MUSCLE FATIGUE ASSESSMENT BY MECHANOMYOGRAPHY AND MUSCLE OXYGENATION DURING ELECTRICALLY-EVOKED WRIST EXTENSION EXERCISE

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Name of Candidate: Nurul Salwani Mohamad Saadon

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Title of Dissertation: Muscle Fatigue Assessment by Mechanomyography and Muscle Oxygenation during Electrically-Evoked Wrist Extension Exercise

Field of Study: Rehabilitation Engineering

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MUSCLE FATIGUE ASSESSMENT BY MECHANOMYOGRAPHY AND MUSCLE OXYGENATION DURING ELECTRICALLY-EVOKED WRIST EXTENSION EXERCISE

ABSTRACT

Repetitive electrically-evoked muscle contraction leads to accelerated muscle fatigue. This study assessed electrically-evoked fatiguing muscle with changes to mechanomyography root mean square percentage (%RMS-MMG) and tissue saturation index (%TSI-NIRS) in extensor carpi radialis (ECR) muscle in able-bodied (AB) and in participants with spinal cord injury (SCI). Due to the limited research from previous studies, it is important to investigate the relationship in AB participants first to understand the natural behavior of the muscle mechanically and physiologically as AB has more power in their muscle to perform exercise compared to SCI participants. AB and SCI performed repetitive electrical-evoked wrist extension to fatigue and results were analysed pre- and post-fatigue, i.e. 50% power output (%PO) drop. Responses of %PO, %TSI-NIRS and %RMS-MMG were correlated while the relationship between %RMS-MMG and %TSI-NIRS were investigated using linear regression. Forty AB (N=40) volunteered in the study. %TSI-NIRS were negatively correlated pre- and post-fatigue with declining %PO as the ability of the muscle to take up oxygen became limited due to fatigued muscle. The %RMS-MMG behaved in two different patterns post-fatigue against declining %PO whereby; (i) group (A) showed positive correlation (%RMS-MMG decreased) throughout the session and (ii) group (B) demonstrated negative correlation (%RMS-MMG increased) with declining %PO until the end of the session. Regression analysis showed %TSI-NIRS was inversely proportional to %RMS-MMG in group A and proportional in group B during post-fatigue. Small gradients in both groups suggested that %TSI-NIRS was not sensitive to the changes in %RMS and they were mutually exclusive. As for SCI, seven SCI participants (N=7) were recruited and %TSI-NIRS was positively correlated with %PO pre-fatigue. At post-fatigue, %TSI-NIRS negatively correlated with declining %PO as the ability of the muscle to take up oxygen became limited due to fatigued muscle. The %RMS-MMG behaved the same way during pre- and post-fatigue against declining %PO whereby both showed positive correlation (%RMS-MMG decreased) throughout the session. Regression analysis showed %TSI-NIRS was proportional pre-fatigue and inversely proportional to %RMS-MMG during post-fatigue. As big gradient was observed from the regression during post-fatigue, it is suggested that changes in %TSI-NIRS were sensitive enough to the changes in %RMS-MMG. Most correlation and regression for both AB and SCI changed significantly post-fatigue indicating that after fatigue, the condition of muscle had changed mechanically and physiologically.

Keywords: spinal cord injury; fatigue; functional electrical stimulation; muscle oxygenation; upper limb.

KELETIHAN OTOT DIUKUR DENGAN MEKANOMYOGRAFI DAN OKSIGENASI OTOT SEMASA SENAMAN PERGELANGAN TANGAN YANG DIGERAKKAN SECARA ELEKTRIK

ABSTRAK

Penguncupan otot yang berulang-ulang mempercepatkan keletihan otot. Kajian ini mengkaji otot-otot yang digerakkan secara elektrik dengan perubahan pada kuadrat *root square* (%RMS-MMG) dan indeks ketepuan tisu (%TSI-NIRS) dalam otot extensor carpi radialis (ECR) dalam individu sihat dan pesakit saraf tunjang. Oleh kerana kajian terdahulu yang terhad, adalah amat penting untuk menyiasat hubungan individu yang sihat terlebih dahulu untuk memahami tingkah laku semulajadi otot secara mekanik dan fisiologi kerana otot mereka lebih kuat untuk melakukan senaman berbanding pesakit kecederaan saraf tunjang. Kesemua individu sihat dan pesakit saraf tunjang melakukan senaman pergelangan tangan yang digerakkan berulang-ulang secara elektrik sehingga keletihan dan keputusan dianalisis sebelum dan selepas keletihan, iaitu keletihan didefinasikan sebagai penurunan output kuasa sebanyak 50%. Tindak balas %PO,%TSI-NIRS dan%RMS-MMG dikolerasikan manakala hubungan antara %RMS-MMG dan %TSI-NIRS diselidiki menggunakan regresi linear. Empat puluh individu sihat (N=40) telah menyertai uji kaji ini dan %TSI-NIRS berkolerasi negatif sebelum dan selepas keletihan dengan %PO yang menurun kerana keupayaan otot untuk mengambil oksigen menjadi terhad disebabkan oleh otot yang keletihan. %RMS-MMG pula berkelakuan dalam dua corak berbeza selepas keletihan seiring penurunan %PO di mana; (i) kumpulan (A) menunjukkan korelasi positif (%RMS-MMG menurun) sepanjang senaman dan (ii) kumpulan (B) menunjukkan korelasi negatif (%RMS-MMG meningkat) dengan penurunan %PO sehingga akhir senaman. Analisis regresi menunjukkan %TSI-NIRS berkadar songsang dengan %RMS-MMG bagi kumpulan A dan berkadar semasa bagi kumpulan B selepas keletihan. Kecerunan kecil dalam kedua-dua kumpulan mencadangkan bahawa %TSI-NIRS kurang peka terhadap perubahan %RMS dan mereka adalah *mutually exclusive*. Tujuh pesakit saraf tunjang (N=7) telah direkrut dan %TSI-NIRS menunjukkan kolerasi positif dengan % PO sebelum keletihan. Selepas keletihan, %TSI-NIRS berkorelasi negatif dengan penurunan %PO kerana keupayaan otot untuk mengambil oksigen terhad. %RMS-MMG pula berkelakuan sama semasa sebelum dan selepas keletihan dengan penurunan %PO di mana kedua-duanya menunjukkan korelasi positif (% RMS-MMG menurun) sepanjang senaman. Analisis regresi menunjukkan% TSI adalah berkadar semasa sebelum keletihan dan berkadar songsang dengan %RMS-MMG selepas keletihan. Kecerunan besar yang dilihat melalui regresi sebelum dan selepas keletihan adalah kerana perubahan dalam% TSI cukup sensitif kepada perubahan %RMS-MMG. Kebanyakan korelasi dan regresi bagi kedua-dua individu sihat dan pesakit saraf tunjang telah berubah dengan ketara selepas keleltihan dan ini menunjukkan bahawa selepas keletihan, keadaan otot telah berubah secara mekanik dan fisiologi semasa senaman yang digerakkan secara elektrik.

Keywords: kecederaan saraf tunjang; keletihan; simulasi elektrik; oksigenasi otot; bahagian atas anggota badan

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LIST OF SYMBOLS AND ABBREVIATIONS

Δ : concentration changes

AB : able bodied

ACC : accelerometers

ACE : arm crank ergometer

ADL : activities of daily living

ATT : adipose tissue thickness

ASIA : American Spinal Injury Association

CF : center frequency

CNS : central nervous system

ECR : extensor carpi radialis

EMG : electromyography

FES : functional electrical stimulation

FV : frequency variance

HHb : deoxyhemoglobin

LCE : leg cycle ergometer

MAV : mean average value

mBF : muscle blood flow

MDF : median frequency

MIZ : microphones

MMG	:	Mechanomyography
MPF	:	mean power frequency
mVO$_2$	:	muscle oxygen consumption
NIRS	:	Near-Infrared Spectroscopy
NMES	:	neuromuscular electrical stimulation
O$_2$Hb	:	oxyhemoglobin
PIZ	:	piezoelectric contact sensors
PO	:	power output
PTP	:	peak to peak
RMS	:	root mean square
SCI	:	spinal cord injury
StO$_2$	:	tissue oxygen saturation
tHb	:	total hemoglobin
TSI	:	tissue saturation index
VMG	:	vibromyography

LIST OF APPENDICES

CHAPTER 1 : INTRODUCTION

This chapter discusses the general idea of the study in brief. This chapter is divided into 8 sections. Section 1 describes the background of the study. Section 2 and 3 explains the motivation and problem statement for the study, respectively. Section 4 lists the objectives of the study. Section 5 and 6 highlight the hypothesis and significance of the study, respectively. Section 7 explains the scope of the study. The last section of this chapter describes the dissertation organization in brief.

1.1 Background of the Study

According to World Health Organization (WHO), every year, between 250,000 and 500,000 people suffer from spinal cord injury (SCI) worldwide. SCI happens when nerve fibre bundles carrying all sensory and motor information is disrupted. SCI can be classified as tetraplegia which results in impairment function of hands as well as legs while paraplegia involves impairment of the legs only (Connolly et al., 2014) .

Cervical spinal cord injuries usually fall into the segment of C5–C7 in spinal cord injury (SCI) individuals (Thorsen et al., 2013). At such high lesions, it may lead to the loss of functionality and sensory and they may have inadequate wrist extension and no grasp left (Thorsen et al., 2001). For this population, wrist extension is the minimum requirement needed in order for them to be independent. As a result, passive forces play an important role in gaining back wrist function which is by using functional electrical stimulation (FES) (Johanson & Murray, 2002) Wrist extension movement with FES can promote recovery and improve tenodesis grip (Thorsen et al., 2001) in both complete and incomplete SCI patients (Adams et al., 2003).

FES is defined as the application of low-level electrical currents to elicit neural activation and produce muscle contractions (Peckham, 1987; Holsheimer, 1998). Individuals with SCI can benefit greatly from this as it increases muscle strength and endurance while improving cardiorespiratory fitness leading to increasing functional exercise capacity (Hettinga et al., 2007). Since the 1960s, FES-evoked muscle contractions have been commonly applied as a rehabilitation intervention for people with SCI especially lower limbs (Davis et al., 2008), not very much in upper limbs. For tetraplegia, the major rehabilitation goals for them is to enhance the function of active tenodesis grasp by strengthening wrist extension (Mangold et al., 2005).

However, muscles fatigue occurs quickly during FES-evoked muscle contraction especially in SCI participants (Ibitoye et al., 2014). Edwards (1981) defines fatigue as an inability to uphold the required force and it is often used in defining muscle fatigue. Due to this, the muscle cannot maintain and continue the expected force anymore when fatigue happens at a certain point. Muscle fatigue can contribute to the risk of musculoskeletal injury (Shin et al., 2016) and in SCI population, individuals may have a lack of sensory and proprioceptive feedback to sense the fatigue themselves. Due to that, it is important to characterize muscle activities in this population in order to monitor muscular forces during FES exercise and muscle fatigue (Hayashibe et al., 2011).

Electromyography (EMG) has been commonly used to assess muscle fatigue during exercise and for understanding muscle activity and its pathological changes (Estigoni et al., 2014). However, EMG is not suitable to assess muscle fatigue during FES contractions since the electrical signal came from the muscle will contaminate the signal from FES thus causing misinterpretation during analysis of the signal (Luca et al., 2010). Therefore, researchers have explored alternative means of muscle fatigue measurement during FES exercise especially for upper limb which is by using mechanomyography (MMG).

MMG records mechanical activity of the muscles (Islam et al., 2013) in which the signals originated from pressure waves due to the changing of dimensional of the active muscle fibers during contraction (Bichler & Celichowski, 2001) that are known as mechanomyogram (Orizio et al., 1999). MMG is suitable to measure muscle fatigue since small changes in force can be reflected in MMG amplitude (Barry et al., 1992). Besides, a few studies verified that MMG is a reliable tool and can be used to measure muscle fatigue development (Akataki et al., 2005; Ibitoye et al., 2014; Yang et al., 2009) during rehabilitation exercises. However, limited number of studies have used MMG to describe muscle fatigue during electrical stimulation (Faller et al., 2009 ; Gobbo et al., 2006).

Besides MMG, near-infrared spectroscopy (NIRS) is a well-known method to assess muscle by measuring muscle tissue oxygenation. NIRS signal depends on the oxygen saturation changes by near-infrared light absorption and scattering characteristics and can be affected at a particular wavelength (Celie et al., 2012). Several studies showed that NIRS is a reliable technique to measure muscle oxygenation during voluntary contractions in erector spinae muscles (Kell et al., 2004), shoulder muscle (Ferguson et al., 2013) and during handgrip exercise (Celie et al., 2012). There are no literatures that looked at NIRS during FES especially throughout muscle fatigue contractions as most studies observed NIRS during voluntary and isometric contractions during exercise.

To obtain more information, some studies assessed muscle during voluntary isometric contractions using EMG and NIRS simultaneously. They suggested that a strong relationship between NIRS and EMG data was observed during the exercise where EMG and NIRS are well associated with each other (Muthalib et al., 2011; Elcadi et al., 2011; Felici et al. 2009; Praagman et al., 2003). However in FES application, EMG is not suitable to use for assessing muscle fatigue (Luca et al., 2010). Due to that, MMG has been used widely as a counterpart for EMG to assess muscle fatigue during FES.

Yoshitake et al. (2001) used MMG to investigate muscle fatigue of lower back pain along with EMG and NIRS simultaneously where they concluded that the concurrent recording system can obtain more promising outcome regarding muscle fatigue. Taken together, these studies have further shown that by recording from different types of sensors, more information about the muscle can be obtained.

To our knowledge, no studies has been done that looked at NIRS during FES-evoked contractions and during muscle fatigue exercise. MMG with concurrent NIRS recordings during FES may offer more detailed information and precise data regarding the mechanism involved during muscle fatigue in wrist extensor muscle based on its mechanical and metabolic characteristics.

1.2 Motivation for this study

Muscle fatigue occurred faster in FES-evoked contraction compared to voluntary contractions. As muscle fatigue can contribute to the risk of musculoskeletal injury, researchers described that it is crucial to recognize the underlying causes of muscle fatigue in order to avoid it from happening during FES exercise.

To date, muscle fatigue assessment which looks at the muscle mechanically and physiologically simultaneously during FES-evoked exercise after SCI remains poorly researched. Even though MMG has been widely used to assess muscle fatigue, quantification of muscle fatigue during FES by NIRS on the other hand is poorly understood (Al-Mulla et al., 2011) especially on small muscles.

This gap motivates the proposed study to investigate the relationship between muscle performance by MMG and oxygenation by NIRS during FES-evoked muscle fatigue contractions. It is also motivating to see how muscle oxygenation relates to muscle mechanomyography and how they affected muscle fatigue during FES-evoked contraction.

A combination of these two systems will provide more information from two different angle; muscle performance and metabolic characteristics during FES. These data can be used in FES feedback mechanism where the system can monitor and predict fatigue during FES-evoked exercise. This feedback mechanism can serve as a warning system and as an indicator to guide the users so they will know when to stop the exercise, hence improving the muscle function while minimizing injury. This will help greatly in rehabilitation field especially for SCI, as this population lost their sensory and cannot sense fatigue themselves (Al-Mulla et al., 2011).

1.3 Problem Statement

During FES-evoked contractions, fatigue occurs earlier and more rapidly in paralyzed or paretic muscles compared to normal muscles. This is because human motor units undergo a reversed recruitment order of motor neurons which preferred the stimulation of large diameter neurons innervating fast-fatiguing muscle fibers (Beck et al., 2004). Muscle fatigue is defined as the inability to sustain maximal muscle force during exercise (Gandevia, 2001). At high level, localized muscle fatigue can be very dangerous and can cause serious injury to the individuals hence it is vital to quantify the muscle’s fatigue state during FES.

During some FES-evoked contractions especially in upper limb, functional muscle fatigue and force decrements cannot be easily monitored leading to health risks. That is why muscle fatigue assessment and detection from MMG and NIRS is the main theme for this study and all the previous studies were found based on how these sensors related with each other in monitor muscle status during muscle fatigue.

Previous studies have been using these MMG and NIRS sensors individually in monitoring muscle fatigue. While MMG have been widely used in FES, usage of NIRS during FES is poorly documented. In addition, they are also focusing more on lower limbs rather than upper limb muscles. There are many parameters that can be used to describe neuromuscular fatigue such as power output and muscle characteristics such as muscle strength and oxygenation.

Due to lack of research concerning muscle fatigue in SCI during FES in upper limb, it is promising to combine both MMG and NIRS assessment during muscle fatigue monitoring as the association of these two different sensors has yet to be investigated. A combination of these two measurements may provide more information from two different perspectives; muscle strength and metabolic characteristics during FES.

Therefore in this study, the aim was to assess muscle fatigue with real-time changes from MMG signals and muscle oxygenation from NIRS within wrist extensor muscle during electrical stimulation-evoked wrist extension exercise in able-bodied (AB) and spinal cord injury (SCI) participants.

1.4 Objectives of the Study

There are three objectives that need to be met during the course of this study:

i. To investigate mechanomyography (MMG) signal responses during electrically-evoked muscle contraction to fatigue wrist extension exercise among AB and SCI participants.
ii. To investigate near infrared spectroscopy (NIRS) pattern during electrically-evoked muscle contraction to fatigue wrist extension exercise among AB and SCI participants.
iii. To determine the relationship between mechanomyography (MMG) and near infrared spectroscopy (NIRS) during electrically-evoked muscle fatigue in wrist extension exercise among AB and SCI participants.

1.5 Hypothesis of the Study

As the changes of MMG and NIRS was determined throughout the repetitive wrist extension, a change in trend before and after fatigue happened was noted. It was hypothesized that a fatiguing muscle would show a clear relationship between mechanomyographic from MMG and muscle oxygenation signal from NIRS after fatigue onset or at pre-defined decrease of muscle power output during repetitive FES-elicited exercise task on wrist extensor muscle.

1.6 Significance of the Study

Based on previous studies, assessing NIRS in FES-evoked contraction especially in fatiguing condition on wrist extensors are not well investigated. The relationship of NIRS with MMG as a mechanical counterpart to EMG during FES also is an important significance that will add to the knowledge value in this study.

Measuring MMG and NIRS simultaneously will provide additional information from two different perspective; muscle performance from MMG and metabolic characteristics from NIRS during FES. By verifying that they are associated with each other during fatigue, these data can be used and applied in FES feedback mechanism where it can monitor and predict the occurrence of fatigue during FES-elicited exercise.

Additional data of muscle oxygen consumption (mVO_2) from NIRS might give additional information regarding muscle oxygenation during FES muscle fatigue wrist extension exercise especially in SCI individuals.

In clinical application, this feedback mechanism can serve as a warning system to guide the users when to stop the exercise. This will help greatly in rehabilitation field especially for SCI, as this population lack of sensory and cannot sense fatigue themselves (Al-Mulla et al., 2011).

1.7 Scope of the Study

This study aimed to study the responses and verifying the relationship of mechanomyographic from MMG and also muscle oxygenation from NIRS during muscle fatigue FES-evoked exercise in AB and SCI individuals. Since this study is a fatigue study, power output (PO) will be used as the measurement of fatigue in this study (50% drop from initial PO) where all the responses will be compared during pre-fatigue (before 50% PO drop) and post-fatigue (after 50% PO drop) points. This point was chosen as we want to see how MMG and NIRS signals from the muscle associated with each other and whether the pattern changed before and after fatigue.

To answer the first two objectives, changes of MMG and NIRS against PO was observed in order to study their responses during the fatigue exercise. Apart from that, mVO_2 data from NIRS may give additional information regarding muscle oxygenation in SCI individuals. In addition, relationship of both MMG and NIRS also will be investigated and verified to see how both of these parameters are associated with each other during fatigue in order to answer the third objective. All of these will be compared during pre- and post-fatigue as we want to observe how the muscle changes mechanically and physiologically especially after fatigue thus increase understanding underlying causes of muscle fatigue.

This study focused only on wrist extensor muscle of AB and SCI individuals and the activity involved in this study was repetitive FES-evoked wrist extension exercise. Since MMG and NIRS are well known in measuring muscle conditions during fatigue, it is exciting to know how well related these two are during FES repetitive wrist extension exercise.

Due to the limited previous studies, it is important for us to know how wrist extensor will react by doing this in AB individuals beforehand before doing it in SCI individuals. However, this study did not compare the differences between AB and SCI participants' data directly with each other. Both AB and SCI participants' data will be discussed separately in different sections in this study.

By knowing the relationship between mechanomyographic and muscle oxygenation simultaneously, more data can be obtained to increase understanding regarding muscle fatigue. Consequently, this study might help individuals with SCI to enjoy their rehabilitation exercises and improve their quality of life. Based on the data from MMG and NIRS, FES feedback mechanism can be implemented where the system can monitor and predict fatigue during FES-evoked exercise, which is not within the scope of this study.

1.8 Dissertation Organization

This dissertation consists of six chapters, which are Introduction, Literature Review, Methodology, Results, Discussion, and Conclusion.

Chapter 1 is the Introduction. It explains the general idea of the study in brief. This chapter also contains the problem statement, research objectives, significance of the study and dissertation organization.

Chapter 2 is the Literature Review. It mainly addresses the critical analysis of the previous relevant studies in relation to the present study.

Chapter 3 is the Methodology. This chapter describes the participants, protocols, and materials that have been used in the study. Participants recruited for this study are AB and SCI participants with specific inclusion and exclusion criteria. Similar protocol and materials were used while carrying out this experiment which involves wrist extension exercise and fatigue exercise.

Chapter 4 is the Results. It contains all the findings of the current study. This chapter describes the results obtained from both AB and SCI participants.

Chapter 5 is the Discussion. This chapter discusses the findings of the current study and clarifies the findings of the current research with previous studies.

Chapter 6 is the Conclusion. This chapter summarizes the findings of the current study and how it can be applied especially in the rehabilitation field. In addition, a few recommendations and suggestions along with study limitations were made in order to improve this study in the future.

CHAPTER 2 : LITERATURE REVIEW

This chapter contains a critical review of currently available literature related to the current study. This chapter is divided into seven sections. The first section explains spinal cord injury in detail along with its classification. The second section describes functional electrical stimulation in the rehabilitation field. The third section explains how muscle fatigue happens during FES exercise. The fourth section on the other hand describes the techniques to assess muscle condition which include electromyography (EMG), mechanomyography (MMG) and near infrared spectroscopy (NIRS) and their role in measuring muscle fatigue respectively. Since this study related to MMG and NIRS, a more detailed explanation will be discussed including the parameters and how they were used in similar exercise with our study. In the fourth section as well, a combination of NIRS and EMG along with NIRS and MMG also will be discussed from previous studies involving healthy and diseased muscle.

2.1 Spinal Cord Injury

SCI is defined as a spinal cord lesion from CNS injuries and disease where it disrupts the nerve fibre bundles that send ascending sensory and descending motor information (Raineteau, & Schwab, 2001). Referring to previous studies, SCI also results in changes to the musculature below the lesion (Bickel et al., 2015; Mccully et al., 2011). Besides affecting muscles, this musculoskeletal degeneration can contribute to the reduction of vascular activity in the paralyzed limbs where long-term immobilization might have caused vascular effects such as reduction in vessel diameter, changes in muscle blood flow and also vascular compliance (Boot et al., 2002; Olive et al., 2002). Due to SCI, individuals will experience losing their upper and lower limb functions depending on their lesion.

2.1.1 Spinal Cord Injury Classifications

According to the American Spinal Injury Association (ASIA) Impairment Scale, the neurological level of injury is determined by a motor and sensory examination. An ASIA A indicates a complete lesion, which there is no motor or sensory function preserved in sacral segments S4-S5. ASIA B, on the other hand is an incomplete lesion in which only sensory is present below the neurologic level which covers sacral segments S4-S5. ASIA C also indicates an incomplete lesion with motor function below the lesion level and the majority of muscles having a grade less than 3 (unable to perform movement against gravity) while ASIA D is an incomplete lesion with motor function below the lesion level and the majority of muscles below the level have muscle grade greater than 3. Last but not least, ASIA E refers to both motor and sensory function are normal (Alaca, 2015).

Along the spinal cord, there are 31 segmental levels that match the nerve roots that exit between each of the vertebrae; 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal (Figure 2.1). Quadriplegia or tetraplegia (paralysis of the four limbs) happens in cervical injury, while lower level injury will lead to paraplegia (paralysis of the lower part of the body). For SCI patients, level of injury and the completeness of it will reflect the level of independence of that person (Connolly et al., 2014).

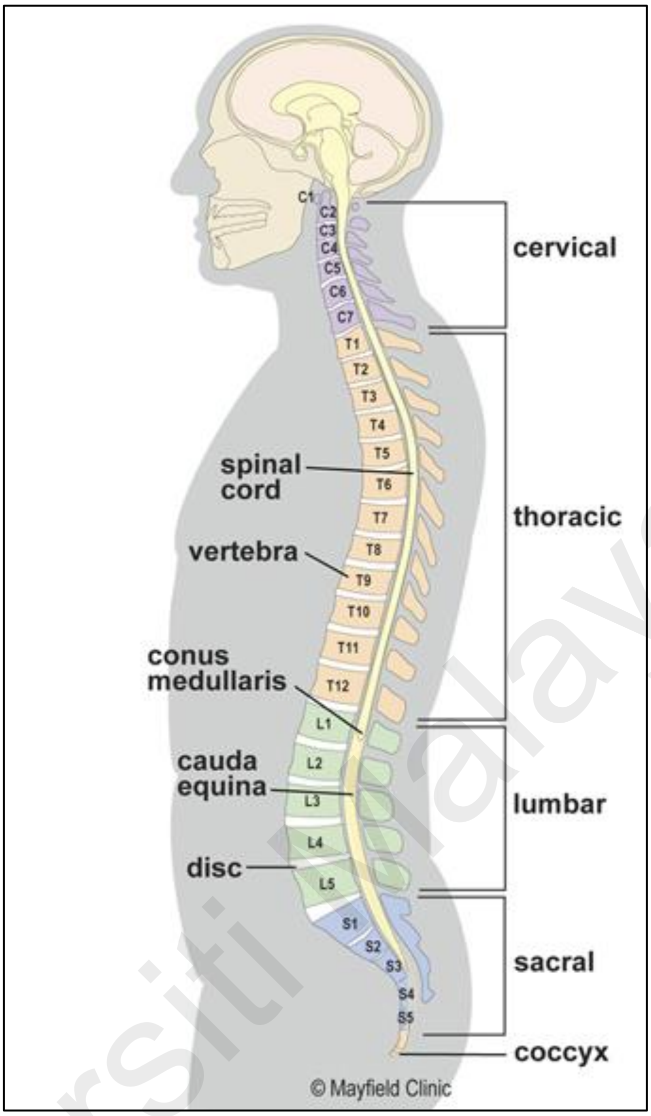

Figure 2.1: Regions of the vertebral column. Retrieved from https://mayfieldclinic.com/pe-anatspine.htm.

2.1.2 Cervical Spinal Cord Injury

In cervical spinal cord injuries, the most frequent lesions are at the C5-C7 neurological levels (Thorsen et al., 2013). At such high lesions, it may cause functionality and sensory loss of one or both hands with inadequate wrist extension and grasping (Thorsen et al., 2001). It is devastating for the individuals as the use of hands is very important in order to carry out their activities of daily living (ADL). As a result, passive forces play an important role in the functional use of the hand after tetraplegia (Johanson & Murray, 2002).

2.1.3 Effects from Spinal Cord Injury

Studies showed that in Malaysia, most males aged less than 40 suffer from SCI had paraplegia. The most common factor of SCI was caused by motor vehicle accident, followed by fall from high place while tumor-related cases made up 40% of non-traumatic causes of SCI (Ibrahim et al., 2013).

Following the injury, muscles beneath the lesions might go through some changes including muscle atrophy, increased intramuscular fat and reduced skeletal muscle mitochondrial function. These changes will then increase the risk of individuals getting cardiovascular and metabolic diseases, osteoporosis, and obesity (Ryan et al., 2013).

2.1.4 Rehabilitation for Spinal Cord Injury

Significant progress have been made in order to manage individuals with cervical level SCI in the past three decades, including electrical stimulation for active arm and hand movements (Mulcahey et al., 1997). Extension causes flexion of the fingers due to the passive forces in the finger flexors. This so-called tenodesis is referred to as the opposition of the thumb and index finger with extension movement of the wrist (Kohlmeyer et al., 1996) and shortening of the finger flexor (Figure 2.2).

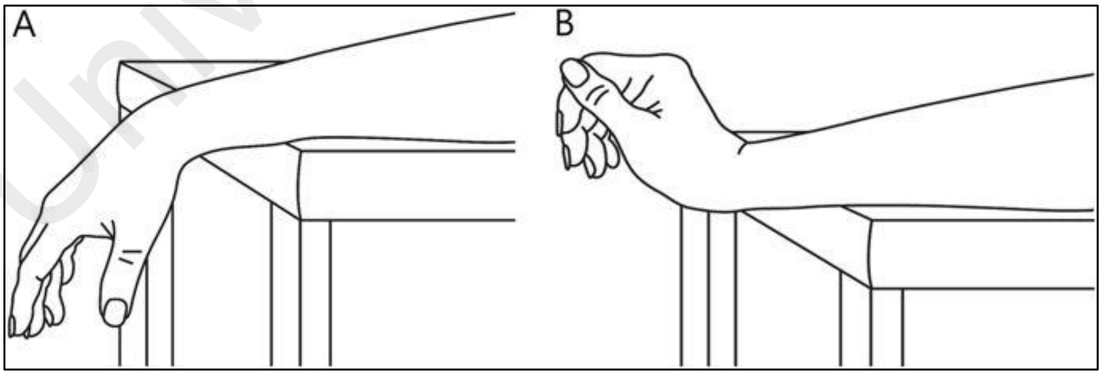

Figure 2.2: Illustrations of the tenodesis grip before (A) and after (B) the movement (Jung, Lee, & Shin, 2018)

As tenodesis grip brings functional advantage to SCI individuals, wrist extension motion can be made as an exercise in rehabilitation. A simple device (Figure 2.3) has been developed to enable physiotherapist to quantify muscle strength in tetraplegia and it has shown that this device is simple yet reliable to measure the strength of wrist extensor and suitable to be used in clinical setting (Glinsky et al., 2010).

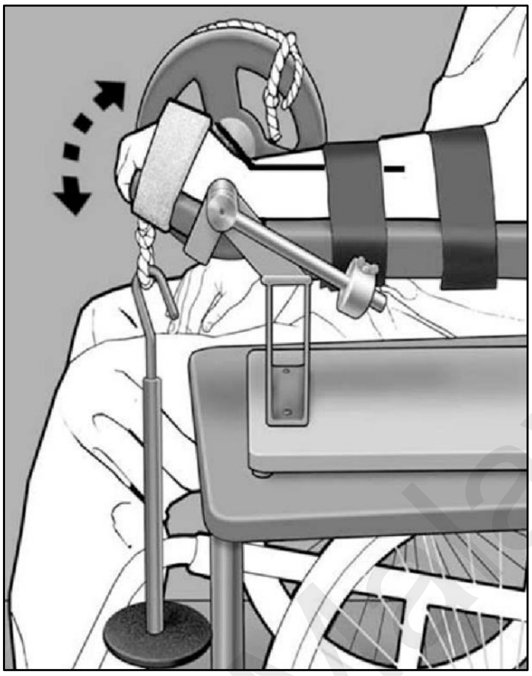

Figure 2.3: A device to strengthen wrist extensor muscle voluntarily with load attached (Glinsky et al., 2010)

2.1.5 Summary

Major rehabilitation goal for tetraplegic individuals with spinal cord lesions at level C6 especially is extension of the wrist (Nas et al., 2015) as in this population, wrist extension is the minimum requirement needed in order for them to be independent in ADL. Wrist extension movement with FES can promote recovery and improve tenodesis grip as well (Thorsen et al., 2001) in both complete and incomplete SCI patients (Adams et al., 2003).

2.2 Functional Electrical Stimulation

Neuromuscular electrical stimulation (NMES) is a promising tool in the rehabilitation of individuals with neuromuscular disease to activate their skeletal muscles (Dudley et al., 1999). FES is one of the examples of NMES that are often used for SCI patients.

Through consistent performance of FES training, individuals can improve their skeletal muscle mitochondrial function and lead to a better health in the future (Ryan et al., 2013).

2.2.1 FES-evoked Exercises

In the last decades, FES has been widely researched and investigated in order to enhance its quality for the improvement of hand functions. Figure 2.4 portrays the types of FES-evoked exercise from 1985-2005 and FES cycling has been the most popular exercise amongst all. Besides the lower limbs, several FES systems have been established in the last four decades in improving the quality of FES and to further enhance hand function.

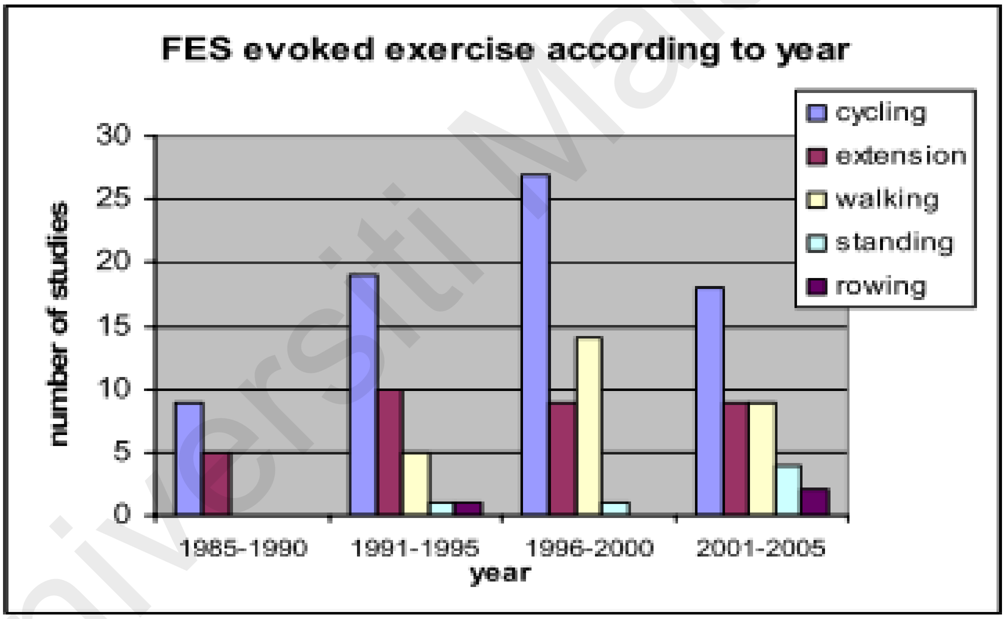

Figure 2.4: FES-evoked exercise categories found in health benefits studies (Hamzaid & Davis, 2006).

FES on upper limbs (Figure 2.5) can be used in the recovery process of some hand functions on patients with SCI (Thorsen et al., 2001). One of the major rehabilitation goals is to enhance the function of active tenodesis grasp; by wrist extension that results in finger flexion movement (Mangold et al., 2005).

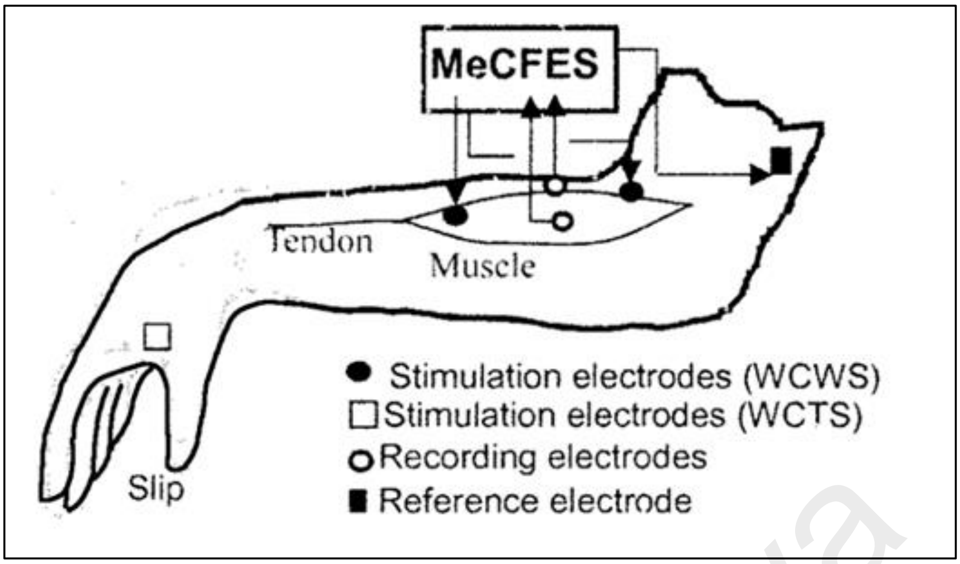

Figure 2.5: The lateral pinch grip aided by the MeCFES[1] on a complete cervical SCI (Thorsen et al., 2001).

A few studies showed that FES had been a great help in improving wrist extension function. Powell et al. (1999) showed that FES evoked exercise of the wrist extensors enhanced the strength of the muscle in hemiparetic stroke patients. As for tetraplegic individuals, Mangold et al. (2005) found that they can benefit from FES system with respect to muscle strengthening, enablement of voluntary muscle activity and also improvement of ADL functions. A study by Thorsen et al. (2001) found that with FES, wrist extension was improved in three out of five SCI patients in addition to improve thumb flexion (Figure 2.6).

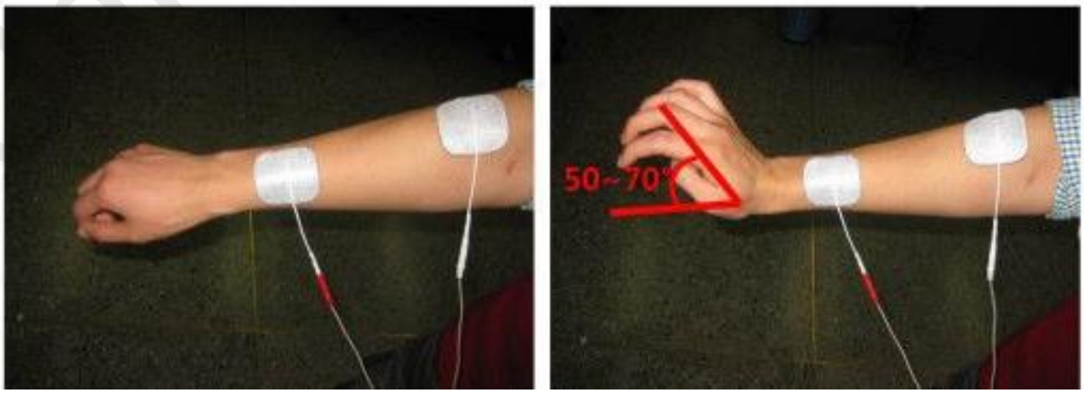

Figure 2.6: Wrist extension exercise with the aid of FES (Joa et al., 2012).

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[1] MeCFES - myoelectrical controlled functional electrical stimulator

2.2.2 Muscle Fatigue during FES-evoked Exercise

However, muscle fatigue occurs rapidly during FES-evoked muscle contraction especially in SCI individuals (Ibitoye et al., 2014). Contractions caused by FES tend to be more susceptible to fatigue than volitional contractions due to their synchronous pattern of motor unit recruitment and the preferential stimulation of large diameter neurons innervating fast-fatiguing muscle fibers (Beck et al., 2004).

Compared to normal recruitment, electrically-evoked muscle contraction causes all fibers in the muscle activated simultaneously instead of a more selective activation pattern. This immense fiber contraction causing muscle ischemia might lead to fatigue. In addition, affected muscles in SCI have a higher proportion of Type II fibres, as well as lower concentration of myoglobin and mitochondria (Lai et al., 2009) thus prone to fatigue faster than Type I. All these factors contribute negatively to muscle oxygenation and causing muscle ischemia which might explain the early onset of muscular fatigue (Hettinga et al., 2007).

2.3 Muscle Fatigue

Packman-Braun (1988) defined muscle fatigue as 50% of the initial force output or 30 minutes of electrical stimulation wrist extension exercise. It is also understood as an exercise-induced reduction in maximal voluntary muscle force and is generally caused either by central (neuronal) or peripheral (muscular) origin, or both (Gandevia, 2001).

2.3.1 Causes of Muscle Fatigue

Central fatigue relates to the central nervous system that relates the connections of the brain to the nerves that are responsible for muscle contraction. Fatigue happens when decreasing activation of these nerves resulting in declining in force output of the muscle. Peripheral fatigue on the other hand is the inability of the muscle to do work. As fatigue approaches, the functionality of the contracting muscles are impaired, causing its ability to exert force to decline because the body cannot meet the increasing energy demand from the muscles (Al-Mulla et al., 2011). Besides that, muscle fatigue can also results from elevating the metabolic cost of muscular contractions or from the recruitment pattern of motor units during stimulation itself (Gorgey et al., 2009).

2.3.2 Effects from Muscle Fatigue

During rehabilitation, low stimulation frequencies are favored compared with high stimulation frequencies as it will delay the development of neuromuscular fatigue (Gorgey et al. , 2009). This is because localised muscle fatigue can contribute to the risk of musculoskeletal injury (Shin et al., 2016) when the level of fatigue is too high. This is due to less energy being absorbed by the fatigued muscles before they are stretched to such an extent where it can cause injuries (Mair et al., 1996). Fatigue at high level can cause harm to the individuals hence it is vital to quantify the muscle's fatigue state during FES.

2.3.3 Importance of Muscle Fatigue Detection

The ability to monitor muscle forces externally and non-invasively can be used to assess muscle fatigue by the decline in the muscle force during stimulation (Mizrahi et al., 1994). The detection of muscle fatigue will be especially beneficial in the rehabilitation field especially for SCI individuals as in this population, they are lack of proprioceptive feedback (Al-Mulla et al., 2011).

2.3.4 Summary

Compared to voluntary contraction, muscle fatigued faster during FES contraction (Beck et al., 2004). Muscle fatigue can lead to musculoskeletal injury (Shin et al., 2016) when the level of fatigue is too high. To avoid this from happening, it important to assess and monitor muscle in order to understand how muscle fatigue happened.

Due to the variability of muscle characteristics for every individual, there is no exact value of muscle load and timing which defines muscle fatigue threshold (Al-Mulla et al., 2011). Many researchers have been investigating muscle fatigue in various conditions involving different muscles with different types of sensors in order to fully understand the condition. There are several of non-invasive techniques available to use in fatigue detection of the muscle during exercise.

2.4 Techniques to Measure Muscle Fatigue

Various techniques can be used to measure muscle fatigue non-invasively, such as by using electromyography (EMG), mechanomyography (MMG) and near-infrared spectroscopy (NIRS).

2.4.1 Electromyography

For the last two decades, EMG has been widely used in rehabilitation to assess muscle fatigue by comprehending muscle activity and predict muscle fatigue during exercise. This is because variables extracted from it can be considered as potential representations of muscle fatigue (Estigoni et al., 2014) by evaluating its motor units firing patterns such as root mean square (RMS), M-wave amplitudes, median frequency (MDF) and mean frequency during FES (Mizrahi, 1994). Among them, MDF and mean frequency were found to be the most consistent and have equivalent repeatability variables in fatigue indices (Merletti et al., 1995).

Electrodes from EMG produce transducer noise when they are in contact with the skin (Al-Mulla et al., 2011) which can lead to saturation of its signal which further limits its accuracy during real-time FES exercises (Haapala et al., 2008; Faller et al., 2009). Since the signal comes from the muscle, it contains some unavoidable and various noises that will contaminate and causing misinterpretation during analysis and this can especially be seen during dynamic contractions (Luca et al., 2010)

That is why EMG is not suitable to assess muscle fatigue during FES contractions as the electrical signal from the muscle will interfere with the signal from FES. Therefore, researchers have explored alternative ways to measure muscle fatigue during FES exercise which is by using mechanomyography (MMG) (Islam et al., 2013).

2.4.2 Mechanomyography

As the mechanical counterpart to EMG, MMG has gained interest from researchers in analyzing isometric and dynamic muscle contractions (Ibitoye et al., 2014) as it is another option to EMG for assessing muscle function and fatigue (Islam et al., 2013). MMG examine mechanical activity of muscles using different types of sensors in order to record muscle vibrations as the muscle fibres move (Islam et al., 2013; Orizio et al., 2003). One of the sensors is VMG which used a sensitive accelerometer to monitor the signal produced by vibrations from muscle contractions. Besides, VMG portrays the contractile properties of the muscle more straightforward compared to EMG (Ng et al., 2015).

2.4.2.1 Parameters from Mechanomyography

MMG can contribute in various areas of interest due to its reliable parameters that can be characterized in the time domain including the RMS, peak to peak (PTP) amplitude and mean average value (MAV), while in the frequency domain it can measure mean power frequency (MPF), median frequency (MDF), center frequency (CF), and frequency variance (FV) (Ibitoye et al.,2014).

Orizio et al. (2003) stated in their study that both time and frequency domain signals may give useful information about the motor control strategies; motor unit recruitment and firing rate of affected muscles during both isometric and dynamic muscle contractions and that MMG is a useful tool in monitoring muscle fatigue under such contractions. The amplitude of MMG is correlated with force production and it is very sensitive even a small change in force can be portrayed in the amplitude (Barry et al., 1992).

2.4.2.2 Advantages of Mechanomyography

MMG is preferred compared to EMG as in monitoring and quantifying muscle fatigue (Sarillee et al., 2014) and can provide more advantages compared to EMG. Some of the advantages are its flexible sensors as well as placement of its sensors are not required to be as precise as EMG's and also it is not easily influenced by impedance from skin due to its mechanical signal. As MMG signals can propagate through muscle and soft tissue, a more accurate signal can be obtained and recorded (Xie et al., 2009; Islam et al., 2013). During NMES protocol, MMG signals will not be interfered from the electrical signal as in as EMG signals can be easily contaminated by electrical noises (Faller et al., 2009).

Besides, a few studies verified that MMG is a reliable tool and can be used to measure muscle fatigue development during electrical stimulation during rehabilitation exercises (Gobbo et al., 2006).

2.4.2.3 Mechanomyography and Muscle Fatigue

A few studies have shown that MMG signal amplitude is often used in monitoring muscle fatigue during dynamic contractions such as exercises (Figure 2.7); as it provides information about the motor unit control strategies (Al-Mulla et al., 2011). It is well researched that the amplitude and center frequency of the MMG signal is related with muscle force. The amplitude of MMG portrays the contraction of the muscle where it will continue to decrease throughout fatiguing contraction. The amplitude also varies with different fiber type composition and motor control (Sarillee et al., 2014).

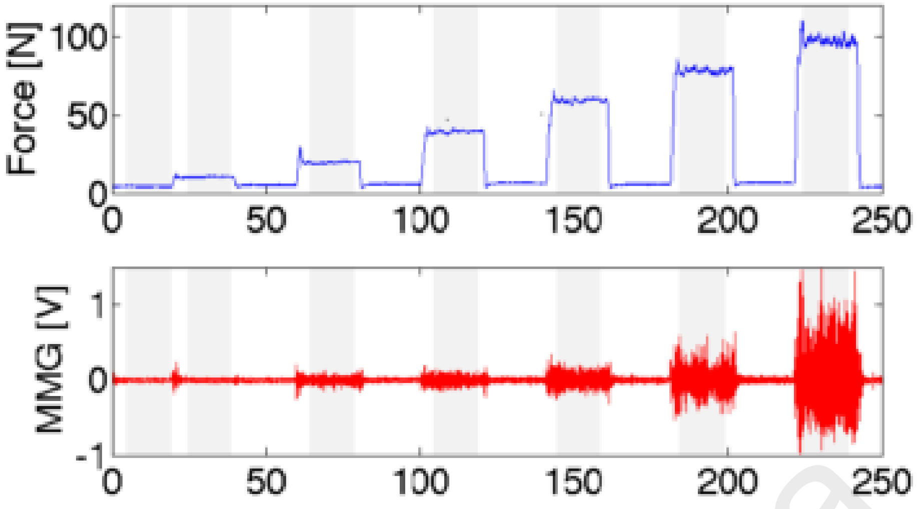

Figure 2.7: An example of an increasing of MMG amplitude with increasing isometric force levels (Ibitoye et al., 2014).

Sarillee et al. (2014) also have reviewed extraction of MMG data from various research which are root mean square (RMS) and variance for time domain, while MPF, MDF and zero crossing from frequency domain. Amongst all, we are interested in RMS from time domain, where RMS amplitude from MMG is the square root of the mean square value for a specific time interval in seconds (Ibitoye et al., 2014).

Akataki et al. (2004) found that motor unit activation strategy is estimated more accurately by MMG-RMS when they investigated an estimation of motor unit activation strategy by voluntary force generation. The amplitude of the signal however varies and depends on the muscle fiber activation and increases along with muscle force as a result from the high contraction level and vice versa. In fatiguing muscle during cyclic contraction, Yang et al. (2009) observed that there was significant change in RMS value with the onset of fatigue. Based on these literatures, RMS is the most suitable in measuring muscle fatigue as it associated with muscle strength and it is considered the most reliable parameter in the time domain (Al-Mulla et al., 2011).

2.4.2.4 Summary

Besides EMG, MMG has been used widely by researchers in assessing muscle fatigue as MMG signal can be propagated even in muscle and soft tissue besides not easily influenced by impedance from the skin.

However, most literatures have used MMG during voluntary contractions, and only a limited number of studies have used MMG to describe muscle fatigue during electrical stimulation (Faller et al., 2009; Gobbo et al., 2006). These studies also were mostly performed only under voluntary isometric exercise with able-bodied human subjects, not in neuromuscular diseased muscles.

2.4.3 Near-Infrared Spectroscopy

Apart from MMG, NIRS has been widely used to assess muscle condition during fatiguing contractions. It measures oxygen consumption, blood flow and oxygen saturation indirectly mitochondrial activity within the muscle (Praagman et al., 2003). It is an optical method that relies on the oxygen saturation changes by near-infrared light absorption and scattering characteristics in biological tissues like bone muscle and skin (Ferrari et al., 2011). The reasoning behind the employment of NIRS to measure oxygenation status in exercising muscle is that localized blood flow is identified to play a major role in the termination of muscle contraction due to fatigue (Yoshitake et al., 2001).

2.4.3.1 Parameters from Near-Infrared Spectroscopy

Some variables can be obtained directly from the NIRS including HHb, O_2Hb, total hemoglobin (THb) and percentage of tissue oxygen saturation (StO_2). On the other hand, muscle oxygen consumption (mVO_2) and muscle blood flow (mBF) can be obtained indirectly through occlusion and some calculations.

According to Ahmadi et al. (2008), in order to estimate mBF, venous occlusions must be applied using blood pressure cuff inflated just above the diastolic pressure lasting for 45 seconds each with a 3 minutes recovery interval. mBF is then estimated by measuring the initial linear increase in THb as in equation 2.1. Concentration changes of THb were expressed in micromole per second (µmol s^{-1}), and converted into units of millilitre per minute per 100 g of tissue (ml min^{-1}per 100 g), using an average Hb concentration of 140 g l^{-1}. The molecular weight of Hb (1 mol Hb is 64.458 kg) and the Hb to oxygen ratio (1:4) were also taken into account (Kooijman et al., 1997; van Beekvelt et al., 2001). Figure 2.8 illustrates how mBF is calculated from the linear increase of THb.

$$mBF = \frac{\left(\frac{\frac{\Delta THb \times 60}{[Hb] \times 1000}}{4}\right) \times 1000}{10} \qquad (2.1)$$

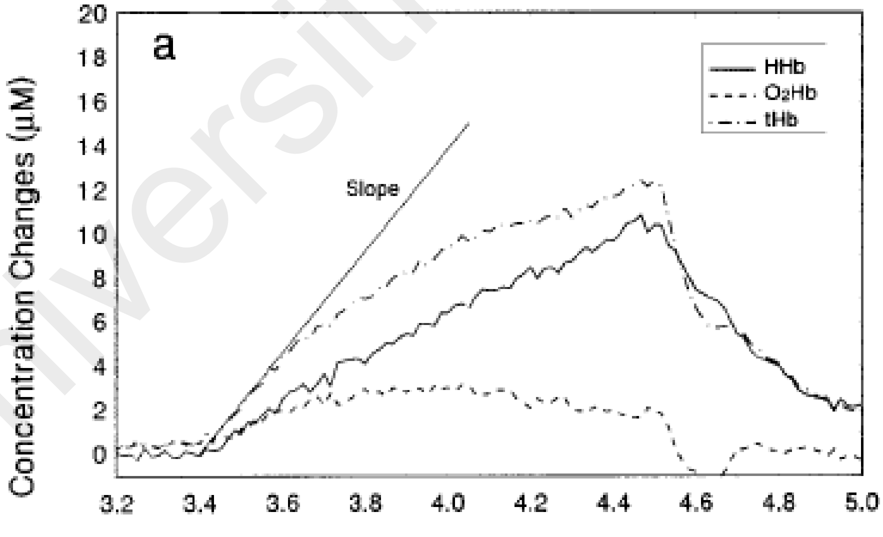

Figure 2.8: Blood flow from venous occlusion can be calculated from the linear increase in THb[2] during occlusion (Kooijman et al., 1997).

As for mVO_2, super-systolic arterial occlusion where cuff air pressure was inflated to 270 mmHg was performed to elicit the minimum and maximum StO_2. Arterial occlusion

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[2] THb – total hemoglobin

was continued until the StO_2 reached the lowest point for at least 5 s, usually after 5–8 min, then the cuff was released immediately and subjects were prepared for the exercise. The initial linear decline in O_2Hb was used to calculate mVO_2 (Kooijman et al., 1997; van Beekvelt, 2002) as in equation 2.2. The changes in HbO_2 given by the spectrophotometer are in micromolar. This can be further converted to millilitres oxygen per minute per 100 g tissue taking into account the following assumptions. The amount of oxygen that binds to hemoglobin (1 mole of Hb binds to 89.6 litres of oxygen, assuming STPD conditions) and the muscle density (1.04 kg per litre) was used to estimate mVO_2. Figure 2.9 shows how to obtain mVO_2.

$$mVO_2 = Abs\left(\left(\frac{\Delta O_2Hb\times 60}{10\times 1.04}\right)\times 4\right)\times\frac{22.4}{1000} \tag{2.2}$$

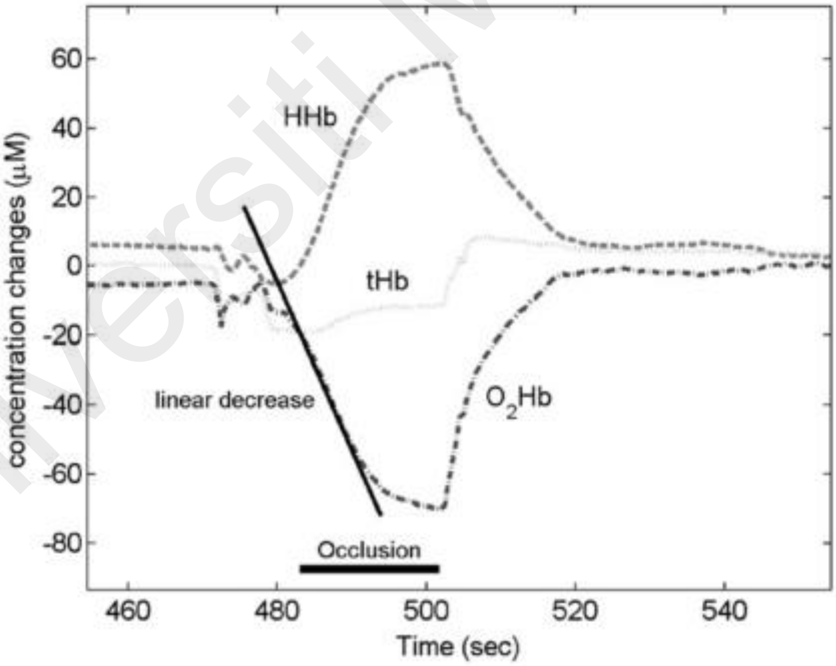

Figure 2.9: Muscle oxygen consumption from arterial occlusion can be calculated from the linear decrease in O_2Hb[3] during occlusion (Praagman et al., 2003).

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[3] O_2Hb - oxyhemoglobin

2.4.3.2 Near-Infrared Spectroscopy in Healthy Subjects

Over the years, NIRS has been employed to measure and examine the trends of muscle oxygenation during both static and dynamic contractions in healthy muscles and in their respective studies, it has proven that it is a reliable technique to measure muscle oxygenation of exercising muscles (Kell et al. 2004; Celie et al. 2012).

Several recent studies has used NIRS to measure small muscles including forearm muscles during isometric exercise. NIRS has proven to be able to detect changes of tissue oxygenation in forearm extensor muscle during low levels of isometric wrist extension (Murthy et al., 1997) and submaximal isometric handgrip (Usaj, 2001; Ušaj et al. 2007). The evidence from these studies showed that NIRS is very reliable and can be used to objectively evaluate muscle oxygenation and fatigue during exercise.

2.4.3.3 Near-Infrared Spectroscopy in Diseased Muscle

Besides measuring NIRS in healthy subjects, NIRS technology also has been able to study muscles in various chronic health conditions, including in SCI population using FES (Hamaoka et al., 2007). NIRS was proven to be capable to monitor changes of oxygenation in spinal muscle (Macnab et al., 2002), measured mitochondrial capacity in vastus lateralis (Erickson et al., 2013) and medial gastrocnemius (Ryan et al., 2013) and measured oxygenation status of vastus lateralis (Bhambhani, et al., 2000) and tibia bone (Draghici et al. 2018) in SCI individuals.

In SCI population, NIRS also was used to measure muscle oxygenation during arm crank ergometer (ACE) as shown in Figure 2.10, as part of a hybrid exercise which included FES-leg cycle ergometer (FES-LCE) in Figure 2.11 with the ACE (Figure 2.12).

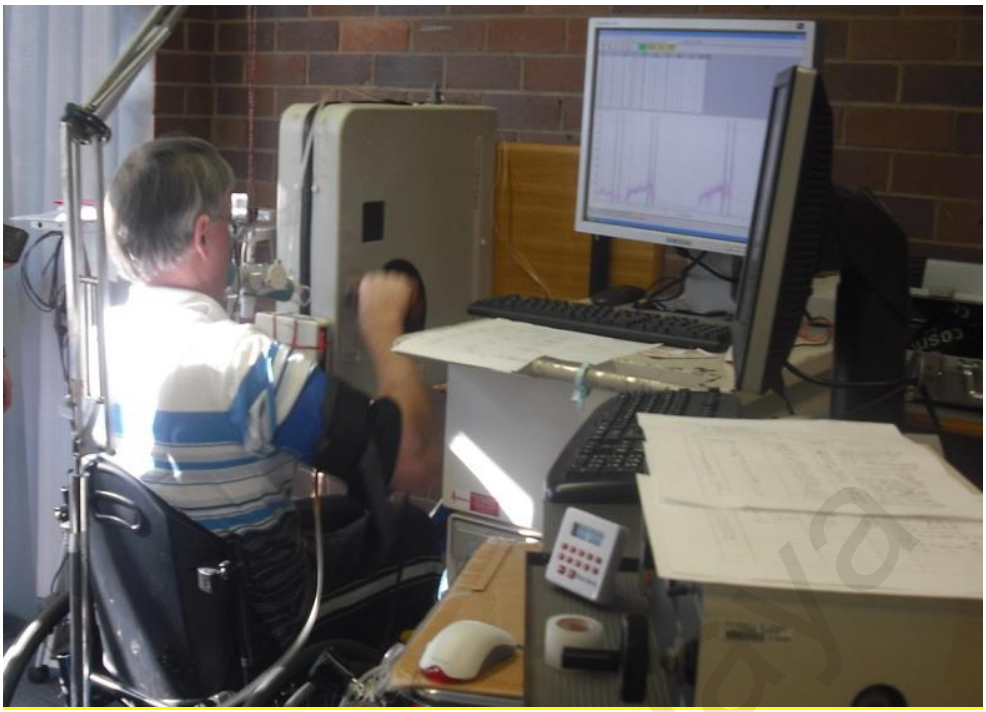

Figure 2.10: Example of ACE[4] exercise (Hasnan, 2015). This picture was taken with patient’s permission


[redacted]
[redacted]

Figure 2.11: Example of FES-LCE[5] exercise (Hasnan, 2015). This picture was taken with patient’s permission

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[4] ACE – arm cranking exercise

[5] FES-LCE - FES-leg cycle ergometer

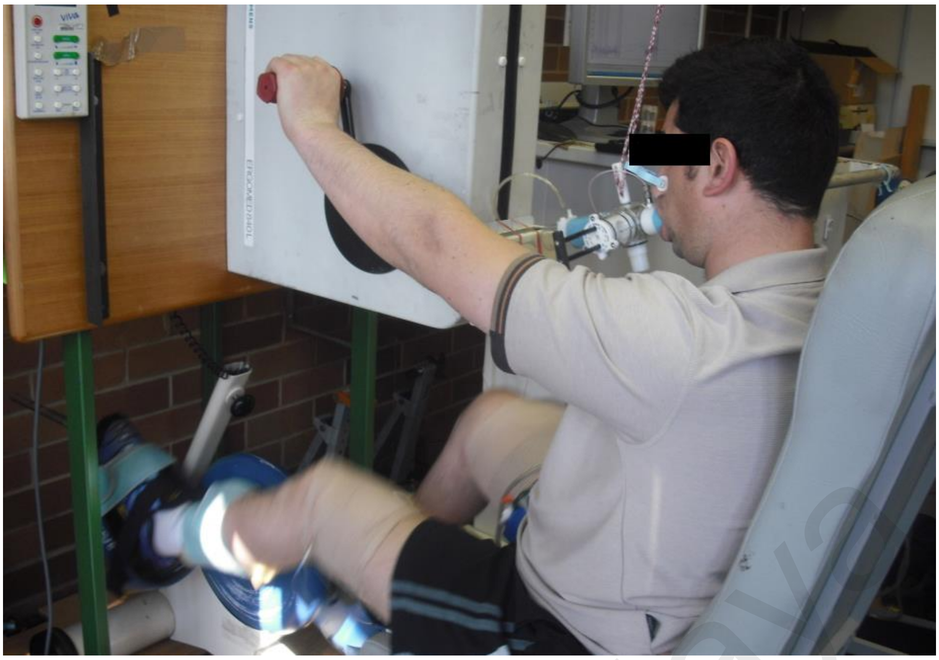

Figure 2.12: Example of hybrid exercise (ACE+FES-LCE) (Hasnan, 2015). This picture was taken with patient's permission

Besides measuring mitochondrial function during voluntary exercise, NIRS also was proven to be able to measure the same thing during FES-evoked exercise since the results for both were comparable and independent of the exercise intensity (Ryan et al., 2013). NIRS also was also reliable in measuring muscle mitochondrial capacity in healthy people as well as SCI individuals and potentially other diseased populations (Erickson et al., 2013). Therefore, if muscle oxygenation can be accurately measured noninvasively using NIRS, then it could be an alternative method in identifying the possible risk of muscle fatigue during repetitive motion (Murthyl & Rempell, 1997).

2.4.3.4 Summary

In previous recent studies, NIRS has been widely used to measure and examine the trends of muscle oxygenation during both static and dynamic contractions. Based on these studies, it shows that NIRS is capable in measuring muscle oxygenation status during FES-evoked exercise among SCI population, where the results were comparable during voluntary exercise and in healthy muscles (Erickson et al., 2013; Ryan et al., 2013). As most studies measure NIRS during FES in lower limbs only, there are no study that looked at NIRS during FES especially throughout muscle fatigue contractions in wrist extensor muscle.

In order to obtain more information regarding the muscle, a few researchers decided to use two sensors simultaneously during contractions. By assessing muscle fatigue using more sensors simultaneously, it could potentially provide more accurate and reliable information in regards to the mechanism underlying muscle fatigue (Yoshitake et al., 2001).

2.4.4 Near-Infrared Spectroscopy with Electromyography

A few studies related RMS from EMG with muscle oxygenation from NIRS during isometric exercises on normal participants at the forearm and shoulder muscle (Muthalib et al., 2011) and extensor carpi radialis (ECR) and trapezius muscles (Elcadi et al., 2011) on able bodied subjects. Elcadi et al. (2011) found that ECR and trapezius oxygen demands during isometric contractions are significantly negative correlated (Figure 2.13) to the muscle EMG-RMS activity and to force.

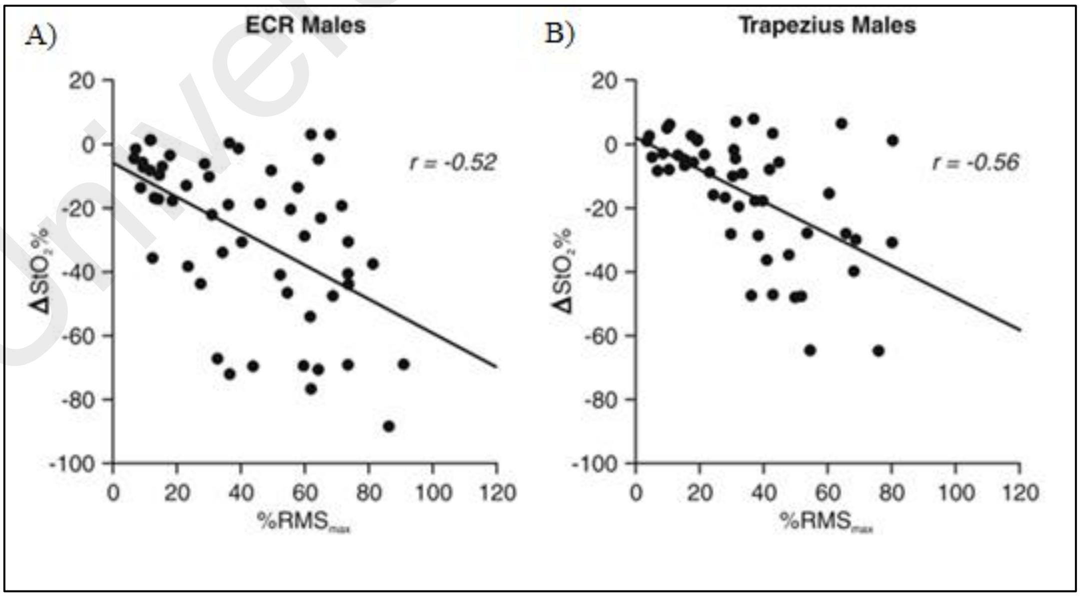

Figure 2.13: Relationship between ΔStO$_2$% and %RMS over force of maximum voluntary contraction in males[6] (Elcadi et al., 2011).

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[6] ΔStO$_2$% and %RMS measured in A) ECR and B) Trapezius muscles

Felici et al. (2009) on the other hand suggests a strong relationship between NIRS and EMG data during exercise on bicep brachii muscle. This study concluded that muscle oxygenation during isometric contractions is influenced not from the type of isometric exercise, but by the type of active motor units. Another research was conducted by Praagman et al., (2003) involving isometric contractions of elbow flexion and pro/supination moments while measuring simultaneous EMG and NIRS. EMG and oxygen consumption were found to increase linearly with the load during exercise.

Moalla et al. (2006) reported that the fatigue due to isometric exercise is related with the decline in muscle oxygenation and blood volume in lower limb of children. Significant correlations between muscle oxygenation and blood volume from NIRS, RMS amplitude and mean power frequency were observed which signifies that fatigue resulting is related to a decrease in oxygenation and blood volume during sustained isometric exercise. By measuring both NIRS and EMG, a better understanding of the fatigue process might be obtained for future research in rehabilitation.

2.4.4.1 Summary

Based on previous studies, the relationship between RMS from EMG to muscle oxygenation from NIRS has a promising interaction and the most associated compared to other parameters. However, these studies where both EMG and NIRS were used only were done during isometric contraction and in healthy subjects only. It is promising to validate this relationship during FES-evoked muscle fatigue contractions in SCI individuals as this was done previously in healthy subjects.

2.4.5 Near-Infrared Spectroscopy with Mechanomyography

In previous studies, authors associated EMG and NIRS of upper limb muscles during voluntary isometric contractions. Since this is a FES study, EMG is not suitable in measuring muscle fatigue along with NIRS. Due to this, MMG is the most practical sensor to be used along with NIRS to replace EMG since this relationship has not been investigated especially when using MMG (Praagman et al. 2003).

Yoshitake et al. (2001) has employed MMG (RMS and MPF) to investigate muscle fatigue of lower back pain along with EMG (RMS and MPF) and NIRS (O_2Hb and blood volume) where they concluded that the simultaneous recording system can obtain a more promising outcome regarding muscle fatigue. As this was done in healthy subjects, it is crucial to validate the reliability and validity of the relationship during FES-evoked muscle fatigue contractions in SCI individuals. This was the main motivation of this thesis investigation.

2.5 Summary

The relationship between the muscle myographic signals using EMG to muscle oxygen saturation using NIRS has promising interaction compared to MMG (Yoshitake et al., 2001). However during FES, EMG is not suitable to be used, hence MMG has been the mechanical counterpart of EMG in measuring fatigue. Most literatures have used MMG during voluntary contractions, and only a limited number of studies have used MMG to describe muscle fatigue during electrical stimulation (Faller et al., 2009; Gobbo et al., 2006).

Since the use of MMG in different aspects of muscle function is increasing over the years, MMG can be one of the most effective tools to examine diverse conditions of muscle activity (Islam et al., 2013) along with NIRS as both MMG and NIRS are reliable and have been used to assess muscle during exercise.

According to Yoshitake et al. (2001), simultaneous recording system can obtain a more promising outcome regarding muscle fatigue. In their study, they did the experiment in healthy subjects, hence it is crucial to validate the reliability and validity of the relationship during FES-evoked muscle fatigue contractions in SCI individuals. As their muscle properties differ from healthy subjects, it is expected that their result might be different. This was the main motivation of this thesis investigation.

In addition, previous studies including Yoshitake et al. (2001) mostly focused on measuring fatigue during voluntary isometric contractions with able-bodied human subjects, not in neuromuscular diseased muscles. No studies yet that measure fatigue in repetitive wrist extension exercise with the aid of FES in SCI. This type of exercise is a very common in rehabilitation especially for cervical SCI patients. Hence, it is important to know and assess the condition of the muscle especially during FES-evoked exercise.

Simultaneous recording of MMG and NIRS in assessing muscle fatigue will provide a clearer picture from mechanical and physiological aspects as well. In the future, it can be used to predict and monitor the occurrence of fatigue. It will help greatly in rehabilitation field especially for SCI patients, since they have no sensory feedback in their muscle and it will be hard for them to feel the fatigue themselves. It can also guide the individuals during exercise and can act as a warning device to notify them before fatigue occur, avoiding unnecessary stretch on the muscle to prevent injury (Al-Mulla et al., 2011).

There are no studies so far that looked at both MMG and NIRS simultaneously to assess muscle fatigue during repetitive FES wrist extension exercise. This study investigated the relationship between MMG and NIRS during repetitive electrically-evoked wrist extension exercise. It was hypothesized that a fatiguing muscle would show a clear relationship between MMG and NIRS during post-fatigue point during the exercise.

Due to the limited research from previous studies in SCI, it is important to investigate the relationship between MMG and NIRS in able bodied (AB) participants first since AB participants has more power in their muscle to perform FES-evoked exercise compared to the participants with SCI. Therefore, we can understand the natural behavior of the muscle mechanically and physiologically during FES-evoked wrist extension exercise to fatigue in AB. This is important as we can set a standard where the relationship of MMG and NIRS during fatigue in participants with SCI could be compared.

CHAPTER 3 : METHODOLOGY

This chapter describes the protocols and materials used in the study. It explains the participants' information, experimental setup, data collection, processing and analysis for able bodied (AB) and spinal cord injury (SCI) participants as both used the same protocol and material.

Pertaining to the first and second objective of the study, the mechanomygraphic (MMG) signals and muscle oxygenation pattern from near infrared spectroscopy (NIRS) including muscle oxygen consumption during repetitive FES wrist extension exercise will be investigated. Last but not least, relationship between MMG and NIRS during repetitive FES wrist extension exercise will be investigated in order to answer the third objective of the study. All of these will be done in AB and SCI participants. Therefore, there are 2 sub-sections for participation section in this chapter; AB and SCI participants.

The next sections discuss regarding the fatigue measurement involving power output (PO), electrode placement and stimulation parameters for functional electrical stimulation, a more detailed explanation on MMG and NIRS along with study protocol. The seventh and eighth sections will discuss regarding how analysis of the data will be done in order to answer our objectives. Correlation analysis between MMG, NIRS and PO reflect the first and second objectives of this study, while correlation and regression analysis between MMG and NIRS reflects the third objective of this study. All the sections reflect all the objectives as both AB and SCI participants employ the same protocol and material.

3.1 Participants

To gain complete representation of the muscle mechanical and physiological behavior among different users, AB subjects as well as SCI patients participated in this study. The study procedure employed was the same for both AB and SCI participants for this experiment. Estimation of the sample size and power analysis were done using GPower

Software where in order to achieve the coefficient of determination of at least 0.8, effect size of 0.89 was needed to determine the sample size required to produce reliable results. 0.8 was used as the power of the correlation which means, if the experiment was repeated with different set of subjects, there will be 80% probability the results produced will be similar. Based on the following parameters, GPower software determined that 6 subjects was the minimal required value.

3.1.1 Able-Bodied Participants

Forty volunteers that were recruited from University of Malaya's students participated in the study. The mean (± standard deviation) characteristics of the subjects were: N = 40: 12 male, 28 female; age: 21.55 ± 1.48 y; skinfold thickness = 4.09 ± 1.56 mm). The participants were recruited based on the inclusion and exclusion criteria (Table 3.1).

Table 3.1: Exclusion and inclusion criteria for AB participants

Inclusion Criteria	Exclusion Criteria
Age 18-80 years old.	Pre-existing bone conditions (e.g. fractures, osteoporosis)
Right-handed	Skin allergies to electric stimulation or electrodes
Able to understand simple instructions	Cardiac pacemaker or other implanted electronic system
In good health with no history of upper extremity musculoskeletal disorder or surgeries	Insulin dependent diabetes
Responsive to functional electrical stimulation	Morbid obesity (BMI > 40)

3.1.2 Spinal Cord Injury Participants

Seven males with motor complete chronic SCI (ASIA A and B, lesion level C5 and above) were recruited for participation in this study. The mean (± standard deviation) characteristics of the subjects were: N = 7; age = 48.86 ± 6.91 y; stature = 1.72 ± 0.02 m;

body mass= 75.14 ± 5.64 kg; skinfold thickness = 8.38 ± 3.26 mm). All the details of the patients are in Table 3.2.

The participants were recruited based on the inclusion and exclusion criteria (Table 3.3) where all the criteria has been discussed with the research team including rehabilitation doctor. One separate session was allocated to do the assessment based on the inclusion and exclusion criteria led by a rehabilitation doctor.

Table 3.2 Physical characteristics of the SCI participants

Participants	Age (y)	Gender	Lesion level	ASIA[7]	Height (m)	Weight (kg)
LE	60	M	C5-C7	B	1.73	80
CH	55	M	C5	A	1.70	75
AN	46	M	C4	A	1.75	70
TH	50	M	C5	B	1.73	70
SA	45	M	C5	A	1.75	75
CO	39	M	C5	A	1.70	85
RL	47	M	C5	A	1.69	71

Table 3.3: Exclusion and inclusion criteria for SCI participants

Inclusion Criteria	Exclusion Criteria
Outpatient, 2 years and above	Pre-existing bone conditions (e.g. fractures, osteoporosis)
Age 18-80 years old.	Skin allergies to electric stimulation or electrodes
SCI C5 and above, ASIA A & B	Wrist contracture; cannot achieve full wrist extension
Able to understand simple instructions	Autonomic dysreflexia, or history of other neurological or psychiatric disorders.
Declared medically stable by attending doctor	Cardiac pacemaker or other implanted electronic system.
Responsive to functional electrical stimulation	Insulin dependent diabetes.
Able to do passive wrist extension and lift minimum load of 100g with the help of functional electrical stimulation	Morbid obesity (BMI > 40)

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[7] ASIA = American Spinal Injury Association; ASIA A indicates a complete lesion, which there is no motor or sensory function preserved in sacral segments S4-S5 while ASIA B is an incomplete lesion in which only sensory is present below the neurologic level which covers sacral segments S4-S5

3.2 Fatigue Measurement

Muscle fatigue has been understood as the decline in muscle ability to generate force or power output (Enoka & Duchateau, 2008) as well as a reduction in movement speed (Sargeant & De Haan, 2006). Packman-Braun (1988) has defined fatigue in his work as 50% from the initial force output. Power output was used as a measurement of fatigue and it could be obtained from equation 3.1.

$$\text{Power }(\text{Nms}^{-1}) = \text{Force}(\text{N}) \times \frac{\text{Displacement (m)}}{\text{Time (s)}} \tag{3.1}$$

A strap attached to the maximum load was placed on the dorsal part of the hand during the exercise (Figure 3.1). Before starting the experiment, one separate session was held to find maximum power output by determining maximum load (force) each participants can lift by FES wrist extension movement. Each participant lifted a maximum load that they can until maximum wrist extension was reached with FES and the amount of load was determined by binary method. The maximum weight of the load and maximum distance of load lifted were recorded. Maximum load for each subject will differ as different muscle will have different tolerance and strength.

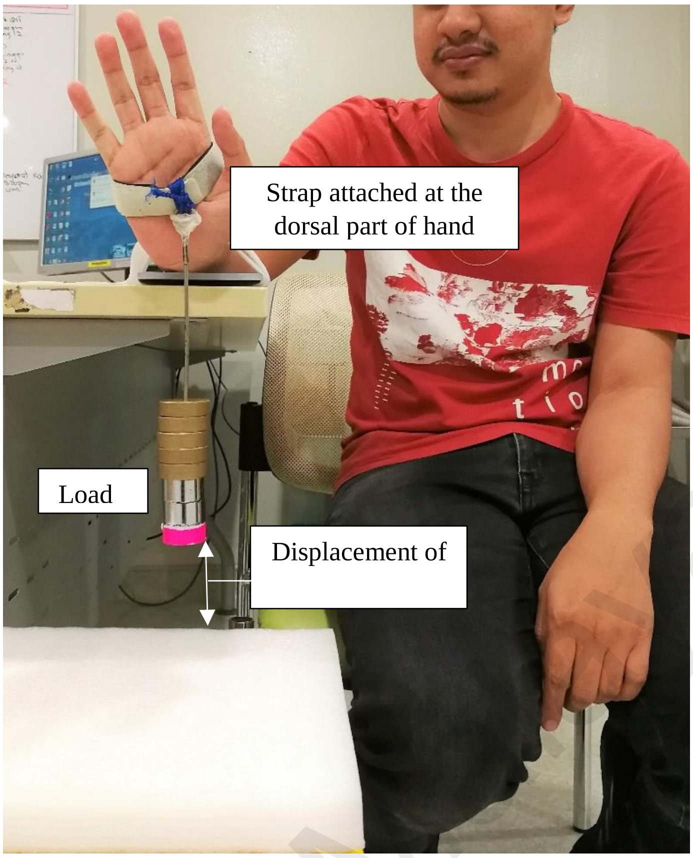

Figure 3.1: Position of the strap attached to the load

Time and displacement during lifting of the load were recorded using a camera recorder and Kinovea software. The exercise session was performed until the participant was unable to lift the load indicating zero power output which was the end point of the exercise.

3.3 Functional Electrical Stimulation

Ottobock STIWELL med4 surface stimulator (MED-EL Elektromedizinische Geräte GmbH, Austria) (Figure 3.2) sends electrical impulses (FES) through the skin, activating the movements. Using electrical pulses, FES can rehabilitate or compensate motor functions failure due to injury or disease such as SCI. Interaction with the nervous system leads to successful therapy in many neurological diseases. STIWELL med4 provides 52 training programs for biofeedback, conventional electrical stimulation therapy of innervated and denervated muscle, functional electrical stimulation, EMG-triggered stimulation and pain therapy. On top of that, 20 customized programs can be saved so that patients can easily use it at home without having to adjust the parameters (Rakos et al., 2007).

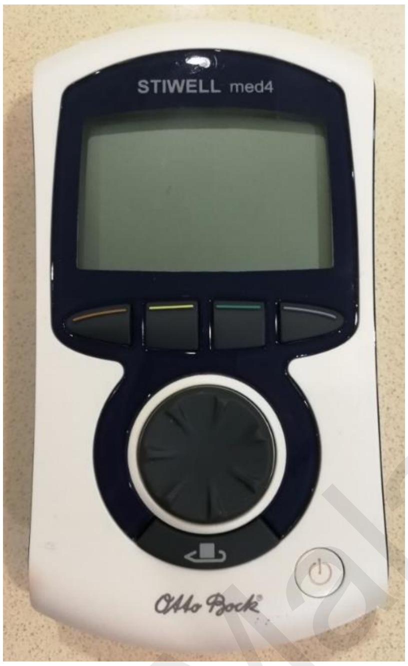

Figure 3.2: Ottobock STIWELL was used to supply FES during exercise

The intensity of stimulation ranged from 10 mA to 30 mA was adjusted according to the subjects' tolerance and pulse width of 250µs to produce full joint extension (Table 3.4). Controlled muscle contraction was achieved by setting with a frequency of 35 Hz. and on/off cycle 4sec/ 4sec with no ramping. Figure 3.3 showed the correct electrode placement to produce balanced radial ulnar wrist extension.

Table 3.4: Stimulation parameters used in this study for SCI participants

Participants	Pulse width (µs)	Frequency (Hz)	Stimulation intensity (mA)
LE	250	35	21
CH	250	35	17
AN	250	35	24
TH	250	35	28
SA	250	35	22
CO	250	35	23
RL	250	35	22

Figure 3.3:Placement of FES electrodes to achieve wrist extension[8](Baker, 2000).

3.4 Mechanomyography

MMG is a technique that reflects contractile properties of muscles more directly. Therefore, it may be useful in aiding investigators to a have better understanding of aspects of neuromuscular control. On top of that, MMG also has shown a noticeably higher ability in detecting muscle fatigue for SCI subjects.

Accelerometer-based MMG sensors, Sonostics VMG BPS II Transducer (Biopac System Inc, USA) (Figure 3.4) with an operational frequency response from 20-200 Hz, sensitivity 50 V/g, maximum range 2000 g was used. The signals were collected at 2 kHz sampling frequency and were digitally band-pass filtered at 20–200 Hz as this is the range recommended by Biopac for assessment of muscle effort. All MMG signals recorded were obtained from the vibration of muscle that caused wrist extension movement.

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[8] One electrode just above the wrist on the dorsal surface of the forearm and the other electrode was placed close to the lateral epicondyle of the humerus

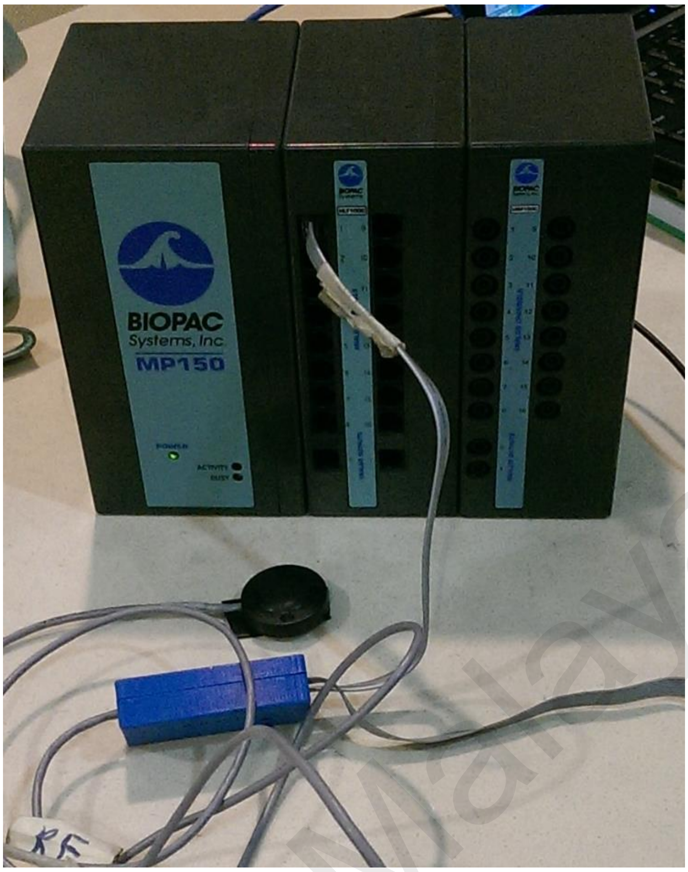

Figure 3.4: Mechanomyography (Biopac System)

In the time domain, the amplitude of MMG was known as the voltage values and its amplitude was retrieved as RMS. RMS-MMG was extracted from the raw MMG signal and was normalized to %RMS-MMG. The amplitude is important to monitor motor unit recruitment during muscle contraction (Orizio et al., 2003). The equation for the RMS processing was defined as equation 3.2:

$$RMS = \sqrt{\frac{1}{N}\sum_{k=1}^{N-1} x_k^2, \;\; for\ k = 1, \ldots, N} \qquad (3.2)$$

where x_k is the raw signal from each segment and N is the number of samples.

3.5 Near Infrared Spectroscopy (NIRS)

NIRS (PortaMon, Artinis Medical Systems, The Netherlands) (Figure 3.5) is a non-invasive, non-ionizing, real-time monitoring and portable system that generated light at two wavelengths of 760 nm and 850 nm with three transmitters and a receiver (Figure 3.6) that was transmitted through body’s skin, muscle, and adipose tissue. It is a direct method to determine muscle oxygenation, hemodynamics, and indirectly mitochondrial activity during exercising.

Based on the amount of light that was absorbed at respective wavelengths into the device, they were then converted to concentration changes of oxyhaemoglobin (ΔO_2Hb), deoxyhaemoglobin (ΔHHb) and total haemoglobin (ΔtHb) from its baseline using a modified Lambert Law. With these concentrations changes, tissue saturation index (TSI) could be calculated.

Figure 3.5: NIRS that is used in this experiment (Portamon)

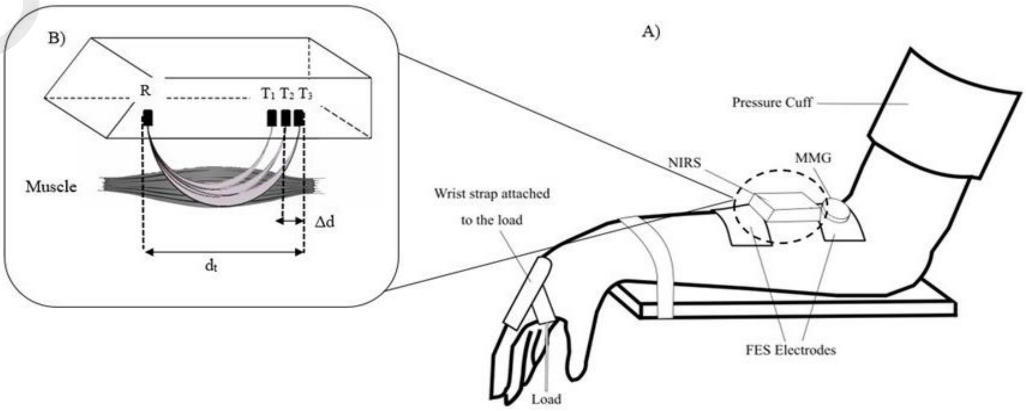

Figure 3.6: A) The setup diagram for the experiment. B) Closer look at the schematic view of a TSI measurement.

Tissue saturation index from NIRS (TSI-NIRS) on the other hand shows the average saturation of the underlying muscle tissue and calculated as $[O_2Hb] / ([O_2Hb] + [HHb]) * 100$). It reflects the dynamic balance between oxygen supply and oxygen consumption in the tissue microcirculation (Buchheit & Ufland, 2011; Jones, Dat, & Cooper, 2014; Billaut et al., 2013). Previous studies have shown that TSI reflects muscle oxygenation more accurately than HHb (Buchheit & Ufland, 2011; Sperlich et al., 2015). %TSI-NIRS therefore showed muscle oxygen utilisation more precisely than ΔO_2Hb and ΔHHB. In addition, this device has more than 50 hours data offline storage at a frequency of 10 Hz. The device weighs 84 grams including the battery with dimensions of 84x42x17 mm (LxWxH).

Physiological calibration was done before starting the experiment to normalize NIRS signals as it provided a range of NIRS optical density unit changes, thus gave an accurate interpretation of change in raw NIRS data. It was an important and the most practical comparisons of oxygenation levels between different subjects and muscle builds. The physiological calibration during the occlusion provided the minimum value during ischemia and maximum value during reactive hyperaemia (or highest point observed during the experiment), and that minimum and maximum values were used as a scaling factor (0% and 100%) for further measurements (Erickson et al., 2013; Hamaoka et al., 2011).

The subcutaneous or fat layer underlying the muscle of interest may influence NIRS measurements. The influence was due to different muscle builds of each individual. To control this, adipose tissue thickness (ATT) was measured for each participant using Skinfold Thickness. ATT is defined as skinfold thickness divided by 2. The maximum penetration depth of NIRS is calculated as half the distance between source and detector. This means that participants with more subcutaneous layer might prevent enough amount of light passing through the muscle and affecting the NIRS measurement (van Beekvelt et al., 2001). For participants with thick fat layers, the signals may be less accurate due to the lower metabolic and blood flow rates in adipose tissue (Mccully & Hamaoka, 2000). This was proved by a study that when ATT increased from 5 to 10mm, there will be a decrease of 50% in absorbance of the NIRS light while a decrease of 25% was observed when fat layer thickness increased from 2.5 to 5 mm (Yamamoto et al, 1998).

mVO_2 was measured as the rate of change in muscle oxygenation during brief arterial occlusions in NIRS signals using linear regression. Hemoglobin and myoglobin both contribute with the changes in NIRS signals where its signal changes are proportional to mitochondrial oxygen consumption due to relative changes in hemoglobin and myoglobin saturation (Erickson et al., 2013). The calculation is shown in 2.2.

3.6 Study Protocol

This study employs cross sectional study design. Three sessions of exercise were conducted with 48 hours of recovery between sessions. All participants underwent written consent given after verbal information with the primary investigator and provided with a participant information sheet, in accordance with the Medical Ethics Committee, University of Malaya Medical Center (MECID.NO: 20166-2552).

Before setting up, investigator first explained to the AB and SCI participants regarding the protocol of the experiment. They were asked to be seated on a chair, with the right hand positioned on a thermoplastic arm rest placed on the table with Velcro strapped along their forearm. The arm rest supported and secured their hands while minimizing other unintended movements throughout the experiment. Arm cuff (Figure 3.7) was strapped around the forearm just above the elbow. Rapid Cuff Inflation System (Hokanson, USA) was used to inflate the cuff during occlusion.

Figure 3.7: Rapid Cuff Inflation System (Hokanson) used during occlusion

One 4x4cm electrode was placed at extensor carpi radialis (ECR), just above the wrist on the dorsal surface of the forearm and the other electrode was placed close to the lateral epicondyle of the humerus for FES. By using small FES electrodes, NIRS probe was able to fit in between the electrode while MMG probe was placed on the proximal FES electrode (Figure 3.8).

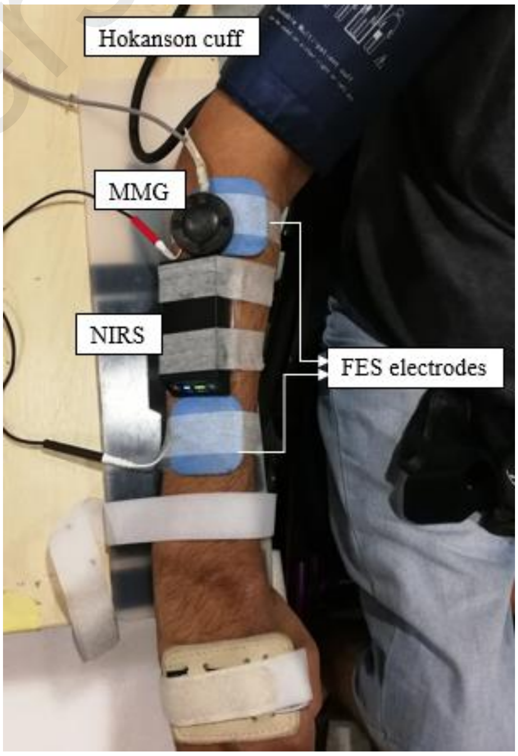

Figure 3.8: Placement of forearm cuff, probes and electrodes

NIRS and MMG's probes were placed along the muscle belly of the extensor muscle and a double-sided tape was used to ensure consistent contact pressure between the sensor and the skin of the ECR area. Both probes were wrapped with an elastic bandage to secure them during exercise. The large unintended movement was avoided by restricting other movements using thermoplastic arm rest with Velcro strapped around the proximal of the wrist. Maximum load was attached and strapped around their palm while doing the exercise.

After 5-minute rest period, a super-systolic arterial occlusion was done where the cuff was inflated to a high pressure of 250 mmHg until the %TSI-NIRS reached a nadir lasting at least 5 s, then the cuff was released immediately. The subjects' muscles were then electrically (FES)-evoked to non-voluntarily performed repetitive wrist extension. The contraction and rest ratio for the exercise was set at 4-sec contraction and 4-sec rest to induce rapid muscle fatigue. The NIRS with MMG signals throughout the entire period of each wrist extension exercise were collected during rest, arterial occlusion and exercise until the load cannot be lifted anymore, indicating zero power output which was the fatigue point. A schematic diagram of the protocol employed in this study is shown in Figure 3.9.

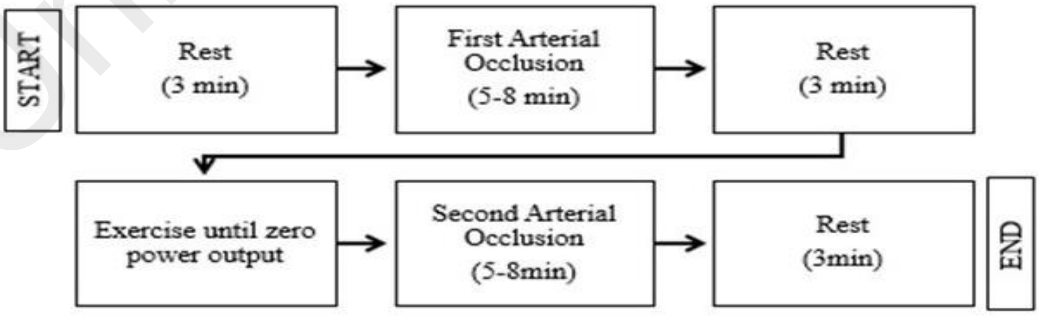

Figure 3.9: Schematic diagram of the experimental protocol for both AB and SCI participants

3.7 Data analysis

The number of contractions was converted to a percentage of contractions as the number of total contractions completed varied between subjects. Percentages of power output (%PO) were calculated using equation 3.1.

The %RMS-MMG were also normalized and the mean amplitude for every 4-sec contraction was computed using epoch analysis while mean percentages %TSI-NIRS from NIRS were obtained during each 4-sec contraction to fatigue. All subjects' mean of %PO, %TSI-NIRS and %RMS-MMG for each 10% increment percentage of contractions were plotted and data are presented as mean ± standard deviation. Muscle oxygen consumption (mVO_2) from NIRS also was calculated and compared pre- and post-exercise.

3.8 Statistical Analyses

All data of %TSI-NIRS from NIRS and %RMS-MMG from MMG along with %PO as a measurement of fatigue for all AB and SCI participants were tested for normality with Kolmogorov–Smirnov normality test by using IBM SPSS Statistics 24 (SPSS Inc., USA).

To answer the first two objectives, correlation analysis were done by pairs; %PO and %RMS-MMG with %PO and %TSI-NIRS in AB and SCI participants respectively. The correlation coefficient (r) measured the strength and the direction of a linear relationship between two variables. The interpretations of correlations were based on these criteria; $r > 0.5$ is a good correlation, $r = 0.3 – 0.5$ is a moderate correlation, and $r < 0.3$ is a poor correlation (Cohen, 1977). mVO_2 in SCI participants also was compared pre- and post-exercise by running paired t-test analysis.

In order to accomplish the third objective, correlation along with regression analysis was done between %RMS-MMG and %TSI-NIRS to determine their relationship with each other during exercise. Linear regression is a type of predictive analysis which makes predictions among variables which have reason and result relation. The main aim of regression is to analyse the relationship between a dependent and independent variables and formulates the linear relation equation between these dependent and independent variables (Uyanık & Güler, 2013). It will also give a p-value which measures the accuracy of the prediction.

As the changes of MMG and NIRS was determined throughout the repetitive wrist extension, a change in trend before and after fatigue happened was noted. Therefore, the correlations and linear regression were done on two points which were pre-fatigue and post-fatigue, of which the fatigue point was the 50% drop of PO.

CHAPTER 4 : RESULTS

This chapter is divided into two types of participants which are able bodied (AB) and spinal cord injury (SCI) participants. All parameters of interest from mechanomyography (MMG) and near infrared spectroscopy (NIRS) will be compared statistically and results are presented in graphs and tables. This study did not compare AB and SCI participants directly, hence the results were portrayed separately for AB and SCI participants.

The overall results will be discussed in the first section to see the general pattern of all parameters for AB and SCI participants pre- and post-fatigue. This includes how root mean square from MMG (%RMS-MMG) and tissue saturation index from NIRS (%TSI-NIRS) progress as percentage of contraction increases. Result for muscle oxygen consumption (mVO_2) from NIRS also will be portrayed in this section where it is compared pre- and post-exercise for SCI participants.

To answer the three objectives, the next three main sections will portray the correlations between %PO with %RMS-MMG, %PO with %TSI-NIRS-NIRS along with correlation and regression between %RMS-MMG and %TSI-NIRS-NIRS pre- and post-fatigue. Each sections will reflect each objectives respectively. Each of the sections will have two sub-sections; AB and SCI participants.

4.1 Overall

Figure 4.1 presents the actual data of the experiment where both NIRS and MMG signals were shown. NIRS data were recorded throughout the experiment while MMG data was recorded during wrist extension exercise only. From MMG, percentage of root mean square (%RMS-MMG) was extracted while from NIRS, percentage of tissue saturation index (%TSI-NIRS-NIRS) was analyzed.

Since each participants had different number of contractions, the number of contractions was converted to % of contractions to make the results comparable. This section showed overall pattern of %PO, %RMS-MMG and %TSI-NIRS-NIRS against % of contractions pre- and post-fatigue where fatigue point was defined as 50% drop of PO from its initial value.

4.1.1 Able Bodied Participants

Figure 4.2 shows %PO, %TSI-NIRS and %RMS-MMG plotted over the percentage of contractions in AB participants. Thirty nine (N = 39) participants' data were analysed as one of the subjects was excluded because the muscle did not reach the pre-defined fatigue point during the experiment i.e. %PO did not reach 50%.

As this was a muscle fatigue experiment, %PO was seen decreasing over increasing number of contractions from 82.30% to 25.63% while %TSI-NIRS behaved in the opposite direction of %PO as it increased by 6.12%. On the other hand, %RMS-MMG was fluctuating and did not have clear pattern over increasing contraction. Figure 4.3 on the other hand, shows the concentration changes and pattern of ΔO_2Hb and ΔHHb from NIRS during exercise. The concentration of ΔO_2Hb was seen increasing similar with %TSI-NIRS while ΔHHb did not show clear changes throughout the exercise.

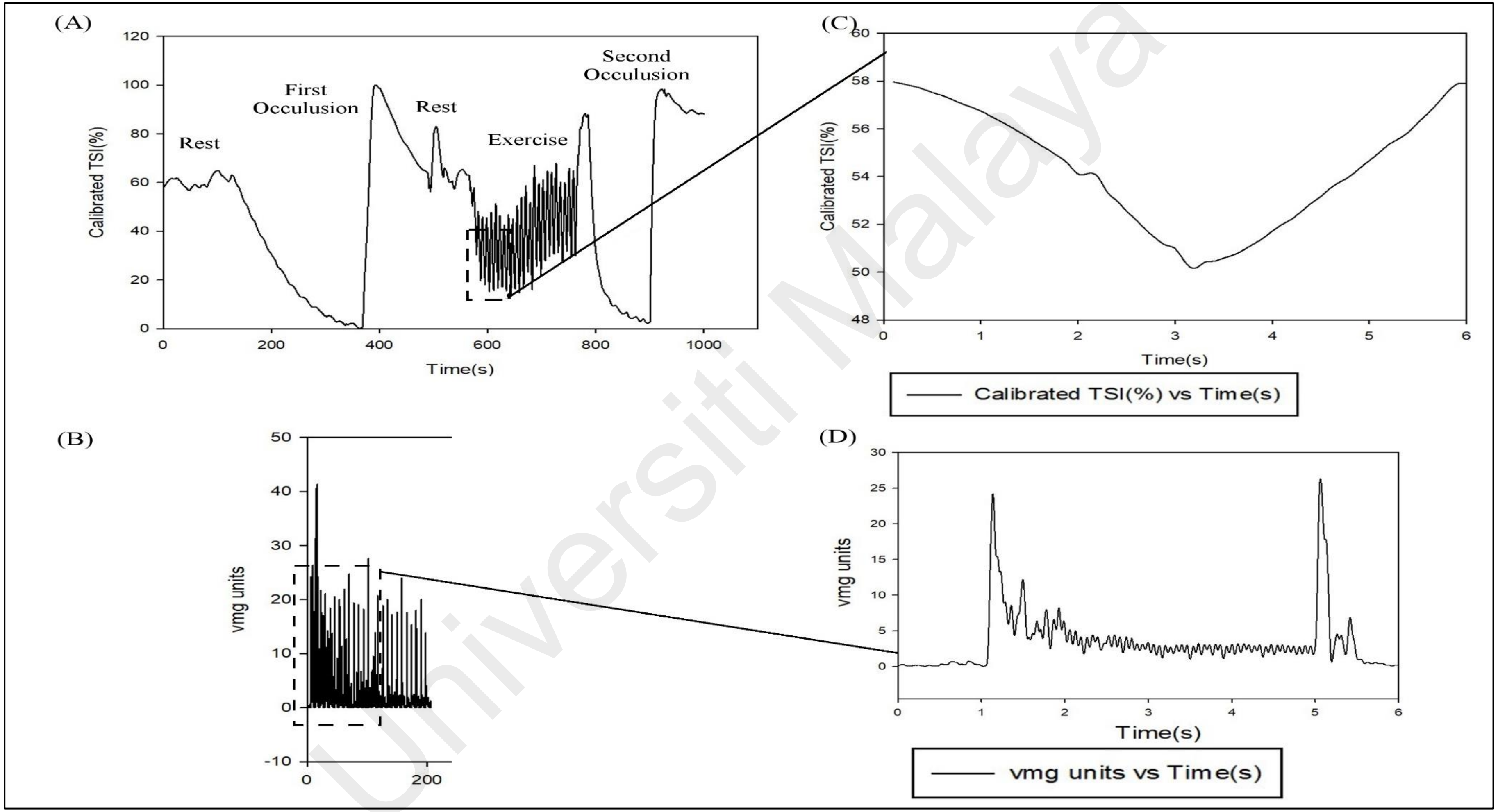

Figure 4.1: A) NIRS signals is recorded throughout the experiment including occlusions and B) MMG signals is recorded during exercise only. C) and D) are a closer look at the signals for one separate contraction from NIRS and MMG.

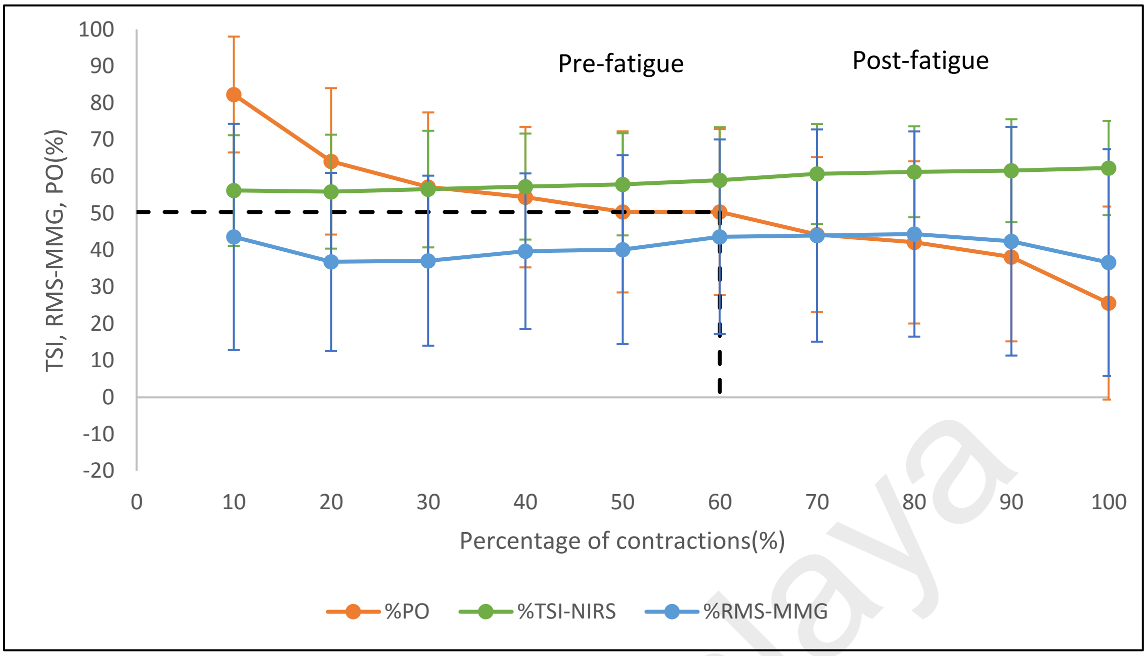

Figure 4.2: Mean for percentage of PO[9], percentage of TSI-NIRS[10] and percentage of RMS-MMG[11] against percentage of contractions for all subjects in AB participants. Data are presented as mean and standard deviation[12].

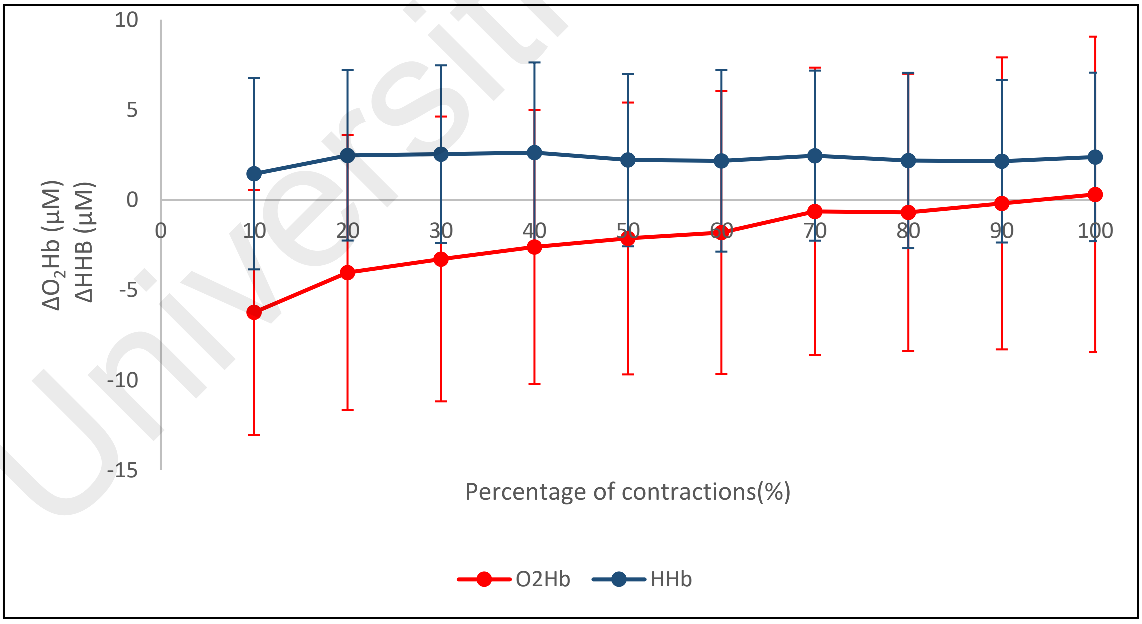

Figure 4.3: Mean of changes in O_2Hb[13] and changes in HHB[14] against percentage of total contractions for all subjects in AB participants. Data are presented as mean and standard deviation.

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[9] PO = power output

[10] TSI-NIRS = tissue saturation index from near infrared spectroscopy

[11] RMS-MMG = root mean square from mechanomyography

[12] Dashed vertical lines denote the point of fatigue (50% drop of PO) where correlations were done at two parts; pre- and post-fatigue.

[13] O_2Hb = oxyhemoglobin

[14] HHb = deoxyhemoglobin

4.1.2 Spinal Cord Injury Participants

Figure 4.4 shows %PO, %TSI-NIRS-NIRS and %RMS-MMG plotted over the percentage of contractions for SCI participants. Six participants' data were analysed (N = 6) as one of the subjects was excluded because the muscle did not reach the fatigue point during the experiment, i.e. %PO did not reach 50%. Paired t-test was done for all three data where each contraction was compared to the contraction prior to it.

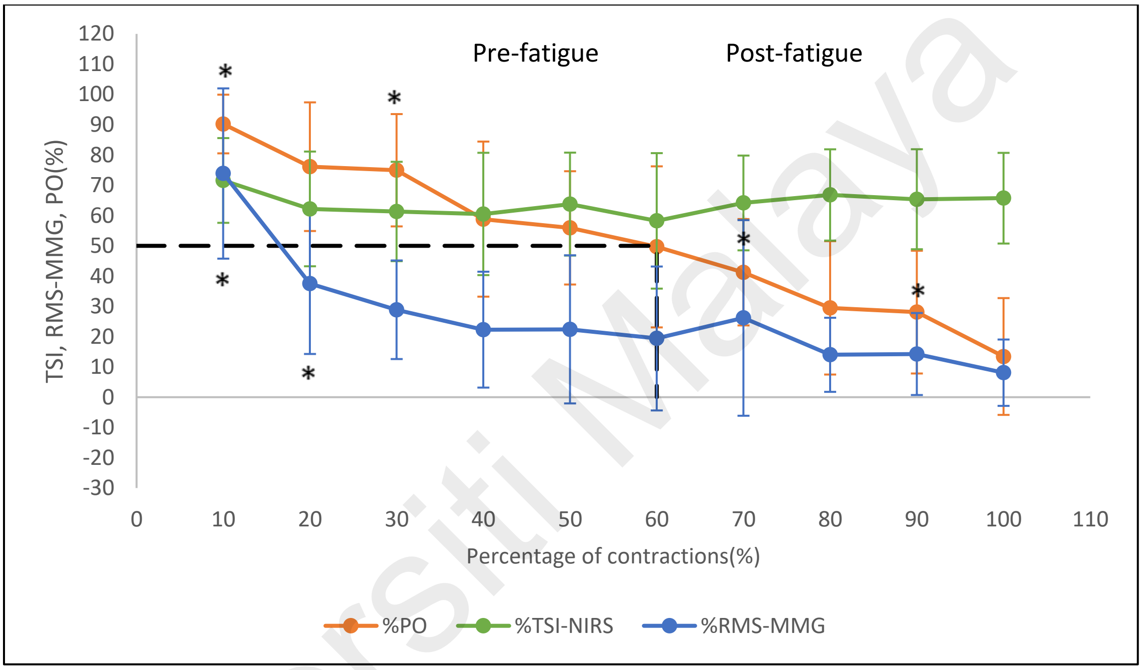

Figure 4.4: Mean for percentage of TSI-NIRS[15], percentage of RMS-MMG[16] and percentage of PO[17] against percentage of contractions for SCI. Data are presented as mean and standard deviation[18].

%PO was seen to decrease over increasing percentage of contractions. %PO was observed to generally decrease but significantly at 10% (-14.09%, p = 0.01), 30% (-16.14%, p = 0.00), 70% (-11.77, p = 0.01) and 90% (-14.66%, p = 0.01) of the contractions respectively. %RMS-MMG displayed a decreasing pattern against contractions and during 10% (-36.35, p = 0.00) and 20% (-8.65%, p = 0.04) of the contractions, %RMS-MMG was seen to decrease significantly. %TSI-NIRS, on the other

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[15] TSI-NIRS = tissue saturation index from near infrared spectroscopy

[16] RMS-MMG = root mean square from mechanomyography

[17] PO = power output

[18] Dashed vertical lines denote the point of fatigue (50% drop of PO) where correlations were done at two parts; pre- and post-fatigue.

hand decreasing during pre-fatigue and increasing during post-fatigue over increasing percentage of contraction numbers but the trend was not statistically significant.

4.2 MMG Signal during FES Wrist Extension Exercise

The first objective in this study was to investigate mechanomyography (MMG) signal responses during electrically-evoked muscle contraction to fatigue wrist extension exercise among AB and SCI participants. MMG signal responses can be obtained by extracting percentage of root mean square (%RMS-MMG) from MMG.

In order to achieve this objective, correlation analysis was done where it measured the direction and how strongly these two pairs of variables are related with each other (Cohen, 1977). Correlation analysis was done to find out how %RMS-MMG progressed against %PO throughout the exercise. The correlation was investigated during pre- and post-fatigue.

4.2.1 Able Bodied Participants

Correlations were done between %PO and %RMS-MMG during pre- and post-fatigue. During post-fatigue, %RMS-MMG had a weak positive correlation of r=0.05, p=0.04 compared to other parameters. As the correlation of %PO and %RMS-MMG pair was weak, another correlation between %PO and %RMS-MMG pair was done pre- and post-fatigue for every subject in order to see the pattern more clearly.

It was discovered that %RMS-MMG behaved in two different patterns post-fatigue, which were either positive correlation against declining %PO, i.e. both parameters decreasing post fatigue (r = 0.26, p = 0.00) or negatively correlated with %PO , whereby the %RMS-MMG increased with decreasing %PO (r = 0.23, p = 0.00). Due to this, all subjects were divided into these two groups depending on how %PO correlated with %RMS-MMG; group A (N = 23) with positive correlation and group B (N = 16) with negative correlation respectively.

Figure 4.5 shows an overall plot of group A for %PO, %TSI-NIRS and %RMS-MMG against the percentage of contractions. A clearer pattern of decreasing %RMS-MMG (-30.74%) was observed along with declining %PO (-54.69%) as the percentage of contractions increasing.

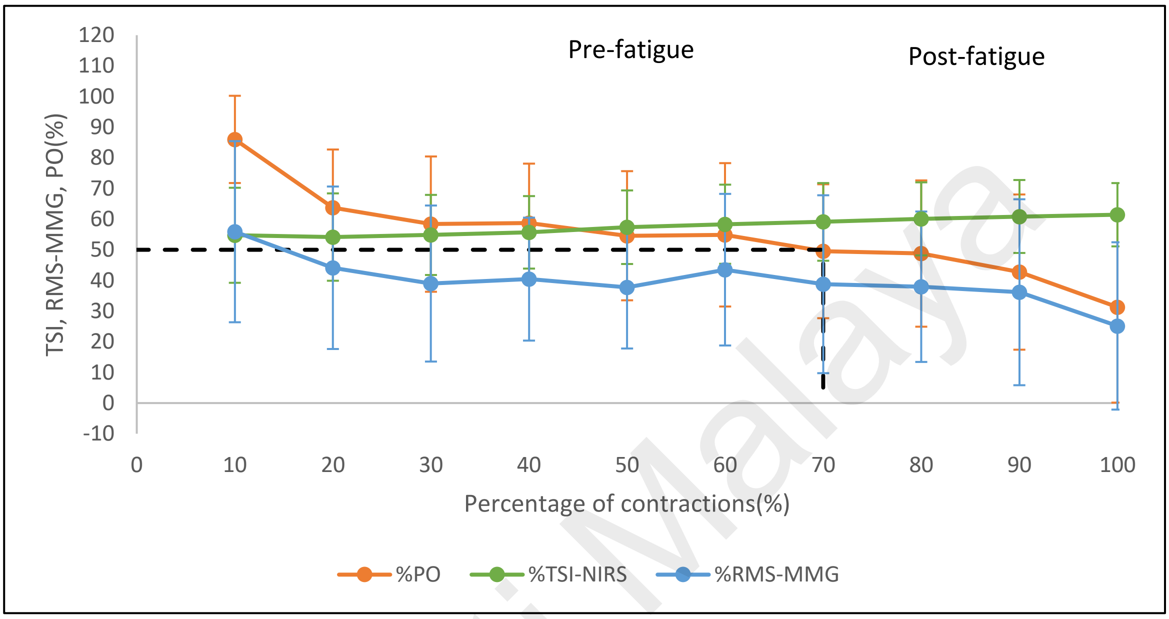

Figure 4.5: Mean of percentage of PO[19], percentage of TSI-NIRS[20] and percentage of RMS-MMG[21] plotted along percentage of contractions for Group A. Data are presented as mean and standard deviation[22].

For group A, correlation during pre-fatigue for %PO and %RMS-MMG pair showed negative correlations (r = -0.02, p = 0.63) but did not portray any significant value. On the contrary, these two parameters showed a significant positive correlation during post-fatigue (r = 0.30, p = 0.00).

Figure 4.6 showed an overall trend by group B where %RMS-MMG was seen increased to 50.78%. %PO on the other hand was seen declined from 75.99% to 13.90% as contractions progressed.

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[19] PO = power output
[20] TSI-NIRS = tissue saturation index from near infrared spectrocopy
[21] RMS-MMG = root mean square from mechanomyography
[22] Dashed vertical lines denote the point of fatigue (50% drop of PO) where correlations were done at two parts; pre- and post-fatigue.

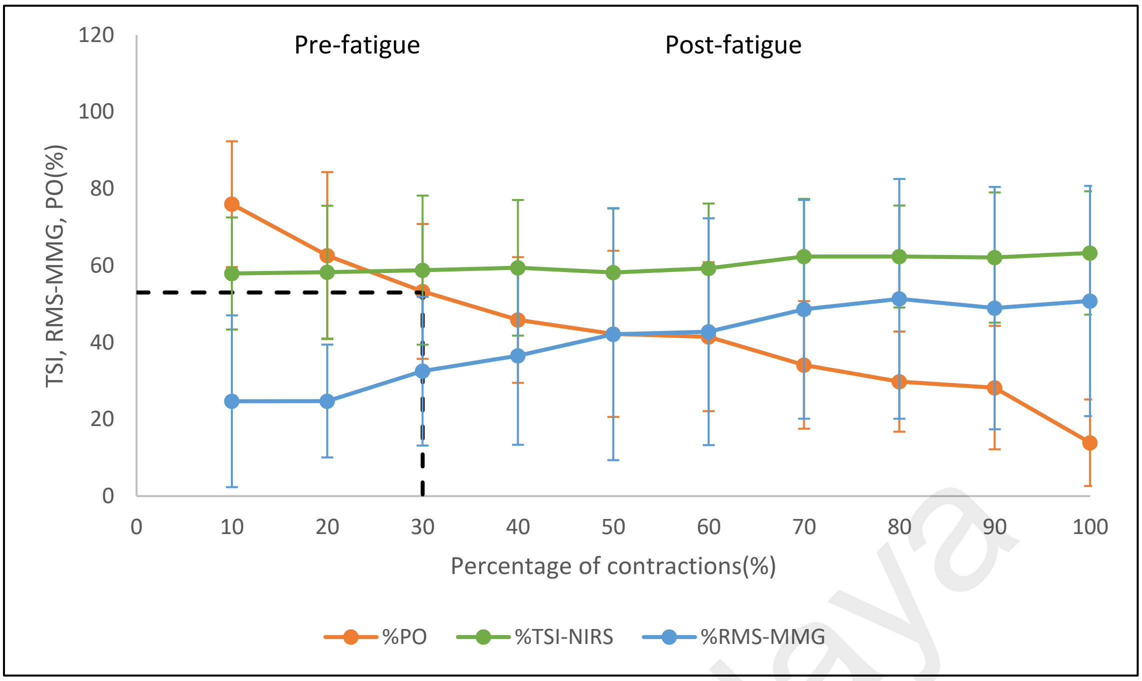

Figure 4.6: Mean for percentage of TSI-NIRS[23], percentage of RMS-MMG[24] and percentage of PO plotted along percentage of contractions for group B. Data are presented as mean and standard deviation[25].

As for group B, significant positive correlations were observed between %PO and %RMS-MMG (r = 0.25, p = 0.00) during pre-fatigue. During post-fatigue, a total opposite pattern was observed where %RMS-MMG moved in a different direction of decreasing %PO with significant and negative correlation (r = -0.14, p = 0.00).

4.2.2 Spinal Cord Injury Participants

Correlations were done between %PO and %RMS-MMG during pre- and post-fatigue. Correlation of this pair showed significant positive correlations pre-fatigue (r = 0.45, p = 0.00). On the other hand, significant correlation was observed post-fatigue where %PO and %RMS-MMG were positively correlated with each other (r = 0.19, p = 0.01).

Since the correlations were significant pre- and post-fatigue, no further correlation analysis was done as in AB participants. The correlation especially during post-fatigue in

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[23] TSI-NIRS = tissue saturation index from near infrared spectroscopy
[24] RMS-MMG = root mean square from mechanomyograpy
[25] Dashed vertical lines denote the point of fatigue (50% drop of PO) where correlations were done at two parts; pre- and post-fatigue.

SCI participants was similar with group A in AB participants, where %PO was positively correlated with %RMS-MMG. All the correlations of %PO and %RMS-MMG for AB and SCI participants were shown in Table 4.1.

Table 4.1: Correlation (r) between percentage of PO[26] and percentage of RMS-MMG[27] during pre-and post-fatigue[28].

Participants	**Pre-fatigue**		**Post-fatigue**	
AB Participants Overall	Correlation(r)	p-value	Correlation(r)	p-value
	0.07	0.06	0.05*	0.04
Group A	-0.02	0.63	0.30**	0.00
Group B	0.25**	0.00	-0.14**	0.00
SCI Participants	0.45**	0.00	0.19**	0.01

4.3 NIRS Signal during FES Wrist Extension Exercise

The second objective in this study was to investigate muscle oxygenation pattern during electrically-evoked muscle contraction to fatigue wrist extension exercise among AB and SCI participants. Muscle oxygenation pattern can be observed by extracting %TSI-NIRS and calculating muscle oxygen consumption from NIRS.

Besides correlation analysis where it measured the direction and how strongly %PO and %TSI-NIRS were related with each other, muscle oxygen consumption (mVO$_2$) also was calculated in SCI participants in order to answer the second objective. Correlation analysis was done during pre- and post-fatigue, while mVO$_2$ was calculated and compared before and after exercise.

4.3.1 Able Bodied Participants

Overall correlations between %PO and %TSI-NIRS during pre-fatigue showed positive correlations but did not have any significant values. On the other hand during

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[26] PO = power output
[27] RMS-MMG = root mean square from mechanomyography
[28] * correlation is significant at the 0.05 level (2-tailed) and ** correlation is significant at the 0.01 level (2-tailed)

post-fatigue, %PO and %TSI-NIRS pair was negatively correlated with each other (r = -0.16, p = 0.00).

In AB participants, there were two groups where it was separated by how %PO correlated with % RMS-MMG. Figure 4.5 shows an overall plot of group A for %PO, %TSI and %RMS-MMG against the percentage of contractions. %TSI-NIRS on the other hand increased by 6.71% with declining of %PO (-54.69%) as the percentage of contractions increasing. For group A, correlation during pre-fatigue for %PO and %TSI-NIRS showed negative correlations (r = -0.03, p = 0.54) but did not portray any significant value. Meanwhile during post-fatigue, %PO exhibited negative correlation but with significant value with %TSI-NIRS (r = -0.10, p = 0.01).

Figure 4.6 showed an overall trend by group B where %TSI was seen increased slightly by 5.26%. %PO on the other hand was seen declined from 75.99% to 13.90% as contractions progressed. As for group B, significant positive correlation was observed (r=0.12, p=0.04) during pre-fatigue. On the contrary, a total opposite pattern was observed where %TSI-NIRS moved in a different direction from decreasing %PO with significant and negative correlation (r = -0.11, p = 0.00).

4.3.2 Spinal Cord Injury Participants

Correlation during pre-fatigue for %PO and %TSI-NIRS portrayed a positive correlation (r= 0.13, p = 0.18) but did not show any significant value. In contrast, the correlation of %PO and %TSI-NIRS post-fatigue revealed a significant negative correlation (r = -0.46, p = 0.00). All the correlations of %PO and %TSI-NIRS for AB and SCI participants were shown in Table 4.2.

Table 4.2: Correlation (r) between percentage of PO[29] and percentage of TSI-NIRS[30] during pre-and post-fatigue[31].

Participants	**Pre-fatigue**		**Post-fatigue**	
AB Participants	Correlation(r)	p-value	Correlation(r)	p-value
Overall	0.02	0.53	-0.16**	0.00
Group A	-0.03	0.54	-0.10**	0.01
Group B	0.12*	0.04	-0.11**	0.00
SCI Participants	0.13	0.18	-0.46**	0.00

By observing the relationship of %PO in both %RMS-MMG and %TSI-NIRS, it was found that the results in SCI participants was similar to group A in AB participants especially during post-fatigue; where %PO was positively correlated with %RMS-MMG while %PO was negatively correlated with %TSI-NIRS.

Skeletal mVO$_2$ was measured as the rate of change in muscle oxygenation during brief arterial occlusions from changes in NIRS signals using linear regression. This technique assumes that changes of NIRS signal are proportional to mitochondrial oxygen consumption due to relative changes in hemoglobin and myoglobin saturation (Erickson et al., 2013). mVO$_2$ was taken pre- and post-exercise for 7 subjects (N=7). Figure 4.7 shows that mVO$_2$ significantly increased from 0.04 mlO$_2$·min^{-1}·100g^{-1} to 0.20 mlO$_2$·min^{-1}·100g^{-1} (p = 0.00) after exercise.

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[29] PO = power output
[30] TSI-NIRS = tissue saturation index from near infrared spectroscopy
[31] * correlation is significant at the 0.05 level (2-tailed) and ** correlation is significant at the 0.01 level (2-tailed)

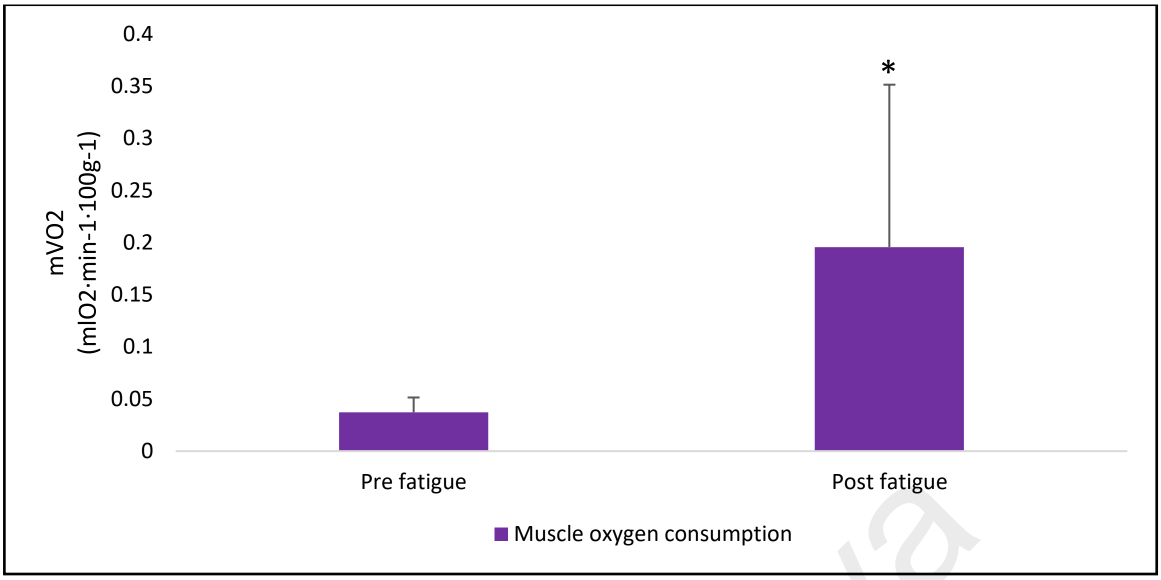

Figure 4.7: Muscle oxygen consumption pre- and post-exercise for SCI participants

4.4 Relationship between %RMS-MMG and %TSI-NIRS

The third and last objective was to determine the relationship between mechanomyography from MMG and muscle oxygenation from NIRS during electrically-evoked muscle fatigue in wrist extension exercise among AB and SCI participants. In order to accomplish this objective, correlation analysis was done between %RMS-MMG and %TSI-NIRS to see how strongly these two with each other.

In addition to that, relationship between %RMS-MMG and %TSI-NIRS was computed by regression analysis where two regression lines from %RMS-MMG and %TSI-NIRS were fitted to each decreasing %PO. Regression is a set of statistical analysis for estimating the relationships among independent and dependent variables; using %PO as the independent variable and %TSI-NIRS or %RMS as the dependent variables.

4.4.1 Able Bodied Participants

As for overall relationship between %RMS-MMG and %TSI-NIRS, they were weakly correlated during pre-fatigue (r = 0.05, p = 0.17) but displayed significant positive correlation post-fatigue (r = 0.36, p = 0.00).

In AB participants, there were two groups where it was separated by how %PO correlated with % RMS-MMG. For group A, correlation during pre-fatigue for %RMS-MMG and %TSI-NIRS portrayed positive correlations pre- and post-fatigue (r=0.16, p = 0.00 and r = 0.17, p = 0.00) and both of them were statistically significant.

Meanwhile for group B, weak positive correlation were observed during pre-fatigue (r = 0.02, p = 0.77) but changed during post-fatigue, where %TSI-NIRS exhibited a significant positive correlation with %TSI-NIRS (r = 0.51, p = 0.00).

Besides correlation, the relationship between %RMS-MMG and %TSI-NIRS was calculated statistically from two regression lines fitted to each decreasing %PO. Using %PO as the independent variable and %TSI-NIRS or %RMS as the dependent variables, while a_0 and a_1 were statistically determined regression coefficients, their relationships are represented by equations 4.1 and 4.2.

$$\%TSI = a_0\%PO + a_1 \tag{4.1}$$

$$\%RMS = a_0\%PO + a_1 \tag{4.2}$$

a_2 and a_3 are the new constants calculated from equations 4.3 describing the relationship between %RMS-MMG and %TSI-NIRS.

$$\%TSI = a_2\%RMS + a_3 \tag{4.3}$$

The regression equations of %RMS-MMG and %TSI-NIRS for group A and group B during pre- and post-fatigue were calculated respectively. For group A, the gradient changed from positive (0.70) to negative (-0.15) while in group B, the gradient stayed positive pre- and post-fatigue respectively (0.27, 0.35).

4.4.2 Spinal Cord Injury Participants

Correlation during pre-fatigue for %RMS-MMG and %TSI-NIRS portrayed a positive correlation during both pre- and post-fatigue (r = 0.40, p = 0.00 and r = 0.29, p = 0.00) with a significant value. All the correlations of %RMS-MMG and %TSI-NIRS for AB and SCI participants were shown in Table 4.3.

Table 4.3: Correlation (r) between percentage of RMS-MMG[32] and percentage of TSI-NIRS[33] during pre-and post-fatigue for AB participants[34].

Participants	**Pre-fatigue**		**Post-fatigue**	
AB Participants	Correlation(r)	p-value	Correlation(r)	p-value
Overall	0.05	0.17	0.36**	0.00
Group A	0.16**	0.00	0.17**	0.00
Group B	0.02	0.77	0.51**	0.00
SCI Participants	0.40**	0.00	0.29**	0.00

Similar with AB participants, the relationship between %RMS-MMG and %TSI-NIRS for SCI participants was calculated statistically from two regression lines fitted to each decreasing %PO using %PO as the independent variable and %TSI-NIRS or %RMS-MMG as the dependent variables. The gradient changed from positive (0.15) to negative (-0.23) pre- and post-fatigue respectively.

Table 4.4 shows the model for regression of %RMS-MMG and %TSI-NIRS for AB and SCI participants during pre- and post-fatigue respectively.

Figure 4.8: Model for regression lines from %TSI-NIRS[33] and %RMS-MMG[32] for AB participants.

	Model for %RMS-MMG and %TSI-NIRS	
Participants	**Pre-fatigue**	**Post-fatigue**
AB Participants Group A	$\%TSI = 0.70\ \%RMS + 22.36$	$\%TSI = -0.15\ \%RMS\ +\ 67.22$
Group B	$\%TSI = 0.27\ \%RMS + 53.10$	$\%TSI = 0.35\ \%RMS\ +\ 50.22$
SCI Participants	$\%\mathrm{TSI} = 0.15\ \%\mathrm{RMS} + 58.08$	$\%\mathrm{TSI} = -2.33\ \%\mathrm{RMS}\ +\ 100.95$

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[32] RMS-MMG = root mean square from mechanomyography

[33] TSI-NIRS = tissue saturation index from near infrared spectroscopy

[34] * correlation is significant at the 0.05 level (2-tailed) and ** correlation is significant at the 0.01 level (2-tailed)

4.5 Summary

In summary, AB participants exhibited two different patterns of %RMS-MMG post-fatigue which represented by group A and group B. Correlation analysis were done by three groups; %PO and %RMS-MMG, %PO and %TSI-NIRS and %RMS-MMG and %TSI-NIRS.

Based on the correlation of %PO and %RMS-MMG in group A, %RMS-MMG was positively correlated with %PO while in group B, %RMS-MMG was significantly negative correlated to %PO. On the other hand, regression analysis between %RMS-MMG and %TSI-NIRS showed inversely proportional relationship post-fatigue in group A while %RMS-MMG and %TSI-NIRS were proportional to each other post-fatigue in group B.

Following AB participants, SCI participants showed a similar pattern of %PO, %RMS-MMG and %TSI-NIRS as well as correlation and regression results with group A from AB participants. As for mVO_2 involving SCI participants, mVO_2 can be seen increased significantly post-fatigue compared to during pre-fatigue.

CHAPTER 5 : DISCUSSION

This chapter discusses all the findings in the study. All three sections in this chapter correspond to the three objectives in this study which are:

i. To investigate mechanomyography (MMG) signal responses during electrically-evoked muscle contraction to fatigue wrist extension exercise among AB and SCI participants.

ii. To investigate near infrared spectroscopy (NIRS) pattern during electrically-evoked muscle contraction to fatigue wrist extension exercise among AB and SCI participants.

iii. To determine the relationship between mechanomyography (MMG) and near infrared spectroscopy (NIRS) during electrically-evoked muscle fatigue in wrist extension exercise among AB and SCI participants.

The first section of this chapter describes the correlation of root mean square from MMG (%RMS-MMG) with %PO during wrist extension exercise. In the second section, the correlation of tissue saturation index pattern from NIRS (%TSI-NIRS) with %PO during wrist extension exercise will be explained. Result for muscle oxygen consumption (mVO2) pre- and post-exercise from NIRS also will be discussed for SCI participants. The third section of this chapter will be discussing on the relationship between %RMS-MMG and %TSI-NIRS and how they are relate with each other.

Due to the limited research from previous studies in SCI, it is important to investigate the relationship between MMG and NIRS in AB participants first since AB participants has more power in their muscle compared to the participants with SCI. From that, we can understand the natural behavior of the muscle during this type of exercise. In this study, AB and SCI participants were not compared against each other, but discussed separately.

Therefore, this chapter is divided into three sections with two sub-sections for each chapter; AB and SCI participants.

5.1 Correlation of %RMS-MMG against %PO

In order to achieve our first objective, correlation analysis was done between MMG signal which is %RMS-MMG and %PO during pre- and post-fatigue in AB and SCI participants.

The %RMS-MMG amplitude from the MMG signal varies and depends on the muscle fiber activation and increases with increasing muscle force as a result of the high contraction level and vice versa (Sarillee et al., 2014). The RMS feature of MMG may therefore correlate with muscle effort and was considered the most reliable parameter in the time domain (Al-Mulla et al., 2011).

5.1.1 Able Bodied Participants

5.1.1.1 Group A

Based on the correlation of %PO and %RMS in group A, %RMS-MMG was positively correlated with %PO, where both of them declined with increasing percentage of contractions post-fatigue. RMS signal varies and depends on the muscle fiber activation and therefore correlate with muscle effort (Sarillee et al., 2014). In this case, RMS decreased with decreasing muscle force as muscle became fatigued.

%RMS-MMG showed a consistent decline pattern throughout the exercise with the declining of %PO. Furthermore, during FES-evoked exercise, larger (fast) motor units with lower excitability threshold were recruited first before the slow twitch muscle units compared to physiological voluntary recruitment order. That was why FES evoked exercise caused a higher rate of fatigue in muscle compared to voluntary exercise causing a more rapidly decreasing %RMS-MMG (Gregory & Scott Bickel, 2005).

5.1.1.2 Group B

On the contrary, %RMS-MMG in group B was significantly negatively correlated to %PO during post-fatigue where %RMS-MMG increased as %PO declined. The increase of %RMS-MMG may be due to the probable recruitment of new single motor unit at low levels of effort (Orizio et al., 2003) as when the fresh muscle started to fatigue, new muscle unit recruitment occurred during exercise (Al-Mulla et al., 2011). This is possible as FES-evoked contractions accelerated muscle fatigue and as muscle started to become fatigued, new muscle unit will be recruited thus increasing %RMS-MMG.

In a voluntary movement, motor unit will be recruited from small which consist of slow motor unit followed by larger and fast motor units. In FES-evoked contraction on the other hand, pattern of motor unit recruitment became reversed where the larger motor unit will be recruited first prior to small (Bickel et al., 2011) and this pattern is more prone to fatigue.

Increase %RMS-MMG also may be due to the intramuscular pressure leading to impairment of the active muscle fiber dimension (Blangsted et al., 2005) in addition to swollen muscle fibers caused by osmotic phenomena and physiologic vibration during the prolonged exercise (Bajaj et al., 2002). Healthy subjects in this study might have faster muscle recovery rate. Muscle recovery affected the %RMS-MMG because the fatigued muscles have already recovered during the 4-sec rest period throughout the repetitive 4-sec contraction 4-sec rest exercise. This occurrence agreed with a study from Clarkson & Tremblay (1988) that an adaptation may have happened where the muscle was more resistant to damage and was repaired at a faster rate among healthy subjects during eccentric exercises (Clarkson & Tremblay, 1988).

5.1.2 Spinal Cord Injury

In SCI participants, %RMS-MMG showed a consistent decline pattern throughout the exercise by the decreasing %PO as they were positively correlated pre- and post-fatigue.

During FES-evoked exercise, previous study had suggested that it will result in recruiting larger motor units before the slow twitch muscle units compared to physiological voluntary recruitment order (Bickel et al., 2011) . This theory is based on two findings in which are the axons of the larger motor units have a lower excitability threshold and demonstrate an increased fatigue with FES compared to voluntary activation. That is why FES evoked exercise is more prone to fatigue (Gregory & Bickel, 2005).

However, Hettinga et al. (2007) stated that all fibres are activated simultaneously instead of a more selective pattern. This massive fiber contraction results in muscle ischemia, which can contribute to muscle fatigue. This concords with our findings that during the exercise, %TSI-NIRS declined pre-fatigue and this condition might cause ischemia to happen as there was insufficient oxygen supply for ECR muscle activation thus the decrease in muscle force represented by %RMS-MMG (Al-Mulla et al., 2011) indicating the muscle has become fatigued.

The decrease in %RMS-MMG also could easily happen in slow-twitch fibers at high contraction level (Yasuhide Yoshitake & Moritani, 1999). On top of that, paralyzed muscles have a higher proportion of Type II fibers, a reduced capillary capacity and a lower mitochondrial density (Lai et al., 2009). All of these factors affect muscle oxygenation and they might explain the early onset of muscular fatigue in this population. MMG also has been associated with intramuscular activities that related to muscle blood flow. During prolonged exercise, there may be an increase in intramuscular pressure that can cause active muscle fiber dimensional to change, leading to inefficient activation of muscles (Orizio et al., 2003).

5.1.3 Summary

Due to the different muscle properties in AB and SCI participants, different trends of %RMS-MMG were seen especially during post-fatigue.

In AB participants, two trends can be seen post-fatigue, where %RMS-MMG decreased in group A while %RMS-MMG increased in group B with declining %PO. As this is a fatigue experiment, %RMS-MMG was expected to decrease as contraction increases as in group A. However, the increase in %RMS-MMG observed in group B was due to the probable recruitment of a new single motor unit since AB participants have faster muscle recovery rate (Al-Mulla et al., 2011; Orizio et al., 2003). In addition, all AB participants also were right handed and this may have affected the results, as muscle in group B may be more resistant to fatigue compared to group A.

While AB participants exhibited two different pattern of %RMS-MMG, SCI participants only showed one pattern where correlations between %RMS-MMG and %PO showed positive correlation (%RMS-MMG decreased) pre- and post-fatigue. This was due to the continuous decreasing effort of the muscle during FES-evoked contractions as muscles in SCI showed less resistance to fatigue (Biering-Sørensen et al., 2009).

5.2 Correlation of %TSI-NIRS-NIRS and %PO

In order to accomplish the second objective in this study, correlation analysis was computed between %PO and %TSI-NIRS along with mVO_2. Correlation analysis was done during pre- and post-fatigue in AB and SCI participants, while mVO_2 was calculated and compared before and after exercise in SCI participants.

Tissue saturation index from NIRS (TSI-NIRS) on the other hand shows the average saturation of the underlying muscle tissue and calculated as $[O_2Hb] / ([O_2Hb] + [HHb]) * 100)$. It reflects the dynamic balance between oxygen supply and oxygen consumption in the tissue microcirculation (Buchheit & Ufland, 2011; Jones et al,, 2014; Billaut et al., 2013). Previous studies have shown that TSI reflects muscle oxygenation more accurately than HHb (Buchheit & Ufland, 2011; Sperlich et al., 2015). %TSI-NIRS therefore showed muscle oxygen utilisation more precisely than ΔO_2Hb and ΔHHB.

5.2.1 Able Bodied Participants

Muscle fatigue was defined as a decline in the ability of ECR muscle to produce power output (Enoka & Duchateau, 2008) and in this study, %PO decreased continuously as a percentage of contractions increased. During pre-fatigue, %TSI-NIRS showed negative correlation in group A (but not significant), while in group B, positive correlation (%TSI-NIRS declined) was observed along with declining %PO. The decrease in %TSI-NIRS pre-fatigue in group B was due to muscle deoxygenation as muscle needed greater oxygen release in order to meet the demands of the ECR muscle causing a larger oxygen debt (Taelman et al., 2011).

The drop in %TSI-NIRS may also be due to the decrease in the ability of oxygen to bind with hemoglobin in the blood known as Bohr Effect, where an increasing number of contractions quicken the production of lactic acid and thus releases hydrogen ions (H+) into the blood which then increasing carbon dioxide output in the blood (Stenberg, et al., 1967; Yoshitake & Moritani, 1999). Hence, the decrease may not be from the metabolic demand, but due to a greater release of oxygen from hemoglobin as part of the metabolic acidosis process.

While %PO decreased, %TSI-NIRS, on the other hand, progressed in a different direction as %PO as they were negatively correlated throughout the exercise in group A and B significantly post-fatigue. %TSI-NIRS gradually increased along with ΔO_2Hb throughout exercise and the findings showed similarities to findings by Muraki et al. where during exercise, StO_2 started to increase along with total haemoglobin and O_2Hb (Muraki et al., 2004).

A similar result can be found in this study where ΔO_2Hb increased with plateau ΔHHb indicating that blood flow was increased with the amount of blood supply exceeding the increased demand related to the contractions (van Dieen et al., 2009). These results suggested that the ability of the muscle to take up oxygen became limited at the middle of the FES-evoked exercise session even though there was enough oxygen supply because the muscle had become increasingly fatigued. It might also be due to a poor oxygen uptake of the ECR itself, and not because of poor oxygen supply into the muscles as ΔO_2Hb increased (Muraki et al., 2004).

As with $\%StO_2$, the general trend was an initial drop with a steady increase throughout the contraction and this trend was reportedly often found in healthy subjects (Elcadi et al., 2014), and this is similar with our study where %TSI-NIRS increased post-fatigue as exercise progressed.

5.2.2 Spinal Cord Injury Participants

In SCI participants, while %PO decreased, %TSI-NIRS on the other hand, progressed in the same direction during pre-fatigue as %PO as they were positively correlated. The same pattern was observed by other authors where arm cranking in healthy subjects showed an earlier decline in $\%StO_2$ due to muscle deoxygenation (Elcadi et al., 2014).

Muscle deoxygenation observed during the exercise as %TSI-NIRS decreased was probably due to a greater need for oxygen release in order to meet the demands of the ECR muscle causing a larger oxygen debt leading to a faster fatiguing process (Taelman et al., 2011). On top of that, McNeil et al. (2006) also concluded that metabolism affected by FES compared to voluntary contractions as FES invoked a greater energy demand.

The drop in %TSI-NIRS also may also be due to the decrease in the ability of oxygen to bind with hemoglobin in the blood known as Bohr Effect (Stenberg, et al., 1967; Yoshitake & Moritani, 1999). As this happened, %TSI-NIRS declined due to a greater release of oxygen from hemoglobin as part of the metabolic acidosis process.

In contrast, %TSI-NIRS increased with declining %PO during post-fatigue as they were negatively correlated and this pattern is similar with AB participants. StO_2 started to increase indicating good oxygen uptake during exercise (Muraki et al., 2004) along with increasing blood flow to the exercising muscles (van Dieen et al., 2009). These results was due to limitation of ECR to take up oxygen during FES-evoked exercise even though there is enough oxygen supply as the muscle has becoming fatigue.

Besides correlation of %PO and TSI, mVO_2 also was measured in order to investigate the muscle oxygenation pattern during FES wrist extension exercise. mVO_2 was measured as the rate of change in muscle oxygenation during brief arterial occlusions from changes in NIRS signals using linear regression. It was taken during rest and immediately after the exercise and the data were compared pre- and post-exercise. Figure 4.5 shows that mVO_2 increased post-exercise.

mVO_2 showed an increase due to the fatigue-induced exercise, based on the assumption of StO_2 represents the dynamic balance between oxygen supply and oxygen consumption in the tissue (Ferrari et al., 2004). The increase may be due to the recovery phase of the muscle from fatigue, therefore the muscle fibers require more oxygen to return back to its resting state. The same pattern was discovered on healthy subjects where mVO_2 of the vastus lateralis muscle increased after an exercise-induced muscle damage (Ahmadi et al., 2008). They concluded that after a single session of downhill walking, the muscle consumed more oxygen to perform other task of isometric contraction at given intensities.

5.2.3 Summary

%TSI-NIRS for both AB and SCI participants on the other hand were positively correlated (%TSI-NIRS declined) along with %PO pre-fatigue (except group A in AB participants but the result was not significant). The decrease in %TSI-NIRS was due to muscle deoxygenation as muscle needed greater oxygen release in order to meet the demands of the ECR muscle causing a larger oxygen debt (Taelman et al., 2011). Compared to type I motor units, muscles in SCI had more of type IIA/B, which contained lower oxidative capacity than type I (Lai et al., 2009) thus promoting muscle deoxygenation during pre-fatigue in SCI.

Conversely, %TSI-NIRS increased with declining %PO (negatively correlated) post-fatigue. The increase was related to the increasing blood supply exceeding the demand to the muscle as muscles need more oxygen during the exercise (van Dieen et al., 2009).

Additional data of mVO_2 was obtained from SCI participants, where it showed an increase after exercise due to the recovery phase of the muscle from fatigue since the muscle fibers require more oxygen to return back to its resting state (Ahmadi et al., 2008). This suggested that sustained FES-evoked wrist extension had affected the ECR muscle especially during post-fatigue.

5.3 Relationship between %RMS-MMG and %TSI-NIRS

The last objective for this study was to determine the relationship between MMG and NIRS and in order to accomplish this objective, regression analysis was done between %RMS-MMG and %TSI-NIRS where two regression lines from %RMS-MMG and %TSI-NIRS were fitted to each decreasing %PO.

5.3.1 Able Bodied Participants

5.3.1.1 Group A

In order to investigate the relationship between %RMS-MMG and %TSI-NIRS, regression analysis was done and their equations are presented in Table 4.4. Group A exhibited positive gradient during pre-fatigue and in this study, the positive gradient showed that the more negative %TSI-NIRS is, the more negative effect of %RMS-MMG becomes on %PO. The proportionality suggested that muscle deoxygenation observed as %TSI-NIRS declined as muscle needed an increased amount of oxygen in order to meet the demands of the ECR muscle during exercise (Taelman et al., 2011). Muscle force also was seen decreased along with %TSI-NIRS which represented by decreasing of %RMS-MMG (Al-Mulla et al., 2011).

Conversely, during post-fatigue, regression analysis between %RMS-MMG and %TSI-NIRS showed negative gradient. The inverse proportionality suggested that as the muscle becoming fatigue, the ability of the muscle to take up oxygen became limited even though there is enough oxygen supply (Muraki et al., 2004) as %RMS-MMG decreased as muscle effort decreased to fatigue (Al-Mulla et al., 2011).

5.3.1.2 Group B

Unlike group A, the gradient remained positive and unchanged during pre-and post-fatigue in group B. The muscle adaptation and recovery can also explain the lack of change in the gradient of the regression line during pre- and post-fatigue as %RMS-MMG and %TSI-NIRS were proportional to each other in group B. This is because muscle in AB participants recovered at a faster rate as their muscles are stronger.

As the exercise progressed, more blood supply was being delivered to the exercising muscle (van Dieen et al., 2009) along with the probable recruitment of new single motor unit (Orizio et al., 2003). These resulted in an increasing pattern for both %RMS-MMG and %TSI-NIRS.

From the equations in Table 4.4, small gradients in pre-fatigue and post-fatigue in both groups A and B suggested that %TSI-NIRS was not sensitive to the changes in %RMS. Small gradient supported that %RMS-MMG and %TSI-NIRS were mutually exclusive.

5.3.2 Spinal Cord Injury Participants

Regression analysis between %RMS-MMG and %TSI-NIRS in SCI participants showed similar results as group A from AB participants where a positive gradient was observed during pre-fatigue. The proportionality observed as %TSI-NIRS declined was with decreasing %RMS-MMG. On the other hand, during post-fatigue, regression analysis between %RMS-MMG and was inverse proportional to %TSI-NIRS.

From the equations in Table 4.4, the small gradient was observed during pre-fatigue showing that %TSI-NIRS was not sensitive enough to the changes in %RMS-MMG. On the contrary, as big gradient observed from the regression during post-fatigue, it is suggested that changes in %TSI-NIRS were sensitive enough to the changes in %RMS-MMG especially during post-fatigue in SCI.

5.3.3 Summary

The relationship between %RMS-MMG and %TSI-NIRS was investigated by regression analysis and in group A, %RMS-MMG and %TSI-NIRS were proportional to each other pre-fatigue and changed to inversely proportional post-fatigue. In group B, both variables were proportional to each other pre- and post-fatigue.

In SCI participants, regression analysis behaved similarly to what was observed in group A from AB participants where %RMS-MMG and %TSI-NIRS were proportional to each other pre-fatigue and changed to inversely proportional post-fatigue.

5.4 Overall Summary for All Parameters Investigated

In summary, it can be observed that FES-evoked exercise affected ECR muscle especially during post-fatigue in both AB and SCI participants. The summary of all the parameters are tabulated in Table 5.1. Most of the correlations showed significant result post-fatigue. This strongly suggested that sustained FES-evoked wrist extension had affected the ECR muscle, both physiologically and mechanically in a similar manner especially during post-fatigue.

Table 5.1: Overall summary for all parameters used in this study[35].

	AB Participants (Group A)	AB Participants (Group B)	SCI Participants	AB Participants (Group A)	AB Participants (Group B)	SCI Participants
Correlation	**Pre-fatigue**			**Post-fatigue**		
%RMS-MMG and %PO	Negative correlation	Positive correlation*	Positive correlation*	Positive correlation*	Negative correlation*	Positive correlation*
%TSI-NIRS and %PO	Negative correlation	Positive correlation*	Positive correlation	Negative correlation*	Negative correlation*	Negative correlation*
Regression	**Pre-fatigue**			**Post-fatigue**		
%RMS-MMG and %TSI-NIRS	Proportional	Proportional	Proportional	Inversely proportional	Proportional	Inversely proportional

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[35] * indicates significant correlation, $p<0.05$

CHAPTER 6 : CONCLUSION

In conclusion, both root mean square from MMG and tissue saturation index from NIRS are well associated with each other especially during post-fatigue and it has been verified in this study. These were reflected by the %RMS for MMG and %TSI for NIRS. It was also found that %RMS-MMG behaved differently in correlation and regression analysis especially after fatigue in both AB and SCI. %TSI-NIRS on the other hand progressed in a same manner for both AB and SCI. As AB and SCI participants had different muscle properties, it is expected that the results obtained also might differ.

To the best of our knowledge, this is the first study to examine wrist extensor muscle fatigue during FES in terms of mechanical and metabolic response recorded simultaneously in AB and SCI participants.

A combination of these two systems will provide more information from two different angle; muscle performance and metabolic concomitants during FES application. This will provide more understanding related to the mechanism of muscle fatigue and can contribute as an additional knowledge in the field. As muscle fatigued faster during FES, these information can be used in FES feedback mechanism where the system can monitor and predict fatigue during FES-evoked exercise.

This feedback mechanism can serve as a warning tool so that the users will know when to stop exercise before the muscle become more fatigued. This will help greatly in rehabilitation field especially for SCI, as this population lost their sensory and cannot sense fatigue themselves (Al-Mulla et al., 2011).

6.1 Recommendations for Future Work

i. Future works involving more AB and SCI participants respectively with larger age range would give better statistical result for this study.

ii. Besides RMS, other variables can be extracted as well from MMG in order to see how they are correlated with NIRS.

iii. Instead of analysing only TSI, O_2Hb, HHb and THb from NIRS can also be analysed in order to observe a clearer oxygen utilization of the muscle during exercise.

iv. It would be useful to add more statistical analysis to directly compare AB and SCI participants as we can see how different MMG and NIRS progressed in healthy and diseased muscle during FES

6.2 Limitations of Study

i. For this study, AB participants undergo one session of experiment. The results may provide more information if more sessions are being done.

ii. In this study, 7 SCI patients were recruited. Perhaps the results would be more convincing if there are more patients or longer duration of experiments.

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LIST OF PUBLICATIONS AND PAPER PRESENTED

The research described in this thesis has led to the presentations and publications of the following:

Journals

1. **N.S. Mohamad Saadon**, N.A. Hamzaid, N. Hasnan, M.A Dzulkifli, G.M. Davis. (2018). Electrically Evoked Wrist Extensor Muscle Fatigue throughout Repetitive Motion as Measured by Mechanomyography and Near-Infrared Spectroscopy. Biomedical Engineering / Biomedizinische Technik (BMT) (Published).
2. N. Hasnan, **N.S. Mohamad Saadon**, M. Teoh, N.A. Hamzaid, S. Ahmadi, G.M. Davis (2018). Muscle oxygenation during hybrid arm and functional electrical stimulation – evoked leg cycling after spinal cord injury. Medicine, 97(43), e12922 (Published).

Proceedings

1. N. Hasnan, **N.S. Mohamad Saadon**, M. Teoh, N.A. Hamzaid, S. Ahmadi, G.M. Davis. (2017). Muscle Oxygenation during Hybrid Arm and FES-evoked Leg Cycling after Spinal Cord Injury. International Functional Electrical Stimulation Society Conference. London Rehab Week 2017, 17th July–20th July 2017, London
2. **N.S. Mohamad Saadon**, N.A. Hamzaid, N. Hasnan, M.A. Dzulkifli, K.B. Gan, M. Teoh and G.M. Davis (2018). Muscle Oxygen Saturation Correlates with Muscle Mechanomyography during Prolonged Electrical Stimulation-Evoked Wrist Extension Exercise. The 10th International Conference on Robotics, Vision, Signal Processing & Power Applications (ROVISP2018), 14th August-15th August 2018, Penang (Published).