-radial amputations. Although one muscle may have been active in all movements for a certain level of amputation, it may not have been the only muscle needed to complete the movement. For instance, biceps were active in all movements of finger flexion in participants with trans-humeral amputations, however anterior deltoid was also active 50% of the time. Table 4.4 visually represents the percent of participants who utilized a target muscle for completing a requested movement, based on level of amputation.

Table 4.4: Percent of Participants Utilizing A Target Muscle for a Specific Movement Based on Level of Amputation

	Finger Flexion				Finger Extension			
	Amputation Level				Amputation Level			
Muscle	WD	TR	TH	SD	WD	TR	TH	SD
FDP	100%	70%	X	X	0%	20%	X	X
EDC	0%	20%	X	X	50%	50%	X	X
P	50%	50%	X	X	50%	10%	X	X
S	0%	20%	X	X	0%	10%	X	X
B	0%	20%	100%	0%	0%	10%	0%	0%
T	50%	10%	0%	0%	0%	0%	0%	0%
D	0%	0%	50%	0%	0%	0%	0%	0%
PM	0%	0%	0%	100%	0%	0%	0%	0%
Trap	X	X	X	0%	X	X	X	0%

	Wrist Flexion				Wrist Extension			
	Amputation Level				Amputation Level			
Muscle	WD	TR	TH	SD	WD	TR	TH	SD
FDP	0%	40%	X	X	0%	0%	X	X
EDC	0%	20%	X	X	100%	50%	X	X
P	50%	40%	X	X	100%	30%	X	X
S	0%	10%	X	X	0%	20%	X	X
B	0%	30%	100%	0%	0%	10%	0%	0%
T	50%	10%	0%	0%	0%	10%	0%	0%
D	0%	0%	0%	0%	0%	10%	0%	0%
PM	0%	0%	0%	100%	0%	10%	0%	0%
Trap	X	X	X	0%	X	X	X	0%

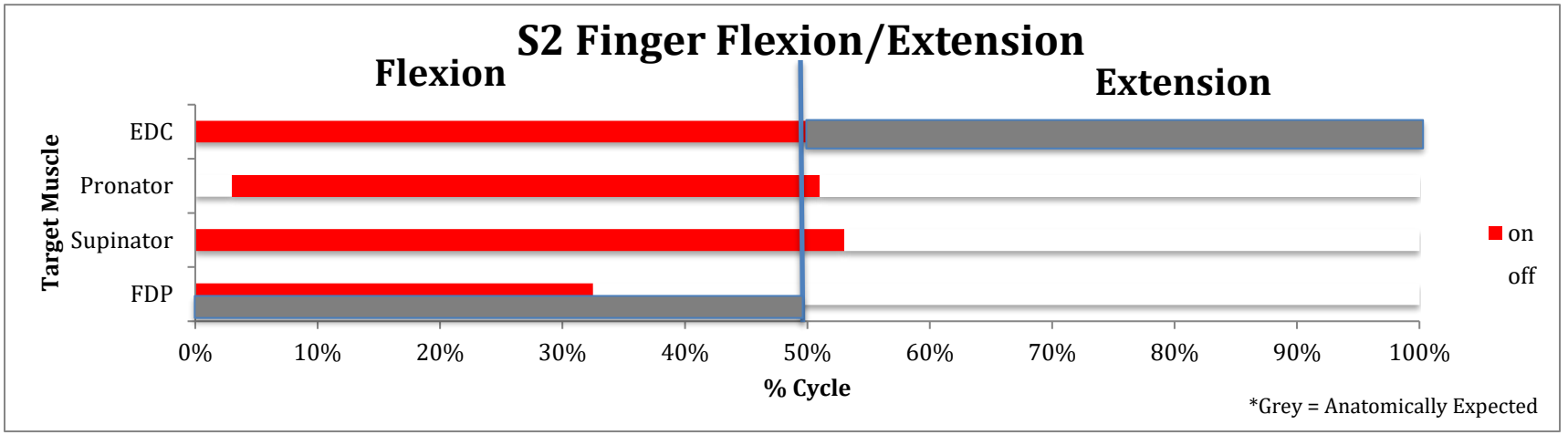
	Wrist Pronation				Wrist Supination			
	Amputation Level				Amputation Level			
Muscle	WD	TR	TH	SD	WD	TR	TH	SD
FDP	50%	0%	X	X	50%	0%	X	X
EDC	50%	30%	X	X	50%	70%	X	X
P	50%	50%	X	X	50%	20%	X	X
S	50%	30%	X	X	50%	50%	X	X
B	0%	10%	0%	0%	100%	50%	0%	0%
T	0%	10%	100%	0%	0%	0%	50%	0%
D	0%	0%	0%	0%	0%	10%	0%	0%
PM	0%	0%	0%	0%	0%	0%	0%	100%
Trap	X	X	X	0%	X	X	X	0%

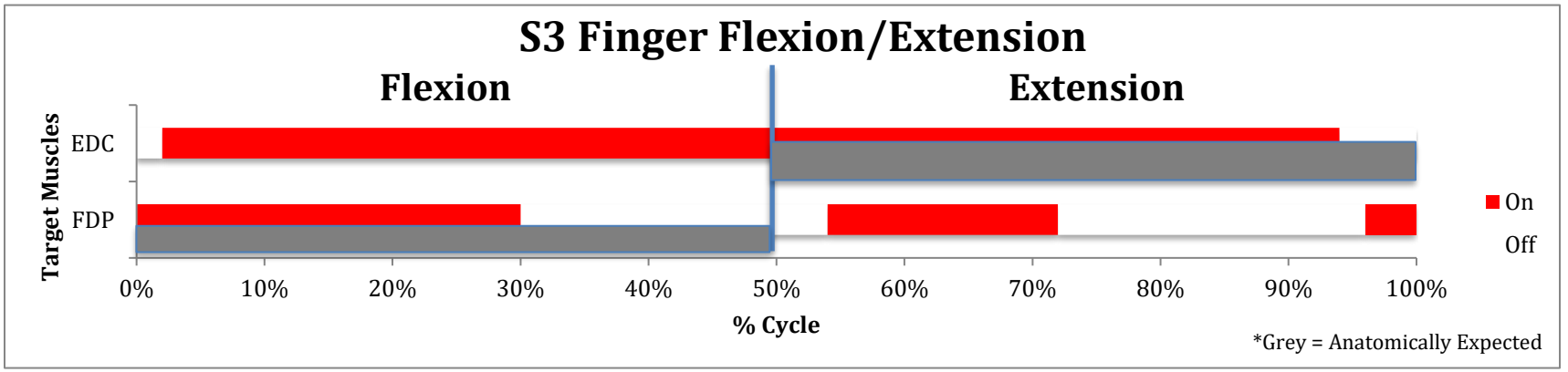
	Elbow Flexion		Elbow Extension	
	Amputation Level		Amputation Level	
Muscle	TH	SD	TH	SD
B	50%	0%	0%	0%
T	0%	0%	100%	0%
D	100%	0%	100%	0%
PM	50%	100%	0%	0%
Trap	X	0%	X	100%

[1]2WD, 10TR, 2TH, 1SD participants completed phantom movements of finger flexion, finger extension, wrist flexion, wrist extension, wrist pronation, wrist supination. 2TH, 1SD participants completed phantom movements of elbow flexion and elbow extension.

[2]Abbreviations: FDP – flexor digitorum profundus, EDC – extensor digitorum communis, P – pronator, S – supinator, B – biceps, T – triceps, D – anterior deltoid, PM – pectoralis major, Trap – trapezius , WD – wrist disarticulation, TR – trans-radial, TH – trans-humeral, SD – shoulder disarticulation, X - Muscle was not targeted

Thirty-five movements out of the 81 with muscle activity (43.2%) were completed with activation of the anatomically expected muscle and co-contractions of muscles not normally involved in the execution of the requested movement. Of those 35 movements, 15 (42.9%) exhibited abnormal co-contraction of the anatomically expected target muscle and its antagonist muscle (Figure 4.3). Five of those 15 involved abnormal co-contraction of only the target agonist and target antagonist muscles. The other 10 movements involved abnormal co-contractions of the agonist, antagonist, and other unexpected muscles. Twenty of the 35 movements involved anatomically expected muscle activation along with co-contractions of unexpected muscles that were not the antagonist. Participants with wrist disarticulation amputations experienced the highest percentage (66.7%) of phantom movements completed by the contraction of anatomically expected muscles in the presence of co-contraction of unexpected muscles (Table 4.2).


S2 Finger Flexion/Extension
Flexion
Extension
Target Muscle
EDC
Pronator
Supinator
FDP
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
on
off
*Grey = Anatomically Expected


S3 Finger Flexion/Extension
Flexion
Extension
Target Muscles
EDC
FDP
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
On
Off
*Grey = Anatomically Expected

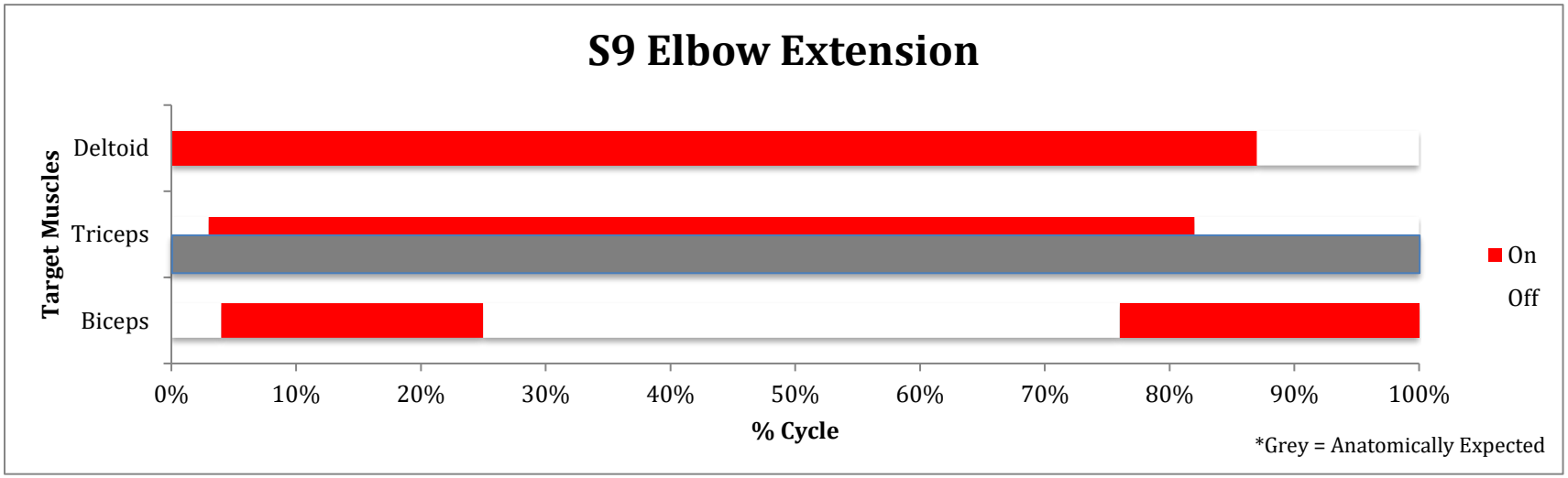
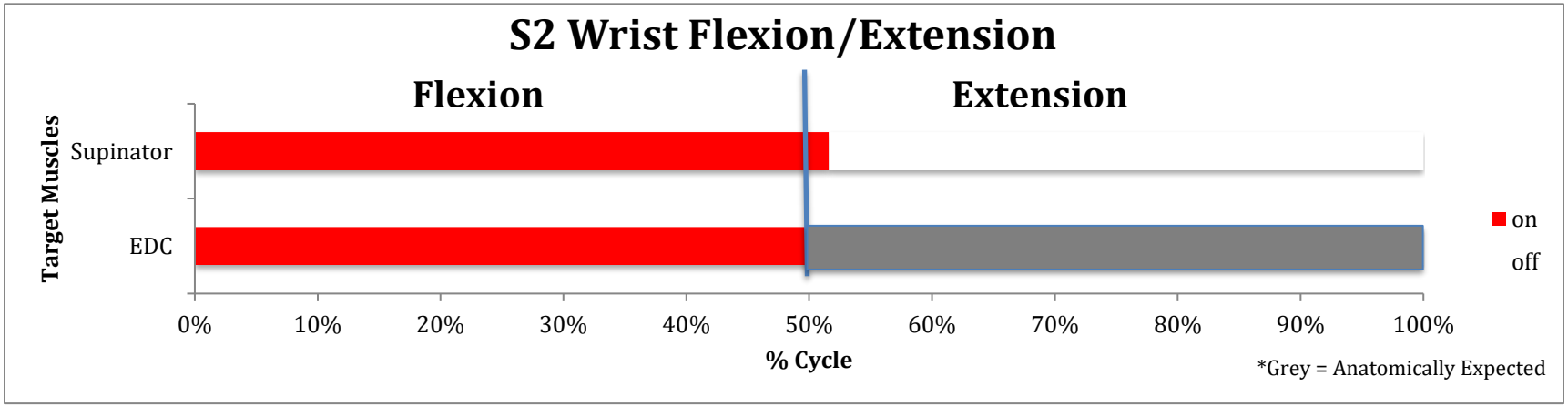


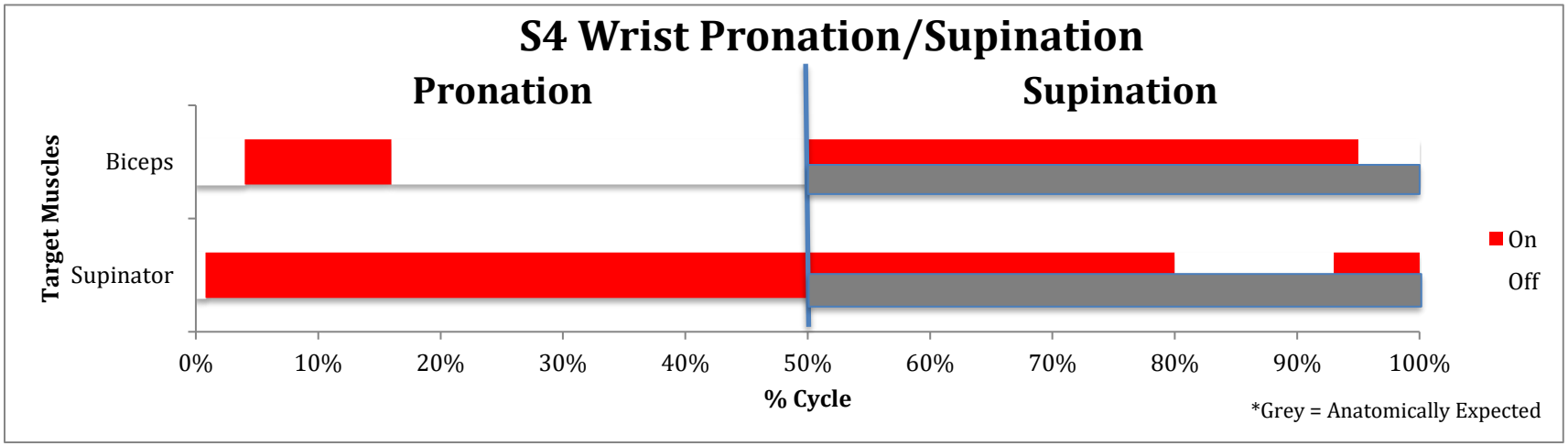
Figure 4.3: Agonist/Antagonist Co-contractions

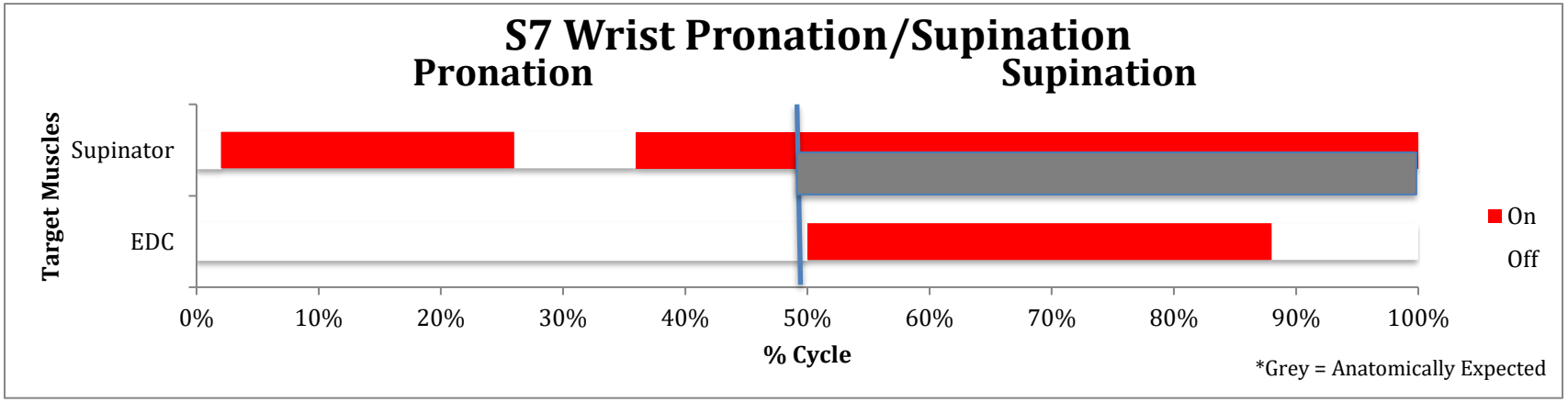
Abnormal co-contractions of the anatomically expected agonist muscle and its antagonist muscle, S2 = FDP and EDC, among other muscles, during flexion of the fingers. S3 = FDP and EDC during both movements of finger flexion/extension. S9 = biceps and triceps, among others, during elbow extension.

Thirty-three movements (34.4%) were completed by anatomically inappropriate muscle activity (threshold of activity above 2SD from rest) (Figure 4.4). In five of these movements, antagonist muscles were active during the completion of an unexpected movement, without activity within the agonist muscle. As the level of amputation increased, so did the amount of movements completed by anatomically inappropriate muscle contractions, however the participants with trans-humeral and shoulder disarticulation amputations presented with the same percentage of anatomically inappropriate muscles completing movements (Table 4.2). EDC and pronator were the most prevalent unexpected muscles active within the completion of phantom forearm movements. EDC was active during wrist supination 66.7% of the time, and pronator was active during finger flexion 50% of the time. Pec major and anterior deltoid were the most prevalent unexpected muscles active during phantom movements of the upper arm. Pec major was active during 50% of elbow flexion movements of participants with trans-humeral amputations and 100% in the participant with a shoulder disarticulation. Deltoid was active during 50% of elbow extension movements in the participants with trans-humeral amputations (Table 4.3).

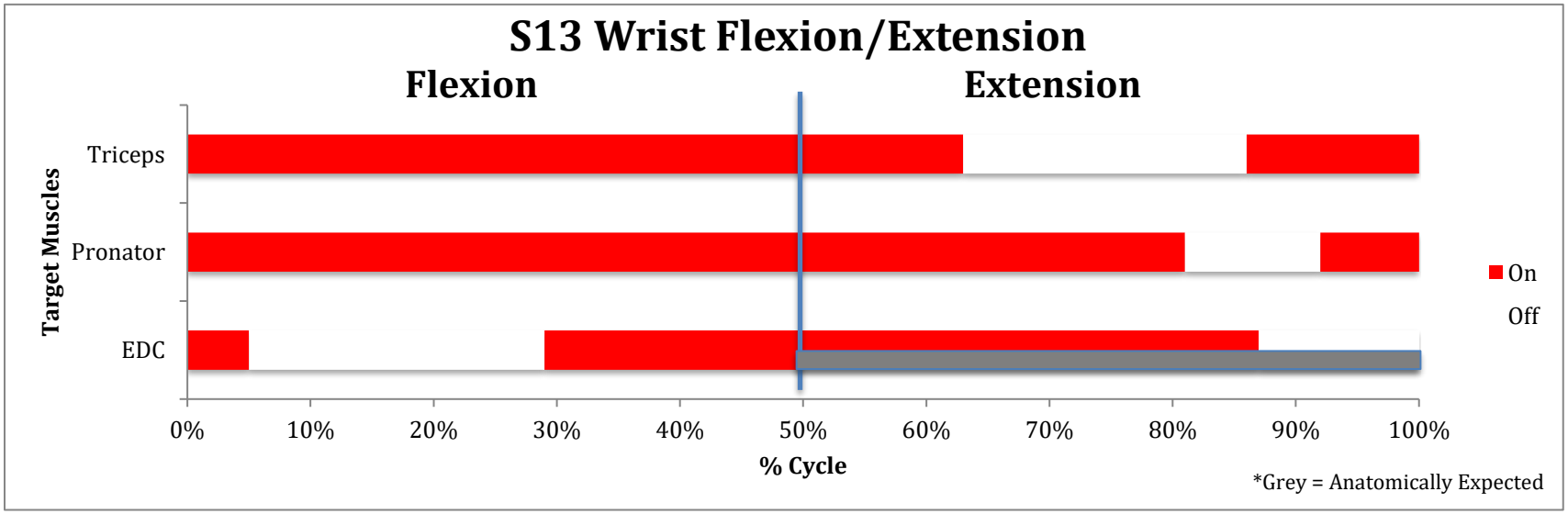
A.

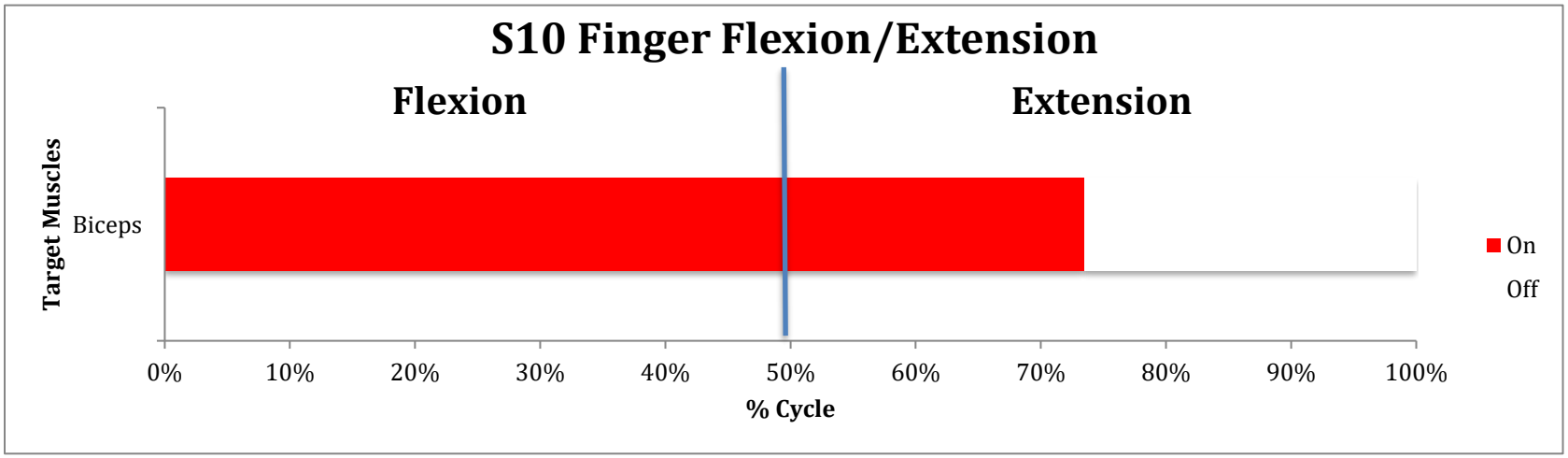

S2 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Supinator
EDC
on
off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

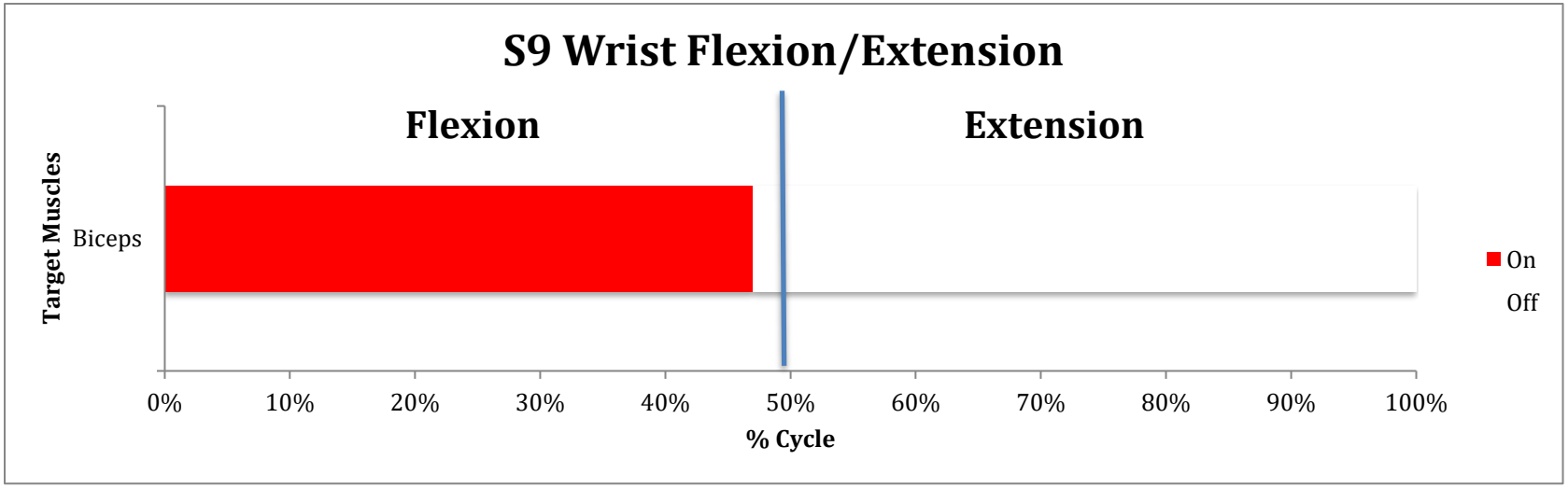

S4 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Biceps
Supinator
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected


S7 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Supinator
EDC
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

B.


S13 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Triceps
Pronator
EDC
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected


S10 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Biceps
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle


S9 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Biceps
On
Off
0%
10%
20%
30%
40%
50%
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70%
80%
90%
100%
% Cycle

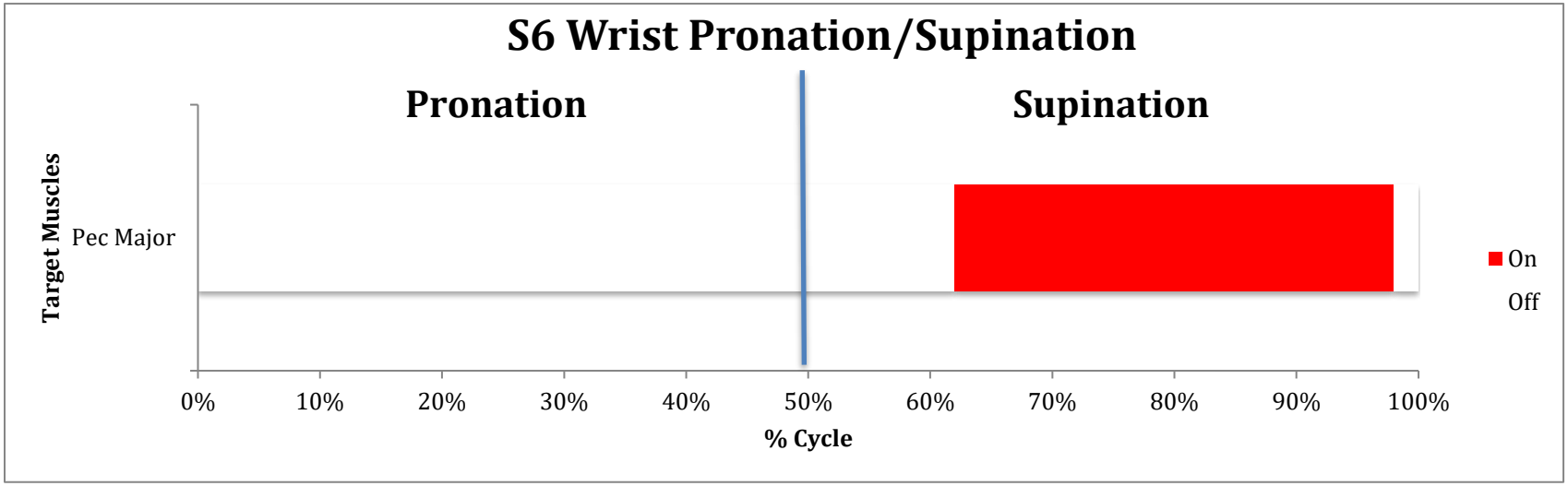
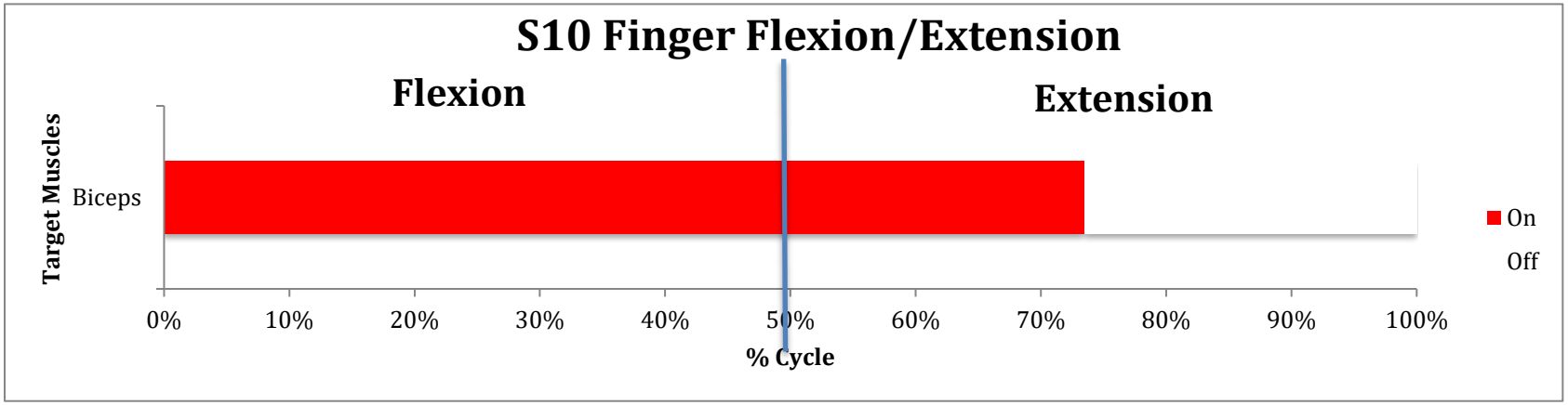


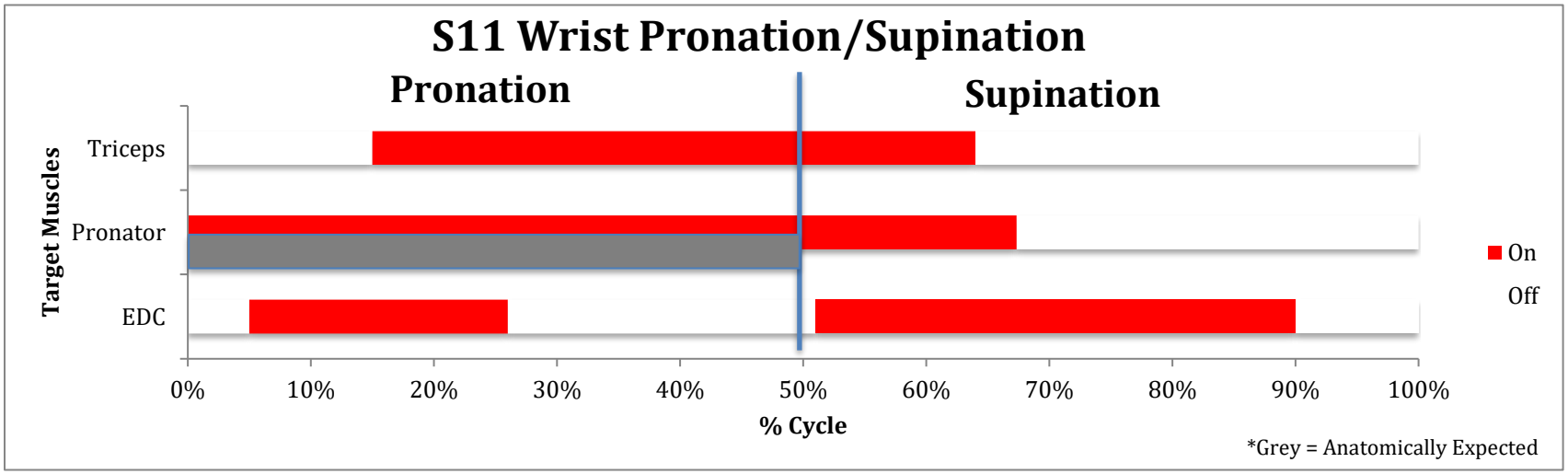
Figure 4.4: Anatomically Inappropriate Muscle Activity

(A) Antagonist muscles active during agonist movements, without activity of the agonist muscle. S2 = EDC during wrist flexion, no activity in FDP. S4 and S7 = supinator during wrist pronation, no activity in pronator. (B) Anatomically inappropriate muscle activity within other muscles besides the antagonist. S13 WD = triceps and pronator for flexion of the wrist. S10 TR = biceps for finger flexion. S9 TH = biceps for wrist flexion. S6 SD = pec major for supination.

Muscle activation patterns were determined to be anatomically unexpected if anatomically inappropriate or abnormal co-contractions occurred. This study further investigated if the frequency of these occurrences, within movements completed by anatomically unexpected muscle activation patterns differed from random chance. The expected frequency, if these occurrences were being executed by chance alone, 31.5 would be completed by anatomically inappropriate muscle activations and 31.5 would be completed by abnormal co-contractions. The frequency of the occurrence of anatomically inappropriate muscle activation patterns (20 occurrences) compared to the occurrence of abnormal co-contractions (43 occurrences) during unexpected muscle activation patterns was different from chance alone, $\chi^2(1, N=63) = 8.397$, $p < .004$. Whether a participant utilized anatomically unexpected muscle activity, or abnormal co-contractions of expected muscles was not a random occurrence.

Prolonged muscle activation is characterized by a continuation of activity within muscles completing the first phase of a movement into the second phase of the movement cycle, including activity continued into the antagonist movement and failure to stop activity before the start of the activity in the antagonist muscle (Brunner & Romkes, 2008; Hallett et al., 1975; Hore et al., 1991). Six participants (40%) exhibited prolonged muscle activation of the muscles completing the first phase of the movement while transitioning into the second phase. Prolonged activity was only seen in one movement cycle for four participants. For one participant it was experienced during both finger and wrist flexion/extension, and for one other participant it was experienced during all movements of the forearm. Figure 4.5 shows examples of prolonged muscle activation in three separate participants.


S10 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Biceps
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle


S11 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Triceps
Pronator
EDC
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

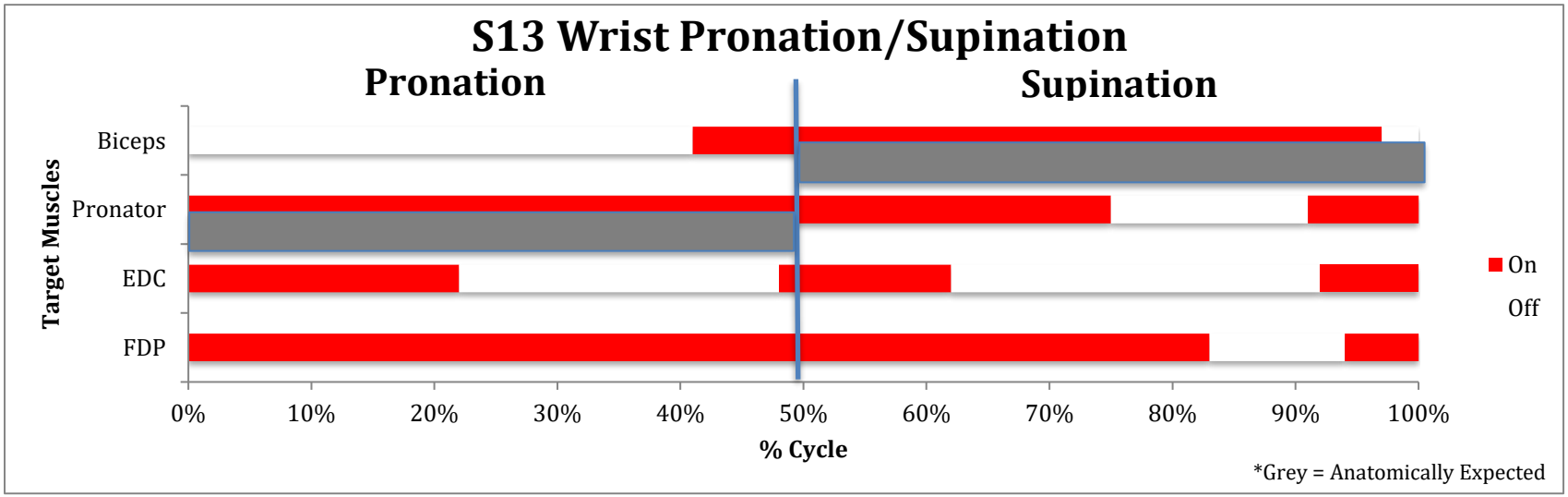
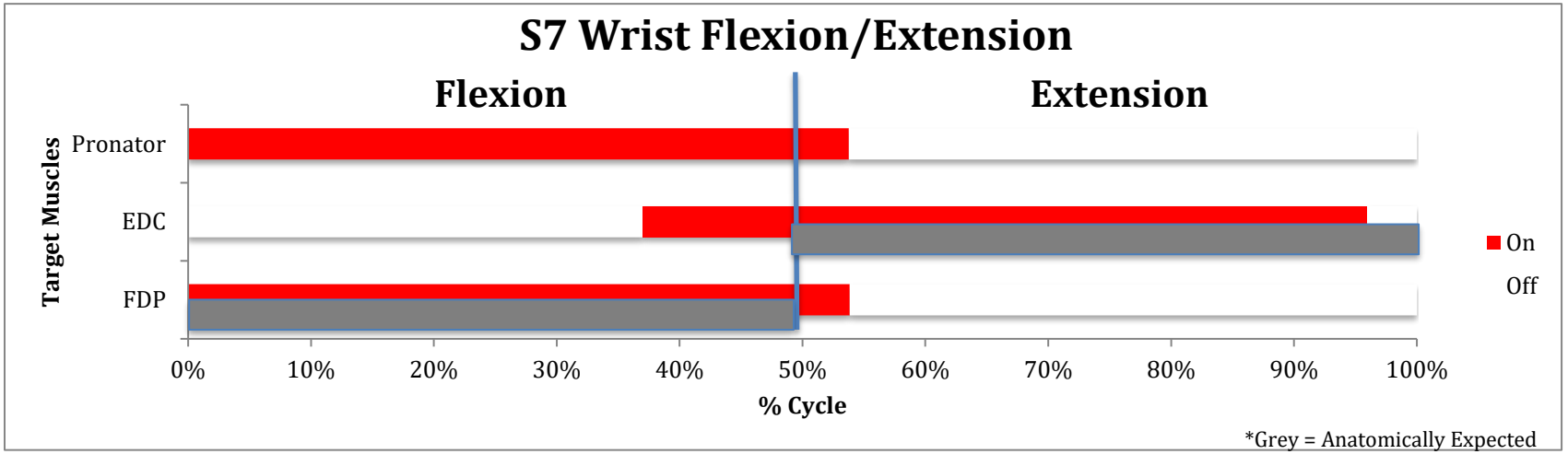
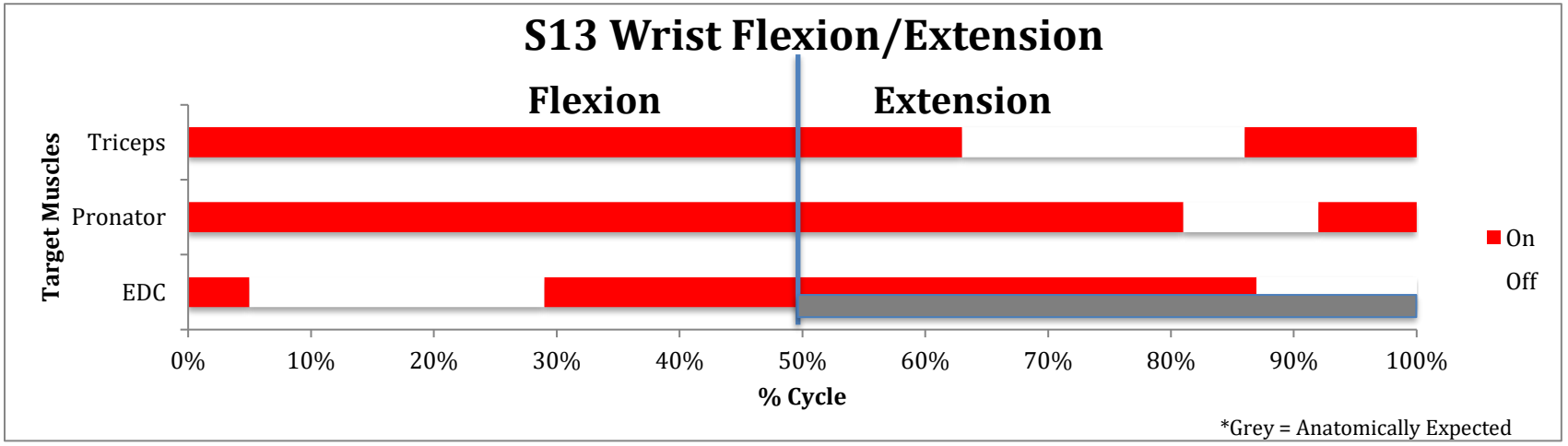


Figure 4.5: Prolonged Muscle Activations

Prolonged activation occurs when muscles completing the first phase of a movement remain active while transitioning into the second phase. S10 = biceps while transitioning from finger flexion to finger extension. S11 = triceps and pronator while transitioning from pronation to supination. S13 = pronator and FDP while transitioning from pronation to supination.

Early onset of muscle activation occurs when the initiation of muscles, active during the second phase of a movement, begin during the first phase of a movement (Brunner & Romkes, 2008). Nine participants (60%) exhibited early activation of the muscles producing activity for the second phase of a movement. This occurred in all forearm movements in three participants, in both wrist movements in one participant, and in only one movement in five participants. Figure 4.6 shows three examples of early muscle activation.


S7 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Pronator
EDC
FDP
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
On
Off
*Grey = Anatomically Expected


S13 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Triceps
Pronator
EDC
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
On
Off
*Grey = Anatomically Expected

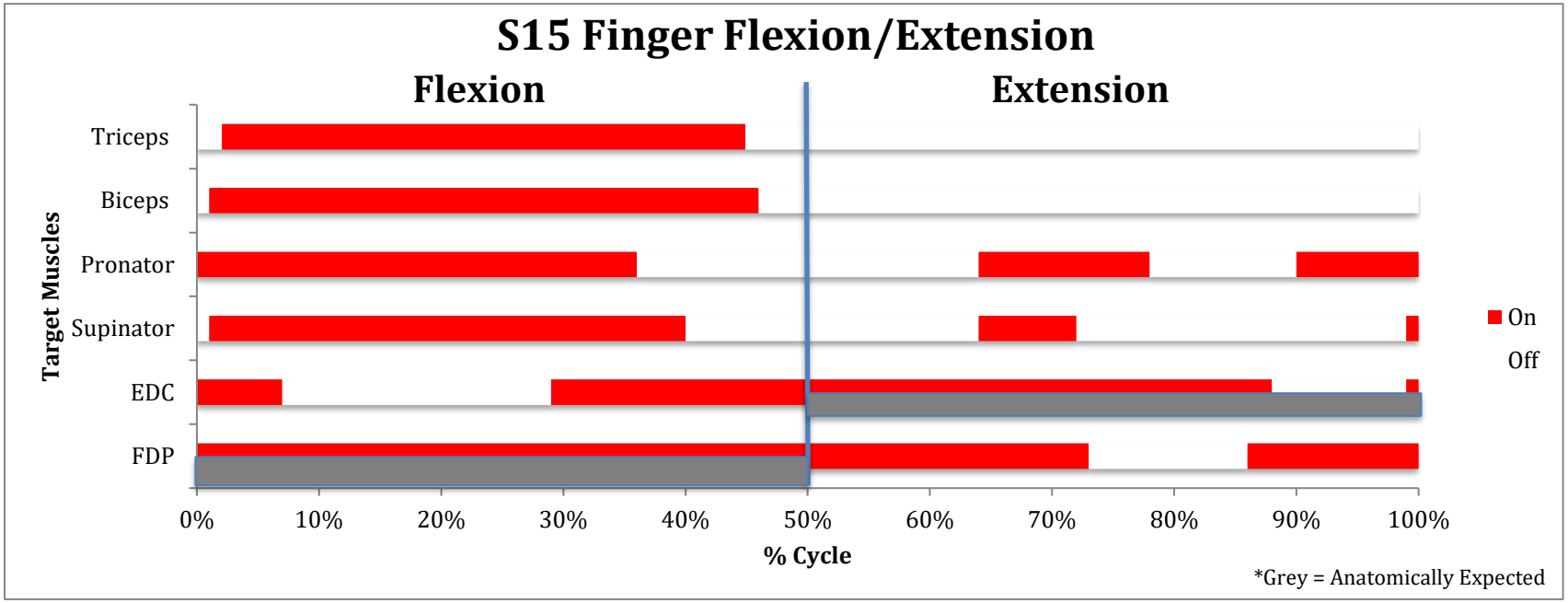
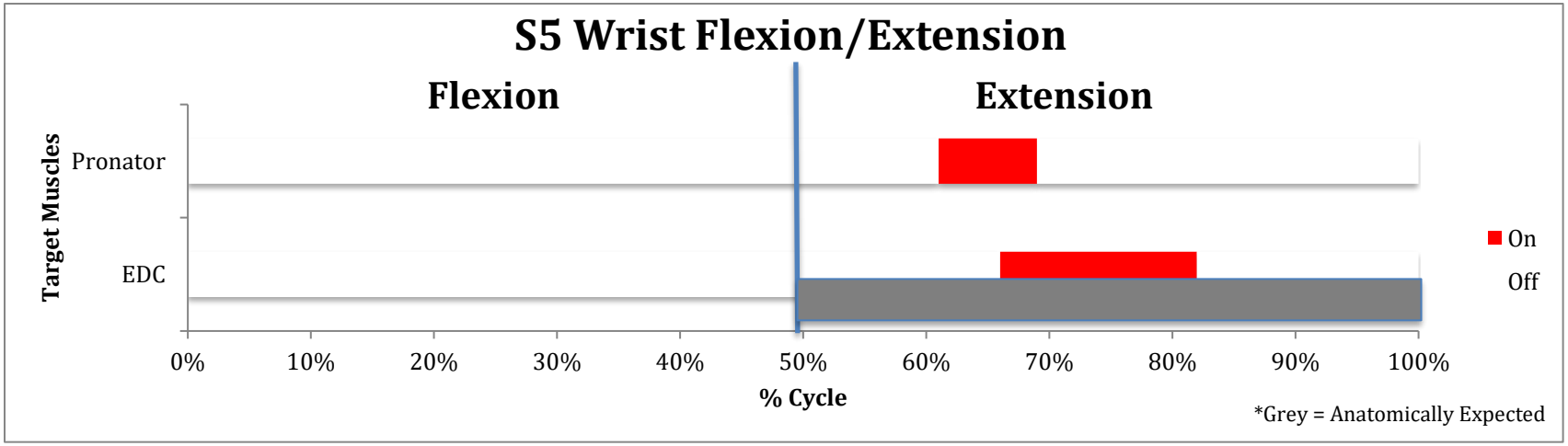
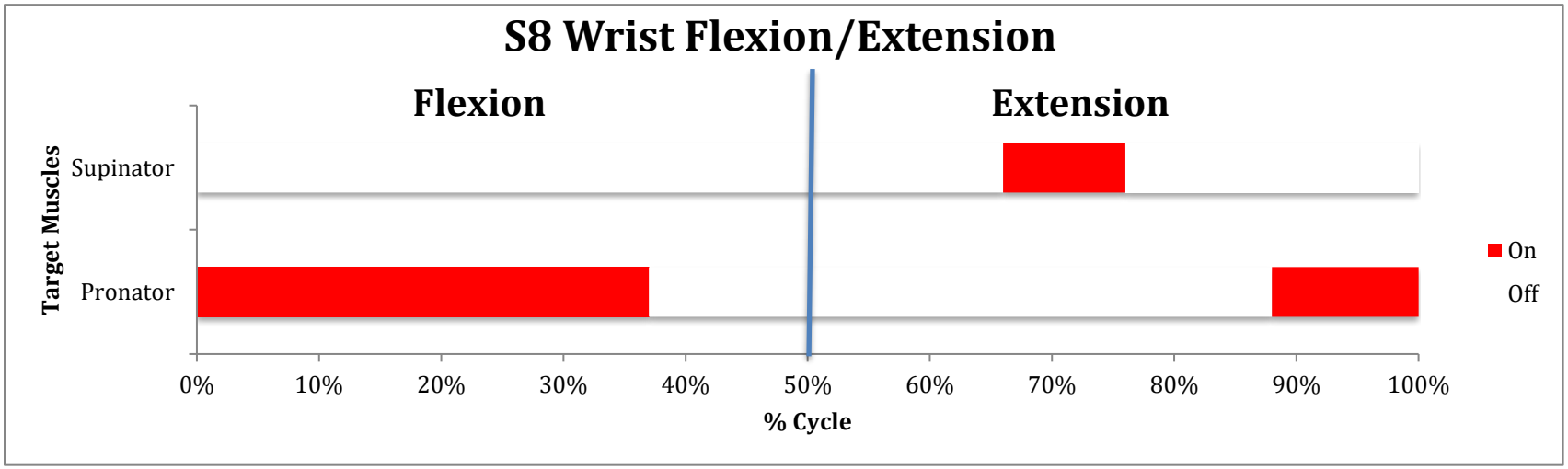


Figure 4.6: Early Onset Muscle Activations

Early activation occurs when muscles producing activity for the second phase of a movement become active during the first phase. S7 = EDC during finger flexion before finger extension. S13 = EDC during wrist flexion before wrist extension. S15 = EDC during finger flexion before finger extension.

Delayed onset of muscle activation occurs when muscles responsible for the movement become active well past the initiation of the movement phase (Hore et al., 1991). Seven participants (46.7%) experienced delayed onset muscle activation. Six participants, with amputations below the level of the elbow (trans-radial and wrist disarticulation), experienced delayed onset of muscle activation while completing the movement of wrist extension. The participant with a shoulder disarticulation experienced delayed onset of muscle activation during wrist flexion and wrist supination. Figure 4.7 shows three examples of delayed onset muscle activation.


S5 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Pronator
EDC
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected


S8 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Supinator
Pronator
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle

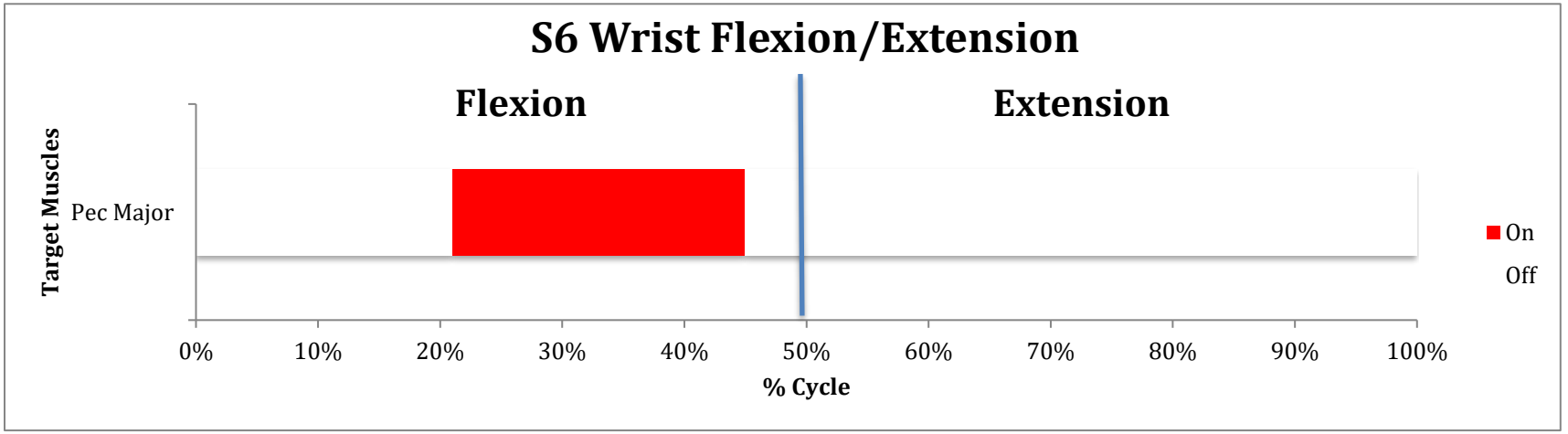


Figure 4.7: Delayed Onset Muscle Activations

Delayed onset of muscle activation occurred in 46.7% of participants. All individuals with amputations below the elbow experienced delayed onset of muscle activation when completing extension of the wrist. S5 = pronator and EDC staring well after the initiation of wrist extension. S8 = supinator starting well after the initiation of wrist extension. S6 = pec major starting well after the initiation of wrist flexion.

4.4 Discussion

When an upper extremity amputation occurs, or a limb is not fully formed, anatomically expected muscles/tendons utilized for control of fine motor movements may be absent. However, people with amputation are capable of controlling movement of the phantom limb (PLC), which requires contractions of residual limb muscles (Brodie, Whyte, & Waller, 2003; Gagné et al., 2009; K. Reilly et al., 2006). PLC remains a poorly understood phenomenon, previously thought to only impact changes in muscle activity in people with amputation above the elbow (Gagné et al., 2009; K. Reilly et al., 2006). This study was designed to test the hypothesis that people with all levels of upper extremity amputation would have muscle activity used to control a phantom limb, and these muscle activity patterns would differ from expected muscle activity patterns used to control an anatomically intact limb.

During a traumatic or disease related amputation peripheral motor nerves, responsible for transporting movement signals from the spinal cord to the muscles, are severed, resulting in the inability of the specific remaining muscles to contract. Some patients can perceive and report the ability to control the phantom limb immediately after amputation. This PLC may be due to inhibitory responses, causing reorganization of neighboring areas within the motor cortex of the brain, to take over for the completion of movement requests (P. Chen et al., 2002; Navarro, 2009; Rossini et al., 1994; Wall et al., 2002). However, Gagne found that PLC negatively correlated with cortical reorganization over time (Gagné et al., 2009), implying that the recovery process of the PNS may reverse cortical reorganization (Giraux et al., 2001; Röricht et al., 2001) and allow for control of the phantom limb. The timeline for cortical reorganization or the reversal has yet to be established.

As a response to injury within the PNS, proximal nerve endings of peripheral motor nerves begin sprouting many new axons, which attempt to establish connections with nearby denervated or injured muscles (Navarro, 2009). Depending on the level of amputation, original target muscles may not be available, resulting in re-innervation of new axons into unexpected muscles (Brushart, 1988; Navarro, 2009; Wu & Kaas, 2000). Similar to the process of re-innervation after traumatic or disease related amputation, congenital limb loss also results in the absence of anatomically expected target muscles, potentially causing peripheral motor nerves to innervate unexpected muscles prior to birth.

Results from the current study show that regardless of cause of amputation, or level of amputation, people with upper extremity amputations utilize contractions of residual limb muscles to control movements of the phantom limb. Out of 96 total phantom limb movements, 81 presented with muscle activity within the residual limb ($p < .001$). Muscles targeted by the electrodes were chosen based on their anatomically expected role in each movement executed by participants, and muscle activity was expected in at least one muscle for each movement. Unfortunately it was not possible to record muscle activity from all residual limb muscles, therefore participants may have used other muscles to complete the desired movements, or they may not have actually been able to complete those phantom limb movements.

The muscle activation patterns utilized during PLC were shown to be different from anatomically expected muscle activation patterns for the same movement. Only 13.5% of 96 total movements were executed by anatomically expected muscle activation patterns. Based on the 61 movements with muscle activation, that could have been completed utilizing anatomically expected muscle activation patterns, anatomically expected muscle activations occurred 13 times, compared to anatomically unexpected muscle activation patterns which occurred 48 times ($p < .001$). Interestingly participants with trans-radial amputations experienced the highest percentage (20%) of anatomically expected muscle activation patterns, above participants with wrist disarticulation amputations (8.3%).

Of the total 96 movements with anatomically unexpected muscle activity, 20 involved anatomically inappropriate muscle activity and 43 involved abnormal co-contractions ($p \leq .004$). Completion of movements by anatomically unexpected muscles (Fig. 4.4) may be occurring due to re-innervation of the peripheral motor nerves, which were denervated from their original target muscles, into new muscles. Co-contractions (Fig 4.3) may be due to re-innervated branches of a peripheral motor nerve, with some branches maintaining original innervation, or potentially a CNS adaptation causing synergistic recruitment of multiple muscles to complete a difficult movement.

Level of amputation did play a role in the amount of movements completed by anatomically inappropriate muscle contractions (Table 4.2). As level of amputation increased, so did the amount of anatomically inappropriate muscles active during completion of phantom limb movements. This number plateaued at the level of trans-humeral amputation, resulting in the same number of movements being completed by anatomically inappropriate muscle activation patterns in all participants with amputation above the elbow. Such a trend was expected due to the lack of anatomically utilized muscles for fine motor movements available within the residual limb as the amputation becomes higher. Biceps brachii, triceps, pectoralis major, anterior deltoid and trapezius are not muscles responsible for movements of an anatomically intact hand, however all participants were able to complete such movements of the phantom hand, even without the presence of typically utilized forearm muscles for hand movements.

Anatomically expected muscle activation patterns involve an agonist and antagonist muscle active in a reciprocal pattern. Some movements, such as wrist supination, are expected to present with activity in multiple muscles (supinator/biceps brachii) (Moore et al., 2015). However, 36.5% of movements completed presented with muscle activity in the anatomically expected muscle plus abnormal co-contractions within unexpected muscles. Of those movements, 42.9% included muscle activity within the antagonist muscle. Participants with wrist disarticulation amputations experienced abnormal co-contractions at the highest rate. Wrist disarticulations were the lowest level of upper extremity amputation included in this study. These participants had the longest residual limbs, implying that they had more of the muscles/tendons anatomically responsible for fine motor movements still intact, compared to other groups of participants. This level of amputation was expected to utilize the most anatomically expected

muscle activation patterns to complete phantom limb movements, however this was not the case. Wrist disarticulation participants had the most abnormal co-contraction activity, in which the anatomically expected muscle was active along with other unexpected muscles. These results were surprising since a muscle must be cut to become receptive to new innervation (Katz & Miledi, 1964) and participants with wrist disarticulations would have the most muscles remaining intact within the residual limb. Although not investigated in this study, it is possible that CNS factors encouraged the recruitment of multiple muscles to complete the movements, especially if the participants found these movements difficult to perform.

4.5 Conclusion

The majority of individuals with upper extremity amputation are capable of controlling movement of their phantom limb, without additional surgery. Further understanding of the natural biological repair process of peripheral motor nerves, may lead to the creation of prosthetic devices that target individual muscle activation patterns utilized by each amputee to control their phantom limb, if a disconnect in muscle activation for completion of these activities does exist. Chapter 5 provides further insight into this area of question. Determining which muscles an amputee uses for PLC and targeting the same muscle activation patterns for control of a prosthetic device would lead to more natural and intuitive control of the device. Additionally, it may be possible to assist peripheral motor nerves in re-innervating specifically chosen muscles during the initial amputation process. Routinely utilizing surgical procedures (such as TMR) at the initial time of amputation, regardless of level of amputation, can encourage specific and controlled re-innervation of severed peripheral motor nerves. Doing so would potentially enhance PLC for all levels of amputation, set amputees up for more intuitive control of prosthetic devices (since specifically innervated muscle would be identified), and diminish the formation of painful neuromas (bundles of sprouting axons that are unable to re-innervate a muscle). More specifically it would be beneficial to initiate these surgical procedures in amputees with all levels of amputation and at the time of amputation, eliminating the need for additional surgery.

Future research should be conducted to determine the process and extent of peripheral motor nerve regeneration and re-innervation after traumatic or disease related amputation and due to congenital limb loss. This study shows that anatomically unexpected muscles are being utilized to control the movement of phantom limbs 86.5% of the time. Although not definitive, these results imply that peripheral motor nerves may be re-innervating unexpected target muscles. Nerve conduction studies and/or retrograde tracing techniques suitable for human research should be utilized to grasp a better understanding of the location of sprouting axon re-innervation. Finally studies should be designed to look at both the changes within the PNS and CNS combined, many studies, much like this one, focus solely on one system or the other. It is very possible that we may not be able to separate the PNS and CNS interaction, however both systems need to be thoroughly investigated.

CHAPTER 5: MUSCLE ACTIVATION PATTERNS UTILIZED FOR PHANTOM LIMB CONTROL COMPARED TO PROSTHETIC CONTROL

5.1 Introduction

Motor skills are either developed through maturation and influenced by genetic factors, and anatomical and neurophysical traits, or achieved through extensive practice and incorporation (Gibson & Pick, 2000; Haibach et al., 2017). Developed motor skills, such as reaching and grasping, are uniform progressions acquired in a specific order over time (Haibach et al., 2017; Zoia et al., 2013). Learned motor skills result from motivation to overcome problems and interact with the environment (Gibson & Pick, 2000). Learning a motor skill transforms a general performance experience into an automatically desired movement that can be recalled at will (Dudai et al., 2015). Unlike developed motor skills, motor learning requires practice and experience before motor control becomes automatic (Schmidt, 1976; Scott Kelso et al., 1983). There are three main stages of motor learning: the *cognitive stage* (requiring a lot of thought and characterized by slow, inconsistent and inefficient movements), the *associative stage* (characterized by a mixture of consciously executed movements and fluid automaticity), and the *autonomous stage* (where movements are executed automatically without the need for conscious thought) (Haibach et al., 2017).

When an amputation occurs, or a limb is not fully formed, amputees experience the sensation that the missing limb is still present, known as a phantom limb (Herta Flor, 2002; Herta Flor et al., 1998). Many amputees have the capability of completing directed, intentional movements of the phantom limb, known as phantom limb control (PLC) (Brodie et al., 2007). PLC does not offer any functional abilities; therefore, some amputees are prescribed a prosthetic device (artificial limb) that they must learn to control. Unfortunately, motor learning to control the terminal device (hook/hand) of a prosthesis is not always achieved by upper extremity amputees, leading to frustration with the device and even total rejection. It is possible that PLC is a recovered motor-developed skill while prosthesis control requires motor learning. To investigate the possibility of this theory, kinesiologic electromyography (EMG) was used to record specific muscle activity within the residual limb, while upper extremity amputees completed movements of their phantom hand/arm, and while completing movements of the prosthesis. It is hypothesized that different muscle activity patterns will be used to control the phantom hand/arm from muscle activity patterns used to control the terminal device of typically prescribed prostheses. For instance, trans-radial body-powered device users are expected to use

upper arm and shoulder muscles to control the device whereas forearm muscles should be used to control the phantom hand/wrist.

5.2 Methods

5.2.1 Participants and Analysis

Participants enrolled in this study included fourteen of the fifteen participants described in Chapter 3. S3 was prescribed a cosmetic only prosthesis, a device that has no functional capabilities, and therefore was not included in the analysis. The average age of participants was 49.6 ± 16.04 years with 19.6 ± 17 years since amputation. Characteristics collected from each participant are outlined in Table 3.1.

All fourteen participants completed all methods outlined in Chapter 3, however only opening and closing movements of the phantom hand were compared to opening and closing movements of the prosthetic device. To obtain the specific outcome measure of this study, muscle activation patterns for phantom hand opening and closing were compared to muscle activity patterns identified during opening and closing of the terminal device. Additionally, wrist supination/pronation was compared in the one participant able to do so.

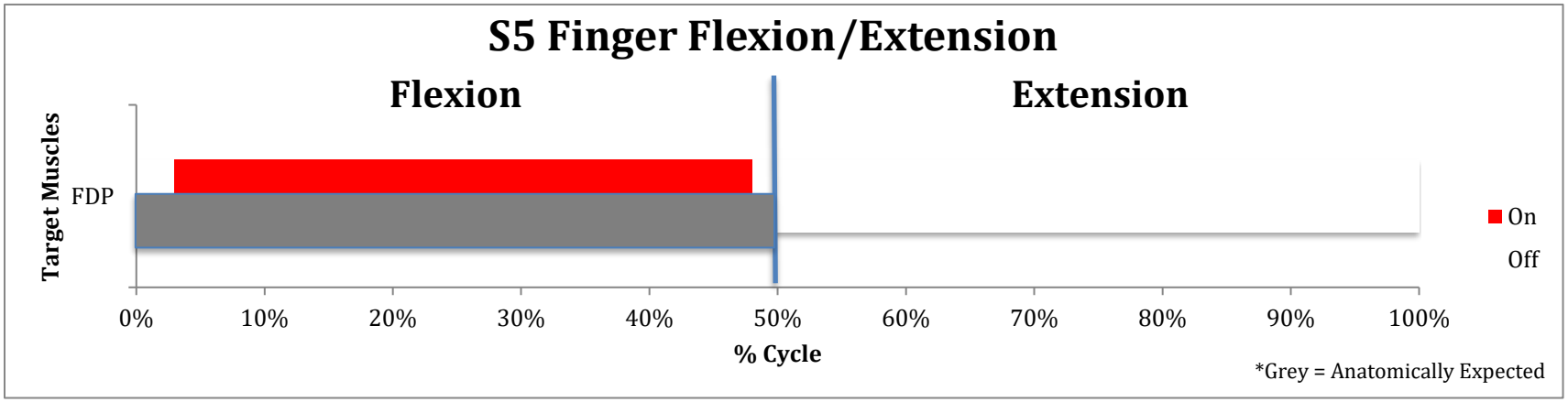
Muscle activation patterns were defined as different if participants utilized completely different muscles to complete the actions, or if activation patterns of the same muscles occurred at opposing time points throughout the cycle of the movement. This analysis is similar to that used for gait analysis where normal muscle activation patterns are compared with test muscle activation patterns throughout the gait cycle. For example, tibialis anterior is normally active during the swing phase of gait. If tibialis anterior were not active during swing, or was active during stance phase, that would be considered abnormal. More specifically, unexpected, early or late onset, and prolonged activity are all common descriptors of muscle activity in cyclic analysis of gait (Brunner & Romkes, 2008). Visual inspection to determine similarities and differences was used, and is a widely used technique for analyzing EMG data (Golabchi et al., 2019). Goodness of fit, Pearson Chi-Square tests were used to examine if occurrences were expected by chance alone. The frequency of occurrences of different muscle activation patterns and similar muscle activation patterns during phantom and prosthetic movements were investigated to determine if they were random occurrences (i.e. 50/50 chance). Additionally, frequency of use of at least one similar muscle during movements of both the prosthesis and phantom limb was investigated to determine if it was a random occurrence. It is theorized that differences in muscle activation patterns used to control a prosthetic device, versus a phantom hand, may be due to extensive motor learning required to control a prosthesis.

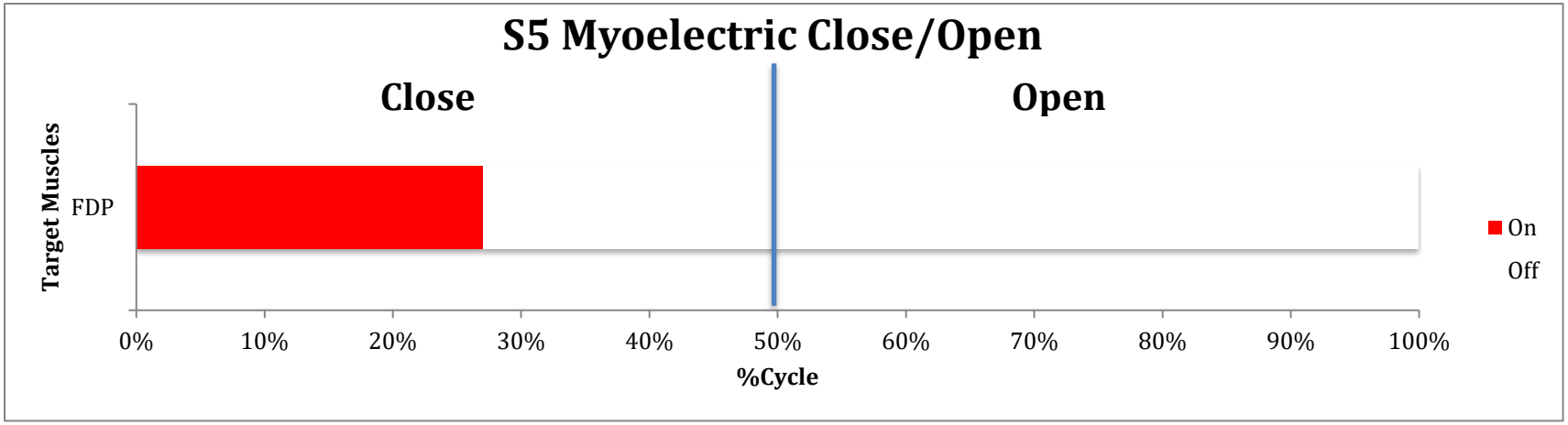
5.3 Results

Out of fourteen participants, thirteen used different muscle activation patterns to open their phantom hand than used to open their prosthetic device (Table 5.1). One participant presented with no contractions of the targeted muscles during opening of the device or phantom

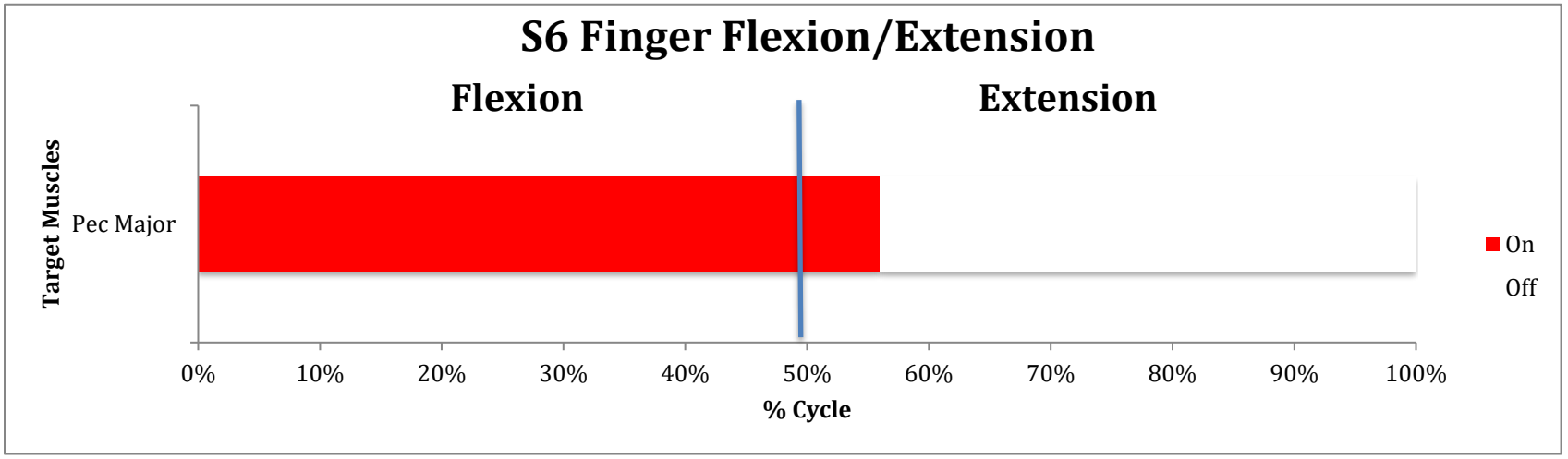
hand; since we were unable to determine which muscles were active for the completion of these movements they were excluded from the analysis. (This participant was most likely utilizing a muscle that was not targeted by an electrode, since no muscle activity was recorded for both phantom and myoelectric control.) Only two of the fourteen participants experienced activity within the same muscles for finger flexion and closing of their prosthetic devices. Figure 5.1 illustrates these similarities.

A.


S5 Finger Flexion/Extension
Flexion
Extension
Target Muscles
FDP
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected


S5 Myoelectric Close/Open
Close
Open
Target Muscles
FDP
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
%Cycle

B.


S6 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Pec Major
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle

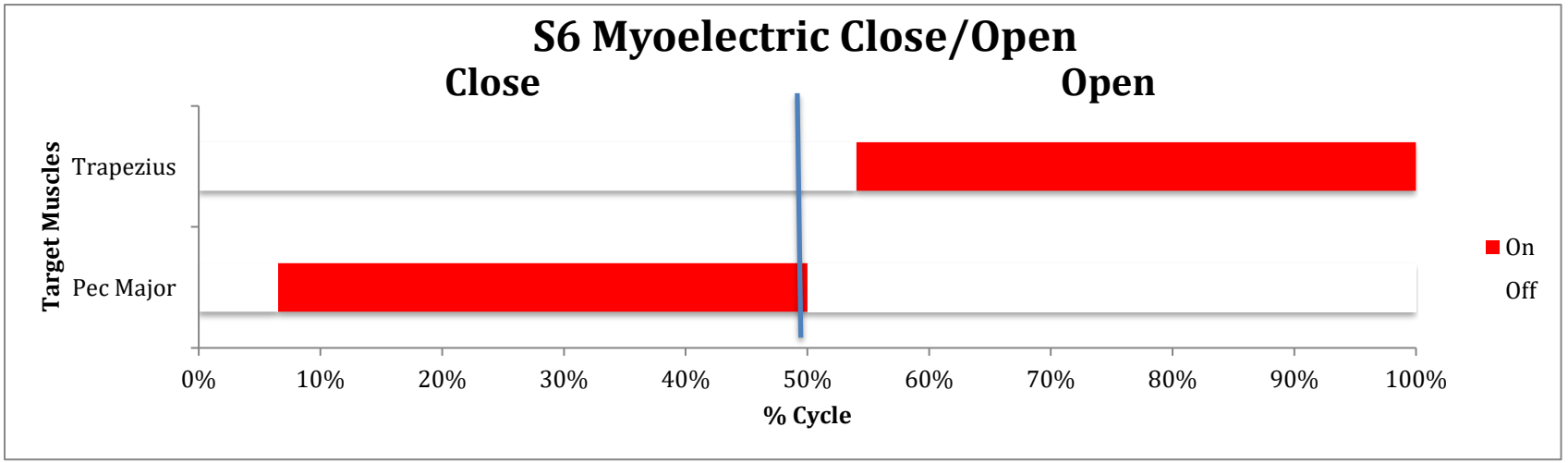


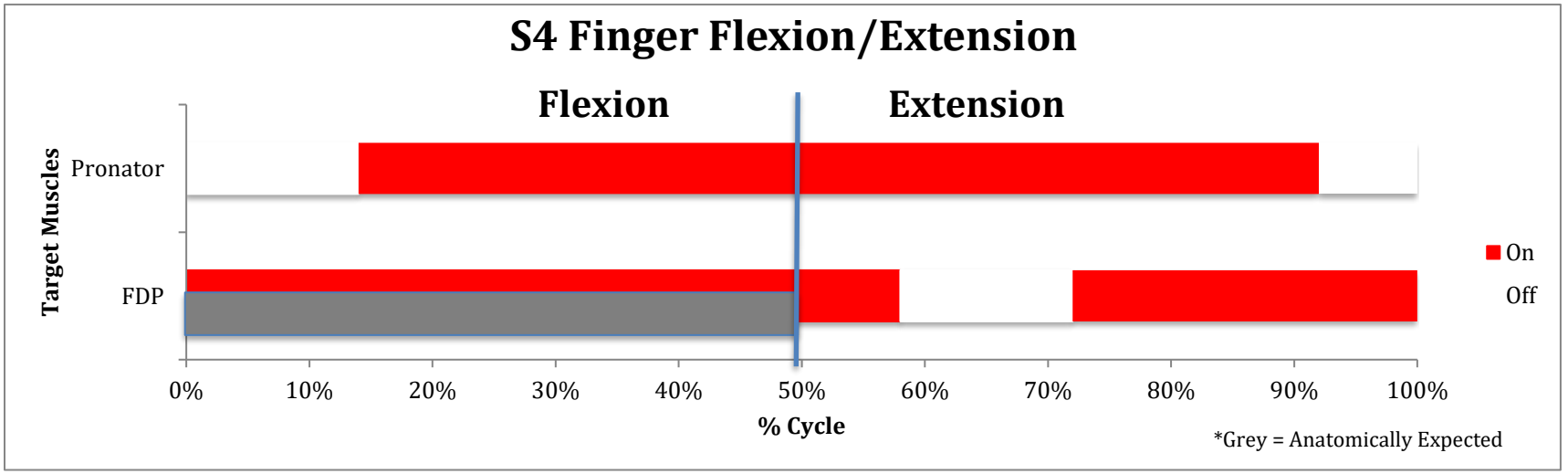
Figure 5.1: Similar Phantom and Prosthesis Closing Activity

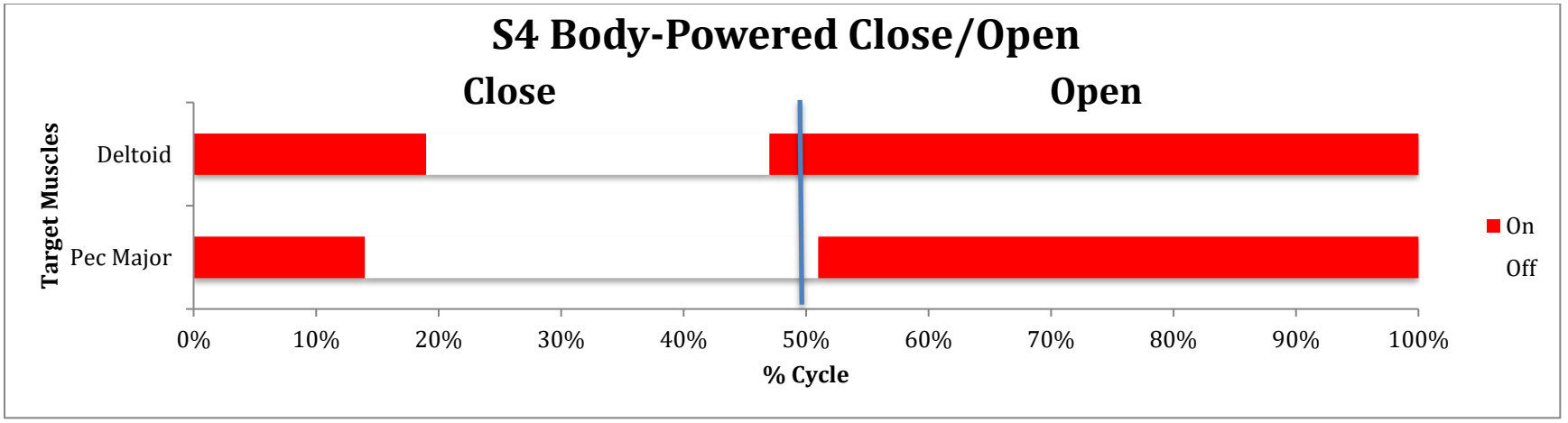
S5, TR, = FDP for both finger flexion and closing of the terminal device. No target muscles active during finger extension or opening of the terminal device. S6, SD = pec major for finger flexion and closing of the terminal device. No target muscles were active during finger extension, however muscle activity was seen within trapezius for opening of the device, specifically where a sensor within the socket was located.

The remaining twelve out of fourteen total participants presented with different muscle activation patterns for both movements of the phantom limb and prosthetic device. The expected frequency, if occurring by random, would be 13.5 movements utilizing different muscle activation patterns and 13.5 movements utilizing the same muscle activation patterns for movements of both the phantom and prosthetic limb. The frequency of the occurrence of different muscle activation patterns used to complete phantom and prosthetic movements (25 occurrences) compared to the frequency of similar muscle activation patterns (2 occurrences) was different from chance alone, $\chi^2(1, N=27) = 19.593$, $p < .001$.

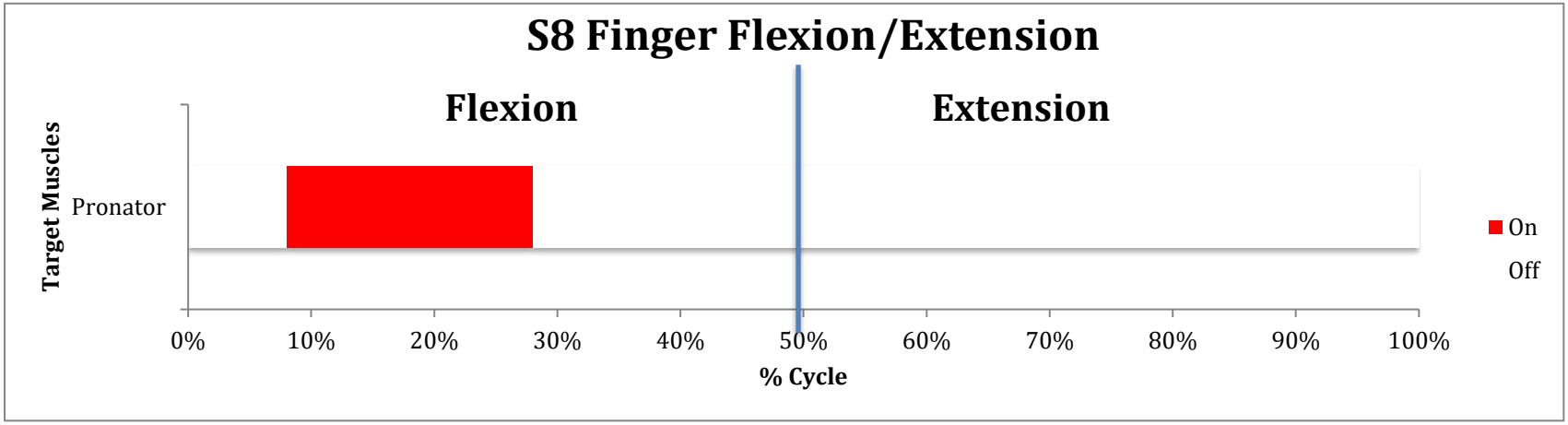
Five participants presented with completely different muscle activation patterns during flexion/extension of the phantom hand and opening/closing of their prescribed prosthetic device, for a total of 10 differences in movements. One of the participants with similar muscle activation patterns during closing of the device and flexion of the phantom hand presented with different muscle activation patterns for opening of the device and extension of the hand. Figure 5.2 provides examples of these differences.

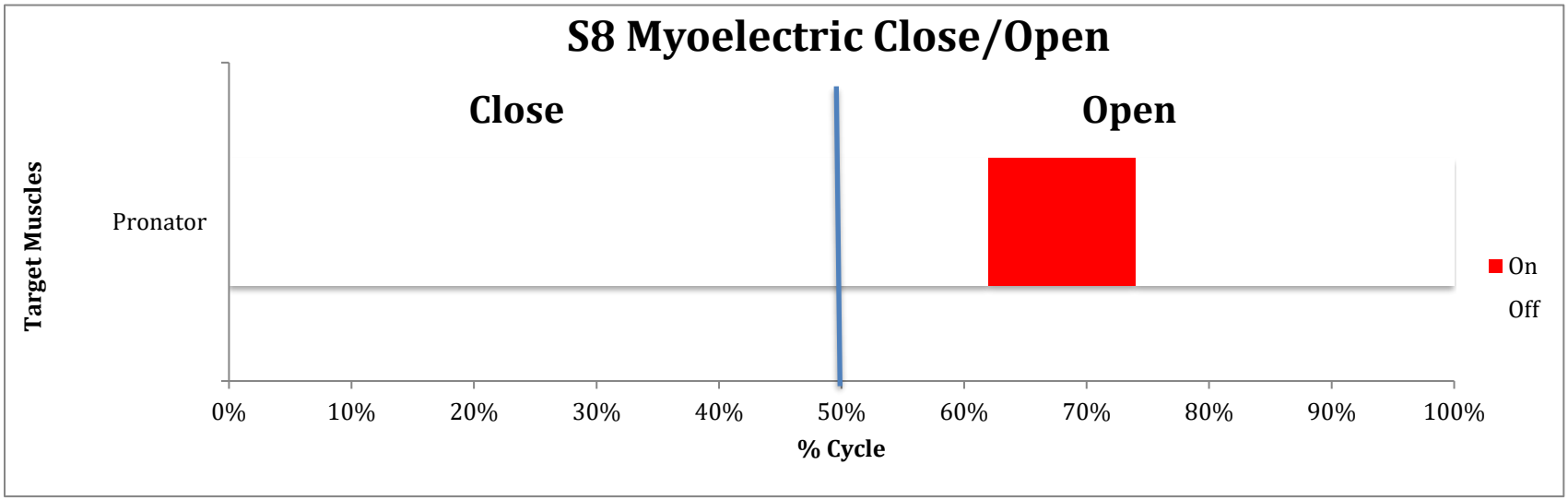
A.


S4 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Pronator
FDP
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

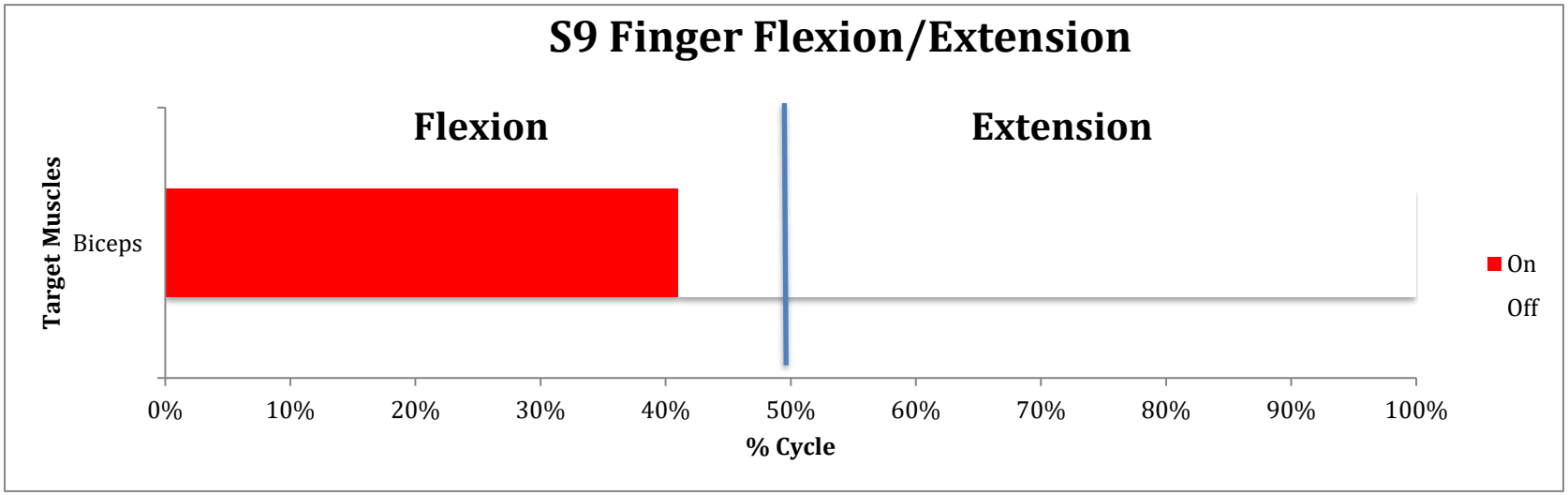

S4 Body-Powered Close/Open
Close
Open
Target Muscles
Deltoid
Pec Major
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle

B.


S8 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Pronator
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle


S8 Myoelectric Close/Open
Close
Open
Target Muscles
Pronator
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle

C.


S9 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Biceps
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle

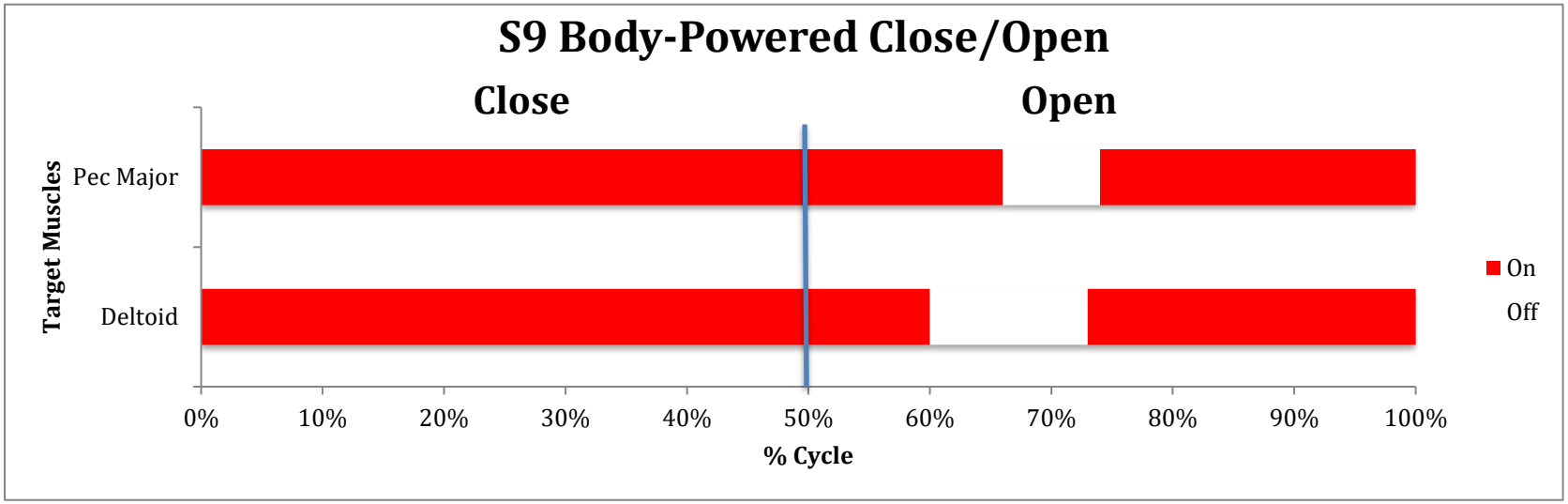


Figure 5.2: Complete Differences in PLC and Prosthesis Activity

S4, TR body-powered prosthesis = FDP and pronator teres active during phantom movements but not prosthetic movements, deltoid and pec major were active during prosthetic movements but not the phantom hand. S8, TR myoelectric prosthesis =. pronator teres active during flexion of the phantom hand and opening of the prosthetic device, no target muscles active during extension of the phantom fingers or closing of the prosthesis. S9, TH, body-powered prosthesis = biceps brachii for finger flexion pec major and deltoid utilized for functional control of the body-powered prosthesis.

The seven other participants had at least one muscle active during the same movement of the phantom hand and the terminal device. The expected frequency, if occurring by random, out of the movements completed by different muscle activation patterns (24 movements), would be 12 completed with at least one similar muscle and 12 without. The frequency of the occurrence of at least one similar muscle contracting for both movements of the phantom and prosthesis (9 occurrences) compared to movements completed without similar muscles contracting (15 occurrences) was not different than chance alone, $\chi^2(1, N=24) = 1.500$, $p=.221$.

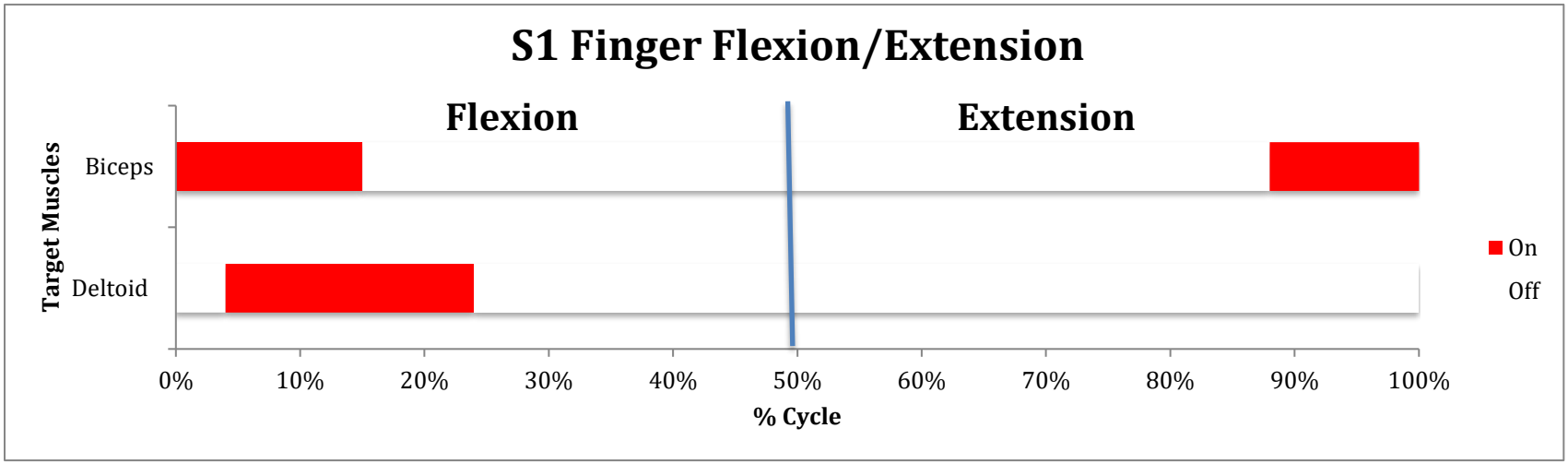
Although these participants did present with muscle contractions in at least one of the same muscles during the completion of the movements of their phantom hand and terminal device, the specific muscle activation patterns were not visually similar. Table 5.1 depicts the muscles that were active for each movement, for each of these seven participants. Figure 5.3 presents three examples of these patterns of muscle activity. Although some of the same muscles became active during movements of the phantom hand and the terminal device of the prescribed prostheses, the patterns of activation are not visually similar.

Table 5.1: At Least One Muscle Active in Both PLC and Prosthetic Movements

Subject	Phantom Close	Prosthesis Close	Phantom Open	Prosthesis Open
1-TH BP	Biceps Deltoid	Biceps (Prolong) Triceps (Delayed)	Biceps (Delayed)	Biceps (Delayed) Triceps (Delayed) Deltoid (Early) Pec Major (Delayed)
2- TR Myo	EDC Pronator Supinator FDP	Pronator (Delayed)	No Targets	Biceps (Delayed) Pronator (Delayed) Supinator (Delayed) EDC (Delayed)
7- TR Myo	Pronator EDC (brief) FDP	No Targets	EDC (Early)	Pronator (Early) EDC (Delayed) Supinator (Delayed)
11- TR Myo	FDP	FDP (Prolong) EDC (Continuous)	EDC	EDC (continuous)
13- WD BP	Triceps(Prolong) Pronator EDC (brief) FDP (Prolong)	Pec Major Pronator Deltoid Triceps	Pronator (Early) EDC (Early)	No Targets
14- TR BP	FDP	Triceps (Prolong) Biceps (Continuous) Pronator (Prolong) Supinator (Prolong) EDC (brief)	FDP (Delayed) Supinator EDC	Biceps (continuous) Pronator (Delayed) Supinator (Delayed) EDC (Early)
15- TR BP	Triceps Biceps Pronator Supinator EDC (Brief) FDP (Prolong)	FDP (Delayed/Prolonged)	Pronator Supinator (Brief) EDC (Early) FDP (Delayed)	Pec Major (Early) Deltoid (Delayed) Triceps (Delayed) Biceps

[1] Abbreviations: TH – Trans-Humeral, TR- Trans-Radial, WD- Wrist Disarticulation, FDP – Flexor Digitorum Profundus, EDC – Extensor Digitorum Communis, BP- Body-powered, Myo- Myoelectric ,

A.


S1 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Biceps
Deltoid
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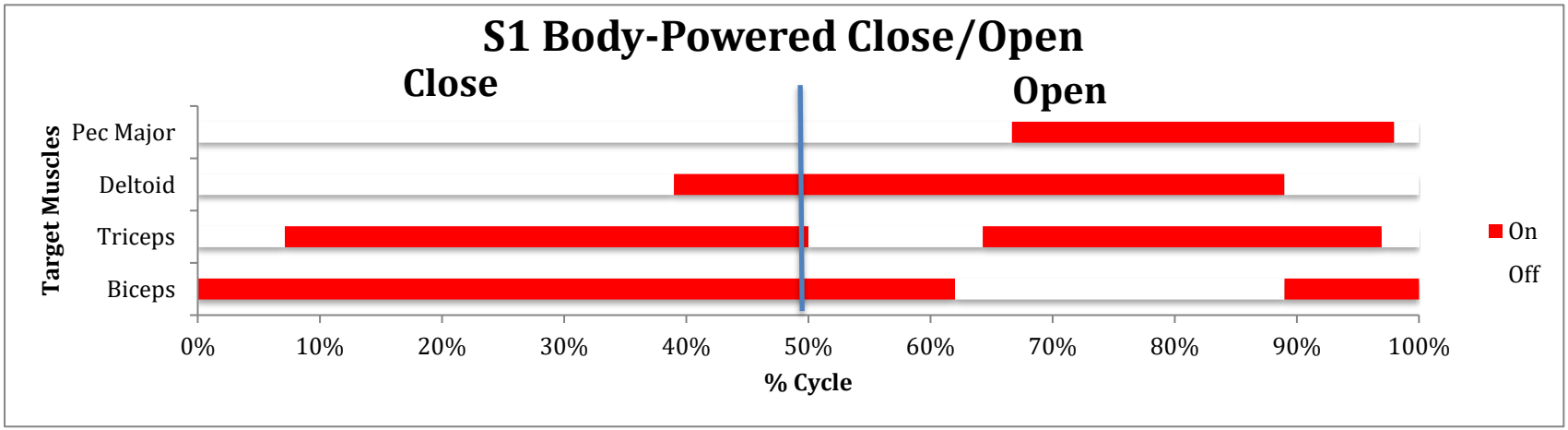
S1 Body-Powered Close/Open
Close
Open
Target Muscles
Pec Major
Deltoid
Triceps
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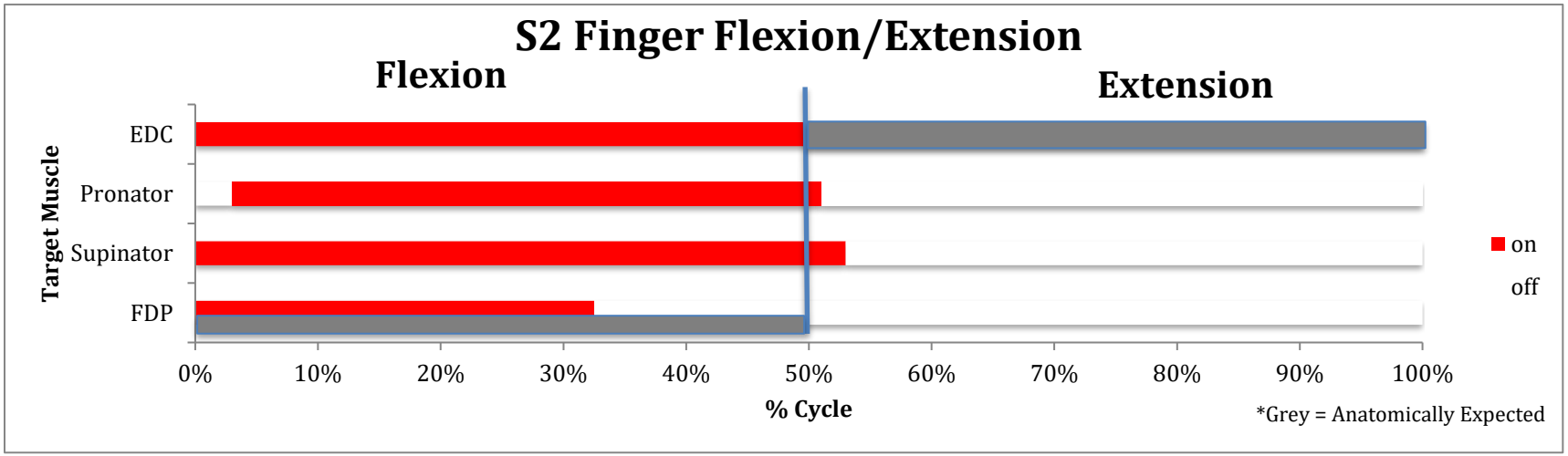
S2 Finger Flexion/Extension
Flexion
Extension
Target Muscle
EDC
Pronator
Supinator
FDP
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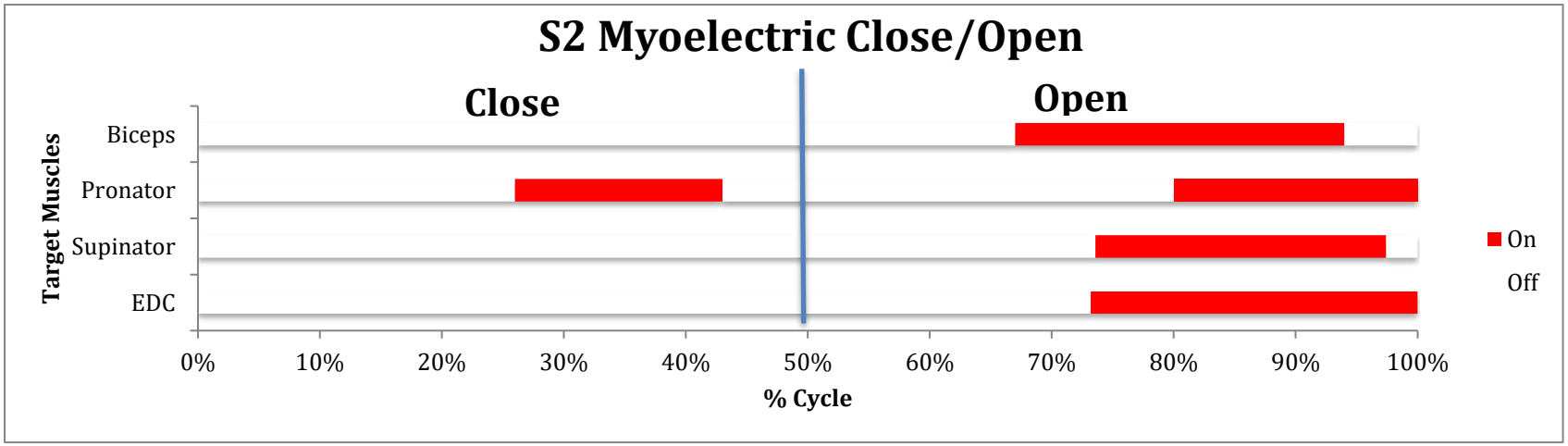
*Grey = Anatomically Expected


S2 Myoelectric Close/Open
Close
Open
Target Muscles
Biceps
Pronator
Supinator
EDC
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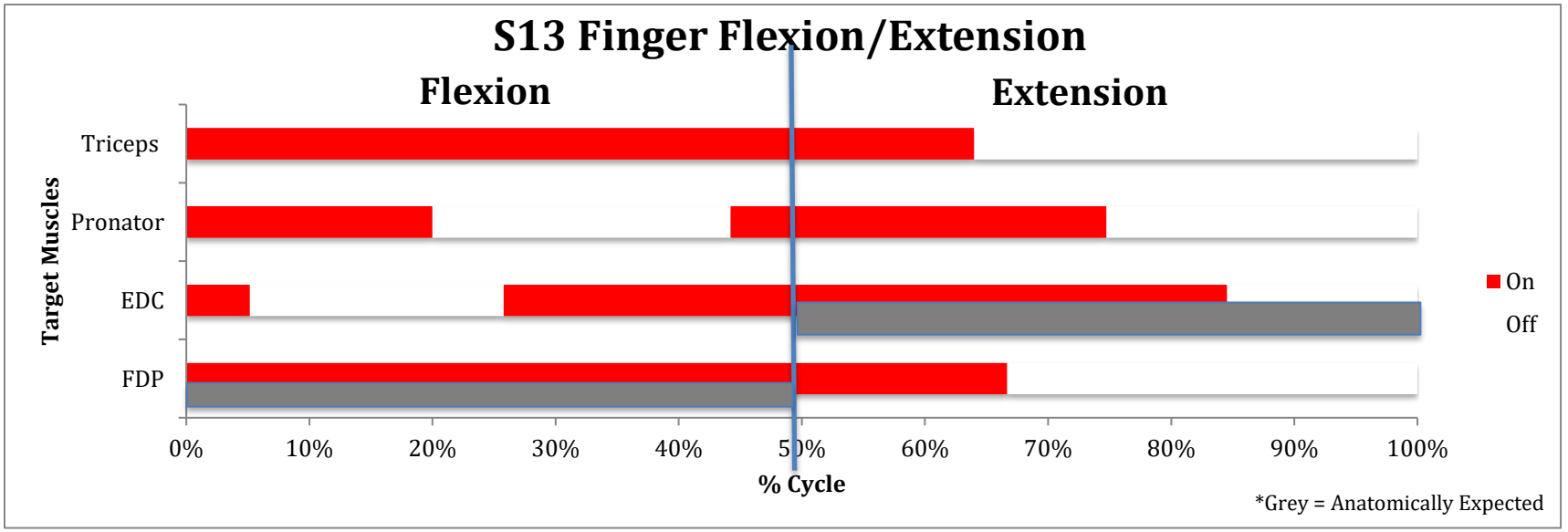
C.


S13 Finger Flexion/Extension
Flexion
Extension
Triceps
Pronator
EDC
FDP
Target Muscles
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*Grey = Anatomically Expected

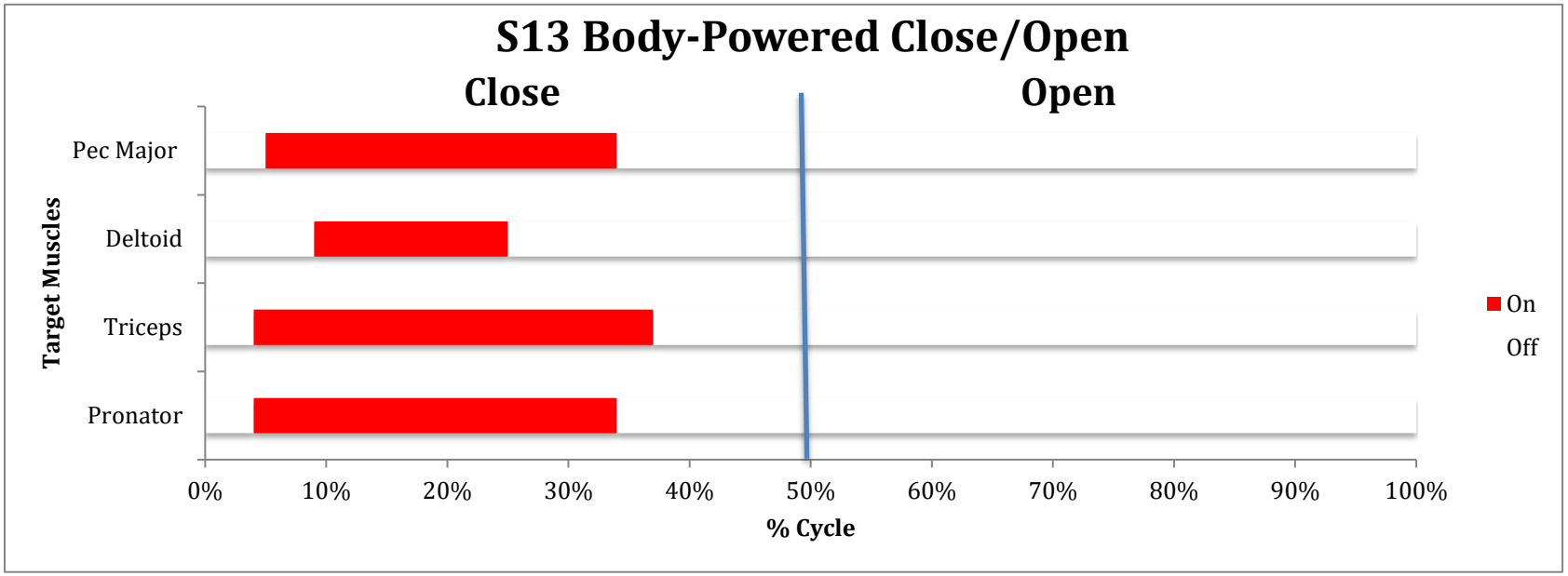


Figure 5.3: Similar Muscles Active, Differing Patterns of Activity

At least one muscle active during both phantom and prosthetic movements, with visually different activation patterns. S1 = deltoid for closing of the phantom hand, and opening of the prosthesis, biceps during both phantom hand closing and prosthesis closing, although the activation patterns are visually different. S2 = pronator and supinator during closing of the phantom hand but opening of the prosthesis. S13 = triceps and pronator for both hand closing and prosthesis closing, however visually different activation patterns.

5.4 Discussion

After injury it is possible to re-acquire motor skills that may have been lost due to injury, known as recovery of function, however acquiring new movements or modifying the execution of previously established movements requires practice and motor learning (Shumway-Cook & Woollacott, 2001). Movement of the upper extremity is a developed motor skill that all individuals obtain in the same successive manner (Shumway-Cook & Woollacott, 2001). It is theorized that movement of a phantom limb is the recovered process of moving the intact limb. In contrast, controlling the movement of a prosthesis requires acquisition of new motor skills through extensive practice. Control of a body-powered device requires movement of upper arm and trunk muscles, regardless of level of amputation. Surface electrodes, typically placed over large flexor/extensor muscle masses, control myoelectric devices. Muscles required for control over prosthetic devices may not be correlated to movements of the intact hand. This study hypothesized that muscle activation patterns used to control a prosthetic device would differ from muscle activation patterns used to control movements of a phantom limb.

Results showed that only two out of fourteen participants utilized similar muscle activation patterns to close both their phantom hands and prosthetic devices, and that the frequency of this occurrence was not random ($p < .001$). Thirteen of fourteen participants (one participant did not have contractions within any of the target muscles during opening movements) utilized different muscle activation patterns for opening their phantom hand and opening their prosthetic device. Twelve out of fourteen participants (85.7%) utilized different muscle activation patterns for closing their phantom hand and closing their prosthetic device. Of the movements with different muscle activation patterns, although statistically similar to chance occurrences, seven participants had muscle activity within at least one of the same muscles during phantom and device movements (3 myoelectric users/4 body-powered users). Although a muscle was active during both movements, timing of the specific patterns of activity within these muscles, throughout the cycle of movement, was not similar. All seven of these participants had visually different muscle activation patterns for opening and closing the phantom hand versus opening and closing the prosthetic device, even if one or more muscles were active during both movements. The remaining five participants presented with muscle activation in completely different sets of muscles for phantom hand movements and prosthetic device movements.

Results from this study show that the majority of participants use different motor control muscle activation patterns to control movement of the phantom limb and prosthetic device and that these were not random occurrences ($p < .001$). These differences are theorized to be due to the incongruity between types of skill. PLC may be a recovered motor developed skill, much like reaching and grasping with the hand, whereas prosthetic control is a motor learned skill, much like shooting a basketball. Unlike PLC, control of the movement of a prosthetic device requires practice before the movement becomes fluid and automatic. Unfortunately, motor learning is not always achieved by upper extremity amputees and may lead to rejection of the prosthetic device.

5.5 Conclusion

More than 30% of all upper extremity amputees reject their prescribed prosthetic device (E. A. Biddiss & Chau, 2007). However, this does not necessarily mean they reject all devices, an individual may have been prescribed a myoelectric device, found it too difficult to control, then switched to a body-powered, or vice versa. Reasons for rejection include difficulty with motor learning to control the device, and an inability to learn multiple patterns of muscle activation required for movement (E. A. Biddiss & Chau, 2007). This study showed that different patterns of muscle activity are required for movement of a phantom limb and movement of a prosthetic device.

The participants in this study tended to use their device for extensive lengths of time (9 participants wear their device 8+ hours) throughout the day, and have not rejected their devices. Such results imply that these participants were able to learn how to control their device efficiently, regardless of the extensive learning required. The next research study investigating muscle activation differences between PLC and prosthesis control should recruit users who have completely rejected any prescribed device, and test them on prosthesis control.

The potential conflict created between differing motor skills, attempting to complete similar actions (opening and closing the hand), may impact muscle activation patterns required for such a movement. (Chapter 6 investigates this theory further.) A prosthetic device that utilize the same muscle activation patterns as phantom limb movements may allow more natural and intuitive control of the device necessitating less practice and decreasing rejection rates.

CHAPTER 6: MUSCLE ACTIVATION PATTERNS DURING PHANTOM LIMB CONTROL BASED ON TYPE OF PROSTHESIS UTILIZED

6.1 Introduction

People with below elbow (wrist disarticulation and trans-radial) upper extremity amputation are typically prescribed a body-powered or myoelectric prosthesis (artificial limb) with either a hook or a hand as the terminal device (Chadwell et al., 2016). Body-powered prostheses are designed to allow the terminal device to be controlled by movements of the shoulder and/or upper body. A cable is supported by a harness, which links proximal body movements to terminal device control (E. Biddiss & Chau, 2007). Typically, movement of the shoulder and/or upper body generates tension on the cable allowing the terminal device to open; when tension is removed from the cable the terminal device closes. Some individuals require devices with active closing rather than active opening, tension on the cable closes the terminal device while relaxing opens the device. Muscle activity required for functional control of a body-powered prosthesis is generated from the muscles of the upper arm and chest; such as biceps, triceps, anterior deltoid, and pectoralis major. Muscle activity within the residual forearm is not necessary for control of the device.

Myoelectric prostheses are controlled by sensors residing within the prosthetic socket that amplify electrical activity generated from specific muscles within the remaining portion of the limb (residual limb) (Chadwell et al., 2016). Myoelectric devices were designed to provide users with more active control over the terminal device by providing more movement options, such as rotation of the wrist, and independent finger movements. Sensor placement is generally situated over large flexor and extensor muscle masses. Muscle activity within the upper arm is not required for functional control of a below elbow myoelectric prosthesis.

Regardless of the type of device prescribed users are required to practice the skill of control. Learning how to control the device requires incorporating different patterns of muscle activity into intuitive, automatic skills. Motor learning is the internal process of obtaining new motor skills, through practice and incorporation, resulting in the automaticity of desired movements (Nieuwboer et al., 2009). Learned motor skills are different from developed motor skills, such as reaching and grasping, which do not require practice (Haibach et al., 2017). Upper extremity amputees are required to practice using their prosthesis before movements become automatic, although not all users achieve automaticity.

Upper extremity amputees are capable of completing movements of the limb that is no longer there; known as phantom limb control (PLC). PLC is thought to be a recovered developed skill rather than a learned process (Brodie et al., 2007; Shumway-Cook & Woollacott, 2001), and as chapter 5 showed, requires different muscle activation patterns. Prosthesis control and PLC in below elbow amputees both accomplish movement commands associated with functions of the hand, and may both become automatic. It is theorized that the practice required to learn a motor skill may impact the execution of recovered developed motor skills. To add potential insight to this theory kinesiologic electromyography (EMG) was used to record specific muscle activity within the residual limb while below elbow amputees completed movements of their phantom hand/wrist. This study was designed as a preliminary, yet critical, step into exploring the potential impact of motor learning to control the terminal device of a prosthesis, on the muscle activation patterns used for the recovered motor developed skill of PLC. It is hypothesized that users of body-powered prosthetic devices will have more muscles of the upper arm unexpectedly active during movements of the phantom hand/wrist than myoelectric prosthetic users. Typically muscles of the upper arm are not active during anatomical movements of the hand and wrist. Myoelectric prosthetic devices also do not require activation of muscles of the upper arm to control. Body-powered prosthetic devices, however, do utilize muscle activity of the upper arm and trunk to control movement. If the process of motor learning, to control the device, has a potential impact on PLC muscle activation, below elbow amputees who regularly utilize a body-powered prosthesis may have more upper arm muscles active while completing phantom limb movements of the hand and wrist than myoelectric prosthetic users.

6.2 Methods

6.2.1 Participants and Analysis

The eleven individuals with amputation below the elbow, who were prescribed a prosthesis with functional capabilities, participated in this portion of the dissertation study; six were prescribed myoelectric prostheses, five were prescribed body-powered prostheses. The average age of participants was 45.3 ± 13.5 years with 24.3 ± 16.2 years since amputation. Characteristics collected from each participant are outlined in Table 3.1.

All participants completed the entire methods outlined in Chapter 3, however only movements of the phantom hand and wrist were analyzed for the purpose of this study. To obtain the specific outcome measure of this study, phantom hand/wrist movements were grouped together by type of prescribed prosthetic device to determine if upper limb muscles were active during control of the phantom hand/wrists among users of the same types of devices. Muscle activation patterns, for each movement of the phantom hand/wrist completed by myoelectric prosthetic users, was compared to the muscle activation patterns used to control the phantom hand/wrist completed by body-powered prosthetic users. Visual inspection to determine similarities and differences was used, and is a widely used technique for analyzing EMG data (Golabchi et al., 2019). EMG data from phantom hand movements, grouped together by type of prosthesis, were inspected to determine if upper arm muscles were active during PLC of the

hand/wrist throughout the two groups of users (body-powered/myoelectric). Differences in upper arm muscle activity used to control a phantom limb were then compared between the two groups. Goodness of fit, Pearson Chi-Square tests were used to examine if the frequency of upper arm muscle activation within the groups and between the groups of prosthetic users were random occurrences. Similarities in muscle activation patterns, used to control the phantom hand/wrist in groups of prosthetic users, may be due to an impact of extensive motor learning required to incorporate a prosthetic device into functional extremity movements.

6.3 Results

EMG data from 11 participants completing movements of the phantom hand and wrist were analyzed. Anatomically unexpected upper arm muscle activity during movements of the distal phantom limb was explored. Table 6.1 documents the muscles active during each movement of the phantom hand/wrist for each participant. Upper arm muscle activity is highlighted for emphasis.

Table 6.1 Muscle Activity for Phantom Hand/Wrist Movements

	Finger Flexion	Finger Extension	Wrist Flexion	Wrist Extension	Wrist Pronation	Wrist Supination
2-M, Congenital	EDC Pronator Supinator FDP	No targets	Supinator EDC	No Targets	Supinator	Supinator EDC
4-B, Trauma 17 years	Pronator FDP	Pronator FDP	FDP	EDC	Biceps**[3] Supinator	Biceps (exp)[3] Supinator
5-M, Trauma 28 years	FDP	No Targets	No Targets	Pronator EDC	Biceps** Pronator Supinator EDC	Biceps (exp) Pronator Supinator EDC
7-M, Congenital	Pronator FDP	EDC	Pronator FDP	EDC	Supinator	Supinator EDC
8-M, Congenital	Pronator	No Targets	Pronator	Supinator	Pronator	Supinator
10-M, Congenital	Biceps	Biceps	Pec Major Biceps	Pec Major Biceps	Biceps Pronator	Biceps (exp)
11-M, Disease 3 years	FDP	EDC	No Targets	Pronator EDC	Triceps Pronator EDC	EDC
12-B, Trauma 28 years	No Targets	No Targets	Biceps Pronator	Triceps	Pronator	Biceps (exp) EDC
13-B, Trauma 13 years	Triceps Pronator EDC FDP	Triceps Pronator EDC FDP	Triceps Pronator EDC	Triceps Pronator EDC	Pronator EDC FDP	Biceps (exp) Pronator EDC FDP
14-B, Trauma 16 years	FDP	Supinator EDC	Pronator Supinator EDC FDP	Pronator Supinator EDC	Biceps** Supinator	Biceps (exp) Supinator EDC
15-B, Trauma 3 years	Triceps Biceps Pronator Supinator EDC FDP	Pronator Supinator EDC FDP	Triceps Biceps FDP	Biceps EDC FDP	Pronator EDC	Deltoid Biceps (exp) Pronator EDC

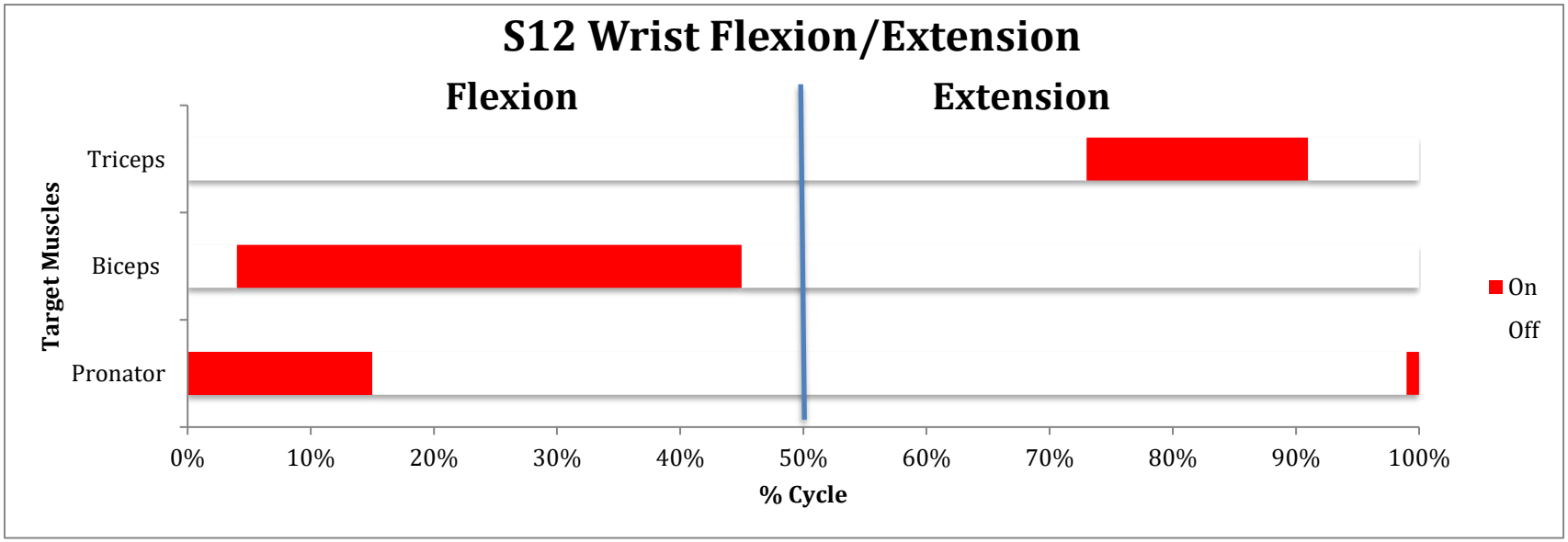
[1] Subjects, type of device utilized (M=myoelectric, B=Body-powered) and cause of amputation.

[2]Upper arm muscle activity of body-powered users is highlighted in blue, upper arm muscle activity of myoelectric users is highlighted in pink.

[3]** indicates bursts of activity in biceps during pronation, which is included in the occurrence of upper arm muscles involved in movements of the hand/wrist. Exp after biceps indicates that this is an anatomically expected muscle activation and therefore not included in the number of movements utilizing unexpected upper arm muscle activation.

Upper arm muscle activity was present during phantom movements of the hand or wrist in all participants who were prescribed a body-powered prosthesis but only in half of the myoelectric prosthesis users. Figure 6.1 shows examples of unexpected upper arm muscle activity during movements completed by body-powered users. Figure 6.2 shows examples of the three out of six myoelectric users who presented with upper arm muscle activation during phantom hand/wrist movements. Of these participants all body-powered users and two myoelectric users experienced muscle activity within biceps brachii during wrist supination movements. Since biceps is a secondary wrist supinator, muscle activity is anatomically expected during supination. Two body-powered users and two myoelectric users also experienced at least a burst of muscle activity of biceps during pronation of the wrist with some experiencing early onset activity when transitioning to supination. Figure 6.3 shows examples of expected biceps activity during supination of the wrist, along with at least a burst of activity during pronation.

A.


S12 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Triceps
Biceps
Pronator
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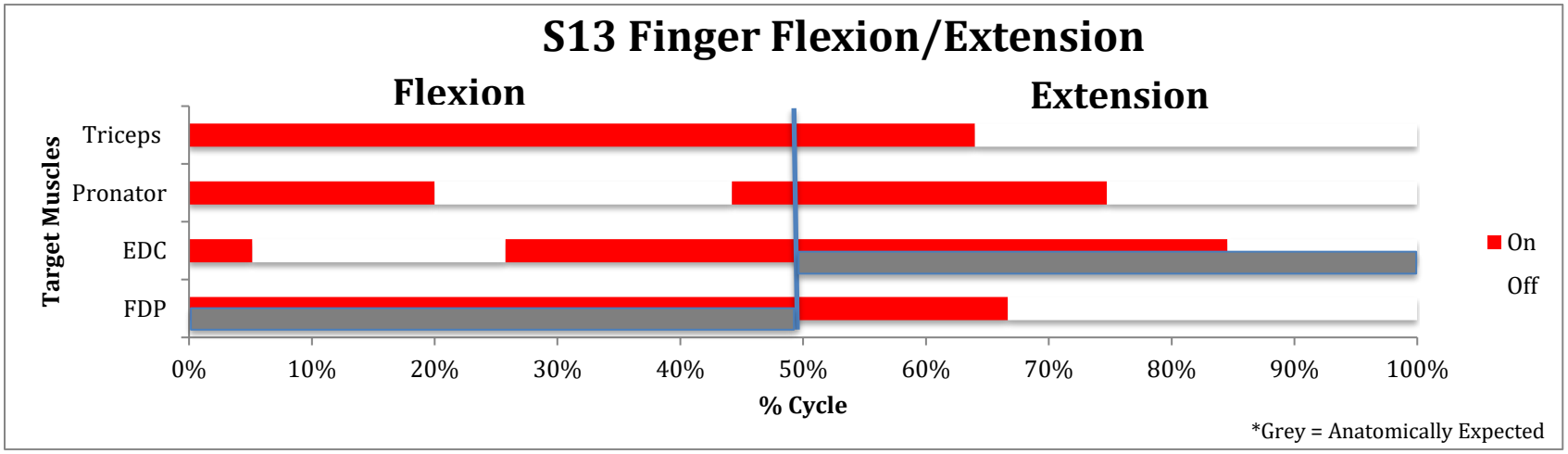
B.


S13 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Triceps
Pronator
EDC
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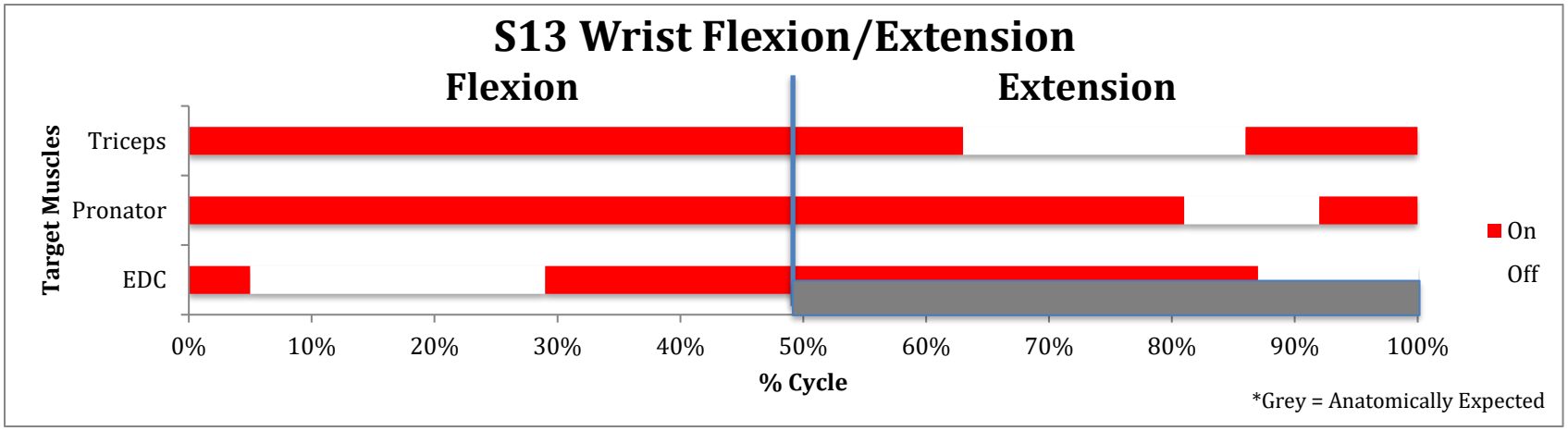
*Grey = Anatomically Expected


S13 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Triceps
Pronator
EDC
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*Grey = Anatomically Expected

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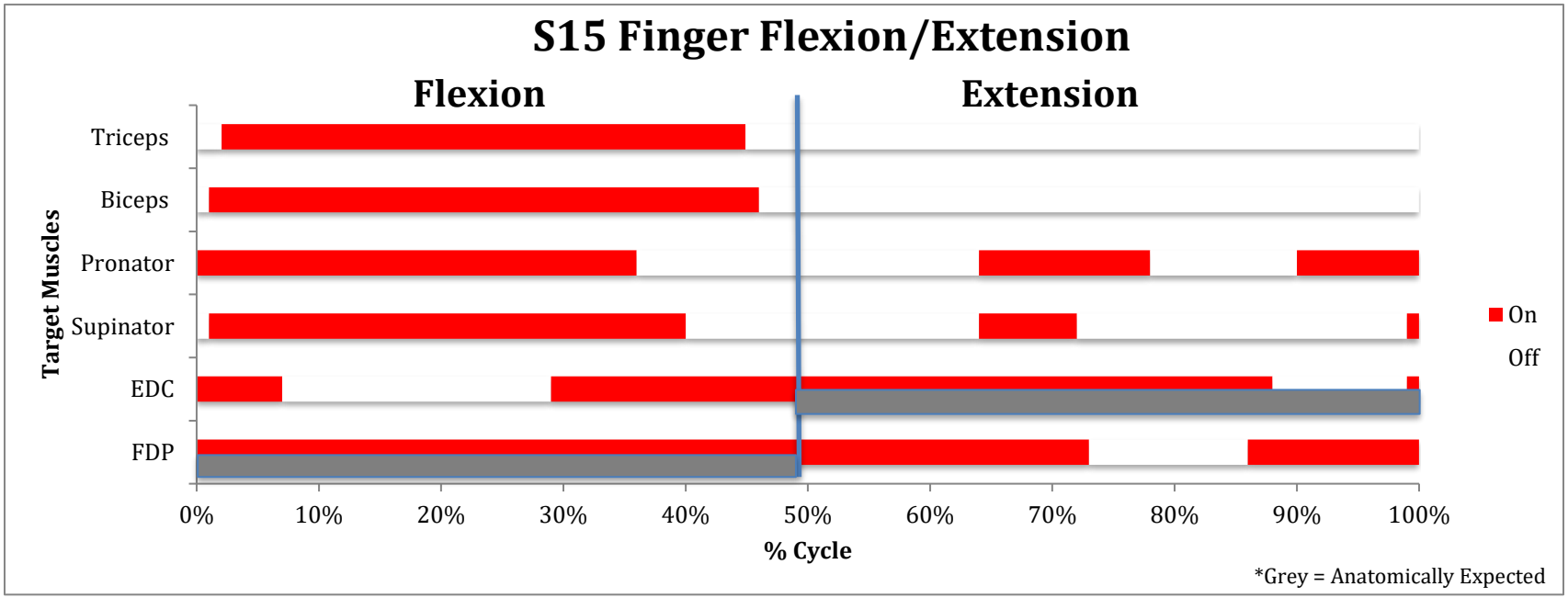
S15 Finger Flexion/Extension
Flexion
Extension
Triceps
Biceps
Pronator
Supinator
EDC
FDP
Target Muscles
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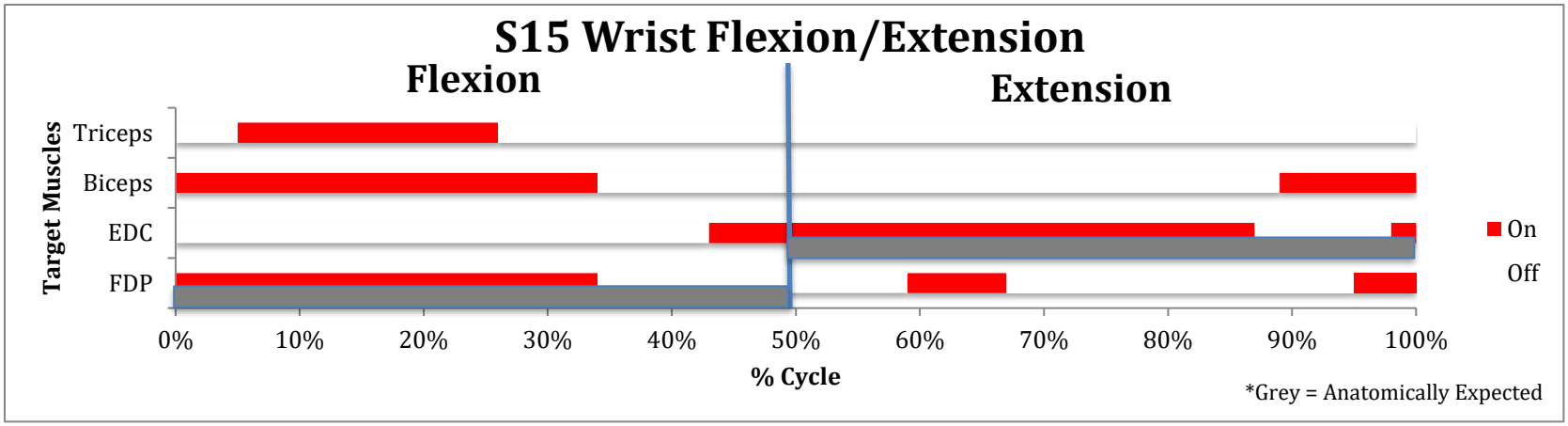
*Grey = Anatomically Expected



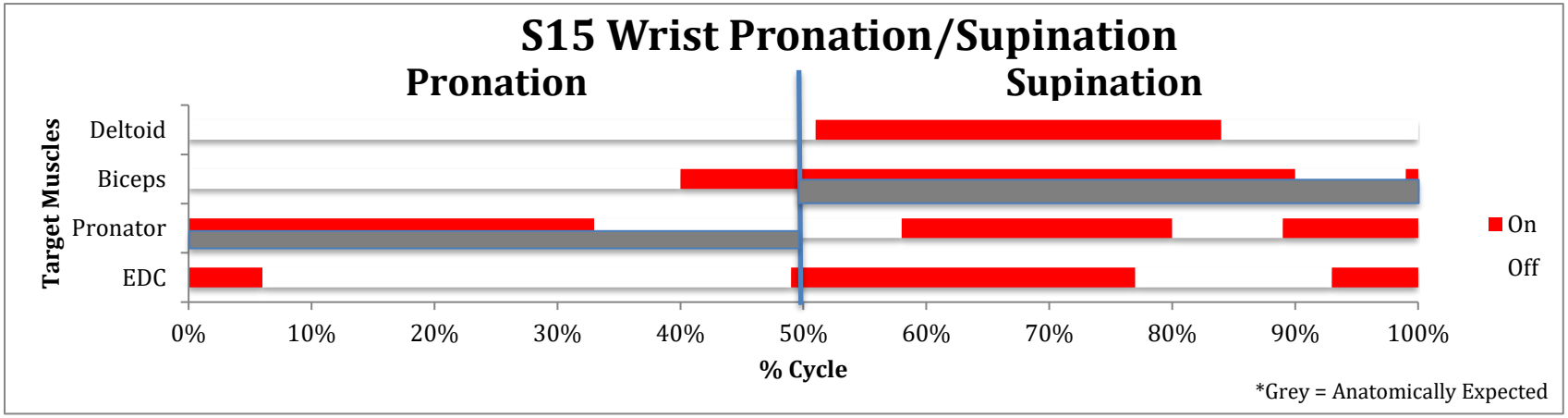
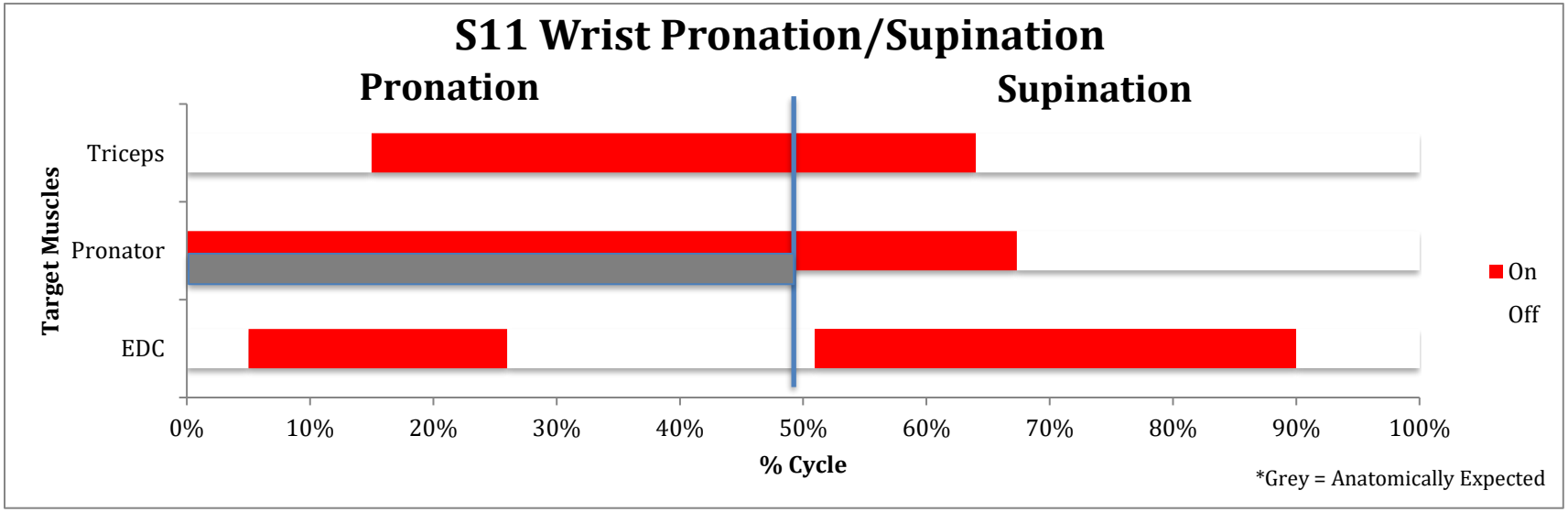


Figure 6.1: Body-powered Unexpected Upper Arm Activity

Body-powered prosthetic users experienced muscle activity in upper arm muscles during phantom hand and wrist movements.

A.


S11 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Triceps
Pronator
EDC
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100%
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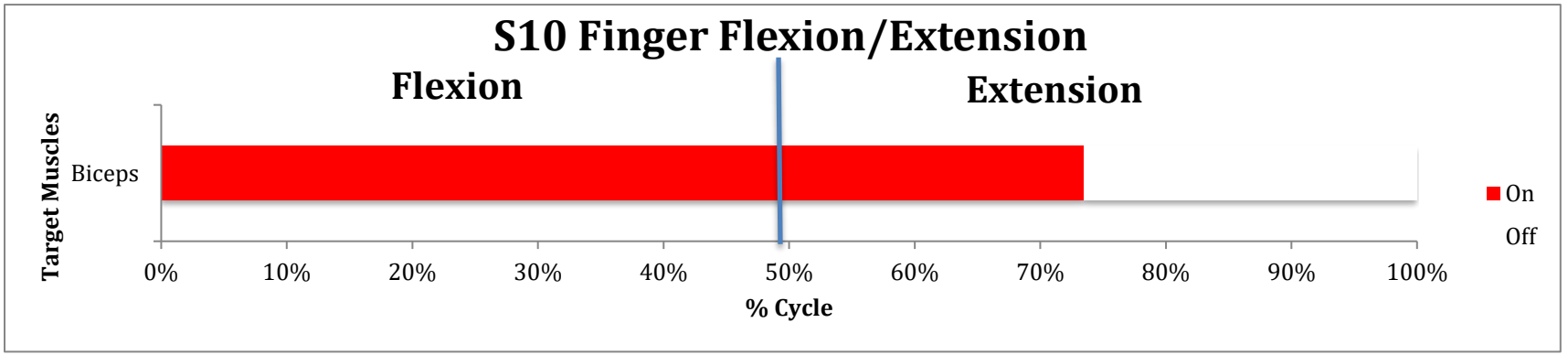
Off
*Grey = Anatomically Expected

B.


S10 Finger Flexion/Extension
Flexion
Extension
Target Muscles
Biceps
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90%
100%
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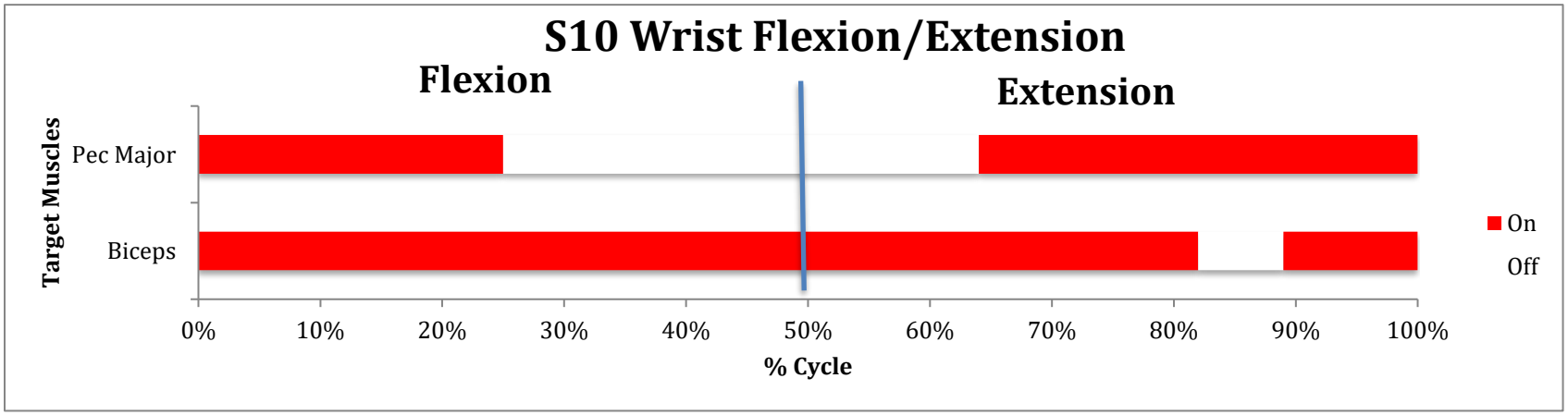
On
Off


S10 Wrist Flexion/Extension
Flexion
Extension
Target Muscles
Pec Major
Biceps
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20%
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40%
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80%
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% Cycle
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Off

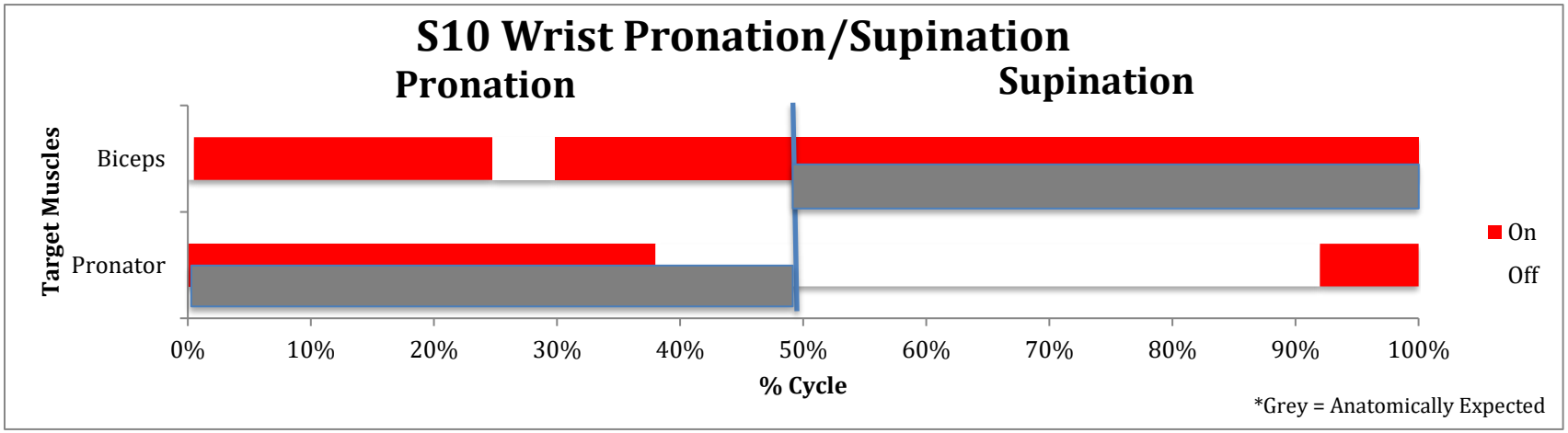
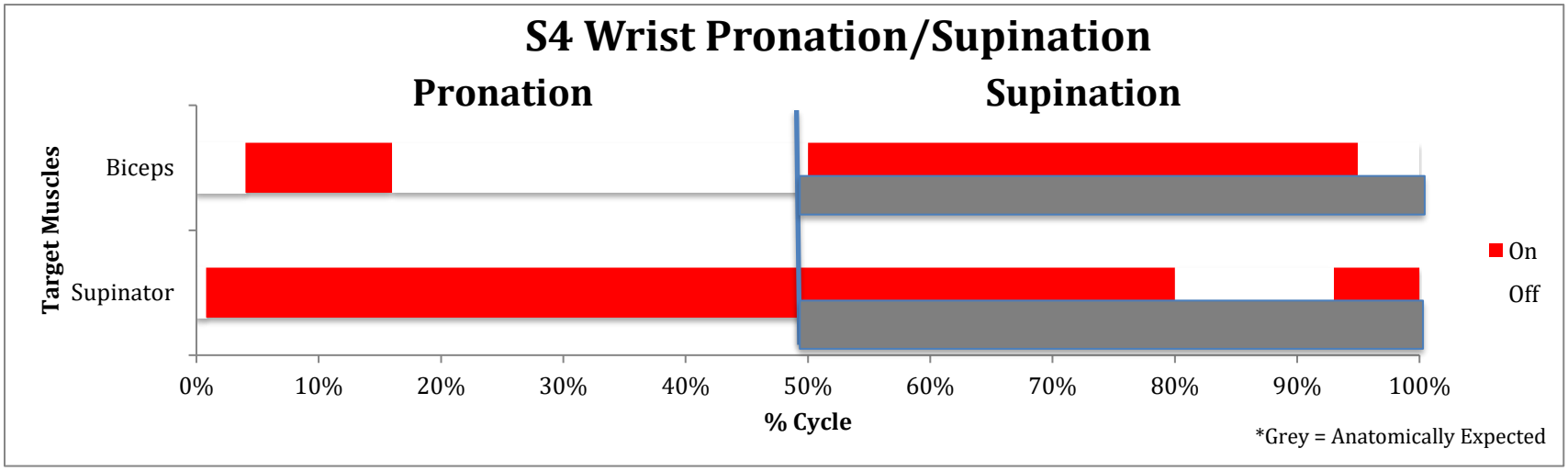


Figure 6.2: Myoelectric Unexpected Upper Arm Activity

Myoelectric prosthetic users experienced muscle activity in upper arm muscles during phantom hand and wrist movements.

A.


S4 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Biceps
Supinator
On
Off
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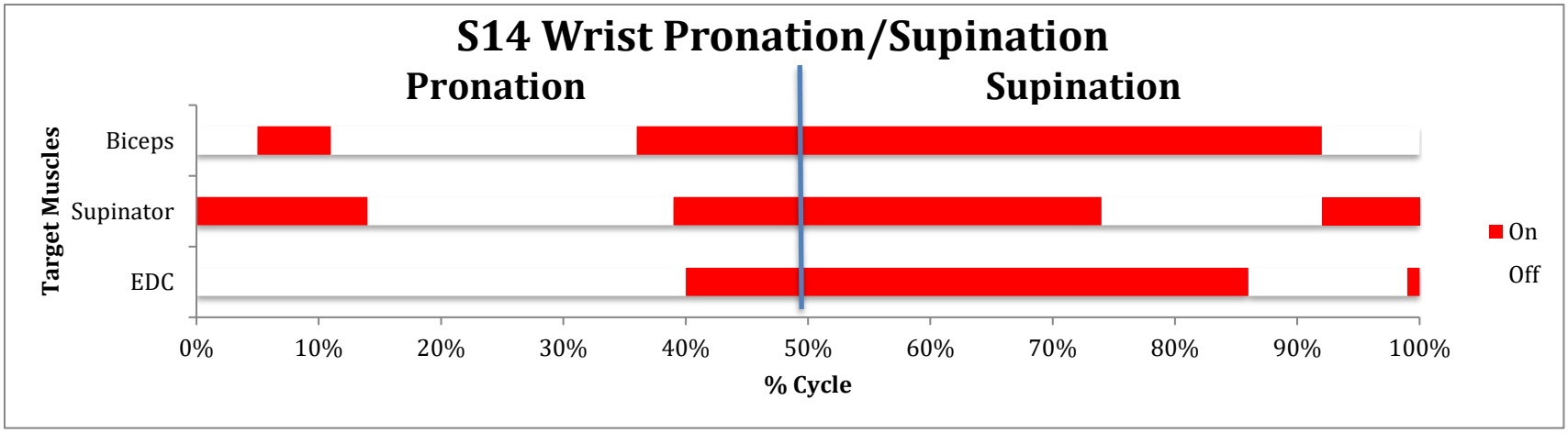
20%
30%
40%
50%
60%
70%
80%
90%
100%
% Cycle
*Grey = Anatomically Expected

B.


S14 Wrist Pronation/Supination
Pronation
Supination
Target Muscles
Biceps
Supinator
EDC
On
Off
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
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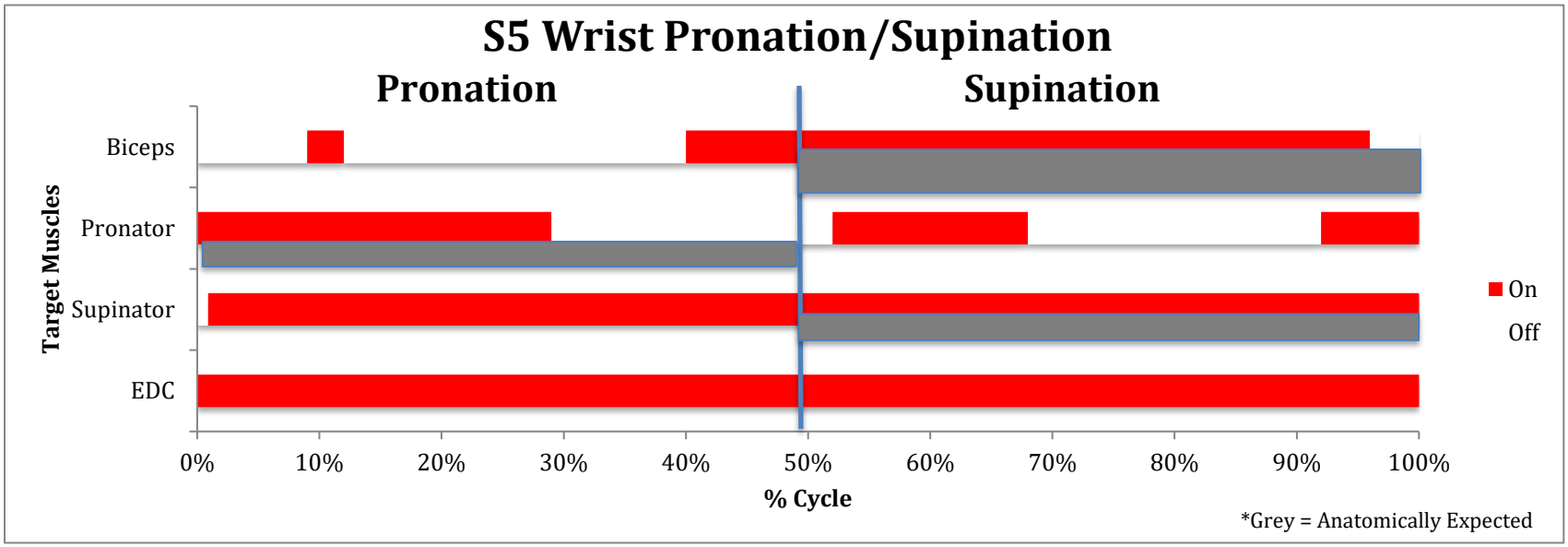

Figure 6.3: Biceps Activation During Wrist Pronation/Supination

Participants who experienced muscle activity within biceps brachii during wrist pronation/supination movements.

Excluding expected biceps activity within supination, upper arm muscles were active during 12 movements of the phantom hand/wrist of body-powered device users. The expected frequency, if occurring by random, would be 15 movements utilizing upper arm muscle activity and 15 movements without upper arm muscle activity for movements of the phantom hand/wrist by body-powered device users. The frequency of the occurrence of upper arm muscle activation during phantom hand/wrist movements of body-powered device users occurred at a frequency no different from chance alone, $\chi^2(1, N=30) = 1.200$, $p = .273$.

Three out of the six participants who were prescribed a myoelectric prosthesis, had muscle activity within the muscles of the upper arm during phantom movements of the hand and wrist. Excluding expected biceps activity within supination, upper arm muscles were active during seven movements of the phantom hand/wrist of myoelectric device users. The expected frequency, if occurring by random, would be 18 movements utilizing upper arm muscle activity and 18 movements not utilizing upper arm muscle activity for movements of the phantom hand/wrist by myoelectric users. The frequency of the occurrence of upper arm muscle activity during phantom hand/wrist movements completed by myoelectric users was different from chance alone, $\chi^2(1, N=36) = 13.444$, $p < .001$.

The frequency of movements completed with unexpected muscle activation of the upper arm (19 occurrences), and movements without unexpected upper arm muscle activation (47 occurrences), based on type of device, for overall movements completed was not a random occurrence; $\chi^2(1, N=66) = 11.879$, $p < .001$. The expected frequency, if occurring by random, would have been 33 movements with upper arm muscle activity and 33 movements completed without upper arm muscle activity. Body-powered prosthetic users had muscle activity within the upper arm during movements of the phantom hand/arm more than myoelectric prosthetic users.

6.4 Discussion

Typically prescribed prosthetic devices are either body-powered or myoelectric. Regardless of the type of prosthesis, people with amputation are required to practice controlling the movement of the device before control becomes fluid and automatic. Prosthesis control is a motor learned skill (E. A. Biddiss & Chau, 2007). In contrast, PLC is thought to be a recovered developed motor skill. PLC and prosthesis control attempt to recreate movements and complete tasks originally executed by the intact hand. Similarities in goal directed movements, and attempts to compensate for the missing limb, may result in interrelated muscle activation patterns for control of the phantom limb, based on type of device prescribed.

Body-powered and myoelectric prosthetic devices require different patterns of muscle activity to complete movements of the terminal device, although design of each type of device is similar for all below elbow amputees. Body-powered devices require activation of the upper arm, scapula and trunk muscles whereas myoelectric devices require activation of forearm muscles. It is theorized that the adaptive process of motor learning, required to functionally control a prosthetic limb, will influence activation patterns utilized to control the phantom hand/arm

between body-powered and myoelectric users, because muscle activity to control each device varies dramatically. Based on the above theory it was hypothesized that users of a body-powered prosthesis would have active muscles of the upper arm while controlling the phantom hand/wrist, whereas myoelectric users would not.

Results showed that all five body-powered device users had muscle activity of the upper arm during phantom limb movements of the hand/wrist. Most muscles of the upper arm are not active during movements of the hand/wrist in an anatomically intact limb. Biceps brachii is an exception to this rule, as it assists in supination of the intact forearm (Karen et al., 2006). Two of these body-powered participants had muscle activity within biceps during wrist pronation/supination. Although biceps are anatomically expected to be active during supination of the wrist, at least bursts of activity were also seen during pronation, an unexpected activation. The remaining three out of five body-powered users had solely anatomically unexpected muscle activity within the upper arm during phantom movements of the hand/wrist.

Three out of six myoelectric device users presented with muscle activity within the upper extremity for movements of the phantom hand/wrist. Activation of most upper arm muscles (biceps for supination is an exception) is not required for completion of hand/wrist movements in an intact limb. Additionally below elbow myoelectric prosthesis users do not require activation of muscles within the upper arm for control of the device, sensors are placed on the forearm. Two of these three participants had anatomically expected activity within biceps during supination of the wrist, however biceps was also active during pronation. The one myoelectric participant, unlike the other 2 participants, who had upper arm muscle activity in more movements than just wrist supination/pronation, was a congenital amputee. This participant experienced upper arm muscle activity during all movements of the phantom hand/wrist. The process of peripheral nerve innervation into residual limb muscles in an individual with congenital absence of a limb has not been previously researched; this study was not designed to determine this biological process, however peripheral nerves of congenital amputees may be able to innervate muscles further away from the site of amputation during initial formation.

Cause of amputation may play an important role in the assignment of muscles utilized to complete movements. All of the body-powered device users were traumatic amputees. Traumatic amputations elicit changes within the central and peripheral nervous systems that inadvertently collaborate to facilitate phantom sensations and control of the movement of the limb (Herta Flor, 2002; Herta Flor et al., 1998). Repair processes and motor learning may impact recovered function of the hand, in the form of PLC. The myoelectric user who presented with the most widespread upper arm muscle activity during phantom hand/wrist movements was a congenital amputee. With congenital amputations it is possible that the biological repair processes initiated by the failure of the limb to form may have impacted motor control patterns of the phantom limb, regardless of motor learning. Congenital amputations are typically caused by failure of the limb to form properly, or a traumatic amputation in utero (amniotic band syndrome) (Gold et al.,

2011). Although specific causes of congenital amputation for all participants was not known, the participant with wide spread biceps activation did not have a traumatic amputation in utero. This individual presented with symbrachydactyly (small fingers) at the end of the stump, unlike the other congenital participants who did not present with residual fingers. Differences in the cause of amputation, (failure to form/traumatic) even in utero, may change the way the body adapts to the amputation. However, no previous research has been conducted on the innervation of peripheral nerves into muscles of the residual limb of individuals born with congenital amputations, regardless of the cause.

Subject 11, a myoelectric user with unexpected triceps activity during pronation, had the most recent amputation out of the group of myoelectric users (3 years). It is possible that cortical reorganization, which occurs within hours of amputation, had not been fully reversed in this individual (P. Chen et al., 2002). Retained cortical reorganization, the activation of neighboring areas within the motor cortex, would explain muscle activation of the triceps during attempted movements of the phantom hand/wrist. When an amputation occurs motor signals from the brain do not result in contraction of the muscles, due to the muscles being denervated. This may result in the areas of the motor cortex responsible for such contractions to become silent (Navarro, 2009). Such silence causes inhibitory factors to become diminished and the stimulation threshold of neighboring cortical areas to be reduced, resulting in the activation of these areas when movements are requested (P. Chen et al., 2002; Navarro, 2009). Triceps are a more proximal muscle that may still have a low activation threshold in this subject. Unfortunately, there have been no studies investigating the timeline of cortical reorganization, or the possibility that initial reorganization is reversed after peripheral nerve repair (a much slower process).

Muscle activation patterns for control of the phantom limb were different between body-powered and myoelectric prosthesis users, and this was not a random occurrence ($p < .001$). All body-powered users experienced unexpected muscle activation within the upper arm during phantom limb movements. Upper arm muscle activation is a critical component for control over the terminal device of a body-powered prosthesis. People with amputation who utilize a body-powered device are taught, and must practice and learn, how to manipulate their upper arm to control the terminal device. Controlling the terminal device and controlling the movement of the phantom hand are very similar goals. It is possible that the extensive learning to open and close the terminal device of the prosthesis, using upper arm muscle activity, may influence the muscles activated to control the phantom hand. Individuals may not be able to fully separate the movements of the prosthetic device and the phantom hand. Myoelectric users more typically did not have unexpected muscle activation of the upper arm during phantom hand/wrist movements, and those who did were either congenital or the newest amputee. Controlling the myoelectric device, although it may use different muscle activations, still relies on muscles of the forearm, similar to control of the anatomical hand. These individuals are taught to activate forearm muscles to control the terminal device of the prosthesis, while not utilizing upper arm muscles. If activation of upper arm muscles during phantom hand movements were not due to motor

learning required for body-powered usage, but the result of another process, such as cortical reorganization after amputation, it would be expected that more myoelectric users would experience this activation as well.

6.5 Conclusion

Muscle activation patterns to control the movement of a phantom hand were different based on the type of device participants used. These results may support the theory that motor control patterns required to execute motor learned skills can influence the execution of recovered developed motor skills. The variance in PLC muscle activation may be related to the differences in motor control required to execute developed skill versus motor learned skill. This study suggests that muscle activity used to control the terminal device may affect muscle activity used to complete phantom limb movements.

Further research needs to be conducted before any definitive conclusions are made regarding the impact of motor learning, especially when motor control varies dramatically from motor developed skills, on phantom limb control and prosthetic acceptance rates. This is the first study that has compared PLC for different prosthetic devices (each in theory, involving a different influence of motor learning) and opens the field up for future exploration.

CHAPTER 7: DISCUSSION

Directed intentional movements of a limb that is no longer there (phantom limb control) are experienced by upper extremity amputees, regardless of the cause of amputation (Estelle Raffin et al., 2012). Many amputees report being able to conduct fine motor movements of the fingers, and wrist and elbow movements of their phantom limb. Motor control of a phantom limb is an unexpected phenomenon considering the anatomic muscles/tendons required to facilitate such movements are absent with congenital limb amputation or may be lost due to traumatic/surgical amputation. To execute movement of a phantom limb, muscles within the residual limb contract, even though these muscles may not have been anatomically responsible for the desired movement (Gagné et al., 2009; K. Reilly et al., 2006).

Previous research indicates that level of amputation influences phantom limb control. It has been reported that trans-humeral amputees utilize different muscle activation patterns to control movement of a phantom limb than would be anatomically expected (Gagné et al., 2009; K. Reilly et al., 2006). Trans-radial amputees were originally thought to retain anatomical muscle activation patterns for phantom limb control, since they have many anatomical nerves and muscles remaining within the residual limb, whereas high-level amputations (shoulder disarticulation) were thought to result in "insufficient survival" of motor neurons inhibiting the movement of a phantom limb (Gagné et al., 2009; K. Reilly et al., 2006). Results from the current study confirm that trans-humeral amputees utilize different muscle activation patterns than would be anatomically expected, at a greater than chance frequency. However, this study challenges the previous findings regarding below elbow (wrist disarticulation and trans-radial) amputees maintaining anatomical activation patterns and the inability of high-level amputees (shoulder disarticulation) to control movement of a phantom limb. All participants, with varying levels of amputation, had muscle contractions of the residual limb during movements of the phantom limb. Muscle contractions occurred during 84.4% of all 96 movements. Although the participant with a shoulder disarticulation did have the highest rate (37.5%) of no activation detected within a movement, they still presented with contractions of the residual limb during 62.5% of phantom limb movements. It is possible that no activation within any of the muscles targeted with electrodes may imply that the participant was unable to conduct those movements, however there is also the possibility that other muscles, not targeted in this study were contracting to facilitate movement.

In addition to control of a phantom limb, residual limb muscle activation is required to enable functional use of a prosthetic device. Prostheses are typically prescribed to upper extremity amputees in an attempt to mimic actions completed by an intact limb. Body-powered

prosthetic devices require activation of muscles within the upper arm, shoulder, and/or upper body to generate tension on a cable that controls the action of the terminal device. Myoelectric prosthetic devices require activation of specific target muscles, sometimes in complicated patterns, beneath sensors embedded within the socket (E. A. Biddiss & Chau, 2007; Bouffard et al., 2012; Bouwsema et al., 2010). Regardless of the type of prosthetic device prescribed, not all upper extremity amputees master intuitive use. More than 30% of prescribed prostheses are rejected, largely due to difficulties with learning how to accurately control the device (E. A. Biddiss & Chau, 2007).

Previous literature has reported that functional and intuitive control of a prosthetic device requires extensive practice and motor learning; unfortunately not all amputees become proficient and may even reject the device (Alcaide-Aguirre et al., 2013; Bouwsema et al., 2010; Dromerick et al., 2008). Rejection has been reported as due to difficulty with learning control over the device and a potential discrepancy between device control and PLC (E. A. Biddiss & Chau, 2007; Bouffard et al., 2012; Bouwsema et al., 2010). Users of body-powered prostheses reported PLC did not influence device control in contrast to myoelectric users who reported PLC did influence device control. (Bouffard et al., 2012). The current studies aimed to expand the understanding of the impact of motor learning, based on type of prosthesis prescribed, on device and PLC. This project confirmed the theory that there is a discrepancy between muscle activation patterns required for PLC and control of a prosthesis, regardless of the type of device prescribed, at a frequency greater than chance ($P \leq .000$). This project also introduced novel results showing that upper arm muscles become active during more movements of the phantom hand/wrist in body-powered prosthetic users compared to myoelectric prosthetic users at a frequency greater than chance ($P \leq .001$). These results may show a potential effect of motor learning for use of prosthetic devices on phantom movements.

The data from the current studies suggests that: (1) Amputees with varying levels of amputation have muscle activity within the residual limb during phantom limb movements and that different muscle activation patterns are used to control movements of phantom limbs than anatomically expected; (2) Different muscle activation patterns are used to control phantom limbs than prosthetic devices, and; (3) Muscle activation patterns for PLC vary between users of different prosthetic devices (myoelectric and body-powered).

Study one found that muscles of the residual limb were active during 84.37% of phantom limb movements completed by participants with varying levels of upper extremity amputation. Of those phantom movements with residual limb muscle activity only 16% were completed by anatomically expected muscle activation patterns. Unexpected muscle activation patterns included any pattern of activity that deviated from anatomically expected muscle activation patterns, specifically; anatomically inappropriate muscle activation, and abnormal co-contractions between expected muscle activity and additional unexpected muscle activity. All participants, regardless of level and cause of amputation, were capable of phantom limb

movements, and experienced anatomically unexpected muscle activation patterns during these movements.

Level of amputation did seem to result in differences of the amount of anatomically inappropriate muscles activated to execute phantom limb movements. Wrist disarticulation participants utilized anatomically expected muscles in addition to co-contraction of unexpected muscles, whereas trans-humeral and shoulder disarticulation participants utilized just anatomically inappropriate muscles. These results were not surprising given the fact that wrist disarticulation participants have the most anatomical muscles/tendons remaining after amputation. Although, it was surprising that participants with wrist disarticulations did not utilize the most anatomically expected muscle activation patterns. Participants with trans-radial amputations have the most muscles that control hand/wrist movements severed, enabling more muscles to become receptive to new axons, suggesting that they should have the highest rate of abnormal co-contractions. However, this was not the case, participants with trans-radial amputations completed movements of the phantom hand/wrist with more anatomically expected muscle activation patterns than participants with wrist disarticulations. These results warrant further investigation into a possible role of the CNS and synergistic muscle activity. For instance it may have been more difficult for the wrist disarticulate subjects to complete the requested phantom movements. An inability, or difficulty executing the movements may have lead to signals being sent to the CNS for the recruitment of additional muscles to complete the task.

As the amputation level moves proximally, such as with trans-humeral or shoulder disarticulations, the amount of muscles/tendons available for severed nerves to regenerate into diminishes, increasing the occurrence of re-innervation and anatomically inappropriate muscles taking responsibility for movements of the hand/arm. This was seen by the highest percentage of anatomically inappropriate muscles completing movements in these participants. Results from study one support the theory that PLC may be influenced by the occurrence of severed peripheral motor nerves regenerating and re-innervating into remaining receptive muscles after amputation or due to congenital limb loss. Peripheral motor nerves must form connections with muscles to illicit contractions and therefore execute movement (Javed & Lui, 2019; Levitan & Kaczmarek, 2015). After an amputation, or with congenital limb loss, peripheral nerves may be forced to find target muscles, which they would not anatomically innervate. However, if the peripheral motor nerves maintain their anatomically expected action, even if unexpected muscles execute the movement, this could explain how PLC is a recovered motor developed movement and does not require motor learning to be intuitive.

Unfortunately this study did not trace the peripheral nerve innervation, or investigate the role of the CNS in PLC, and therefore no conclusions can be drawn regarding the mechanisms of each part of the nervous system or this potential theory. However, the studies do demonstrate a drastic need for further research regarding the changes that occur within the PNS, throughout the entire process of recovery, and how these changes impact the CNS. Emphasis for future research on how the PNS impacts the CNS is supported by a 2013 EEG study before and after TMR on 2

individuals and 2017 study investigating cortical mapping in individuals who elected to have TMR compared to individuals without TMR and to healthy controls (A. Chen, Yao, Kuiken, & Dewald, 2013; Serino et al., 2017). The 2013 study recruited 3 participants before and after TMR surgery to investigate electroencephalogram (EEG) activity during movements of the phantom limb. The study showed that EEG activity seemed to move more closely to the presumed location prior to amputation, based on the intact side. However, some shifts of activity seemed to move further away from prior locations, and closer to proximal neighboring regions of the arm, such as the hand toward the elbow. The author speculates that this may be due to the TMR process in which the entire peripheral nerve is innervated into a single muscle, rather than a group of muscles that enable intact limbs to control separate yet similar movements. Unfortunately, this may also make separate phantom movements difficult to complete. The participants with more accurate presumed pre-amputation activity were tested further away from the surgical date, potentially allowing for more regeneration to occur and for individual axon terminals to re-innervate different segments of the muscle. These patients reported a better ability to complete different, separate, movements of the phantom hand (A. Chen et al., 2013). This study supports the theory that peripheral re-innervation may reverse initial cortical reorganization, identifying that cortical representations of the amputated limb reverse initial reorganization once peripheral nerves have re-innervated new target muscles (A. Chen et al., 2013). Unfortunately, this study did not report on the patient's ability to control phantom limb movements prior to TMR surgery. Based on the presence of cortical reorganization prior to TMR, it can be assumed that these patients had minimal PLC, (Gagné et al., 2009; Osumi et al., 2015) possibly leading to the election for TMR surgery to enhance this ability. The 2017 study recruited 3 participants with TMR, 6 participants without TMR, and 12 able bodied individuals. Participants were asked to complete movements of their phantom limb and/or intact limbs while in an fMRI. Interestingly results showed that cortical motor maps of the participants with TMR showed similar activation within the motor cortex to healthy controls, whereas participants without TMR had different activation maps. These researchers hypothesized that needing to activate the motor cortex for control over a prosthetic limb has the ability to reactivate motor maps similar to normal controls (Serino et al., 2017). This is an impactful study in the fact that it shows similar cortical maps between patients with TMR and able bodied individuals, however PLC in the non-TMR patients was not queried, all but one reported phantom limb pain, and only two utilized a prosthetic device capable of functions. Unfortunately without an fMRI study prior to and after TMR, there is no way to compare and concretely say that TMR reversed the cortical reorganization. It is possible that these maps were different due to the non-TMR patients having minimal PLC, and/or PLP. Future research should look at the difference in cortical maps of individuals with PLC and no pain compared to patients who have undergone TMR; results may be strikingly similar.

In contrast to PLC, control of a prosthetic device requires extensive practice and motor learning, if the movement is to become intuitive. Results from study two showed that thirteen of fourteen participants used different muscle activation patterns to open their phantom hand than

they used to open the terminal device of their prosthesis (one participant presented with no contractions of the target muscles during opening movements of either the device or phantom hand). Twelve out of fourteen participants maintained this disconnect in muscle activation patterns used to close their phantom hand and close their terminal device. Seven participants had muscle activity within at least one of the same muscles for both PLC and prosthesis control, however patterns of muscle activation were visually different for each movement. Utilization of different muscle activation patterns for PLC and terminal device control, in an attempt to recreate movements and function of the anatomical hand/arm, may inhibit intuitive control of a prosthetic device, which in turn may lead to the high rejection rate of upper extremity prostheses. Results from study two supports the theory that PLC is a recovered motor developed skill whereas prosthetic control is a motor learned skill, requiring different muscle activation patterns for execution.

Advancements in prosthetic device design are attempting to utilize the findings presented by study two (the comparison of muscle activation patterns of the phantom hand/arm to muscle activation patterns used to control the terminal device of a prescribed prosthesis) currently, however device designs are not being widely accepted by users. In order to allow the user to control a prosthetic device with more natural movements, prosthetic limbs are using pattern recognition software. Pattern recognition involves multiple electrodes placed circumferentially around the forearm within the prosthetic socket. The device is designed to learn the natural muscle contraction patterns required for each movement of the device. Amputees are must commit to extensive, time consuming, training processes with frequent and persistent retraining sessions to master device capabilities (Samuel et al., 2019). Direct control devices may be preferred over pattern recognition devices due to the failure of pattern recognition devices to work properly in real life situations outside of the training lab (Franzke et al., 2019; Kyranou, Vijayakumar, & Erden, 2018; Samuel et al., 2019). The simple movement of a subject, (for instance walking) while attempting to control a pattern recognition device causes an 11.35% error effect (Samuel et al., 2019). Such errors are due to variations in limb position compared to training position, variations in muscle contraction forces during daily life activities, movement of the socket on the limb, and weight on the end of the terminal device (such as while holding something) (Franzke et al., 2019; Kyranou et al., 2018; Samuel et al., 2019). Pattern recognition devices will need to overcome these limitations if they are to allow for natural control in daily life situations (Scheme & Englehart, 2011).

Conflicts between muscle activation patterns needed to execute motor developed skills and motor learned skills might influence muscles used for completion of both movements. Study three involved a novel study designed to investigate the muscle activity required to control a phantom limb, based on type of prescribed device. This was the first study of its type. Movements of the phantom limb, and movements of the prosthesis, regardless of the type of device, are attempts to mimic anatomic hand/arm movements. However, neither movement is executed utilizing anatomically expected muscle patterns; muscle activation patterns are different

for both PLC and prosthesis control, and both types of devices require different muscle activation patterns.

Results from study three showed that body-powered device users typically had muscle activity of the upper arm during movements of the phantom hand, muscles not required for hand movements but required for prosthetic control. Myoelectric users tended to not have muscle activity within the upper arm for phantom hand movements, which are also not required for prosthetic control. These results suggest that motor learned skills may influence motor developed skills. These differences were more apparent when the muscles used for each movement are different, for example upper arm muscles required for terminal device control even though forearm muscles are present.

Overall, results from this dissertation enhance the field of research involving PLC and prosthetic control. Study one supported previous findings of unexpected muscle activity during phantom limb control in trans-humeral amputees, while also introducing new research regarding physiological differences at multiple levels of amputation. Study two provided data to support the theory that there is a disconnect between muscle activation patterns used for PLC and prosthetic device control. Study three provided data to support the theory of different muscle activation effects due to type of prosthesis. Study three was novel in the fact that it provided data comparing two types of prosthetic devices prescribed as an indirect indication of motor learning, on muscle activation patterns for PLC. Results of this dissertation are preliminary, however they open the field to further investigation of routinely utilizing surgical procedures that complement the biological process of re-innervation in the initial surgery (such as TMR), and the potential of prosthetic devices that utilize natural muscle activity for PLC rather than extensive learning processes.

However, limitations were present within the methodological design and statistical analysis of the results. Limitations in methodological design included the inability of the researchers to visualize movement of a phantom limb. To address this participants were required to mirror movements of the phantom limb with the intact limb. A member of the research team observed and pressed a trigger device identifying the movement occurring during half of a movement cycle. Although this was minimized by instructing the participant to hold the extremes of the position, the identification of the exact timing of movement initiation from one may have been delayed. This may also have affected opening and closing of the prosthesis, especially the myoelectric devices. Muscle activation is required for the initiation of a movement; this initial activation was unable to be captured exactly by the researchers throughout the cycle, especially when delayed and/or prolonged activation was present. It is also possible that there is a delay in the ability of the prosthetic socket to pick up the initial muscle contraction, or a difference in sensitivity between the kinesiologic EMG electrode and the prosthetic electrode. Future studies should focus on incorporating a methodological plan that can capture the precise start and stop times of muscle activity required for movement of a phantom limb and prosthetic device.

The statistical approach in the studies is novel and limited by a lack of prior knowledge of expected occurrences of muscle activity outcomes in amputees. Previous research has focused on descriptive and not statistical presentations of the results. This is the first study to utilize goodness of fit, Chi-Square tests to determine if results were expected by chance frequency. Chance frequency was the best option given the fact that there are no data available on what the expected frequency of each occurrence should have been. Future studies will be able to utilize the results presented in this study and adjust the expected frequencies accordingly. Additionally, a lack of independence of observations for the Chi-Square tests may exist. Individual movements were categorized as independent based on previous literature stating that upper extremity amputees have different muscle activation patterns for each movement (K. Reilly et al., 2006). Participants were required to complete three trials of each movement, then an average activation of each trial was used. Movements made by each participant, however, originated from the same CNS and therefore may not be completely independent of each other. Independence of observations may need to be addressed in future studies by recruiting larger numbers of participants and comparing only muscle activation patterns for each individual movement.

Study three incurred another limitation within the subject population. To obtain similar numbers of myoelectric and body-powered device users we were required to enroll participants with any cause of amputation. Study three was the first study to investigate the differences between type of device prescribed on muscle activation patterns, and presents crucial preliminary results for future studies. Future studies should aim to recruit not only equal numbers of type of device users, but cause of amputation as well. Study three resulted in important findings, however they would have been enhanced had we been able to recruit more traumatic myoelectric users and more congenital body-powered users. Regardless of the limitations, the results are nonetheless important to progress the field of amputee research.

CHAPTER 8: CONCLUSIONS

The goal of this dissertation was to: (1) Compare muscle activation patterns of the phantom hand/arm to documented muscle activation patterns of an anatomical limb during like movements, (2) Compare muscle activation patterns of the phantom hand/arm to muscle activation patterns used to control the terminal device of a prescribed prosthesis, and (3) Compare whether users of body-powered prosthetic devices have more muscles of the upper arm unexpectedly active during movements of the phantom hand/wrist than myoelectric prosthetic users.. To complete these studies, kinesiologic EMG was used to record muscle activity of specific target muscles during phantom limb and prosthetic device movements. Muscles were determined active when EMG amplitude reached two standard deviations above rest. Results showed that muscle activation patterns of phantom hand/arm movements were different from anatomically expected muscle activation patterns. Muscle activation patterns of phantom hand/arm movements were also different from muscle activation patterns used to control the terminal device of prostheses. Finally, body-powered prosthesis users had more upper arm muscles active during movements of the phantom hand/wrist than myoelectric users.

Implications from this dissertation will contribute to practical enhancements for amputees and future research. The first major practical contribution of the present research is that it exposes an understudied biological process that may play a role in the ability of amputees to control the movement of their phantom limb. It is possible that future research could show positive implications for routinely manipulating regeneration and re-innervation during the initial surgical procedure, in all levels of amputation, rather than the more frequently conducted secondary surgery. Study one showed that different muscles than anatomically expected contract to control phantom limb movements. It is possible that peripheral motor nerve re-innervation, into unexpected target muscles after amputation, or with congenital limb loss, is playing an important role in this process. Re-innervation of peripheral motor nerves, to specific target muscles, is being utilized to control myoelectric prosthetic devices through the surgical procedure TMR (Todd A. Kuiken et al., 2009). Originally TMR was focused for amputation above the elbow, however more recently it has been investigated in trans-radial, lower extremity amputations, and for neuroma prevention. However, the goal of TMR remains to produce strong, isolated EMG signals for prosthetic control (Todd A Kuiken, Barlow, Hargrove, & Dumanian, 2017). This may not be the only benefit of re-innervating peripheral nerves to targeted muscles. Many amputees could potentially benefit from increased PLC as it correlates to a reduction in PLP, without ever being interested in using a myoelectric prosthesis. Reports from discussions with many amputees suggested that myoelectric devices do not hold up during manual labor and therefore many farmers and mechanics have no interest in their use. However, they would benefit from phantom pain reduction, which may be connected to successful peripheral nerve re-innervation. Further understanding of the biological process of peripheral motor nerve repair after amputation may enable surgeons to devise new initial amputation procedures that can

specifically choose target muscles for each nerve, enhance PLC, and eliminate the need for an invasive secondary surgery.

The second major practical contribution of the present research is that it provided further evidence for a disconnect between PLC and control of prosthetic devices. More than 30% of upper extremity amputees reject the prosthesis they are prescribed (E. A. Biddiss & Chau, 2007). This study showed that muscle activation patterns used to control the phantom limb are not the same ones needed to control typically prescribed prostheses. Developing prosthetic devices that can be controlled by the same natural muscle activation patterns used to control the phantom hand, during activities of daily living (walking/climbing stairs/varying hand positions) may make the device more intuitive to use, reduce the difficult, time consuming, process of motor learning for active users and potentially diminish rejection rates. This was the first study to investigate the relationship between type of prosthetic device (body-powered or myoelectric) and muscle activation patterns of phantom limb movements. Results showed that device type might alter muscle activation patterns during PLC. In theory, this may be due to extensive motor learning that is required to intuitively control a prosthesis. Overall these results imply that prosthetic devices should be designed so they utilize similar natural muscle activation patterns as each individual uses to control their phantom limb. Doing so may diminish the need for extensive motor learning, and reduce rejection rates. Pattern recognition devices were designed with this in mind, however they have not yet shown to be superior to other devices outside the lab environment and still require extensive training and retraining sessions. Implantable electrodes (similar to fine wire electrodes) used to control the device may prove to be the best option. If this turns out to be true, it will be that much more important to understand the specific muscles that individual amputees are using to control their phantom limb. No participants presented with similar muscle activation patterns for phantom limb control; they were all individualized. Such individualization may be the result of how the peripheral nerves recover after injury. This can either need to be rectified surgically, all residual nerves re-innervated to the same pre-determined muscles, or prosthetic devices will have to be designed based on the unique muscle activation patterns of each user, there may not be a generalizable catch all solution.

Future research should be conducted on injury response occurring within the PNS, how this physiological response impacts phantom limb experiences, how these changes impact or are impacted by the CNS, and how to utilize the bodies natural response to injury to enhance control and function of prosthetic devices. Previous research has been done to understand peripheral motor nerves and muscle responses to injury, however not specifically after amputation. The peripheral nervous systems natural repair process after an amputation, or with congenital limb loss, has not been investigated, however it is being manipulated during TMR. Research studies that investigate where peripheral motor nerves naturally re-innervate, due to amputation, is the first step to grasping an understanding of PLC. Additionally, future research should explore how the CNS responds not only to amputation, but after the peripheral repair process of re-innervation. It is possible that initial CNS changes are reversed after the recovery and re-

innervation of the peripheral nerves is completed, this statement is supported by the cortical changes that occur after TMR (A. Chen et al., 2013; Serino et al., 2017). Finally, extensive research needs to be conducted on the impact of motor learning on motor developed skills, especially when both skills facilitate similar actions such as with PLC and prosthetic control. The disconnect between muscle activation patterns for PLC and muscle activation patterns for the learned motor skill of prosthetic control may be a critical factor in the high rejection rates experienced by upper extremity amputees.

Overall this study provided practical and research based implications. It has explored novel ideas regarding the ability of amputees to control movement of a phantom limb, and gleaned important insight into the possible effects of motor learning necessary for prosthetic control. Although this research was novel and impactful, future research needs to be continued to gain a more complete understanding of the role that peripheral nerve re-innervation after amputation plays on PLC and prosthetic control.

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APPENDIX:

A.1:

Subject number with level and cause of amputation, device type and muscles active for all movements completed. Anatomically expected muscle activity is green. FF – finger flexion, FE – finger extension, WF – wrist flexion, WE – wrist extension, WP – wrist pronation, WS – wrist supination, EF – elbow flexion, EE – elbow extension, FDP – flexor digitorum profundus, EDC – extensor digitorum communis, P – pronator, S – supinator, Bic – biceps, Tri – triceps, Del – anterior deltoid, Pec – pectoralis major, Trap – trapezius

Subject	Amputation Level	Cause of Amputation	Device Type	FF	FE	WF	WE	WP	WS	EF	EE	Prosthesis Close	Prosthesis Open
1	Trans Humeral	Trauma	Body Powered	- - - - Bic - Del -	- - - - Bic - - -	- - - - Bic - - -	- - - - - - - -	- - - - - Tri - -	- - - - - - - -	- - - - Bic - Del -	- - - - Bic Tri Del -	- - - Bic Tri - -	- - - Bic Tri Del Pec
2	Trans Radial	Congenital	Myoelectric	FDP EDC Pro Sup - - - -	- - - - - - - -	- EDC - Sup - - - -	- - - - - - - -	- - - Sup - - - -	- EDC - Sup - - - -	X	X	- - Pro - - - - -	- EDC Pro Sup Bic - - -
3	Trans Radial	Trauma	None	FDP	FDP	FDP	-	- EDC	- EDC	X	X	X	X

				EDC - - - - - -	EDC - - - - - -	EDC - - - - - -	EDC - - - - Del -	- - - - - -	- - - - - -				
4	Trans Radial	Trauma	Body Powered	FDP - Pro - - - -	FDP - Pro - - - -	FDP - - - - - -	- EDC - - - - -	- - - Sup Bic - - -	- - - Sup Bic - - -	X	X	- - - - - - Del Pec	- - - - - - Del Pec
5	Wrist Disarticulation	Trauma	Myoelectric	FDP - - - - - -	- - - - - - -	- - - - - - -	- EDC Pro - - - -	- EDC Pro Sup Bic - - -	- EDC Pro Sup Bic - - -	X	X	FDP - - - - - - -	- - - - - - - -
6	Shoulder Disarticulation	Disease	Myoelectric	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -	- - - - -

				- - Pec	- - -	- - Pec	- - -	- - -	- - Pec	- - - Trap	- - Pec	- - Pec	- - - Trap
7	Trans Radial	Congenital	Myoelectric	FDP - Pro - - - - -	- EDC - - - - -	FDP - Pro - - - - -	- EDC - - - - -	- - - Sup - - - -	- EDC - Sup - - - -	X	X	- - - - - - -	- EDC Pro Sup - - - -
8	Trans Radial	Congenital	Myoelectric	- - Pro - - - - -	- - - - - - -	- - Pro - - - - -	- - - Sup - - - -	- - Pro - - - - -	- - - Sup - - - -	X	X	- - - - - - -	- - Pro - - - - -
9	Trans Humeral	Trauma	Body Powered	- - - - Bic - - -	- - - - - - - -	- - - - Bic - - -	- - - - - - - -	- - - - - Tri - -	- - - - - Tri - -	- - - - Bic Tri Del -	- - - - - - Pec	- - - - - - Del Pec	- - - - - - Del Pec
10	Trans Radial	Congenital	Myoelectric	-	-	-	-	-	-	X	X	FDP	FDP

				- - - Bic - - -	- - - Bic - - -	- - - Bic - - Pec	- - - Bic - - Pec	- Pro - Bic - - -	- - - Bic - - -			- - - - - - -	- - - - - - -
11	Trans Radial	Disease	Myoelectric	 FDP - - - - - - -	- EDC - - - - - -	- - - - - - -	- EDC Pro - - - - -	- EDC Pro - - Tri - -	- EDC - - - - - -	X	X	FDP EDC - - - - - -	- EDC - - - - - -
12	Trans Radial	Trauma	Body Powered	- - - - - - - -	- - - - - - - -	- - Pro - Bic - - -	- - - - - Tri - -	- - Pro - - - -	- EDC - - Bic - - -	X	X	- - - - - Tri Del Pec	- - - - - Tri Del Pec
13	Wrist Disarticulation	Trauma	Body Powered	 FDP EDC Pro - - Tri	FDP EDC Pro - - Tri	- EDC Pro - - Tri	- EDC Pro - - Tri	FDP EDC Pro - - -	FDP EDC Pro - Bic -	X	X	- - Pro - - Tri	- - - - - - -

				- -	- -	- -	- -	- -	- -			Del Pec	- -
14	Trans Radial	Trauma	Body Powered	FDP - - - - - -	- EDC - Sup - - - -	FDP EDC Pro Sup - - - -	- EDC Pro Sup - - - -	- - - Sup Bic - - -	- EDC - Sup Bic - - -	X	X	- EDC Pro Sup Bic Tri - -	- EDC Pro Sup Bic - - -
15	Trans Radial	Trauma	Body Powered	FDP EDC Pro Sup Bic Tri - -	FDP EDC Pro Sup - - - -	FDP - - Bic Tri - -	FDP EDC - - Bic - - -	- EDC Pro - - - - -	- EDC Pro - Bic - Del -	X	X	FDP - - - - - - -	- - - - Bic Tri Del Pec