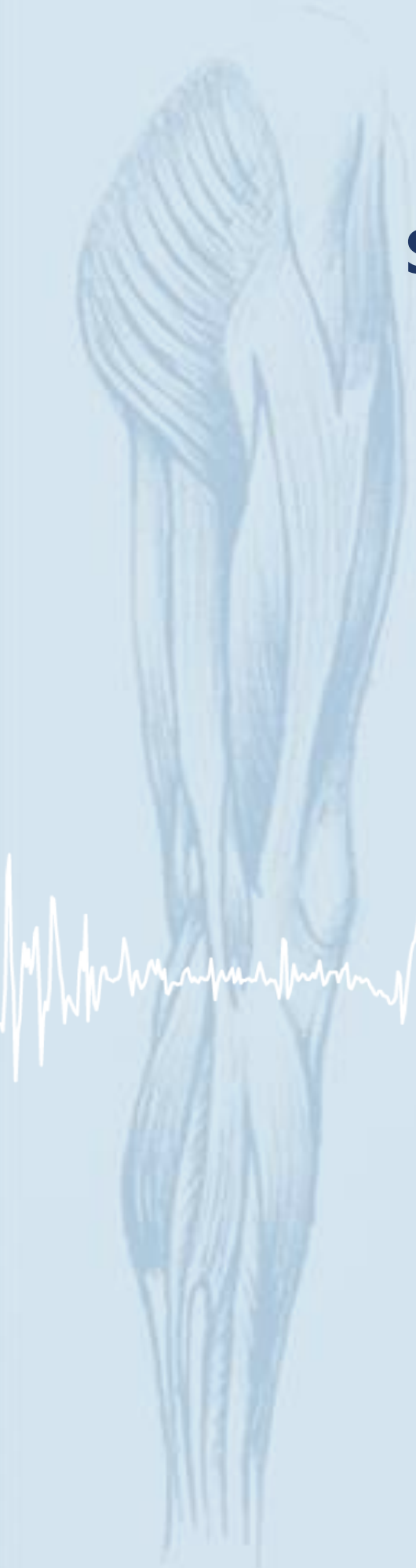
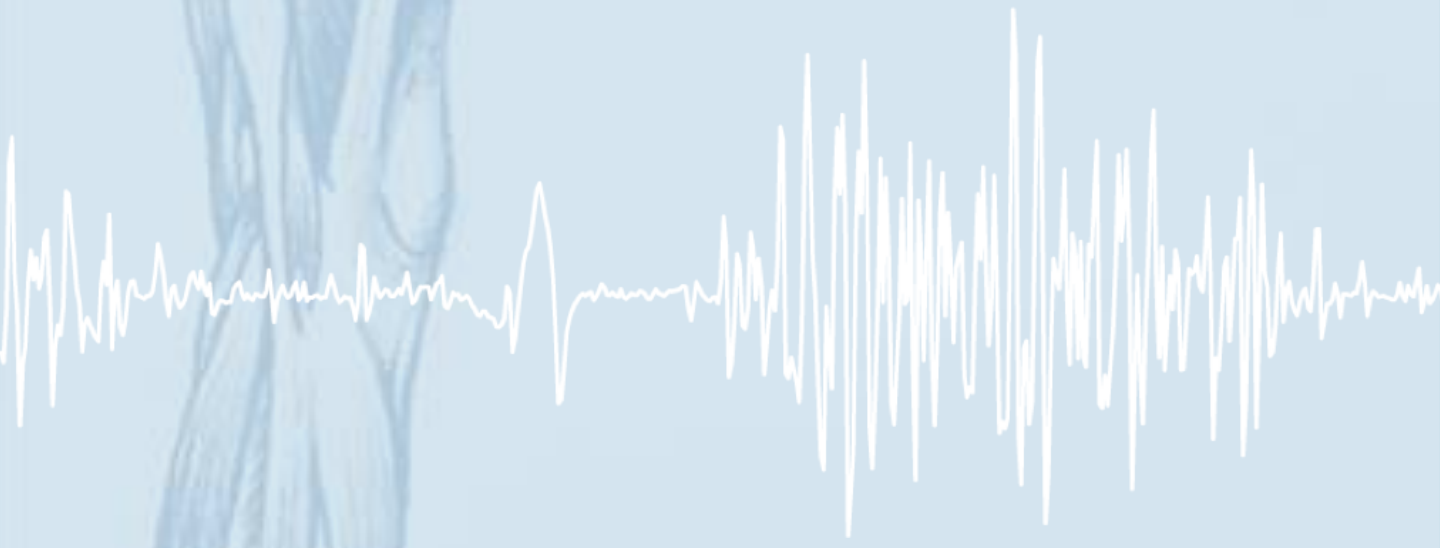


Spasticity Deciphered:
The effects of intrathecal baclofen treatment determined by electromyography in spasticity.

MSc. Thesis Technical Medicine

Center for Pain Medicine – Erasmus Medical Center

Roos Kolthof



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SPASTICITY DECIPHERED: THE EFFECTS OF INTRATHECAL BACLOFEN TREATMENT DETERMINED BY ELECTROMYOGRAPHY IN SPASTICITY.

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Preface

The end of my master thesis is also the end of almost eight years of studying. I am forever grateful for all the opportunities to improve myself on knowledge and experience. From the years of my Bachelor's, where I gained insights into my strengths and weaknesses. I then proceeded to complete my Bachelor's with an eye-opening minor in neuro-rehabilitation at Rijndam Rehabilitation Centre in Rotterdam, which helped me make the decision to pursue the Master's in Technical Medicine – Sensing and Stimulation track. I am thankful for the opportunities to gain comprehensive experience of the hospital setting during my master's internships. It has helped me to discover my genuine interests and skills. The final year of my master proved to be a significant period of personal growth and development. In particular, the period of study abroad in Lausanne has been an inspiring experience.

My interest in neurology and rehabilitation has been longstanding, but it was during my minor and my first year of the master's program that I began to grow. Completing my master's with a research project in the field of neuro-rehabilitation represented an ideal opportunity to finish my studies.

Throughout the writing of this thesis I have received a great deal of support and assistance. In particular, I would like to thank my supervisors, who have provided me with guidance and encouragement throughout the project. My technical supervisor, dr. ir. Cecile de Vos, for asking the relevant questions, which enabled me to gain deeper understanding of not only my project, but also myself. Furthermore, I would like to express my gratitude to my supervisor and thesis committee chair, Winfred Mugge, for sharing his experience and enthusiasm in research. As well as his comprehensive explanations on signal analysis, which were consistently supported by illustrations, helping me to understand the matter more effectively. Furthermore, I also want to thank my medical supervisor, drs. Eugene Quant, who has shared his profound knowledge on baclofen treatment and the distinctive characteristics of the patient population. But also for offering me the opportunity to present my research at the C4HC symposium. In addition, gratitude towards all members of the baclofen treatment team and C4HC team with whom I have had the privilege of working.

Lastly, I would like to thank all my colleagues in the Na-17 department for their support. Given by countless coffee breaks with baked sweets, calls on Python coding, and sharing knowledge. The opportunity to share this experience with such a group supported me during this period. And I would like to thank my roommate for supporting me at home and always being honest. Furthermore, I want to express my special thanks to my sister, who has consistently provided me with support, encouragement and enough post-its for my planning. And to my parents for always supporting me in finding my own path. And of course thank you to all my family and friends for supporting me in this period.

With my final thanks for my uncle, for sending his support to me.

Roos Kolthof
Rotterdam, May 2024

Abstract

Background
Spasticity is a condition that affects patients who have sustained an upper motor neuron lesion. Such lesions include for example cerebral palsy (CP), of which 35% is affected by spasticity, and stroke, of which 90% is affected by spasticity. Pharmacological therapy often involves the prescription of oral baclofen. However, due to the difficulty of medication in crossing the blood-brain barrier, high dosages of oral baclofen are required to achieve the desired therapeutic effect, which in turn leads to an increase of the incidence of negative side-effects. For patients with severe spasticity, the intrathecal baclofen (ITB) pump is indicated for more effective drug delivery. To monitor the efficacy of the treatment and quantify the level of spasticity, the Modified Ashworth Scale (MAS) is employed. Nevertheless, the moderate inter- and intra-rater reliability indicates that the subjectivity of the approach represents a potential limitation. Therefore, a more objective approach is required. Surface electromyography (sEMG) can measure direct muscle activity and is an objective and non-invasive approach. Yet, there is no research available on sEMG measurements to assess the change in muscle activity as a result of ITB treatment.

Objective
The primary objective of this exploratory study is to assess the effect of intrathecal baclofen on lower limb muscle activity using sEMG. The secondary objectives are assessing the correlation between the sEMG feature values and MAS scores, and between the sEMG feature values and Patient's Global Impression of Change (PGIC) scores.

Method
sEMG masurements were performed during standard assessment of the MAS on patients receiving an ITB single shot trial (SS) and/or pump implantation. The following features were analysed: (1) Root Mean Square (RMS), (2) Peak Amplitude Value (PAV), (3) Median Frequency, and (4) Co-Contraction (CCR). A comparative analysis was conducted to assess the change in mean feature value of each individual muscle between pre- and post-treatment for the purpose of study aim 1. The Spearman's rank correlation coefficient was calculated in order to assess the relationship between changes in feature values and changes in MAS scores. Furthermore, the Spearman's rank correlation coefficient was calculated to assess the relationship between the changes in most effective feature and the PGIC scores.

Results
A total of twelve patients were included in the study, diagnosed with a variety of conditions including spinal cord injury (SCI), multiple sclerosis (MS), traumatic brain injury (TBI) and CP. Following ITB treatment, the RMS demonstrated a statistically significant decrease for three out of eight muscles: the left semitendinosus *($p = 0.020$)*, the right rectus femoris *($p = 0.025$)* and the right tibialis anterior *($p = 0.002$)*. The PAV presented a decrease in 3-8 out of 10 patients following SS baclofen treatment. The changes in median frequency exhibited considerable variability between patients following ITB treatment. The CCR decreased in six out of ten patients for the left leg following SS baclofen treatment. A significant correlation was observed between the change in MAS scores and change in RMS in the medial gastrocnemius ($p = 0.027$) and the change in median frequency in the semitendinosus ($p = 0.002$). A low correlation was observed between the change in RMS and the PGIC score.

Conclusion
In conclusion, this study demonstrates the potential of sEMG features, such as RMS, in assessing the impact of ITB treatment on muscle activity. Future work could validate these findings by increasing the sample size and improving certain methodological aspects.

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Nomenclature

Abbreviations

Abbreviation	Definition
AUC	Area Under the Curve
BMI	Body-Mass Index
BTX-A	Botulinum Toxin Type A CCR
Co-Contraction Ratio	
CNS	Central Nervous System
CP	Cerebral Palsy
CSF	Cerebral Spinal Fluid
EMC	Erasmus Medical Centre
FFT	Fast Fourier Transform
GABA-B	Gamma-Aminobutyric Acid-B
ITB	Intrathecal Baclofen
LMN	Lower Motor Neuron
MAS	Modified Ashworth Scale
MS	Multiple Sclerosis
PGIC	Patient's Global Impression Scale
PAV	Peak Amplitude Value
PSD	Power Spectral Density
RMS	Root Mean Square
ROM	Range Of Motion
SCI	Spinal Cord Injury
sEMG	Surface Electromyography
SENIAM	Surface EMG for Non-Invasive Assessment of Muscles
SS	Single Shot
TBI	Traumatic Brain Injury
UMN	Upper Motor Neuron
X-ADL	X-linked Adrenoleukodystrophy

Symbols

Symbol	Definition	Unit
U	Voltage	[μV]
f	Frequency	[Hz]
t	Time	[s]

1 Introduction

1.1. Spasticity

Spasticity is a disease of the motor system of the human body, which is divided into upper and lower motor neurons. Upper Motor Neurons (UMN) initiate and modulate voluntary movements, while lower motor neurons (LMN) directly control the muscles that ensure the execution of these movements [2], as can be seen in Figure 1.1. A sign of an UMN syndrome is spasticity, which is defined by Pandyan et al. (2005) [3] as "*a disordered sensori-motor control, resulting from an upper motor neuron lesion, resenting as intermittent or sustained involuntary activation of muscles*". Damage to the UMN can be caused by stroke, traumatic brain injury (TBI), cerebral palsy (CP), spinal cord injury (SCI), and inflammatory, neurodegenerative, or metabolic diseases such as multiple sclerosis (MS) [4]. Of the above causes, spasticity affects approximately 35% of stroke patients, more than 90% of CP patients, about 50% of the TBI patients, 40% of the SCI patients, and between 37% and 78% of the MS patients [4]. Spasticity manifests through a range of symptoms, including muscle hypertonia, overactive reflexes, involuntary movements, contractures, muscle weakness, and pain [5]. As a result of these symptoms, patients experience limitations in activities of daily living, participation and in receiving care, leading to a reduced quality of life [6]. Therefore, the treatment of spasticity is a high priority in the rehabilitation plan of patients with UMN lesions.

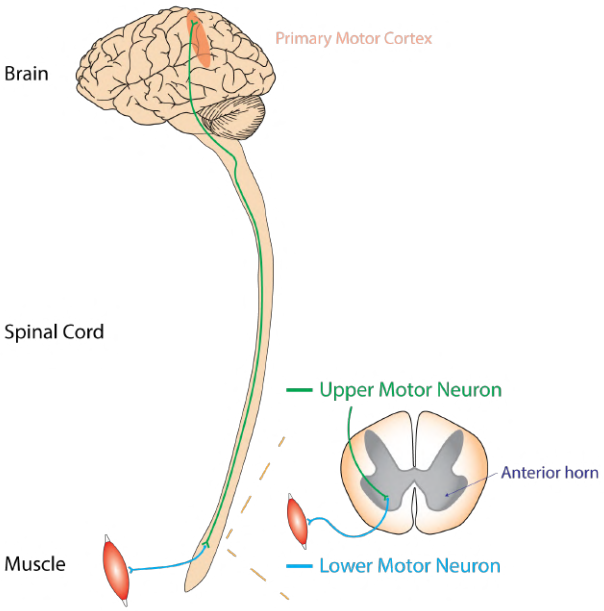


Figure 1.1: Illustration of the Upper and Lower Motor Neuron. [1]

1.2. Treatment

Early intervention strategies for spasticity include identifying and avoiding harmful stimuli such as infection, urinary retention or pressure ulcers. If these stimuli remain unaddressed or have already been addressed and the spasticity persists, the intervention will progress to include physiotherapy, such as manual stretching or the use of orthotics, and eventually pharmacotherapy [4]. Oral baclofen is the most commonly prescribed spasmolytic agent for pharmacological treatment, targeting the spinal cord centrally. It stimulates the gamma-aminobutyric acid-B (GABA-B) receptors, located in the central nervous system (CNS) leading to pre-synaptic suppression, resulting in reduction of spasms and sensitivity of reflexes. However, dose-dependent side-effects are described in studies on baclofen, such as sedation, drowsiness, fatigue, and dizziness [7, 8]. Furthermore, drugs have difficulty crossing the blood-brain barrier, so high oral doses are required to achieve a concentration in the Cerebral Spinal Fluid (CSF) that results in the desired therapeutic effect. However, increasing the dose of the drug increases the systemic bio-availability and therefore the risk of side effects [9].

1.3. Intrathecal Baclofen

An alternative approach can be considered for patients with severe spasticity, whose symptoms are under treated but also experience side-effects [9]. This alternative involves the direct delivery of low doses of baclofen to the intrathecal space of the spinal cord, via an implanted programmable pump with a refillable reservoir. Local administration of baclofen increases the concentration at the target site and reduces the risk of (systemic) adverse side effects. A screening test will be performed either as a single shot baclofen (SS) trial or by receiving an external pump for one week. The purpose of this test is to evaluate the response to baclofen. A positive response is characterized by a reduction in muscle tone, and improvement in functional capacity. If the initial test proves to be beneficial, a patient can be included for implantation of a permanent ITB pump [10].

1.4. Monitoring of treatment effect

For the evaluation of the screening test, the Modified Ashworth Scale (MAS) is used. This clinical scale is widely used to measure muscle tone, related to spasticity levels, using a 0-4 point scale, as can be seen in Table 1.1 [8]. The physiotherapist performs the measurements by moving the patient's limbs. Muscle activity is evoked by fast passive stretches. This scale is easily applicable in the clinical setting and does not require any additional hardware. However, this method is sensitive to subjectivity due to moderate inter- and intra-rater reliability [11]. The results are partly depend on the strength that the physiotherapist can deliver to counteract the muscle tension in the limbs, the training and the experience of the physiotherapist. In addition, the differentiation is limited to six levels, which restricts the ability to detect possible changes in muscle activity in response to treatment at higher levels of detail. It would be optimal to evaluate the screening test and eventual treatment effect of ITB using a more objective method with greater levels of differentiation.

Table 1.1: Descriptions of the Modified Ashworth Scale grades with, corrected grades used for calculation. [12].

MAS corrected for calculation	Grade	Description
0	0	Normal muscle tone
1	1	A slight increase in muscle tone, with a slight catch when the limb is moved in flexion and extension.
2	1+	A slight increase in muscle tone, with minimal resistance at the end of movement.
3	2	A more marked increased muscle tone through most of the Range Of Motion (ROM) but affects part(s) easily moved.
4	3	Considerable increase in muscle tone, passive movement difficult.
5	4	Affected part(s) rigid in flexion or extension.

1.5. Surface electromyography

Muscle activity can be detected by sEMG which is currently used by neurophysiologists in the clinic to diagnose neural pathology. This measure of skeletal muscle tone and functional capacity is objective and non-invasive, making it a suitable addition or alternative to the MAS. Literature presents different methods where sEMG is applied for spasticity quantification. Abraham et al. (2015) [13] used sEMG measurements to observe changes in muscle activity after surgery in patients with compressive cervical myelopathy. The researchers concluded that surface electromyography (sEMG) is an objective tool for detecting improvements in spasticity following surgical treatment. Even in patients who did not show an improvement in MAS, sEMG was able to detect improvements in spasticity after treatment. Lee et al. (2008) [14] used sEMG to measure changes in elbow spasticity over time following botulinum toxin type A (BTX-A) injection in the upper extremities of stroke patients. This study on BTX-A effect, demonstrated the ability to detect early spasticity relapse. Furthermore, the quantitative approach using sEMG, demonstrated by Lee et al. and Abraham et al, provides valuable information for clinicians when making decisions regarding additional rehabilitation interventions. However, no results are presented on the change in muscle activity after intrathecal baclofen treatment, measured by sEMG in adults.

1.6. sEMG features

For this exploratory study, I have chosen features from either the time *(t)* or frequency *(f)* domain to analyse sEMG signals [15]. This decision was based on my literature review, see Appendix O. In the time domain three features were extracted, in the frequency domain one feature:

Root Mean Square (t)
The RMS of the sEMG signal is frequently described in literature and is a measure of muscle activation intensity [16]. A study of Hu et al. (2018) [17] described the correlation between the RMS value and the muscle tension (as a measure of spasticity). They concluded that a higher mean RMS value indicates an increase in muscle tension.

Peak Amplitude Value (t)
Cooper et al. (2005) described the PAV for evaluating stretch responses to determine the validity of the MAS as a measure of spasticity. The hemiparetic patient group showed a higher PAV compared to the healthy control group [18]. The sEMG amplitude is often analyzed using the signal envelope, which is derived by rectification and low-pass filtering. The term ”amplitude of sEMG” is used in the literature to describe the voltage variation of the sEMG signal, defined as the signal’s time-varying standard deviation [19]. In other words, it describes how the peak amplitude of the sEMG signal fluctuates or changes throughout the duration of the measurement. The standard deviation is therefore important in the calculation of the amplitude value, as it accounts for individual differences in baseline sEMG activity.

Median Frequency (f)
The spectral characteristics of sEMG can provide valuable insights into motor unit synchronization and recruitment [20]. To assess changes in the frequency spectrum for this study objective, the median frequency was calculated. This value reflects the frequency content of an action potential. The frequency content is related to the size of the motor units responsible for generating the action potential. The power spectrum is divided equally on both sides of the median frequency [21].

Co-Contraction Ratio (t)
Activation of the antagonist muscle, while the agonist muscle is activated, is called co-contraction and leads to joint stiffness [22]. Current clinical methods for evaluating co-contraction are limited, but understanding its mechanism could enhance patient rehabilitation [23]. Ohn et al. (2013) used the CCR to measure spasticity induced co-contraction. Finding higher CCR values in affected upper limbs of stroke patients, compared with the unaffected upper limbs of the patients and the dominant upper limbs of the healthy subjects. Additionally, patients with higher MAS scores were found to have higher CCR values [22]. For this study the CCR approach will be applied to evaluate the effect of baclofen on co-contraction [22].

1.7. Study aim

The primary aim of this exploratory study is to assess the effect of ITB on muscle activity in the lower limbs using sEMG. Feasibility of sEMG recordings during MAS assessment has been established at the Erasmus Medical Center (EMC).

- **Study aim 1: To assess the effect of ITB on lower limb muscle activity using sEMG.**
  The objective focuses on assessing whether sEMG can detect changes in muscle activity during passive movements, resulting from intrathecal baclofen treatment. This involves evaluating differences in sEMG feature values from pre- and post-treatment measurements.
- **Study aim 2: To assess the correlation between sEMG feature values and MAS scores.**
  The objective is to investigate the potential correlation between the MAS scores and the calculated sEMG features. This information can contribute to future research on quantification of spasticity using sEMG.
- **Study aim 3: To assess the correlation between sEMG feature value differences and Patient Global Impression of Change (PGIC) scale.** The patient’s perspective on the changes following ITB treatment provides valuable insights beyond the obtained MAS scores. Both the Modified Ashworth Scale (MAS) and patient experience are subjective. Therefore, a comprehensive analysis using multiple measures is recommended [24].

1.8. Hypotheses

1.8.1. Aim 1: Electromyography Features

The following section outlines my expectations regarding the change of each feature after ITB treatment.

Root Mean Square (t)

An increase in the mean RMS value indicates an increase in muscle tone [17]. This is due to the activation of alpha-motor neurons in a reflex response to passive motion, which leads to an increase in excitation of motor neurons and thus electrical activity. After administering baclofen, the release of excitatory neurotransmitters is suppressed by the GABA-B receptors, resulting in a muscle relaxant effect. This leads to less muscle activity and therefore less electrical activity. Based on this, I hypothesize that there will be a decrease in mean RMS values after ITB treatment.

Peak Amplitude Value (t)

In previous research using the PAV a higher value was observed in spastic hemiparetic stroke patients. Additionally, a significant increase in PAV was observed in the sEMG response between contracted muscles compared to non-contracted muscles [18]. The suppression of the GABA-B receptors by baclofen will result in less activation of motor units. Since the PAV is directly related to the amount and size of activated motor units of the muscle, I hypothesize that there will be a decrease in PAV after ITB treatment.

Median Frequency (f)

Hyperpolarization of presynaptic type 1a inhibitory neurons is caused by the binding of baclofen to GABA-B receptors. This makes it more difficult for the neurons to reach the action potential threshold. Consequently, the action potential of the postsynaptic motor neurons that innervate the muscle spindles is reduced. This leads to fewer activated muscle spindles and a decrease in spasticity [10]. In addition, larger motor units require more depolarization to reach the action potential threshold and are represented in the spectral analysis by higher frequency values compared to smaller motor units [25]. As baclofen impedes the depolarization of motor neurons and larger motor units require more energy to reach the action potential threshold, I hypothesize that the median frequency will increase following baclofen administration. This is based on the knowledge that low-frequency components in sEMG signals are often associated with larger motor units composed of slow-twitch muscle fibers [26].

Co-Contraction Ratio (t)

The results of Ohn et al. [22] presented significant differences between the CCR of stroke patients, compared to the unaffected upper limbs of the patients and the dominant upper limbs of the healthy subjects. I hypothesize that there will be a decrease in the CCR after ITB treatment, since these results indicate that a lower CCR is associated with a reduction in spasticity. And the anticipated treatment effect of ITB is reduction of spasticity.

1.8.2. Aim 2: Modified Ashworth Scale

In my secondary objective I aim to assess the correlation between feature values extracted from sEMG data and MAS scores. The comparison between the MAS and sEMG features may be affected by the subjectivity of the MAS due to moderate intra- and inter-rater variability. Therefore, I expect a moderate correlation between the sEMG feature values and MAS scores.

- **Root Mean Square:** for the RMS I expect to see a decrease after ITB administration. I expect to observe a similar trend for the MAS score after administration. Consequently, I expect a moderate positive correlation between the RMS and MAS.
- **Peak Amplitude Value:** I expect that a moderate positive correlation will be observed for the PAV. Since it is expected that this feature will demonstrate a decrease following ITB administration.
- **Median Frequency:** I expect that the median frequency will increase following ITB administration. Conversely, it is expected that the MAS score will exhibit a decrease, thereby demonstrating a moderate negative correlation between the two.
- **Co-Contraction Ratio:** I expect the CCR to decrease after ITB treatment. However, the MAS is not designed for clinical quantification of co-contraction. Therefore I expect a low positive correlation between the CCR and MAS score.

1.8.3. Aim 3: Patient's Global Impression of Change

Assessing an objective evaluation method is informative, but patient experience should not be forgotten. To capture information from the patient's perspective on the severity of spasticity symptoms, several rating scales are available: the Numeric Rating Scale for Spasticity (NRS-S) and the PGIC scale. According to literature, there is a consistent association between the validity of these scales [27]. In my study the PGIC is used, and clinically important improvement is considered by a score of 'much improved' and 'very much improved' (2 and 1 points out of 7 on Likert scale) based on literature [27]. When for example the sEMG feature RMS presents a small decrease after treatment with baclofen, the effect of this decrease can be experienced differently for each patient. This depends on the severity of the spasticity and how the patient responds to ITB treatment. But also on the patient's mindset, cognitive ability and expectations. I expect to see a moderate correlation between the PGIC score and the sEMG feature value differences. I expect a low correlation between the MAS scores and the PGIC, since both are subjective measures. This comparison offers useful information since it translates on how well the patient can quantify the effect of treatment, compared to how it is quantified clinically.

2
Methods

This study is a mono-centre, prospective, explorative study in Erasmus Medical Centre, Rotterdam. The objective was to assess the effect of ITB on muscle activity in the lower limbs using sEMG. sEMG measurements were performed in participants receiving an ITB screening test as single shot (SS) and/or a permanent implanted ITB system for treatment of spasticity. The retrieved sEMG signals were analyzed by the chosen features.

2.1. Population

From November 2023 to March 2024, patients who received baclofen treatment were recruited. All participants had to meet the following inclusion criteria: (1) Receiving a SS ITB or permanent implanted ITB system; (2) experiencing unilateral or bilateral spasticity in the lower limbs; (3) able to undergo MAS and sEMG measurements; (4) capable of understanding and complying with verbal instructions. The following exclusion criteria were applied: (1) age under 18 years old; (2) high sensitivity of lower limb skin. The Medical Ethical Committee of the Erasmus MC approved the study and all patients provided written informed consent before data collection and assessment.

2.2. MAS Assessment

Measurements were performed during the standardized MAS assessment before and after treatment with ITB (either SS or implantation). The newest version of the MAS includes six different levels of spasticity, see table 1.1. The physiotherapist moves the limb, creating a fast passive stretch on the muscle of interest, to evaluate the spasticity level. For each muscle this movement was repeated three times. The hip flexors and extensors are evaluated through flexion and extension movements of the hip, with the knee joint placed in a 90-degree angle. Subsequently, the adductors are assessed through adduction of a stretched leg. This is followed by the rectus femoris, which is tested by placing the hip in 90 degrees and performing knee flexion. Subsequently, the hamstring is evaluated by positioning the knee at a 45-degree angle and allowing the knee to bend until the leg is fully extended. Finally, the hip and knee joint are positioned at a 90-degree angle and the dorsiflexion of the foot is performed to assess the soleus muscle. The same movement is performed to assess the gastrocnemius muscle, but now with a stretched hip and leg. See table 2.1 for an overview of the muscles groups evaluated during the procedure and see Appendix A for a visualisation of the movements performed during MAS assessment. Four muscles were identified for each leg: the medial gastrocnemius, rectus femoris, semitendinosus, and tibial anterior muscles, as can be seen in Figure 2.1. The following section provides an explanation of the muscle's localisation and function.

Abbreviation	Muscle Group
Rest	30 seconds of rest, no contact with the bed or patient
MAS HFHE	Hip Flexors and Extensors
MAS AD	Adductors
MAS RF	Rectus Femoris muscle
MAS HAM	Hamstrings: semitendinosus, biceps femoris, semimembranosus
MAS SOL	Soleus muscle
MAS GAS	Gastrocnemius muscle

Table 2.1: Abbreviations and corresponding muscles groups of the Modified Ashworth Scale assessments.

2.2.1. Muscles of interest

Rectus Femoris muscle

The rectus femoris is one of the four muscles that form the quadriceps group in the thigh. It functions as a hip flexor and knee extensor, opposing the action of the hamstrings. The muscle has two origins: the anterior inferior iliac spine (AIIS) and acetabular ridge on the ilium bone. It inserts proximally on the straight head and reflected head of the ilium bone, and distally at the patella as the ligamentum patellae, see figure 2.1a. [28]

Semitendinosus muscle

On the posterior side of the thigh the semitendinosus muscle is located, medial to the biceps femoris and lateral to the semimembranosus. This group of muscles is also known as the hamstrings. The semitendinosus originates from the ischial tuberosity of the pelvis. This insertion is at the upper part of the medial surface of the tibia, as can be seen in figure 2.1a. This makes the muscle a bi-articular muscle with hip extension and knee flexion as main function. [29]

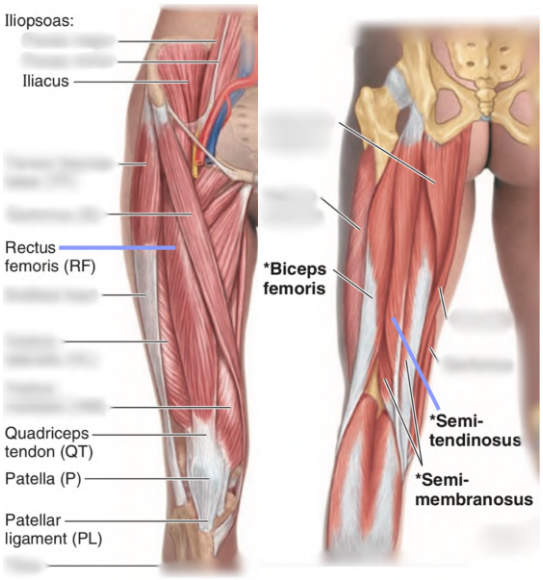
Medial Gastrocnemius muscle

The medial gastrocnemius muscle is one of the posterior lower limb muscles that make up the triceps surae. The triceps surae consists of three heads, the medial and lateral gastrocnemius heads and the deep soleus head. This group of muscles is responsible for plantar flexion and supination of the foot and knee flexion. It originates from the medial condyle of the femur and inserts on the calcaneus with the achilles tendon, as shown in figure 2.1b [30]

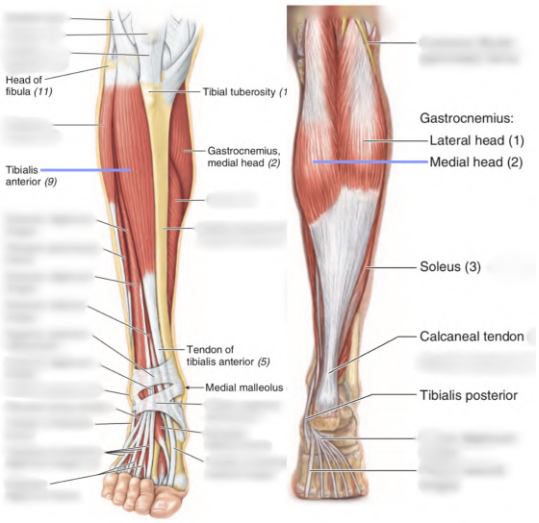
Tibial Anterior muscle

Four muscles are located on the anterior side of the lower leg, with the tibialis anterior muscle being the largest, see figure 2.1b. It originates from the lateral tibia and inserts at the distal medial border of the foot, playing a crucial role in dorsiflexion and inversion of the foot [31].

The rectus femoris and semitendinosus function as antagonistic muscle pairs. Similarly, the tibialis anterior and medial gastrocnemius function as antagonistic muscle pair. In cases of spasticity, the rectus femoris and medial gastrocnemius tend to generate more force compared to the semitendinosus and tibialis anterior. As a result, fixed postures of knee extension together with hip flexion and plantar flexion and inversion of the foot are more likely to be observed.



(a) Representation of the anatomy of the rectus femoris and semitendinosus muscle (marked with purple).



(b) Representation of the anatomy of the medial gastrocnemius and tibial anterior (marked with purple).

Figure 2.1: Overview of the anatomy of the lower limbs. Defining the location and orientation of the muscles of interest. Images retrieved from MOORE Clinically Orientated Anatomy [32].

2.2.2. Preparation

The protocol of SENIAM [33] (Surface EMG for Non-Invasive Assessment of Muscles) for non-invasive assessment of muscles was followed for the placement of the electrodes and preparation of the skin, see Figure 2.2 for electrode locations. This included identification of the belly of each corresponding muscle and after that scrubbing with scrub-gel (Nuprep, Weaver and Company, USA) and disinfecting with sanitizer (Sterillium MED, Hartmann Group, Germany). On the belly of each corresponding muscle two electrodes (Red Dot snap electrodes, 3M, Minnesota, USA) were attached 2 cm apart, for a bipolar signal registration. Additionally, the reference electrode was placed on the patella and the ground electrode on the opposite, lower leg. The electrodes were connected to the EEG headbox, functioning as amplifier (Schwarzer AHNS, Schwarzer GmbH, Germany), by snap-on EMG cables (Reusable snap leads, 2m cable, 5/pk, Natus Neurology, Wisconsin, USA). The headbox was connected to a computer, that ran software (BrainRT, BrainLab, Germany) for data sampling (fs = 2,0 kHz) and storage. Before starting a measurement all other electronic devices were disconnected from the power socket to reduce noise.

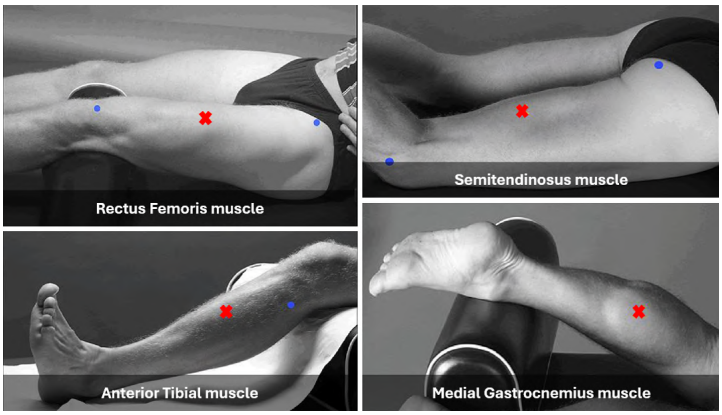


Figure 2.2: Red crosses mark the location for electrode placement, which is the belly of the muscle. The blue dots mark the location of the origo and insertion of the muscle. Images retrieved from SENIAM protocol [33].

2.2.3. sEMG Recording

Each measurement started with a period of 30 seconds rest, during which the patient was positioned lying horizontally in bed and asked to relax as much as possible. No contact was permitted with the bed or patient during this period. This rest period was followed by the standard procedure of the MAS assessment. In order to be able to calculate the different MAS scores for further evaluation, the following correction is applied. A score of 1+ is corrected to 2 and so on until MAS score 4 (corrected 5), as can be seen in Table 1.1. For more accurate analysis the repetitions of each MAS sub-type were manually labelled in BrainRT, with the corresponding muscle name. Each measurement session started with the left leg, followed by the right leg after repositioning the snap-on electrodes.

2.3. sEMG analysis

Raw sEMG signals were exported from BrainRT as .EDF+ files, together with the time labels as .XML files. The pre- and post- baclofen measurements were performed on both legs, resulting in four file sets per participant, per event (either SS or implantation). The files were named according to the participant ID and measurement number. This measurement number referred to the the type of event (1-4 = SS, 5-7 = implantation), with the odd numbers corresponding to the left leg, and even numbers to the right leg. The data of the MAS assessments of the adductor muscles (MAS AD) and soleus muscle (MAS SOL) were left out of the analysis, since these muscles were not recorded with sEMG. For further data analysis Python 3.12.0 was used within the Spyder 5.5.0 environment. A complete overview of the sEMG data processing is visualized in Appendix B.

2.3.1. Re-referencing

The initial stage of data analysis involved re-referencing the EDF+ files to correct for bipolar measurement set-up during data sampling. A reference channel was used during the measurements to record background noise. To eliminate the recorded noise, the reference channel was subtracted from the bipolar channels of each muscle, see Equation 2.1. Next, new virtual channels were defined by taking the difference between the anode and the corresponding cathode, see Equation 2.1 as well, where one represents the anode, and two the cathode. This was calculated for each measured muscle, which resulted in a data frame of four channels, corresponding to the four muscles.

$$Y(t) = X_1(t) - X_2(t) \tag{2.1}$$

2.3.2. General Pre-processing

To improve data quality, the sEMG data was pre-processed. The first step was to remove 50 Hz in the frequency domain to eliminate noise from the mains current. To achieve this, each channel was converted to the frequency domain, using the Fast Fourier Transform, see Equation 2.2. To reduce the impact of this interference, the magnitude values of time samples covering frequencies between 49.9 and 50.1 Hz were set to zero. Following this, the signal was corrected using a fourth-order Butterworth bandpass filter (15-500 Hz). For the time labels, the software applied a sampling frequency that was twice as small as the sampling frequency of the sEMG signal. Therefore, the .XML files had to be corrected by a factor of 2. To extract the sEMG data of interest, the labels were used as the extraction method. Only the data samples within the labelled time windows were stored in a new data frame with the corresponding assessment labels, as defined in Table 2.1 .

$$X(k) = \sum_{n=0}^{N-1} x(n) \cdot e^{-j2\pi \frac{kn}{N}} \tag{2.2}$$

where:

- $X(k)$ is the FFT output at frequency bin k
- $x(n)$ is the input signal sample at time n
- N is the total number of samples in the input signal
- k is the frequency bin index, ranging from 0 to N-1
- j an imaginary unit, $j^2 = -1$

2.3.3. Root Mean Square

The RMS is a representation of the average power of the signal, over a defined set of samples. It was calculated by taking the square root of the mean of the squares of the sample values, see Equation 2.3. Interpreting the RMS value in sEMG analysis provides insights into the muscle activation level. The RMS value was calculated for each time window of a MAS assessment, as can be seen in Figure 2.3. As each type of MAS assessment is repeated three times, this resulted in three RMS values, for each assessment, per measurement.

$$rms = \sqrt{\frac{x_1^2 + x_2^2 + x_3^2 ... + x_n^2}{N}} \tag{2.3}$$

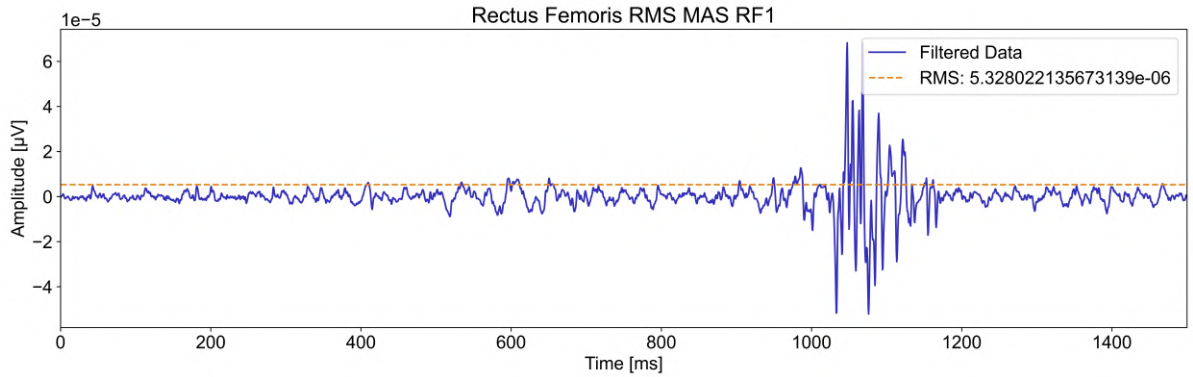


Figure 2.3: Representation of the Root Mean Square (orange dotted line) of an sEMG signal of a fast passive stretch reflex. It is a representation of the rectus femoris (RF) muscle during the first repetition of the MAS assessment of the rectus femoris (MAS RF1).

2.3.4. Peak Amplitude Value

To enable comparison of the PAV among different muscles, over time, and between individuals, it is necessary to normalise the sEMG signal. This means it must be normalised in relation to a reference value obtained under standardised and reproducible conditions [34]. Therefore, the approach defined by Cooper et al. [18] was used for this study to calculate the PAV, see Equation 2.4. In the equation the mean value and standard deviation of the sEMG data during 30 seconds of rest for normalization are used. Furthermore the highest peak value of the corresponding time window was used by Cooper et al. for analysis. However, this creates the risk of calculating the PAV based on an outlier. Therefore, the ten highest values within the defined time frame were detected, where 6-10 were averaged. This averaged peak value is used for the parameter *PeakEMG* in Equation 2.4.
Prior calculating the PAV, additional pre-processing was conducted based upon the pre-processing steps of Cooper et al. The signals generated by the muscles contained both positive and negative values. To obtain the linear envelope, full-wave rectification was applied to ensure no loss of relevant data when averaging. A low-pass Butterworth filter of 100 Hz was used (second order, zero phase lag). Zero phase lag means that the filter was applied bidirectional to correct for phase lag shifts. A second order filter results in a 12 dB correction, thus bidirectional filtering results in 24 dB correction. Figure 2.4 presents a visualisation of the PAV of the sEMG signal during a MAS repetition.

$$PAV = \frac{(PeakEMG - MeanRestingEMG)}{SDRestingEMG} \tag{2.4}$$

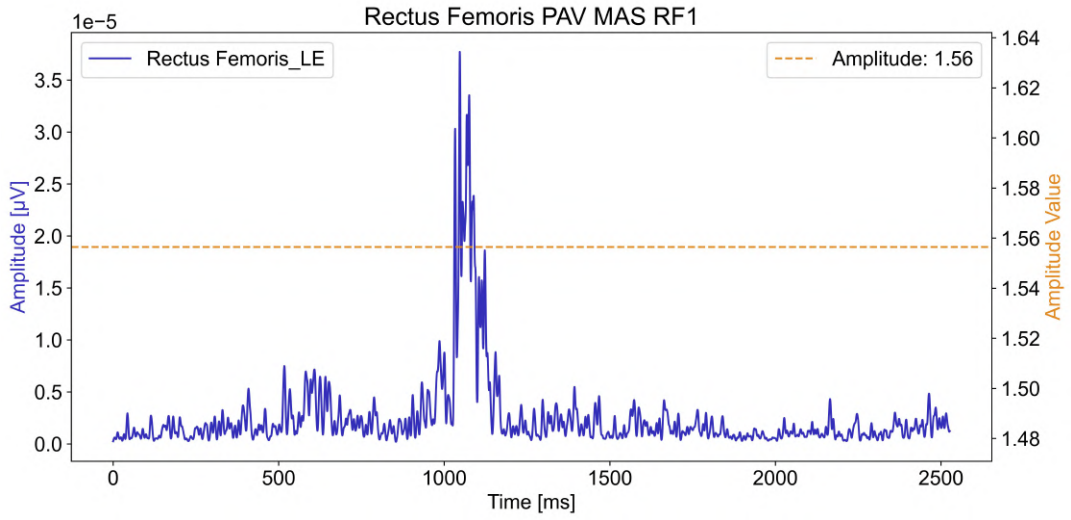


Figure 2.4: Representation of the Peak Amplitude Value (orange dotted line) of an sEMG signal. It is a representation of the rectus femoris (RF) muscle during the first repetition of the MAS assessment of the rectus femoris (MAS RF1).

2.3.5. Median Frequency

Power Spectral Density - Welch's Method

Power Spectral Density was conducted for spectral analysis of the median frequency of the sEMG signal. Analysing the signal in the frequency domain provides additional insight into the distribution of frequencies and their corresponding magnitudes or power. The PSD was calculated using Welch's method. This method iterates over the signal, taking separate signal windows. For each window the Fast Fourier Transform (FFT) is used to convert the signal into the frequency domain to produce a local estimate of the PSD, see Equation 2.5. To obtain a comprehensive overview of the PSD of the entire signal, the individual PSD estimates were averaged, see Equation 2.6 and Figure 2.5. Welch's method, which has a lower frequency resolution compared to a full FFT, has the advantage of reduced variance. This trade-off makes Welch's method particularly suitable for analyzing non-stationary signals, such as sEMG, where changes in signal characteristics over time need to be captured.

$$P_i(f) = \frac{1}{N} |\text{FFT}(x_i)|^2 \tag{2.5}$$

where:

- $P_i(f)$ is the periodogram estimate of the power spectral density for the i-th segment.
- N is the length of the segment.
- $\text{FFT}(x_i)$ represents the Fourier Transform of the i-th segment of the signal.

$$S_{\text{Welch}}(f) = \frac{1}{M} \sum_{i=1}^{M} P_i(f) \tag{2.6}$$

where:

- $S_{\text{Welch}}(f)$ is the Welch-estimated Power Spectral Density.
- M is the total number of overlapping segments.
- $P_i(f) = \frac{1}{N} |\text{FFT}(x_i)|^2$ is the periodogram for the i-th segment.
- N is the length of each segment.
- f is the frequency.

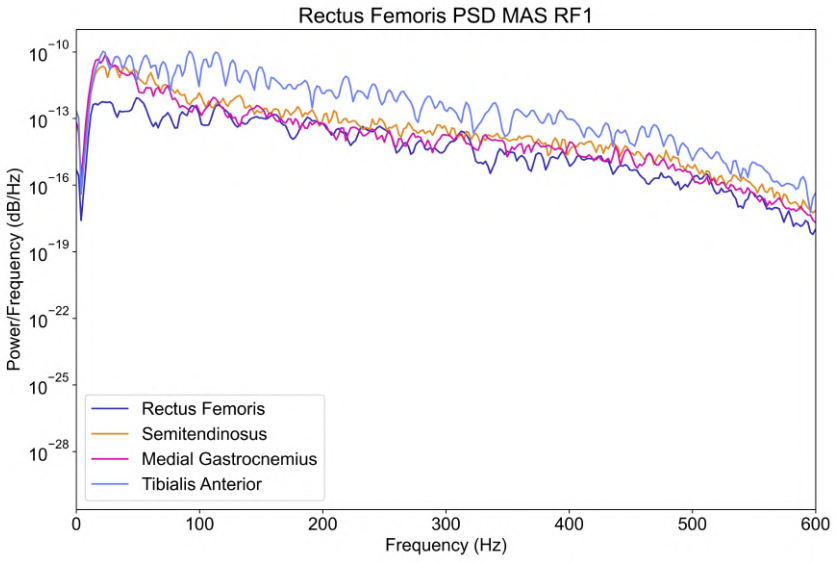


Figure 2.5: Representation of the Power Spectral Density of the sEMG signal of all four muscles during MAS assessment of the Rectus Femoris (RF).

Median Frequency

The number of samples per signal window (*nperseg*) used for the FFT is determined by a logarithmic scale. Increasing the parameter value, improves the frequency resolution, but reduces noise rejection. As parameter value *nperseg* 2^{10} was chosen, taking 1024 samples per segment. The sample frequency of the sEMG signal was 2000 Hz, then following the Nyquist principle at least a frequency of 1000 Hz is necessary to assure all information is captured when transforming the the frequency domain. Furthermore, to ensure that the frequencies of interest (15-500 Hz) can be observed, the sampling rate should at least be twice the maximum frequency following Nyquist principle. This results in a sampling frequency of at least 1000 Hz as well.

To gain insight into the frequency distribution the median frequency was calculated. This involves the determination of the frequency below which 50 percent of the total power spectrum is located. The median frequency provides a robust measure that reflects the central tendency of the frequency distribution in the signal. To calculate the median frequency the integral of the product of the PSD and frequency over the frequency range, was divided by the integral of the PSD over the frequency range, see Equation 2.7. These integrals are also known as Area Under the Curve (AUC). This resulted in a ratio of the two integrals and is used as an estimate of the median frequency. Figure 2.6 is a visual representation of the median frequency of the rectus femoris muscle during MAS assessment of the rectus femoris.

$$\text{Median Frequency} = \frac{\sum_{i=1}^{N} \text{PSD}(f_i) \cdot f_i}{\sum_{i=1}^{N} \text{PSD}(f_i)} \tag{2.7}$$

where:

- $\text{PSD}(f)$ is the Power Spectral Density as a function of frequency f.
- N is the number of frequency points.
- f_i and $\text{PSD}(f_i)$ are respectively the i-th frequency and its corresponding Power Spectral Density.

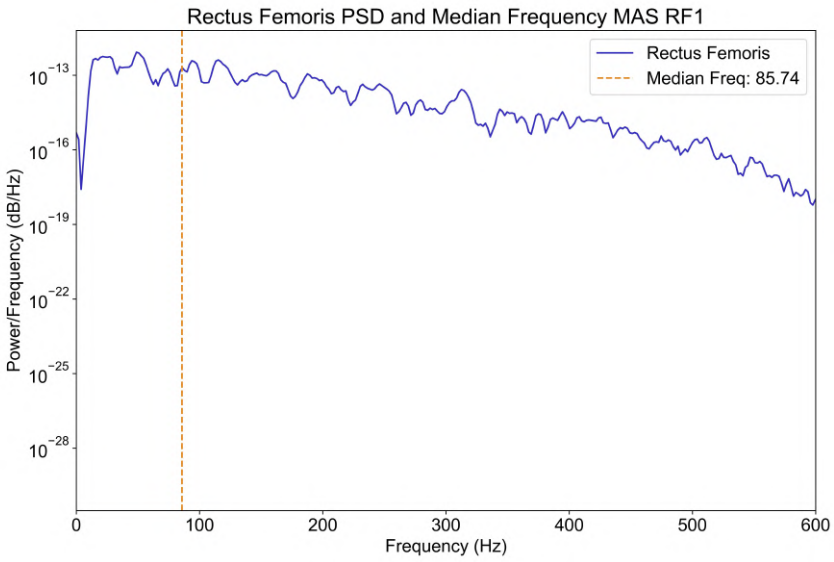


Figure 2.6: Representation of the median frequency (orange dotted line) of the power spectral density of the rectus femoris (RF) muscle during MAS assessment of the rectus femoris (MAS RF).

2.3.6. Co-Contraction Ratio

To calculate the CCR, the method of Ohn et al. [22] was used for analysis: the equation involves dividing the RMS of the target muscle or agonist by the RMS of the reference muscle or antagonist, defined in Equation 2.8 and visualized in figure 2.7. The RMS was calculated over a time window of the corresponding MAS event for the agonist or antagonist muscle. Thus, for the CCR of the rectus femoris, the time windows labelled MAS RF were used for calculation. The CCR was determined for three muscles, rectus femoris, semitendinosus and medial gastrocnemius.

$$\text{Co-Contraction Ratio} = \frac{RMS_{\text{agonist}}}{RMS_{\text{antagonist}}} \tag{2.8}$$

where:

- CCR RF (during MAS RF) = $RMS_{\text{Rectus Femoris}}/RMS_{\text{Semitendinosus}}$
- CCR HAM (during MAS HAM) = $RMS_{\text{Semitendinosus}}/RMS_{\text{Rectus Femoris}}$
- CCR GAS (during MAS GAS) = $RMS_{\text{Gastrocnemius muscle}}/RMS_{\text{Tibial Anterior Muscle}}$

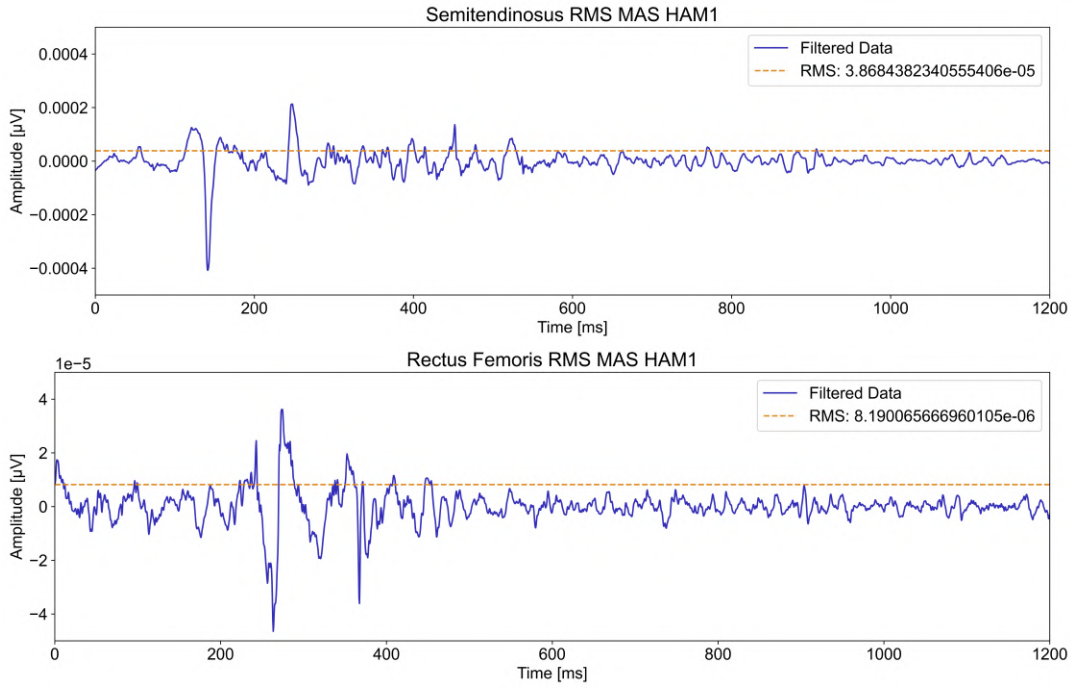


Figure 2.7: sEMG signals after standard pre-processing of the rectus femoris muscle and semitendinosus muscle during MAS assessment of the hamstrings. RMS value is presented as the orange dotted line. Co-activation of the antagonist muscle is seen, causing co-contraction.

2.4. Comparative analysis

2.4.1. Aim 1: To assess the effect of ITB on muscle activity in the lower limbs using sEMG

The average feature values, across all MAS repetitions for each muscle, were compared as pre- and post SS or pre- and post implantation.

2.4.2. Aim 2: To assess the correlation between sEMG feature values and MAS scores.

The feature value of each repetition of the same MAS sub-type, for the corresponding muscle, were averaged (e.g. MAS RF1/2/3 for the rectus femoris resulting in MAS RF). The percentage differences before and after baclofen administration of these these averaged values were calculated for each muscle, see Equation 2.9. In order to ensure a comparable analysis with the MAS score, only the MAS assessment of the corresponding muscle was utilised. The tibial anterior muscle is not evaluated during the MAS assessment, therefore this muscle was excluded for this analysis.

$$\text{Percentage Difference} = \frac{\textit{feature value after baclofen} - \textit{feature value before baclofen}}{\textit{feature value before baclofen}} \times 100 \quad (2.9)$$

Spearman's Rank Correlation Coefficient

To calculate the correlation coefficient, the '*spearmanr*' function from the '*scipy.stats*' module in Python was used, which computes the correlation coefficient using Equation 2.10. Spearman's rank correlation coefficient was chosen because the MAS scores are considered ordinal, and the feature values are all numerical [35, 36]. The same method was applied in other studies evaluating correlation between the MAS and sEMG feature values [22]. This coefficient allows to assess whether there is a monotonic relationship between the ranks of the percentage difference and ranks of the MAS score, without assuming linearity. A correlation coefficient (ρ) close to zero indicates that there is no monotonic relationship between the two variables. Conversely, ρ = 1 indicates a positive rank correlation, which means that when one variable increases in rank, the other variable also increases in rank. A correlation coefficient ρ = -1 indicates a negative rank correlation. This implies that an increase in the rank of one variable correlates with a decrease in the rank of the other variable. The evaluation of the strength of the correlation is based on the definitions by Kuckartz et al. (2013) [37], as can be seen in Table 2.2.

$$\rho = 1 - \frac{6 \sum d_i^2}{n(n^2 - 1)} \quad (2.10)$$

where:

- ρ represents the correlation coefficient
- d_i is the difference in ranks between two variables
- n is the number of observations

2.4.3. Aim 3: To assess the correlation between sEMG feature values and Patient Global Impression of Change scale.

To achieve this goal, the Spearman rank correlation coefficient was determined for the PGIC vs. the change in MAS score and PGIC vs. the change in the best performing feature value. This test is suitable for either ordinal vs. ordinal correlation analysis or ordinal vs. numerical correlation analysis. The PGIC gives an impression of the change a patient experiences after treatment. The decision to include a patient for implantation after the single shot trial is clinically based on the effect of the treatment on the most severely affected muscle. Therefore, the MAS score and sEMG data (of the best performing feature) of the muscle with the highest MAS score pre-treatment was used as input for the Spearman rank test. For the best performing feature in study aim 1, the percentage differences, calculated as described in section 2.4.2, were used for analysis.

2.4.4. Statistical Analysis

A statistical analysis was conducted to identify potential insights into the significance of changes in feature values following baclofen treatment. Given the exploratory nature of the study and the lack of full measurement availability, as well as the fact that the study has not been powered for statistics, it is necessary to interpret the statistical results with caution.

The data for study aim 1 was paired but not normally divided, thus a non-parametric test, Wilcoxon Signed-Rank test, was employed for statistical analysis. The data was organised into groups based on the muscle and anatomical side. For each group, the test was employed to ascertain the significance of changes in feature values. The Wilcoxon Signed-Rank test was applied to each feature individually. In order to ensure sufficient sample sizes for statistical analysis, patients treated with SS or those who underwent implantation of a definitive system were combined. In order to identify any statistically significant differences, a significance level of 0.05 was applied.

In order to address the issue of multiple comparisons, a Benjamini-Hochberg correction was applied, given that the study tested four muscles and two anatomical sides [38].This method is based on the False Discovery Rate control (FDR), which refers to the probability of incorrectly rejecting a hypothesis, resulting in an increased number of false positives in the findings.

The Spearman rank correlation coefficients were evaluated according to the following indications, as presented in Table 2.2.

Table 2.2: Indications of strength of the correlation, based on the Spearman's rank correlation coefficient [37].

Amount of r	Strength of the correlation
0.0 <0.1	No correlation
0.1 <0.3	Low correlation
0.3 <0.5	Medium correlation
0.5 <0.7	High correlation
0.7 <1	Very high correlation

3
Results

This chapter is subdivided into sections that correspond with the study aims: assessing the effect of ITB on muscle activity in lower limb muscle activity (Aim 1: section 3.2), assessing the correlation between sEMG feature values and MAS scores (Aim 2: section 3.3) and assessing the correlation between sEMG feature values and the PGIC scores (Aim 3: section 3.4). Patient characteristics are described in section 3.1.

3.1. Patient Population

Patient Demographics

Twelve patients (58% female, 42% male) treated with ITB were included in this study, with a mean age of 53 years [SD 13]. The pathology's presented in the patient group were MS (4 out of 12), CP (1 out of 12), TBI (2 out of 12), SCI (2 out of 12) and other (3 out of 12) (X-ADL, KNCB1 Encephalography and Cavernous Malformations). A mean MAS score of 3 (4, after correction for calculation) was documented for 5 out of 12 patients. A mean MAS score of 4 (5 after correction for calculation) was reported for 1 out of 12. One patient exhibited spasticity in only the medial gastrocnemius muscle, therefore the average MAS score results in zero. See Table 3.1 for the patient demographics, including the mean MAS score pre- ans post treatment (over all muscles of both legs). For additional details on patient characteristics see Appendix C. For the MAS scores of individual muscles for each patient see Appendix D.

Two patients diagnosed with rare diseases were included, KNCB1 and X-ADL. The underlying pathology for KNCB1 is a disorder of potassium channels that causes abnormal signal transduction in nerves. X-ADL is a rare genetic disorder that damages the central and peripheral nervous systems by accumulation of fatty acids. The accumulation causes damage the myelin sheaths and disrupts normal nervous system function [39, 40].

Patient data Single Shot

Three patients had both SS and implantation event data available. Eleven patients had measurements taken before and after SS treatment. All patients received a baclofen dosage of 50 µg during SS treatment, except EMGITB010 she received 25 µg. Due to technical difficulties, data were available for 10 patients for left leg SS and 10 patients for right leg SS. In addition, one patient had a torn hamstring. Therefore, data were available for 9 patients for the right semitendinosus muscle.

Patient data Implantation

Four patients underwent measurements before and after the implantation of a definitive ITB system. Of the four patients, three were diagnosed with MS, and one (EMGITB007) with X-ADL. During the measurements on EMGITB007, excessive spasticity occurred in the left rectus femoris muscle, which made it not possible to retrieve correct labelled sEMG data. Therefore, data is available on the left rectus femoris for three patients. The catheter tip of the implanted ITB system was located at a thoracic spinal level in all patients. The specific levels are provided in Appendix C, which contains further details of the patients' clinical characteristics. This also applies to the dosage settings of the pump, which varied between patients, ranging from 1.04 µg/h to 4.2 µg/h.

Table 3.1: Patient Demographics. For the Modified Ashworth Scale score 1+ is corrected for calculation to 2. Meaning a score of 5 represents a MAS score of 4. MS = Multiple Sclerosis, CP = Cerebral Palsy, ABI = Acquired Brain Injury, SCI = Spinal Cord Injury, X-ADL = X-linked Adrenoleukodystrophy. *For the Modified Ashworth Scale the mean of all muscles, of both extremities pre- and post-intervention is calculated. **One patient exhibited spasticity in only the medial gastrocnemius, therefore the average MAS results in zero.

Variables	**Total** (n = 12)	**Single Shot** (n = 11)	**Implantation** (n = 4)
Age			
Mean [SD]	53 [13]	54 [13]	58 [9]
Sex			
Female	7 (58%)	8 (73%)	3
Male	5 (42%)	4 (27%)	1
Pathology			
MS	4 (33%)	4 (36%)	3
CP	1 (8%)	1 (9%)	
TBI	2 (17%)	2 (18%)	
SCI	2 (17%)	2 (18%)	
Other	3 (25%)	2 (18%)	1
Average MAS Score* pre treatment		**Single Shot** (n = 11)	**Implantation** (n = 4)
0	-	0	1**
1	-	3 (27%)	0
2	-	3 (27%)	1
3	-	0	1
4	-	4 (36%)	1
5	-	1 (9%)	0
Average MAS Score* post treatment		**Single Shot** (n = 11)	**Implantation** (n = 4)
0	-	6 (55%)	1
1	-	2 (18%)	1
2	-	1 (9%)	1
3	-	1	0
4	-	1	0
5	-	0	1

3.2. Aim 1: To assess the effect of ITB on muscle activity in the lower limbs using sEMG

In this section, I present the results of the analysis of the different feature values between pre and post ITB treatment, which addresses study aim 1. The values of all MAS assessments for a single muscle were averaged, resulting in one value per muscle. The RMS presented a decrease for 7 out of 10 patients after ITB treatment across the left and right leg muscles. This is supported by a significant decrease for three muscles across all participants. After SS treatment 3-8 out of 10 patients presented a decrease in the PAV for both left and right leg. The number of patients presenting a decrease in the median frequency was just as high as the number of patients presenting an increase (36 over 44 for all muscles). The left leg presented a decrease in CCR in 6 out of 10 patients after SS baclofen treatment across all muscles. All other three features (PAV, median frequency and CCR) did not present a significant decrease when comparing pre- and post treatment feature values. Figures 3.1, 3.3, 3.5, 3.7 present the results of the feature values for one patient of interest. For supplemental patient data see Appendices E (RMS), F (PAV), G (Median Frequency) and H (CCR). The statistical analysis results for each feature are presented in heat maps in Appendix I.

3.2.1. Root Mean Square

For the measurements after SS, for all muscles 7 out of 10 patients presented a decrease in RMS value on the left leg.There was a greater degree of variation in the number of patients exhibiting a decrease in the right leg muscles. The RMS value for the rectus femoris muscle decreased in 8 out of 10 patients. The smallest group of patients with a decrease in RMS after SS was for the right semitendinosus and medial gastrocnemius, as well as the left tibial anterior muscle (5 out of 10).

For the pre- and post-implantation measurements, an average of 3 out of 4 patients presented a decrease in the RMS value of the left leg muscles. For the left medial gastrocnemius, one patient (*EMGITB010*) presented a decrease in RMS value, as can be seen in figure 3.1. For 3 out of 4 patients a decrease in RMS value for the right leg muscles was measured. For the tibial anterior muscle, 4 out of 4 patients presented a decrease after implantation. Number of patients presenting a decrease are presented per muscle in Table 3.2. For the mean RMS across all patients see Figure 3.2. Where outliers are seen for the pre SS measurements of the tibial anterior muscle. Limited variability in RMS value is seen across all patients.

Statistical analysis demonstrated a significant decrease in RMS value for the left semitendinosus *(p = 0.020*), right rectus femoris (*p = 0.025*) and tibialis anterior (*p = 0.002*), as can be seen in Appendix I.

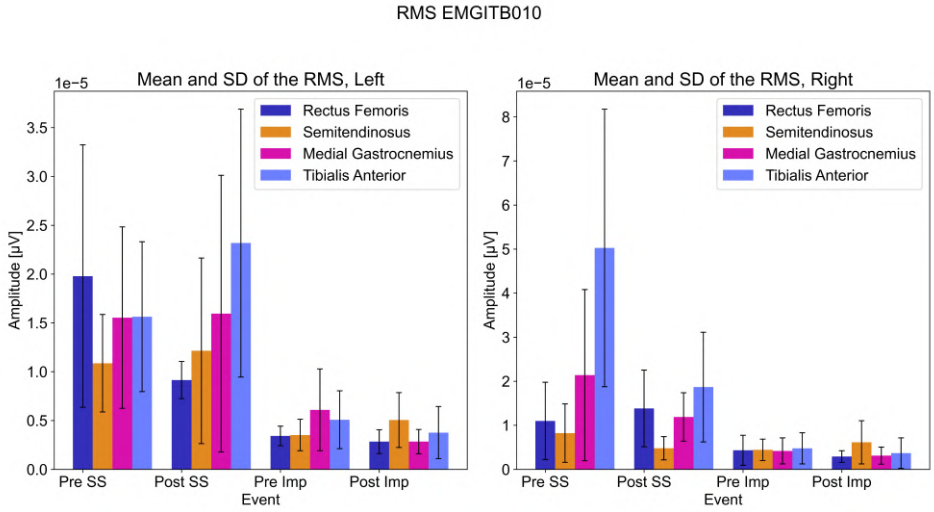


Figure 3.1: Bar charts of the average RMS values for each muscle of EMGITB010. The average is calculated across all MAS repetitions.

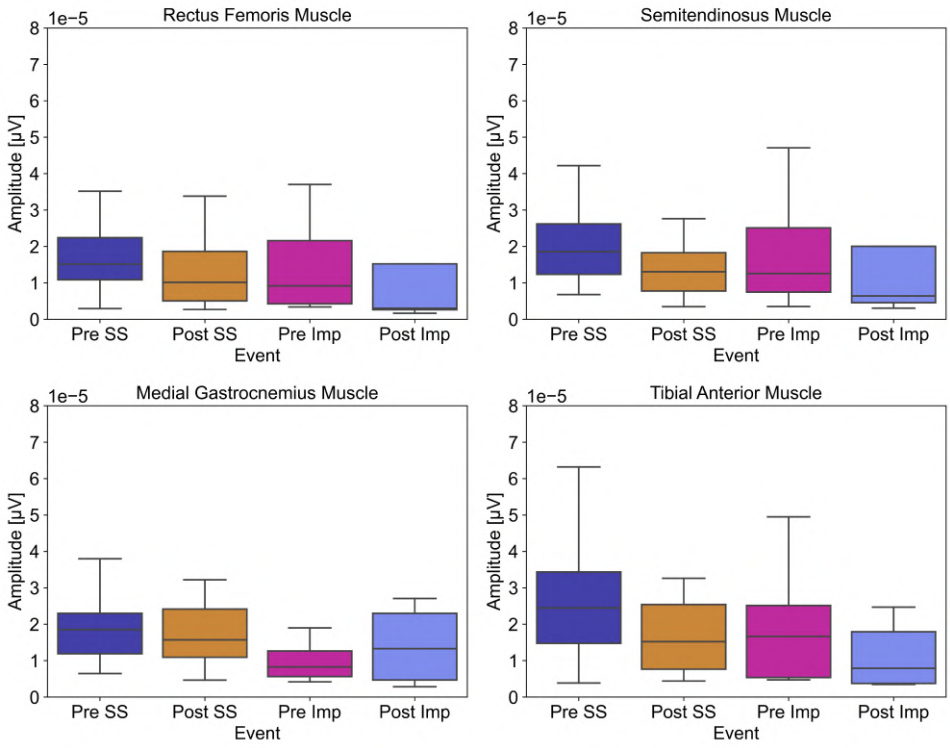


Figure 3.2: Box plots for each muscle of the mean RMS value of all patients per event. Pre SS/Post SS = pre- and post Single Shot baclofen trial. Pre Imp/Post Imp = pre- and post implantation of permanent ITB system.

3.2.2. Peak Amplitude Value

For measurements after SS, over all muscles of the right leg 5-9 out of 10 patients presented a decrease. For the left leg, across all muscles 3-8 out of 10 patients presented a decrease. The PAV for the left medial gastrocnemius muscle decreased in 9 out of 10 patients. A decrease in PAV was reported for the right semitendinosus muscle in 3 out of 9 patients. Three patients exhibited limited (less than four muscles) decrease in PAV following SS treatment.

For the pre- and post-implant measurements, 2-3 out of 4 patients presented a decrease in PAV of the left leg muscles. For the right medial gastrocnemius, one patient (*EMGITB007*) presented a decrease in PAV, as can be seen in Figure 3.3. On average, 1 out of 4 patients presented a decrease in PAV for the right leg muscles. No patients presented a decrease in the right rectus femoris muscle. And one patient (*EMGITB007*) presented a decrease in the right tibialis anterior muscle. Number of patients presenting a decrease are presented per muscle in Table 3.2. In Figure 3.4 the mean of all patients is presented per muscle. A greater variability is seen for the Pre SS measurements of the rectus femoris and medial gastrocnemius. Large outliers are detected for the tibialis anterior muscle during pre implantation measurements.

No statistical differences were presented for the PAV, the p-values varied from $p = 1.00$ towards $p = 0.078$ for the left leg and from $p = 0.502$ and $p = 0.903$ for the right leg, as can be seen in Appendix I.

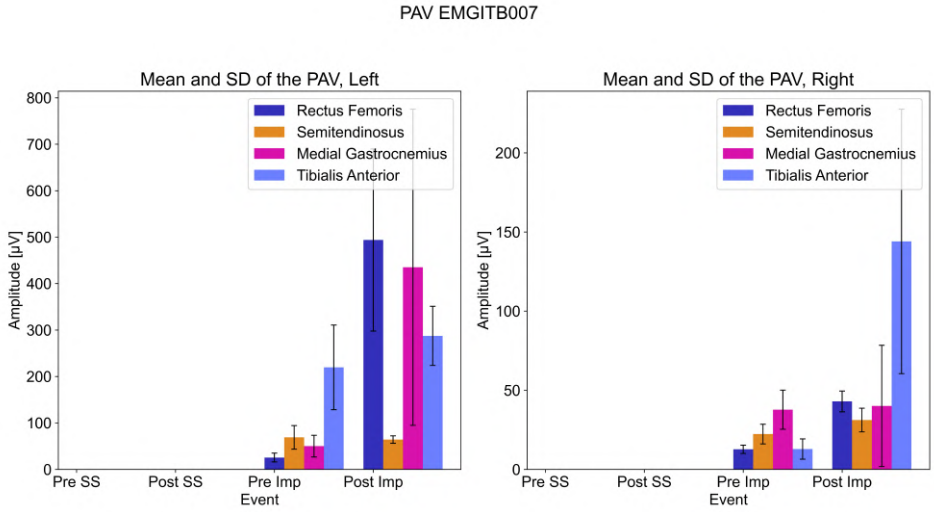


Figure 3.3: Bar charts of the average PAV values for each muscle of EMGITB007. The average is calculated across all MAS repetitions.

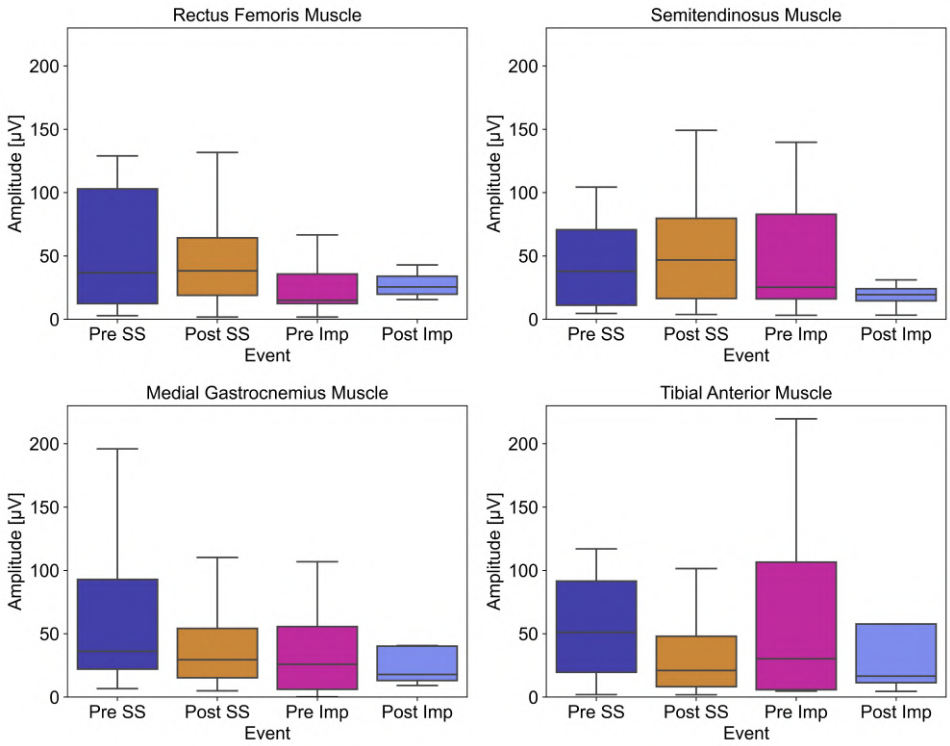


Figure 3.4: Box plots for each muscle of the mean PAV value of all patients per event. Pre SS/Post SS = pre- and post Single Shot baclofen trial. Pre Imp/Post Imp = pre- and post implantation of permanent ITB system.

3.2.3. Median Frequency

For the SS measurements of the left leg, the results varied between the four muscles. On average, 6 out of 10 patients presented an increase in the median frequency after SS baclofen treatment. The median frequency in the left tibial anterior muscle increased for 3 out of 10 patients. For the right rectus femoris and medial gastrocnemius, 5 out of 10 patients presented an increase. An increase was measured in the right semitendinosus muscle for three patients.

For both the pre- and post-implant measurements, an average of 3 out of 4 patients exhibited an increase in the median frequency of the left leg muscles. On average across all muscles for the right leg, 2 out of 4 patients presented an increase of the median frequency. Number of patients presenting a decrease are presented per muscle in Table 3.2. Notably, for the right semitendinosus muscle, one patient (*EMGITB001*) presented an increase of the median frequency, as can be seen in Figure 3.5. For the distribution of the mean value across all patients see Figure 3.6. Large outliers are seen for both the pre- and post SS measurements of the medial gastrocnemius. The variability in data is less in the pre- and post implantation data set, compared to the pre- and post SS.

No statistical significant differences were reported for all muscles of both legs. P-values varied from $p = 0.078$ to $p = 0.855$ for the left leg and from $p = 0.194$ to $p = 0.952$ for the right leg. The left rectus femoris presented $p = 0.078$, being the p-value closest to the statistical level of $p = 0.05$.

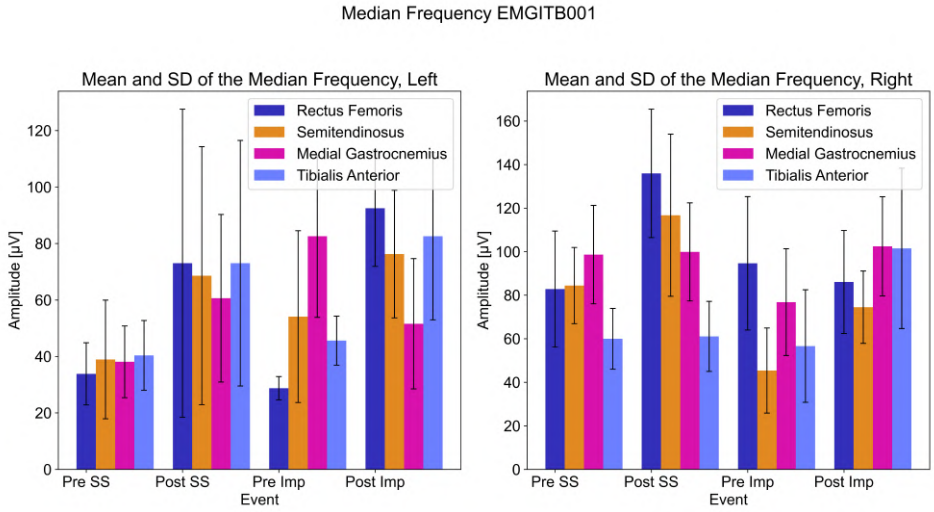


Figure 3.5: Bar charts of the average median frequency for each muscle of EMGITB007. The average is calculated across all MAS repetitions.

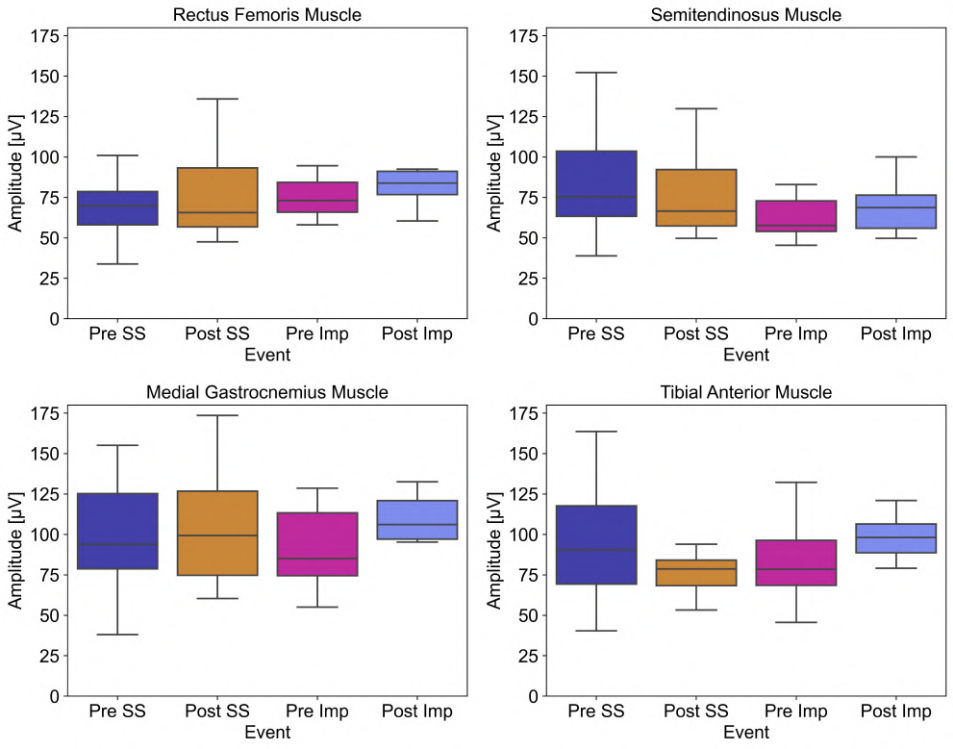


Figure 3.6: Box plots for each muscle of the mean median frequency over all patients per event. Pre SS/Post SS = pre- and post Single Shot baclofen trial. Pre Imp/Post Imp = pre- and post implantation of permanent ITB system.

3.2.4. Co-Contraction Ratio

The CCR of the left leg muscles decreased on average in 6 out of 10 of the patients, while the right leg muscles presented an average decrease in 4 out of 10 of the patients. The right semitendinosus CCR decreased in 2 out of 10 patients, and the right medial gastrocnemius CCR decreased in 4 out of 10 patients. The measurements performed before and after implantation presented a decrease in CCR for 2 out of 4 patients in the left leg. The CCR for the right leg was decreased for 1 out of 4 patients on average. The decrease of CCR for the right rectus femoris and medial gastrocnemius after implantation did not imply to the same patient. The decrease for the right rectus femoris, for *EMGITB005*, is presented in Figure 3.7. Number of patients presenting a decrease are presented per muscle in Table 3.2. For the variation in the mean CCR value of all patients, see Figure 3.8. For the semitendinosus muscle larger variability in mean CCR across all patients is seen, together with outliers for the measurements post SS and implantation.

For all three muscles across all patients no significant decrease was reported, where the medial gastrocnemius presented p-values closest to the statistical level ($p = 0.091$ left, $p = 0.135$ right).

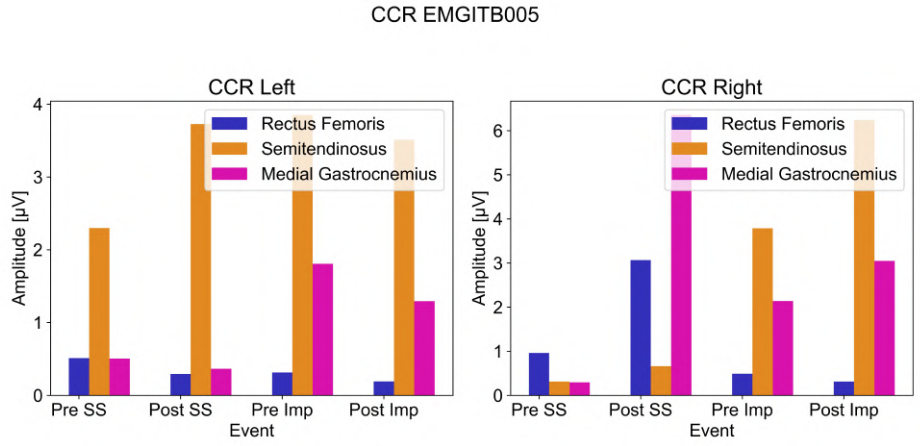


Figure 3.7: Bar charts of the average CCR for each muscle of EMGITB005.

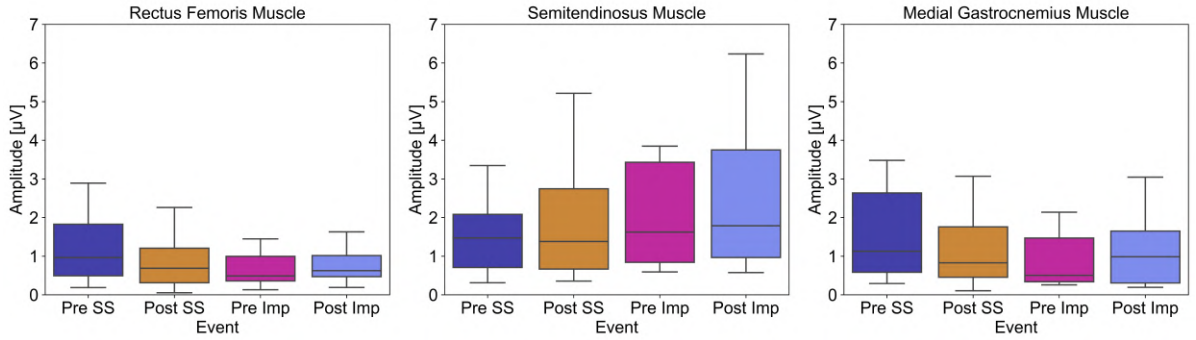


Figure 3.8: Box plots for each muscle of the mean CCR value of all patients per event. Pre SS/Post SS = pre- and post Single Shot baclofen trial. Pre Imp/Post Imp = pre- and post implantation of permanent ITB system.

Table 3.2: Number of patients with the hypothesized in- or decrease after ITB treatment, across all MAS events for each muscle. Detailed for each feature; Root Mean Square, Peak Amplitude Value, Median Frequency and Co-Contraction Ratio. And detailed for each event (Single Shot (SS) or implantation of definite system (Imp) and each leg; left or right. The tibial anterior muscle was not included in CCR analysis.

Feature	Rectus Femoris	Semitendinosus	Medial Gastrocnemius	Tibial Anterior
RMS				
SS Left	7 out of 10	7 out of 10	7 out of 10	6 out of 10
SS Right	8 out of 10	6 out of 9	5 out of 10	8 out of 10
Implant Left	3 out of 4	2 out of 4	1 out of 4	3 out of 4
Implant Right	3 out of 4	2 out of 3	3 out of 4	4 out of 4
PAV				
SS Left	5 out of 10	5 out of 10	9 out of 10	8 out of 10
SS Right	5 out of 10	3 out of 9	4 out of 10	8 out of 10
Implant Left	2 out of 4	3 out of 4	2 out of 4	3 out of 4
Implant Right	0 out of 4	2 out of 3	1 out of 4	1 out of 4
Median Freq				
SS Left	8 out of 10	7 out of 10	6 out of 10	3 out of 10
SS Right	5 out of 10	3 out of 9	5 out of 10	3 out of 10
Implant Left	2 out of 4	3 out of 4	3 out of 4	3 out of 4
Implant Right	2 out of 4	1 out of 3	3 out of 4	2 out of 4
CCR				
SS Left	7 out of 10	6 out of 10	6 out of 10	
SS Right	5 out of 10	2 out of 10	4 out of 10	
Implant Left	2 out of 3	2 out of 4	3 out of 4	
Implant Right	1 out of 4	2 out of 4	1 out of 4	

3.3. Aim 2: To assess the correlation between sEMG feature values and MAS scores.

In this section I present the results of the correlation between sEMG feature values and MAS scores, which adresses study aim 2. The results are divided in a paragraph for each feature, reporting the results for the Spearman Rank correlation coefficient. The values of each repetition of a MAS assessment of the corresponding muscle were averaged, and then a percentage difference was calculated. The MAS assessments analyzed are: Rectus Femoris (MAS RF), Semitendinosus (MAS HAM) and Medial Gastrocnemius (MAS GAS). The Spearman's rank correlation coefficients for all features, for each muscle, are presented in Table 3.3. The percentage differences are plotted next the MAS scores in Figure 3.9 for each feature. The correlation between the MAS scores and features values was significant for the RMS in the medial gastrocnemius *(p = 0.027)* and for the median frequency in the semitendinosus *(p = 0.002)*.

Table 3.3: Spearman's rank correlation coefficient (p-value) for all sEMG features, listed per muscle. The coefficient represents the correlation between the percentage difference in feature value for the muscle during the corresponding MAS assessments vs. difference in MAS score given by the clinician during the same MAS assessments. * indicates significant correlation.

Feature	Rectus Femoris	Semitendinosus	Medial Gastrocnemius
RMS	0.211 (0.290)	0.106 (0.593)	0.417* (0.027)
PAV	0.108 (0.591)	-0.146 (0.458)	-0.190 (0.332)
Median Frequency	0.122 (0.545)	0.557* (0.002)	-0.109 (0.580)
CCR	0.230 (0.249)	-0.245 (0.209)	0.142 (0.470)

3.3.1. Root Mean Square

Between the RMS percentage differences and MAS score differences a low and moderate positive correlation across all three muscles is found. A significant correlation is found for the medial gastrocnemius (*p = 0.027*). For more detailed results on the percentage differences of RMS values between pre- and post treatment and MAS differences, see Appendix J.

3.3.2. Peak Amplitude Value

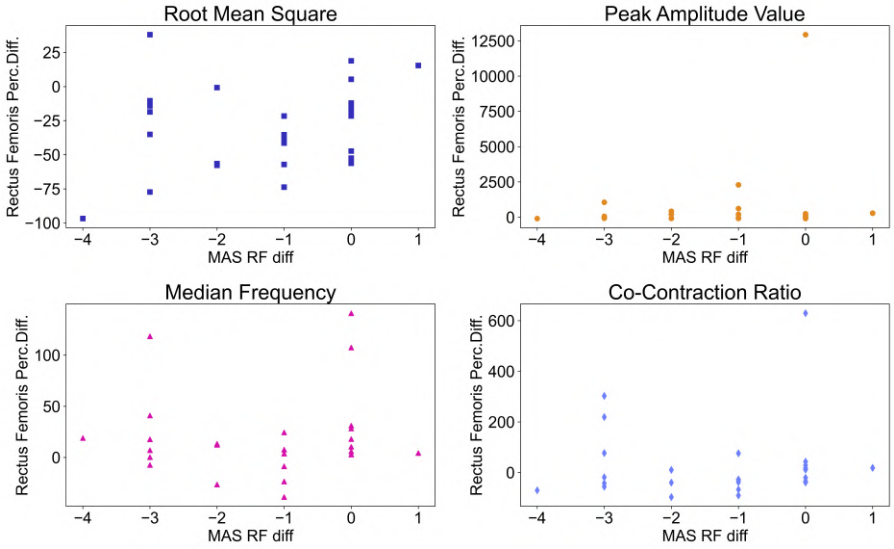
For the PAV no significant correlations were found when comparing the percentage differences with the MAS score differences. For all muscles the correlation coefficient is between 0.1 and 0.3, indicating low correlation. For more detailed results on the percentage difference of PAV and differences in MAS scores, see Appendix K.

3.3.3. Median Frequency

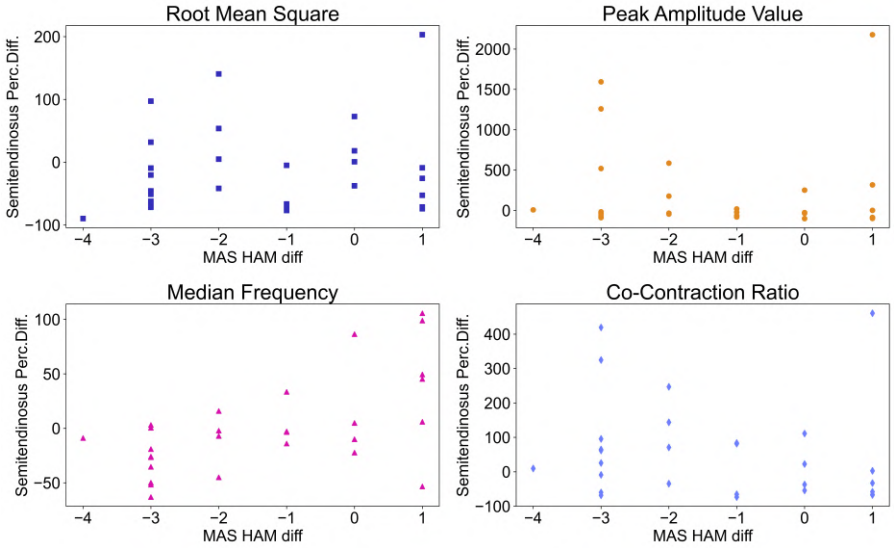
The correlation coefficient for the median frequency presented a significant positive correlation for the semitendinosus muscle (*p = 0.002*). The coefficients for the other two muscles were either positive or negative, both between 0.1 and 0.3, indicating low correlation. For more detailed results on the percentage differences of median frequency values between pre- and post treatment and MAS differences, see Appendix L.

3.3.4. Co-Contraction Ratio

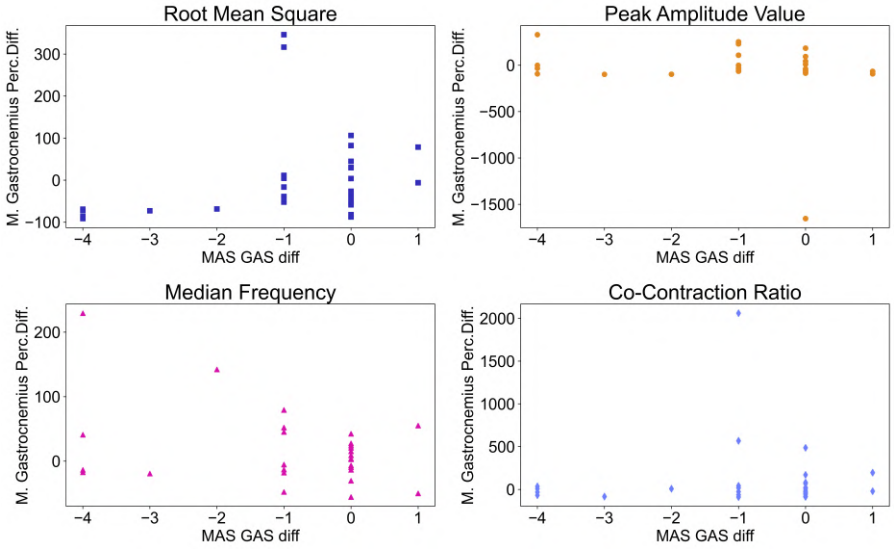
The percentage differences in CCR did not significantly correlate with the percentage differences in MAS scores. For the rectus femoris and medial gastrocnemius muscle a low positive correlation was seen, but for the semitendinosus a low negative correlation was seen. For more detailed results on the correlation between the difference in MAS scores and percentage difference in CCR, see Appendix M.



(a) Feature value differences vs Modified Ashworth Scale for Rectus Femoris



(b) Feature value differences vs Modified Ashworth Scale for Semitendinosus



(c) Feature value differences vs Modified Ashworth Scale for Medial Gastrocnemius

Figure 3.9: Scatter plots of the Root Mean Square, Peak Amplitude Value, Median Frequency and Co-Contraction Ratio versus the values of the Modified Ashworth Scale (MAS). Presented for all three muscles a: Rectus Femoris, b: Semitendinosus, c: Medial Gastrocnemius.

3.4. Aim 3: To assess the correlation between sEMG feature values and Patient Global Impression of Change scale.

3.4.1. Spearman correlation

The feature that performed best in assessing the change in muscle activity after baclofen treatment according to study aim 1 was the RMS. Therefore, the percentage differences of this feature were used for Spearman rank correlation analysis with the PGIC. The percentage differences, PGIC scores and changes in MAS scores for each patient's most severe muscle are listed in Appendix N.
A correlation coefficient $\rho = 0.182$ was found for the RMS vs. PGIC, with $p = 0.405$. According to Table 2.2, this indicates a low correlation between the percentage difference in the RMS value of the most severe muscle and the PGIC score. A correlation coefficient of $\rho = 0.334$ with $p = 0.119$ was found between the PGIC and the change in the MAS score of the most severe muscle. This result indicates a moderate correlation between the change in the MAS score of the most severely affected muscle and the PGIC.

Table 3.4: Correlation coefficients of the percentage differences in RMS vs. the PGIC scores.

Calculation	Correlation coefficient (ρ)	P-value
RMS (%diff) vs. PGIC	0.182	0.405
MAS vs. PGIC	0.334	0.119

4

Discussion

In this study, I investigated the change in muscle activity, before and after ITB treatment, using sEMG in patients with UMN lesions. My analysis included sEMG features from time and frequency domain: RMS, PAV, median frequency and CCR. Furthermore, correlation between these features and the MAS and PGIC was assessed.
For the RMS significant differences for three out of eight muscles, after baclofen treatment is seen. The results on the PAV do suggest potential in detecting change in muscle activity after baclofen treatment. But improvement of the feature calculation methodology is recommended to increase the predictive value. The results regarding the median frequency highlight the uncertainty of the effects of ITB on spectral characteristics. For the CCR, around 50% of the patients presents a decrease after baclofen treatment. These results reflect the uncertainties associated with the calculation methodology of the CCR.

4.1. Aim 1: To assess the effect of ITB on muscle activity in the lower limbs using sEMG.

These findings represent the overall activity of each muscle, across the entire sEMG measurement, without differentiation on muscle activity during specific MAS sub-types.

4.1.1. Root Mean Square

In this paragraph, the results on RMS after ITB will be further interpreted. I expected to see decrease in RMS after treatment. Across all muscles of the left and right leg, a decrease in RMS for 7 out of 10 patients is seen after SS treatment. After implantation of an ITB pump 3 out of 4 patients presented for most muscles a decrease in RMS, see Table 3.2 and Appendix E for the exact difference values of patients per muscle. Based on the Wilcoxon Signed-Rank test results, statistically significant differences were observed in the RMS across different muscles and anatomical sides following baclofen treatment (left semitendinosus; $p = 0.020$, right rectus femoris $p = 0.025$, right tibialis anterior $p = 0.002$), as can be seen in Appendix I. These findings contribute to the evaluation of the positive predictive value of RMS in response to the treatment. These results are in line with my hypothesis on the change of the RMS after ITB administration.
Limited or no decrease in RMS after SS treatment was seen for three patients for the muscles of either one or two legs. For these patients, the underlying pathology was either equal or the patient did not exhibit a positive response to baclofen. These patients will be further evaluated in the following paragraphs on single shot and implantation.

Single Shot
Following SS treatment, patient EMGITB001 presented an increase in RMS on the right leg muscles, while patient EMGITB008 demonstrated an increase in RMS on the left leg muscles. Patient EMGITB010 presented an increase in RMS on the left leg muscles. Patients EMGITB001 and EMGITB010 are both diagnosed with Multiple Sclerosis (MS).
In EMGITB001, spasticity predominantly affected the right lower muscles (medial gastrocnemius and soleus), however for all right leg muscles the mean RMS increased after baclofen treatment, which

is the opposite than hypothesized. Further analysis of the mean percentage difference for the medial gastrocnemius only over the time window of the MAS assessment of the gastrocnemius muscle (MAS GAS) revealed a decrease. Furthermore, it is important to note that the data quality for this patient may be limited due to her high Body Mass Index (BMI), which can affect the signal quality of the sEMG measurements. The presence of adipose tissue can impede the electrical activity of the muscle, thereby reducing the likelihood of obtaining sufficient signal quality. Additionally, having more fat tissue between the leg and skin allows for greater electrode movement across the muscle. This makes it difficult to ensure consistent measurement of the same motor unit.
For patient EMGITB010, the root mean square (RMS) of the more affected, left leg is observed to increase following the administration of baclofen in contrast to my expectations. An decrease is onlys een for the rectus femoris. The most severe left leg muscle was the medial gastrocnemius, MAS score of 3 pre-treatment and 0 post-treatment.
For the analysis of study aim 1, the average of all different MAS assessments from one muscle is used. When looking into the percentage differences of the medial gastrocnemius during the MAS assessment of the medial gastrocnemius, a decrease is seen. This is revealed for both EMGITB001 and EMGITB010, suggesting that the influence of the other MAS assessments, other than the one of the corresponding muscle, do influence the calculated mean RMS value per muscle.
The third patient, EMGITB008, demonstrated no reduction in RMS following ITB administration. This patient suffers of spasticity due to a spinal cord injury (SCI) at Th7, caused by a cavernous hemangioma (venous malformation). The left leg presented an increase in RMS following ITB administration, which is consistent with the mean MAS scores of the left leg, which showed no improvement. The MAS scores of the left leg muscles increased, decreased or remained the same after treatment, see Appendix D. This indicates that the ITB therapy did not have an effect on the spasticity in all muscles of the left leg, and thus no decrease in mean RMS can be expected.

Implantation
After implantation of an ITB system, EMGITB007 presented no decrease in 6 of the 8 leg muscles of the lower limbs. Furthermore, EMGITB001 (1), EMGITB005 (1) and EMGITB010 (2) present no decrease in RMS for the left medial gastrocnemius (1) and left and right semitendinosus (2) muscles.
EMGITB007, suffering of X-ADL, exhibited heightened spasticity in the left leg. Limited research on ITB treatment for X-ADL suggests its potential benefit, though further investigation is needed to understand its mechanisms and validate hypotheses about changes in electromyography (sEMG) readings [41].

Results similar to this study were reported in literature by Castilho et al. [42], investigating the impact of neural mobilization on sEMG activity, in patients with spasticity. The methodology employed in this study is comparable to that employed in my own study, investigating the measurement of sEMG during passive movements. Their results indicate a reduction in the mean RMS for approximately two-thirds of the patient group. However, the statistical analysis conducted by Castilho et al., using the Pearson test, did not yield statistically significant results [42]. In order to elaborate on the promising results for RMS, it is recommended to repeat the analyses after increasing the patient cohort and review the calculation methodology for comparative analysis.

4.1.2. Peak Amplitude Value

For the PAV I expected to see a decrease after ITB treatment. In 5-9 out of 10 patients a decrease in the PAV was seen for the left and right leg muscles after SS treatment. After implantation a decrease in the PAV of the left leg muscles was seen for 3 out of 4 patients and for the right leg muscles 1 out of 4 patients, as can be seen in Table 3.2 and Appendix F. However, three patients presented limited reduction in PAV following SS treatment. The patients presenting results that are not in line with my expectations for either SS treatment of after implantation, are discussed in the following paragraph. Additionally, no significant differences were obtained for the PAV within the study, as can be seen in Appendix I. But statistical analysis was conducted to only identify potential insights in to the significance of changes in feature values following baclofen treatment. The study has an exploratory nature and has not been powered for statistics.

Single Shot
The data from patient EMGITB002 with cerebral palsy (CP) reveals a distinct pattern of response to treatment. Only the tibialis anterior of the right leg presented a small reduction in PAV. However, the left leg, being more affected by spasticity, only demonstrate a small reduction in PAV for the medial gastrocnemius. No other patients with cerebral palsy were included in the study to enable comparisons to be made. Following SS treatment, the desired therapeutic effect was achieved, with a reduction in spasticity from MAS 4 to 1 for the left leg. This highlights the interest in the correlation between the PAV and MAS, which is discussed in section 4.2.
Following SS treatment, the PAV increased for all muscles for patient EMGITB009. However, clinical assessment and patient experience reported improvement after treatment. No clarification on these results can be made from clinical characteristics.
EMGITB011 is another patient who presented an increase in PAV for 5 out of 8 muscles. The cause of spasticity in this patient is a rare mutation on the KCNB1 gene. The patient's left side had more severe spasticity, and many contractures were diagnosed. In addition, the growth of a considerable amount of hair on the lower limbs may have resulted in an additional distortion of the measured sEMG signal, which could explain why no decrease was observed in all muscles. The decision not to shave the patient's hair was made due to the cognitive impairment and spastic response to touch on the lower limbs.
Patient EMGITB012, diagnosed with MS, presented no consistent decrease of the PAV after treatment in the right leg muscles. Unlike other patients, there is no reported side dominance in terms of severity, and the response to baclofen treatment was positive. Despite the observed increase in PAV for the right leg muscles, no direct explanation for this phenomenon can be derived from evaluating the clinical presentation of this patient.

Implantation
The number of patients exhibiting a decrease after implantation is limited, primarily due to a measured increase in PAV for EMGITB010. The pathology of this patient was discussed in the paragraph on RMS. No additional clinical characteristics of this patient can explain the unexpected increase in PAV, other than those already discussed.

The variability in the PAV data suggests that the methodology used to extract this feature needs improvement. The variability in the acquired sEMG signal amplitude can be caused by different influences, such as electrode application, perspiration, temperature, movement velocity, muscle length and crosstalk from neighbouring muscles. When comparing amplitude values across measurements, it becomes necessary to normalise the data in order to ensure a uniform scaled signal for all patients [19]. In my study, the data is normalised by using the standard deviation and mean of sEMG signals collected during a 30-second resting period. This standardised condition allows for the comparison of data across patients. The protocol addressed the influence of external factors. One such example is the practice of cleansing the skin prior to electrode application. However, no correction was applied for differences in temperature and fat tissue thickness between inpatients, which influence the conduction of the signal. Addressing these factors could enhance the signal quality and thus the predictive value of the PAV.

4.1.3. Median Frequency
I anticipated that the median frequency would demonstrate an increase following ITB treatment. Following SS treatment, an increase in median frequency was observed in 3-8 out of 10 patients across the left leg muscles. An increase was observed in the median frequency for 3-5 of the 10 patients in the right leg muscles. Following implantation, 1-3 out of 4 patients presented an increase in median frequency for both legs. The Wilcoxon Signed-Rank test did not result in significant differences. The variation between the group sizes is notable and therefore, patients not presenting the expected increase are discussed in the following section for the SS and implantation.

Single Shot
For the median frequency a high variance in is seen in the number of patients per muscles, presenting an increase in the median frequency after ITB. For the left rectus femoris muscle 8 out of 10 patients presented an increase, however the for the right tibial anterior muscle this is just 3 out of 10.
EMGITB004 and EMGITB008 present contradicting results. Despite EMGITB004 experiences greater

impairment on the right side, this patient primarily presented a decrease of the median frequency after treatment for this leg, which is in contrast with my expectations.
For EMGITB008 the right leg was reported as the anatomical side with more severe spasticity. However, the right leg presented a decrease of the median frequency after ITB administration, indicating the opposite effect. Although, the evaluation of the SS trial had a positive outcome.
Patients EMGITB009 (TBI), 011 (KCNB1 mutation) and 012 (MS) all had a decrease of the median frequency for 3-4 out of 4 muscles. No overlap in pathology is seen for this group of patients that could be an explanation on decreasing median frequencies for all muscles.
In addition to patient characteristics, other factors can influence the identification of meaningful differences before and after ITB treatment. Specifically, the quality of the sEMG signal can be affected by various external factors, which can limit the data quality and interfere with the analysis. However, I attempted to limit this influence as much as possible through data pre-processing.

Implantation
For the results on the effect ITB after implantation one patient (EMGITB001) presented a decrease for all muscles, except left gastrocnemius and right rectus femoris. This patient suffers from MS and clinically a positive response on the effect of the ITB pump was reported.

The diverse range of pathology's that affect the UMN can result in various underlying mechanisms that induce spasticity. Consequently, baclofen's effects may vary depending on the specific pathology, resulting in potential differences in frequency composition alterations. For example, for EMGITB011 (KCNB1 mutation), disruption occurs at the cellular-channel level, whereas for EMGITB012 (MS) it is due to damage to the myelin sheath. The type of pathology might influence the frequency composition of the muscle activity. For example a study conducted by Yao et al. [43] compared the paretic side (affected by spasticity on MAS 3 level or lower) with the contra-lateral side in stroke patients, using spectral analysis of sEMG signals. The median frequency was significantly lower for the paretic side, than for the contra-lateral side. Furthermore, the effect of oral baclofen on the median frequency is studied in healthy participants by Hornby et al. [44]. No statistically significant differences in median frequency were observed between the pre- and post-baclofen conditions (pre-baclofen: mean = 47 (SD 11) Hz; post-baclofen: mean = 49 (SD 10) Hz; $P > 0.30$). It is noteworthy that the effective dose differs when the medication is administered orally and not intrathecal. I recommend to conduct further research to ascertain the manner in which spectral characteristics change following baclofen treatment for each type of pathology. The existing literature and the results of my own research indicate that there is considerable variation in the trends observed. Some studies have indicated an increase in median frequency post-treatment, while others have demonstrated a decrease.

4.1.4. Co-Contraction Ratio

For the CCR I expected to see a decrease after ITB treatment. Across the left leg muscles 6-7 out of 10 patients presented a decrease in CCR SS treatment. The group of patients presenting a decrease in CCR for the right leg muscles after SS, was 2-5 out of 10. After implantation for the left leg muscles 2-3 out of 4 patients presented a decrease in CCR. And for the right leg 1-2 out of 4 presented a decrease. These outcomes do not all align with my hypothesis, particularly in regard to the implantation measurements. Additionally, the Wilcoxon Signed-Rank test did not yield statistically significant results. One patient (EMGITB001) presented no decrease in CCR for all muscles in the right leg after SS treatment and for the left leg after implantation. EMGITB010 also presents no decrease in CCR after implantation for all muscles of the right leg. EMGITB012 presents no decrease in CCR for both legs, on the semitendinosus and medial gastrocnemius muscles. Patients mentioned above will be discussed in the next section, followed by an evaluation of the CCR methodology.

Single Shot
Patient EMGITB001 was diagnosed with MS and exhibited particularly pronounced spasticity in the medial gastrocnemius. For the right leg, higher MAS scores were reported. However, the RMS for this patient was discussed in Section 4.1.1, as no decrease was observed for all muscles. This explanation also applies for the results on the CCR that were against my expectations, since the RMS is used for the calculation of the CCR.
Patient EMGITB012, diagnosed with MS, presented no decrease in the CCR for the semitendinosus

and medial gastrocnemius muscles. The CCR calculation is based on the RMS value, and a decrease in the RMS for the semitendinosus of the right leg was not observed. This outlier resulted in the CCR of the semitendinosus increasing as well, when dividing it by the decreased RMS of the rectus femoris. The outcome suggests that the co-contraction of the right leg did not decrease following ITB treatment. Consequently, the reflex response of the semitendinosus muscle remains as high as before. However, this also highlights the sensitivity of this method to outliers, which will be further explained in the following paragraph.

Implantation
EMGITB010, also diagnosed with MS, presented no decrease in the CCR for the right leg muscles after implantation. Additionally, a slight decrease was observed in the RMS values for the tibial anterior, rectus femoris and medial gastrocnemius. An increase was observed in the RMS values for the semitendinosus following ITB implantation, as can be seen in Appendix H.

While a decrease in CCR post-treatment is expected, supported by the study of Ohn et al. [22], this is seen for approximately 50% of the patients. With the promising results on the RMS, more was expected on the results of the CCR. However, more cautious interpretation of the CCR, compared to RMS, is warranted, due to the calculation methodology. For example, if both agonist and antagonist muscles experience decreased activity due to the effect of baclofen, the CCR may remain unchanged. Looking from a pharmacologic perspective, from a research conducted by Wang et al. (2010) [45], it is known that baclofen does affect the GABA-B receptors on the interneurons. Indicating that baclofen could influence the disrupted communication between agonist and antagonist muscle pairs.
Given the complexity of assessing CCR in patients with spasticity undergoing ITB treatment, exploring alternative methods may provide new insights. One such method, proposed by Sgouros et al. (2002), involves assessing co-contraction using surface electromyography (sEMG) after intrathecal baclofen (ITB) administration [46]. The findings suggest a decrease in synchronous activation and correlation between agonist and antagonist muscles following treatment. Although this method is suitable for exploratory research, it may not align with the clinical setting of my study and the patient population due to the use of a mechanical chair supporting for the movement of the limbs. Nevertheless, integrating aspects of Sgouros et al.'s approach in future investigations could improve understanding of the underlying mechanisms of co-contraction dynamics in spasticity management and decrease the uncertainties that arise with the calculation of the CCR used in my study.
While existing data suggests a potential influence of baclofen on co-contraction, further investigation is required to identify the underlying mechanisms and to assess the therapeutic effect using sEMG.

4.2. Aim 2: To assess the correlation between sEMG feature values and MAS scores.

In this section the Spearman's rank correlation coefficient is interpreted for each feature. The scatter plots presented in the results section, see Figure 3.9, provide insight into the trend of the data of each feature for all muscles. The values presented in Appendix J (RMS), K (PAV), L (Median Frequency), M (CCR) are calculated by taking the average over all MAS repetitions of the muscles's corresponding MAS assessment, resulting in one value per muscle. The objective of the statistical significant tests is to gain further insight into the potential outcomes of this research. The study is not powered to yield statistical significant results.

4.2.1. Root Mean Square

For the RMS I expected to see a moderate positive correlation. A low correlation is seen for the rectus femoris (*0.290*) and semitendinosus (*0.106*) muscles. However, the medial gastrocnemius presented a statistical significant moderate correlation (*0.417, p = 0.027*). This indicates that, for medial gastrocnemius, the RMS values does increase when the MAS scores increased as well. Research of Wang et al. [47] also used the Spearman rank correlation analysis to assess the correlation between RMS and MAS score in stroke patients. The findings of this study revealed significant correlations for both the biceps ($\rho = 0.249$, $p = 0.007$) and triceps ($\rho = 0.391$, $p = 0.001$) muscles. This variation can be attributed to the differing sizes of the patient groups. My study involved 12 patients, whereas Wang et al. included a total of 39 patients, all presenting with the same pathology. The homogeneity in pathology reduces the variability within the patient group, thereby increasing the probability of finding significant correlations. Furthermore, the data used for the Spearman rank correlation in my study are the differences in RMS and MAS, while Wang et al. used the absolute values of MAS and RMS for this analysis. To increase the possibility on finding more and stronger correlations for this feature and the MAS, I would recommend to include more patients and do an additional analysis with the absolute values of pre- and post treatment.

4.2.2. Peak Amplitude Value

For the PAV I expected to see a moderate positive correlation. Although, for both the semitendinosus and medial gastrocnemius the correlations were negatively low. This indicates no or low negative correlation between the PAV and MAS scores for these muscles, as defined in Table 2.2. For the rectus femoris muscle the correlation coefficient was positive, but very close to zero, indicating no correlation. Taking together, the values for the Spearman rank correlation coefficient show variety in direction and strength of correlation. However, the results of Cooper et al. [18], presenting the methodology on the normalization of the amplitude, presented a small positive correlation between the sEMG amplitude and MAS scores for the affected muscles of stroke patients ($\rho = 0.21$, $p = 0.022$). The difference in size of patient population can influence the significant results. Important to note that in the study of Cooper et al. the sEMG measurements of passive stretches were not derived during the actual passive stretches for the MAS assessment.

As can be seen in the scatter plots, Figure 3.9, the PAV does include some high outliers. For the rectus femoris, the outliers correspond to the same patient, during the same event (EMGITB010, after implantation). Looking into the dataset, increased mean and SD for the rectus femoris is seen. A difference in value magnitude, between pre- and post-treatment measurements is therefore seen. Calculating the absolute difference between these two values, will result in an exceptional high value, as outlier. Since the normalization methodology is based on SD and mean of the resting period, no correction for this increase is performed. My hypothesis is that the observed increase in SD and mean values is likely due to an increase in impedance. Since the electrodes are applied for 24 hours before measuring post-implantation, it is possible that the adhesiveness may have decreased. Furthermore, during surgery, the patient is moved and stabilised, which may result in movement of the electrode.

4.2.3. Median Frequency

For the median frequency I expected to see a moderate negative correlation. However a high correlation with significance was seen for the semitendinosus muscle. For the rectus femoris and medial gastrocnemius the correlations were close to zero, indicating low or no correlation following the standards from Table 2.2. The significant correlation indicates that the median frequency decreases, when

the MAS scores decrease after ITB treatment. This is against my hypothesis on the effect of ITB on the median frequency.
The study of Wang et al. [47], also applied the median frequency as sEMG feature. Their results on the correlation between MAS score and median frequency did not result in significant differences as well. No correlation for either the biceps (ρ = *-0.060, p = 0.524*) or triceps (ρ = *-0.012, p = 0.900*) was reported. These results are more in line with the results of my study, except for the semitendinosus. No clarification on the limited correlation between the median frequency and MAS is given by Wang et al [47]. The results indicate a need for further knowledge on the spectral characteristics of muscle activity following baclofen treatment. This is to identify a spectral feature that can assess the change in muscle activity following baclofen treatment and can be used in the clinical setting.

4.2.4. Co-Contraction Ratio

For the CCR I expected to see a low positive correlation. This was seen for the rectus femoris (ρ = *0.230*) and medial gastrocnemius (ρ = *0.142*). However, the semitendinosus muscles present a low negative correlation with the MAS (*-0.245*), following the standards from Table 2.2. The results of my study indicate that there is low correlation between the differences in the CCR and the percentage differences in the MAS scores. This is as I expected, since the MAS is not designed to quantify co-contraction in spasticity. Clinically functional tests, EMG and clinical observations are often used. However, Sgouros et al. (2002) report improved MAS scores of -1 or -1.5 after ITB treatment, while the measure for co-contraction also demonstrated improvement. The authors included correlation and time lag differences between agonist and antagonist activation as co-contraction measures. This can be explained by the fact that co-contraction can limit the range of motion which is a criterion within the description of MAS score 3, as can be seen in Table 1.1.

4.3. Aim 3: To assess the correlation between sEMG feature values and Patient Global Impression of Change scale.

In this section the Spearman rank correlation coefficients for the PGIC are evaluated. The percentage differences of the RMS, MAS scores and PGIC scores for each patient are listed in Appendix N. By evaluating this correlation, more can be said about how the patient can quantify the effect (on the Likert scale) of treatment. I expect to see a moderate correlation between the PGIC score and the sEMG feature value differences and a low correlation between the MAS scores and the PGIC.
A low correlation was reported between the PGIC and the RMS percentage difference *(ρ = 0.182)*. This comparison between objective measured values (RMS) and a subjective scale (PGIC) was expected to be moderately correlated. Patient EMGITB007 provides an illustrative example of the limited correlation. No improvement in the Modified Ashworth Scale (MAS) was reported, yet an increase in the RMS was observed. However, the patient's self-reported PGIC score was 1, indicating "very much improved." In contrast, patient EMGITB010 demonstrated opposite results for the measurements of the left leg after implantation. The MAS score improved by four levels, while the RMS presented a decrease. Nevertheless, the PGIC was scored with 4, indicating "no change." It is important to note that the data set used for this analysis was the RMS percentage difference for the most severely affected muscle. This would suggest that the patients may have experienced the majority of their complaints with this muscle, and thus experience most of the treatment effect for this muscle.
The limited sample size available for this correlation analysis might have influenced the results as well. But these tests are performed to form an indication on what can be expected when continuing this research. After including more patients, the correlations between the PGIC and MAS might increase.
The results indicate that the patient's ability to quantify the actual change in muscle activity is limited. The correlation coefficients indicate a moderate and low correlation between the two variables. It is of significant importance to consider the patients' experience when interpreting the results. However, these results do confirm that this parameter cannot be the sole factor for decision-making regarding treatment.

4.4. Limitations

This section acknowledges the limitations and challenges of my research and provides insight into the validity and reliability of my findings. This limitations include aspects related to study design and external factors affecting data collection and analysis.

4.4.1. MAS Assessors

The MAS assessments were conducted by six different assessors as part of this study. In order to eliminate the potential for intra-patient differences, the same assessors conducted both the pre- and post-assessment for each patient. Taking into account intra-rater variability, the high number of assessors, can influence the inter-rater reliability. Research conducted by Meseguer et al. [11] indicates that the reliability of MAS scores is negatively impacted by the use of a larger number of assessors. Their explanation states that the absence of a standardised protocol for the application of the MAS procedure can result in limited reliability. The protocol should include details of the test position, the number of repetitions, the order of the right-left leg test and the testing time. It is therefore recommended for future research that either one assessor is appointed for all MAS assessments or a robust, standardised protocol is established.

4.4.2. Number of patients

A limited amount of patients was included during the study. A smaller patient population limits the ability to generalise the results for the whole ITB patient population and results is limited statistical power. Several factors contributed to the limited inclusion of patients, including logistical challenges in the pre- and post-operative process and patient anxiety prior to surgery, which affected their willingness to complete the measurements. In addition, a significant proportion of patients receiving a baclofen pump had cognitive impairment, which further complicated the assessment process. In addition, many patients had multiple co-morbidity's in addition to spasticity, necessitating admission to the post-anaesthesia care unit (PACU) rather than the ward. Here, patient safety concerns outweighed the measurements. To address these limitations, I recommend that future research focuses on the inclusion of patients presenting for SS treatment rather than patients receiving a definitive implanted system. SS measurements offer a more standardised condition with less logistical dependencies and external factors.

4.4.3. Stretch Reflex Onset

A limitation of this study is the potential for observational bias in the labelling of MAS repetitions within the sEMG software. As the researcher, I manually label MAS repetitions based on my subjective perception of when the repetition begins. This method is inherently influenced by individual interpretation and may introduce variability and bias into the analysis. To address this limitation, future research could explore automated methods, such as those proposed by Hu et al. [17]. Their method is based on the Stretch Reflex Onset detection and can improve accurate and reliable labelling of the MAS repetitions. Of the 44 cases analysed in their research, 42 cases (95.5%) were successfully recognized using the SRO detection algorithm.

4.4.4. Pharmacokinetics of baclofen

The limitations in assessing the effect of baclofen on muscle activity stem from gaps in understanding its pharmacokinetics. The mechanism by which baclofen spreads in the cerebrospinal fluid (CSF), and subsequently its effect on specific muscles, remains unclear. Factors such as breathing and heart rate might influence the flow of CSF [48], which could affect the distribution of baclofen within the central nervous system. The lack of knowledge on the distribution of baclofen makes it difficult to determine which dermatomes, and therefore which muscles are predominantly affected after ITB treatment.
In addition, concentration differences between the spinal cord and the cerebrospinal fluid also play a role in the therapeutic effect. Initially after administration, there are low concentrations in the spinal cord and high concentrations in the cerebrospinal fluid. Later, the concentration in the spinal cord increases, leading to an effective reduction in spasticity. This is followed by gradual excretion from the surrounding tissues, resulting in diminishing effects within approximately four hours after administration. It is reported in literature that there are inter-individual variations in the concentrations of baclofen in the cerebrospinal fluid (CSF) [49]. Not all patients are assessed at the same time after administration, leading to variations in baclofen levels between patients, and therefore measured therapeutic effects.

4.5. Future Recommendations

This report presents the findings of an exploratory study and identifies several aspects that are worth further investigating. The study will continue by including more patients receiving baclofen treatment. The following recommendations are intended to enhance the quality of the data, the methodology employed in the analysis, and the study protocol.

4.5.1. Averaging MAS repetitions

The substantial amount of data gathered for each patient, measurements from both legs, four muscles, and six Modified Ashworth Scale (MAS) events, with each three repetitions, results in a considerable volume of data points. With four features extracted from each event, SS and implantation, the total dataset per patient can quickly grow. The quantity of data necessitates careful consideration and decision-making during analysis and interpretation. For the data analysis and evaluation of the results of study aim 1, choices had to be made regarding data reduction. As this is an exploratory study, it was important to avoid eliminating too much data. Since it can potentially lead to biased or incomplete conclusions. Based on the assumption that the muscle activity in other muscles than the one assessed for the MAS would be limited, all different MAS events were averaged for one muscle. For example, the time window of the MAS assessment of the rectus femoris muscle is particularly relevant for the rectus femoris. Consequently, it can be assumed that the MAS GAS assessment will have a negligible effect on the RF muscle activity, in comparison to activity follow by the MAS RF assessment.
However, the evaluation of the RMS values led to the rejection of the aforementioned assumption. The results of the RMS for EMGITB001 and EMGITB010 were not in accordance with the hypothesis. Upon examination of the data from each MAS assessment, it was observed that the signal intensity of the medial gastrocnemius was increased during the MAS RF assessment, after treatment. Consequently, when averaging over all MAS assessments, the mean value demonstrated an increase when comparing pre- and post-treatment values. However, when only the MAS GAS time window for the medial gastrocnemius was taken into account and the values were compared pre- and post-treatment, a decrease was observed.
An alternative approach considered was the averaging of data across all muscles of a patient's leg. This approach would not account for potential inter-patient variability in muscle function. Furthermore, in clinical practice, it has been observed that not all muscles are equally affected by spasticity.
Based on these observations I recommend the following data analysis approach for future research, regarding study aim 1.
The decision to include patients for ITB implantation is based on the principle that the most severely affected muscle should benefit from treatment. Consequently, the most severely affected muscle of each patients should be used when evaluating the feature values. For that muscle, the corresponding MAS assessment repetitions should be employed. For example, if the medial gastrocnemius is the most severely affected muscle, only the repetitions of the event MAS GAS should be considered for analysis. This will result in a smaller dataset for each patient, thereby reducing the necessity of averaging for data reduction.

4.5.2. Features

For further analysis of sEMG features, I make the following recommendations. For PAV, the influence of external factors should be further analysed as the sEMG amplitude is a sensitive parameter to noise. In addition, the pre-processing and normalization methods used should be reviewed due to the outliers seen in the absolute and percentage differences. A suggestion can be removing the offset of the signal, isolating the specific muscle activity of interest from the baseline nose.
In a review of Sousa et al. [34] on normalization of EMG signals an approach is presented for normalisation of isokinetic actions. This approach is based on the Maximal Voluntary Contraction, the express EMG as a percentage of the maximum neural activity. However, for the patient population of this study maximal contractions are not always possible due to their UMN. Another approach to consider in future research is to use the mean amplitude of the defined MAS repetition, instead of the peak amplitude. It is reported by Halaki et al. [50] that this approach is either comparable or better as normalization technique.
For the median frequency I recommend to conduct further research to ascertain the manner in which spectral characteristics change following baclofen treatment for each type of pathology. The existing

literature and the results of my own research indicate that there is considerable variation in the trends observed. Some studies have indicated an increase in median frequency post-treatment, while others have demonstrated a decrease.
For the CCR I recommended to consider additional information regarding interpretation of the CCR. When both agonist and antagonist muscles decrease simultaneously, the ratio remains unchanged, which may lead to misinterpretation of muscle activity. From literature the time-lag between activation of the antagonist and agonist muscle, following agonist activation is suggested [46]. The additional information could assure more refinement on the CCR results and therefore enhance the accuracy of the assessment of co-contraction.

4.5.3. Statistical Analysis

Given the exploratory nature of the study a statistical analysis was conducted to identify potential insights into the significance of changes in feature values following baclofen treatment. For future statistical analysis, I recommend two additional approaches. First, to perform additional statistical analysis, by grouping the patients according to their pathology. This may provide further insight into the impact of baclofen on different pathology's. To enable this analysis more patients need to be included.
Secondly, to perform the Spearman rank correlation coefficient and the corresponding p-value calculation for the MAS scores and feature values, both pre- and post-treatment, separately. This approach may facilitate the identification of new insights regarding the relationship between feature values and MAS scores. This approach differs from the current methodology, which calculates the correlation between the change in feature value and the change in MAS score. The calculation of the change in feature value or MAS score is based on the assumption that both the pre- and post-measurement conditions are identical. However, data analysis has revealed that there are differences between the pre- and post-measurements. For instance, the change in electrode impedance affects the signal's standard deviation. This new approach offers insight into the correlation between feature values and MAS scores, thereby avoiding the limitations of previous methodologies.

4.5.4. Study protocol

In order to create a more homogeneous patient group, I recommend to add an inclusion and exclusion criteria to the study protocol. The inclusion would state that the Body Mass Index (BMI) of the patient should be within the ranges of 'normal' (18.5-24.9). This is to ensure that no patients are included with levels of body fat that are too high, which could negatively influence the sEMG signal quality [51]. The exclusion criteria would state that the patient is included for implantation of a definitive implanted ITB pump. The conditions surrounding the surgery present challenges in ensuring a sufficient number of included patients and sufficient data quality. Pre-surgery patients often experience nerves and discomfort, which may influence their willingness to participate. Additionally, post-surgery, limited time is available to perform measurements since post-operative imaging and transportation to the rehabilitation clinic is planned. In addition, external factors may also affect the quality of the sEMG signal, such as differences in dosage, given that each pump is installed according to the patient's needs. Furthermore, the potential impact of anaesthetics administered during surgery on muscle activity.

4.5.5. Automation

In the context of the assessment of muscle activity changes post-baclofen treatment through sEMG, the integration of machine learning techniques presents a promising approach for future research. The recommendation to implement machine learning algorithms in future research is based on a study by Wang et al. (2017) [47]. The objective of this study was to evaluate the use of support vector machine (SVM) to classify the grade of spasticity. They included patients with upper limb spasticity resulting from a stroke. The root mean square, mean power frequency and median frequency were chosen as sEMG features. The accuracy of the SVM using only sEMG features was found to be 70.9%. When combining sEMG with mechanomyography (MMG) data, the accuracy increased to 91.7%. These promising results indicate that the application of SVM with sEMG and MMG data is meaningful in the evaluation of muscle activity. Furthermore, this research demonstrates that the positive predictive value can be improved when features are combined. The use of machine learning algorithms for signal analysis presents a number of advantages over manual signal analysis, making it worthy of consideration for future research. First, as the volumes of data increase, including more patients or analysing multiple features, machine learning algorithms can process it more efficiently. Second, the potential for bias or

subjectivity is limited due to the objective approach of the algorithm, which improves the reliability of the results [52, 53]. Finally, a machine learning algorithm can recognise complex patterns within data, allowing for identification of subtle changes or trends in signal patterns that could translate treatment effects.

5
Conclusion

In conclusion, the objective of this study was to assess the impact of intrathecal baclofen (ITB) treatment on muscle activity in the lower limbs using surface electromyography (sEMG). Through the analysis of sEMG features, several key findings have appeared.
First, the RMS demonstrated a significant difference in 3 out of 8 muscles, and suggesting it is a suitable sEMG feature for assessing the effect of baclofen on muscle activity. However, it is advised to review the analysis method on averaging across MAS assessments used for comparative analysis. The results for the RMS feature indicates a moderate correlation with the MAS scores. Additional analysis involving more patients is recommended to confirm these promising results in a larger cohort of patients.
Second, the PAV appears to have moderate potential as an indicator of changes in muscle activity following ITB treatment. The PAV analysis presented variability in correlation direction and strength with the MAS. This variability points out the necessity to review the methodology of signal acquisition and normalization of the PAV, all to minimize the influence of external factors on the amplitude value.
Third, the median frequency, not yet presenting valuable insights on changes in muscle activity after baclofen treatment or on correlation with the MAS. The results indicate that more knowledge is needed about the changes in the spectral characteristics of muscle activity after baclofen treatment to identify a spectral feature that can assess these changes.
Finally, the CCR demonstrated a moderate ability as predictive value on change in muscle activity after baclofen treatment and low correlation with the MAS scores. Limitations regarding the calculation method are noted, suggesting additional approaches to quantify co-contraction using sEMG.

The moderate correlations on the PGIC analysis emphasise the importance of integrating subjective patient experiences alongside objective measures in treatment decision-making processes.

This research provided valuable insights into the sEMG features that were used for analysis, on their changes after baclofen treatment. The study underscores the complexity of muscle activity patterns related to spasticity and their relationship with ITB treatment. Continuing this research will help to gain more knowledge about the influence of ITB on sEMG characteristics. This will be accomplished by following the recommendations on the calculation methodologies of the sEMG features and increasing the patient cohort.

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A

MAS Movements

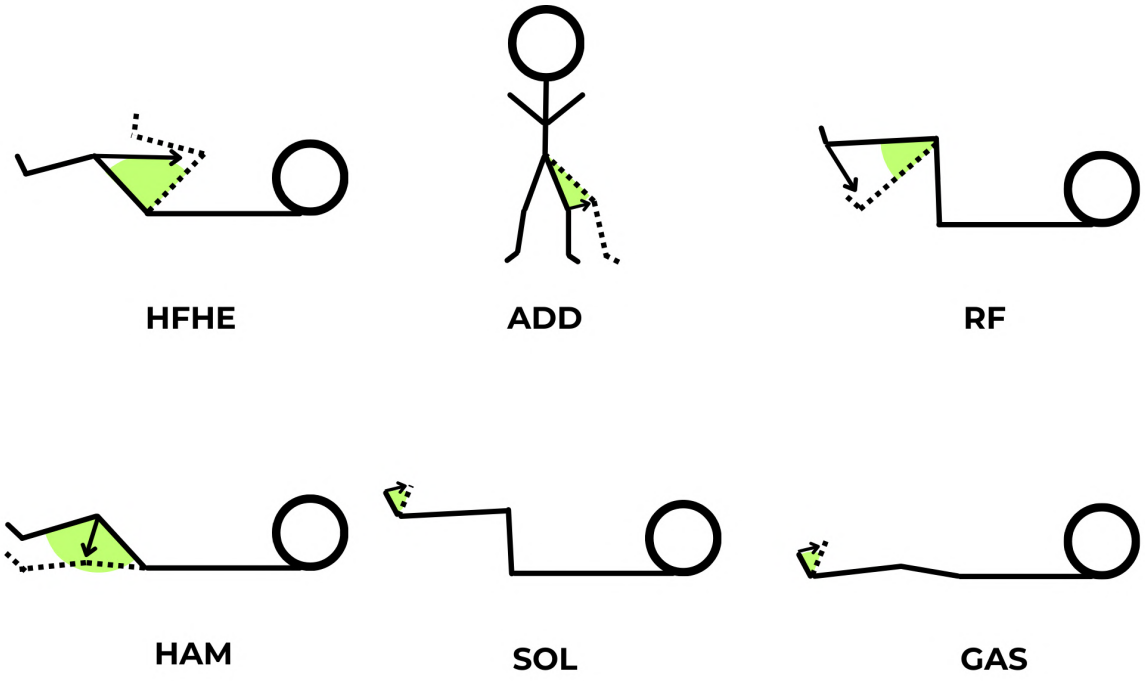

Figure A.1: Movements performed during assessment of the Modified Ashworth Scale. HFHE = Hip Flexors Hip Exentensors; ADD = Adductors; RF = Rectus Femoris; HAM = Hamstrings; SOL = soleus muscle; GAS = Gastrocnemius muscle

B

Pipeline Data Processing

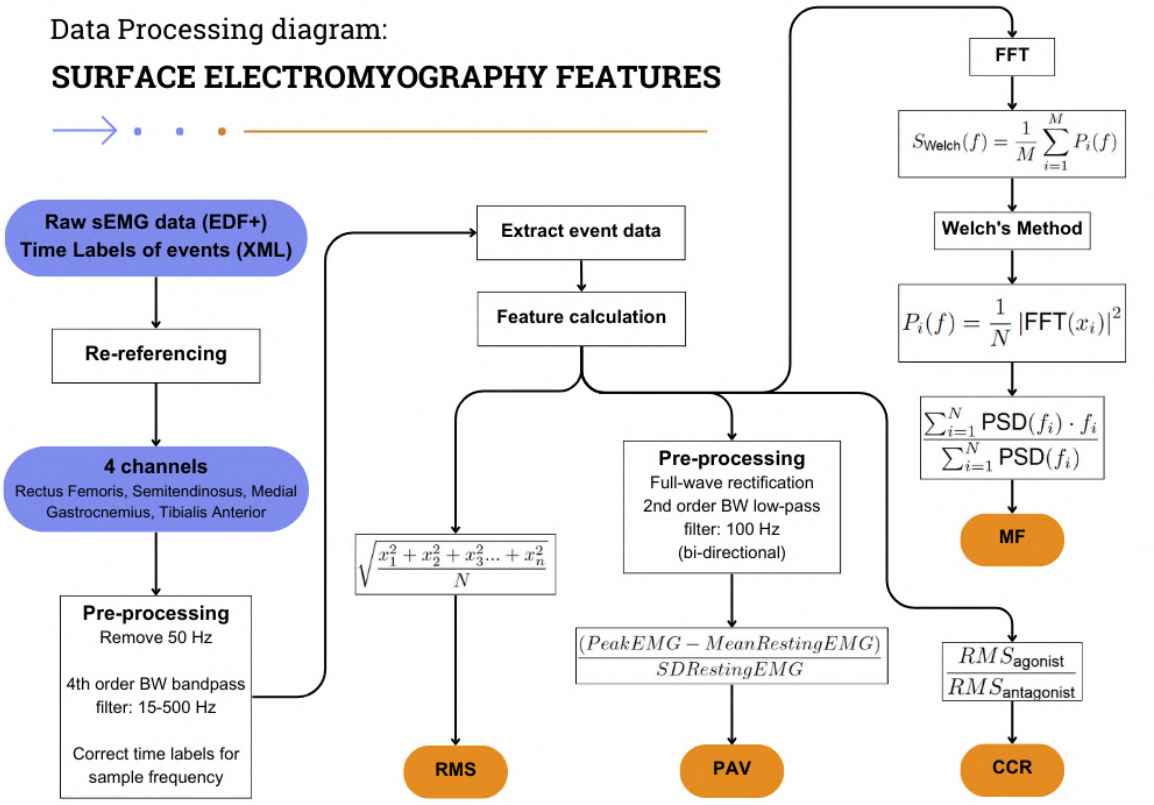

Figure B.1: Flowchart of data processing: from raw EDF. files to features.

C

Patient Demographics

Table C.1: Specifications of the patient population. MS = Multiple Sclerosis, CP = Cerebral Palsy, ABI = Acquired Brain Injury, SCI = Spinal Cord Injury, X-ADL = X-linked Adrenoleukodystrophy, CM = Cavernous Malformations. (Part 1).

ID	Pathology	Age	Gender	Dosage SS (µg)	Oral Baclofen Dosage
EMGITB001	MS	54	F	50	4dd 20 mg
EMGITB002	CP	52	F	50	3dd 20 mg
EMGITB003	NAH	31	M	50	-
EMGITB004	CM	72	M	50	7dd 10 mg
EMGITB005	MS	63	F	50	4dd 12.5 mg
EMGITB006	SCI (Th10)	55	F	50	4dd 20 mg
EMGITB007	X-ADL	47	M	-	3dd 10 mg
EMGITB008	SCI (Th7)	65	M	50	3dd 20 mg
EMGITB009	NAH	34	F	50	Other anti-spasmolytic
EMGITB010	MS	68	F	25	4dd 10 mg
EMGITB011	KCNB1	41	M	50	3dd 15 mg
EMGITB012	MS	59	F	50	3dd 15 mg

Table C.2: Specifications of the patient population. No specification on spastic side, indicates both sides were even affected.(Part 2).

ID	Dosage pump	More spastic side	Katheter Tip Level
EMGITB001	25.05 µg (1,04 µg/uur)	Th5	Right
EMGITB002	-	-	Left
EMGITB003	-	-	Right
EMGITB004	-	-	-
EMGITB005	100.0 µg (4.2 µg/uur)	Th6	Right
EMGITB006	-	-	-
EMGITB007	100.0 µg (4.2 µg/uur)	Th7	Left
EMGITB008	-	-	Right
EMGITB009	-	-	-
EMGITB010	50.06 µg 2.09 µg/uur	Th8	Right
EMGITB011	-	-	Left
EMGITB012	-	-	-

D

MAS Scores

Table D.1: Overview of the MAS scores of each individual patient. Presented for the hip flexors and extensors (HFHE), the rectus femoris (RF), the semitendinosus (HAM) and the medial gastrocnemius (GAS). The scoring is corrected for data analysis: 0 = 0; 1 = 1; 1+ = 2; 2 = 3; 3 = 4; 4 = 5.

Patient	MAS HFHE	MAS RF	MAS HAM	MAS GAS
EMGITB001				
Left Pre SS	0	0	0	2
Left Post SS	0	0	0	0
Right Pre SS	0	0	0	1
Right Post SS	0	0	0	0
Left Pre Imp	1	0	1	0
Left Post Imp	0	0	0	1
Right Pre Imp	1	0	1	2
Right Post Imp	0	0	0	2
EMGITB002				
Left Pre SS	5	5	5	5
Left Post SS	1	2	5	5
Right Pre SS	5	4	3	4
Right Post SS	0	2	3	4
EMGITB003				
Left Pre SS	3	3	3	3
Left Post SS	0	0	0	0
Right Pre SS	4	4	4	4
Right Post SS	0	1	1	1
EMGITB004				
Left Pre SS	1	1	1	1
Left Post SS	0	0	0	0
Right Pre SS	1	1	1	1
Right Post SS	0	0	0	0
EMGITB005				
Left Pre SS	4	4	3	1
Left Post SS	0	1	0	0
Right Pre SS	4	3	-	1
Right Post SS	0	0	-	0
Left Pre Imp	4	3	4	3
Left Post Imp	3	3	1	3

Continued on next page

Table D.1: Continued from previous page

Patient	MAS HFHE	MAS RF	MAS HAM	MAS GAS
Right Pre Imp	5	3	-	4
Right Post Imp	3	3	-	3
EMGITB006				
Left Pre SS	4	4	4	5
Left Post SS	4	4	3	5
Right Pre SS	4	4	4	5
Right Post SS	4	4	4	5
EMGITB007				
Left Pre Imp	5	5	5	4
Left Post Imp	5	5	5	3
Right Pre Imp	5	4	4	3
Right Post Imp	5	5	5	4
EMGITB008				
Left Pre SS	0	1	0	0
Left Post SS	0	1	1	0
Right Pre SS	4	4	4	0
Right Post SS	3	2	3	0
EMGITB009				
Left Pre SS	5	4	4	5
Left Post SS	1	1	1	5
Right Pre SS	4	4	4	5
Right Post SS	1	1	1	5
EMGITB010				
Left Pre SS	1	1	3	4
Left Post SS	0	0	1	0
Right Pre SS	1	0	0	1
Right Post SS	1	0	1	1
Left Pre Imp	1	1	3	4
Left Post Imp	0	0	1	0
Right Pre Imp	1	0	0	1
Right Post Imp	1	0	1	1
EMGITB011				
Left Pre SS	4	4	3	0
Left Post SS	3	3	0	0
Right Pre SS	4	4	3	0
Right Post SS	3	3	0	0
EMGITB012				
Left Pre SS	3	4	4	4
Left Post SS	0	0	0	0
Right Pre SS	3	2	3	4
Right Post SS	0	0	0	0

E

RMS and ITB

Table E.1: Mean RMS value, standard deviation and absolute difference for each muscle, per patient. The mean (SD) is calculated over all MAS repetitions for each muscle. The absolute difference is the difference in mean RMS pre- an post treatment.

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
EMGITB001				
Medial Gastrocnemius				
Left	Pre SS	2.68E-05	2.11E-05	-7.33E-06
Left	Post SS	1.95E-05	1.70E-05	
Left	Pre Imp	4.27E-06	3.00E-06	6.09E-06
Left	Post Imp	1.04E-05	9.29E-06	
Right	Pre SS	8.22E-06	2.38E-06	8.60E-08
Right	Post SS	8.30E-06	1.17E-06	
Right	Pre Imp	8.02E-06	4.42E-06	-2.79E-06
Right	Post Imp	5.23E-06	1.02E-06	
Rectus Femoris				
Left	Pre SS	3.01E-05	1.68E-05	2.54E-06
Left	Post SS	3.27E-05	2.76E-05	
Left	Pre Imp	1.65E-05	8.35E-06	-1.23E-05
Left	Post Imp	4.22E-06	2.38E-06	
Right	Pre SS	6.35E-06	3.43E-06	1.14E-06
Right	Post SS	7.49E-06	1.43E-06	
Right	Pre Imp	4.07E-06	2.86E-06	-8.97E-07
Right	Post Imp	3.18E-06	2.05E-06	
Semitendinosus				
Left	Pre SS	3.05E-05	2.71E-05	-1.21E-05
Left	Post SS	1.84E-05	8.36E-06	
Left	Pre Imp	8.51E-06	5.57E-06	-5.44E-06
Left	Post Imp	3.07E-06	1.60E-06	
Right	Pre SS	6.81E-06	2.55E-06	1.76E-06
Right	Post SS	8.56E-06	4.04E-06	
Right	Pre Imp	1.10E-05	6.56E-06	-7.83E-06
Right	Post Imp	3.17E-06	1.56E-06	
Tibialis Anterior				
Left	Pre SS	2.48E-05	2.54E-05	-1.24E-05
Left	Post SS	1.24E-05	1.52E-05	
Left	Pre Imp	4.95E-05	0.000118	-4.36E-05
Left	Post Imp	5.85E-06	6.12E-06	
Right	Pre SS	5.45E-06	2.74E-06	2.01E-06

Continued on next page

Table E.1: Continued from previous page

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
Right	Post SS	7.45E-06	8.98E-06	
Right	Pre Imp	5.51E-06	3.53E-06	-2.04E-06
Right	Post Imp	3.47E-06	1.97E-06	
EMGITB002				
Medial Gastrocnemius				
Left	Pre SS	3.80E-05	1.61E-05	-1.23E-05
Left	Post SS	2.57E-05	6.97E-06	
Right	Pre SS	5.00E-05	1.87E-05	-1.78E-05
Right	Post SS	3.22E-05	9.04E-06	
Rectus Femoris				
Left	Pre SS	3.12E-05	1.56E-05	-1.26E-05
Left	Post SS	1.87E-05	3.67E-06	
Right	Pre SS	2.16E-05	6.83E-06	-6.96E-07
Right	Post SS	2.09E-05	5.22E-06	
Semitendinosus				
Left	Pre SS	1.44E-05	5.50E-06	-7.21E-06
Left	Post SS	7.23E-06	2.10E-06	
Right	Pre SS	1.43E-05	3.19E-06	1.22E-04
Right	Post SS	1.36E-04	3.14E-04	
Tibialis Anterior				
Left	Pre SS	3.51E-05	4.21E-05	-7.42E-06
Left	Post SS	2.77E-05	1.54E-05	
Right	Pre SS	6.32E-05	1.67E-05	-4.16E-05
Right	Post SS	2.15E-05	1.07E-05	
EMGITB003				
Medial Gastrocnemius				
Left	Pre SS	8.88E-06	4.16E-06	-3.37E-06
Left	Post SS	5.51E-06	2.52E-06	
Right	Post SS	4.95E-06	2.67E-06	3.30E-06
Rectus Femoris				
Left	Pre SS	2.95E-06	1.78E-06	4.34E-07
Left	Post SS	3.39E-06	1.22E-06	
Right	Post SS	3.96E-06	2.08E-06	
Semitendinosus				
Left	Pre SS	1.06E-05	4.28E-06	-7.17E-06
Left	Post SS	3.47E-06	1.43E-06	
Right	Post SS	8.92E-06	3.56E-06	
Tibialis Anterior				
Left	Pre SS	3.87E-06	2.57E-06	9.02E-07
Left	Post SS	4.77E-06	2.90E-07	
Right	Post SS	8.24E-06	3.51E-06	
EMGITB004				
Medial Gastrocnemius				
Left	Pre SS	4.75E-05	4.66E-05	-3.59E-05
Left	Post SS	1.17E-05	7.64E-06	
Right	Pre SS	1.24E-05	1.11E-05	1.48E-05
Right	Post SS	2.73E-05	2.32E-05	

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Table E.1: Continued from previous page

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
Rectus Femoris				
Left	Pre SS	1.01E-05	8.89E-06	-4.81E-07
Left	Post SS	9.60E-06	2.25E-06	
Right	Pre SS	2.15E-05	1.71E-05	-1.15E-05
Right	Post SS	1.00E-05	8.71E-06	
Semitendinosus				
Left	Pre SS	2.50E-05	1.70E-05	-1.41E-05
Left	Post SS	1.08E-05	7.03E-06	
Right	Pre SS	2.71E-05	2.35E-05	-1.25E-05
Right	Post SS	1.47E-05	1.01E-05	
Tibialis Anterior				
Left	Pre SS	3.52E-05	3.07E-05	-7.45E-06
Left	Post SS	2.78E-05	8.23E-06	
Right	Pre SS	2.60E-05	2.09E-05	5.41E-07
Right	Post SS	2.66E-05	2.78E-05	
EMGITB005				
Medial Gastrocnemius				
Left	Pre SS	1.55E-05	7.70E-06	6.83E-07
Left	Post SS	1.61E-05	2.06E-06	
Left	Pre Imp	1.31E-05	1.28E-05	1.01E-05
Left	Post Imp	2.32E-05	2.81E-05	
Right	Pre SS	6.46E-06	4.81E-06	1.41E-05
Right	Post SS	2.06E-05	5.31E-06	
Right	Pre Imp	1.90E-05	1.81E-05	-2.73E-06
Right	Post Imp	1.62E-05	5.25E-06	
Rectus Femoris				
Left	Pre SS	1.37E-05	6.99E-06	-9.98E-06
Left	Post SS	3.72E-06	2.44E-06	
Left	Pre Imp	9.29E-06	8.98E-06	-7.38E-06
Left	Post Imp	1.91E-06	1.76E-06	
Right	Pre SS	1.79E-05	2.80E-05	-7.64E-06
Right	Post SS	1.03E-05	1.04E-05	
Right	Pre Imp	9.07E-06	4.87E-06	-7.42E-06
Right	Post Imp	1.65E-06	8.28E-07	
Semitendinosus				
Left	Pre SS	2.59E-05	1.13E-05	-1.68E-05
Left	Post SS	9.06E-06	3.56E-06	
Left	Pre Imp	1.78E-05	9.75E-06	-1.10E-05
Left	Post Imp	6.75E-06	1.59E-06	
Tibialis Anterior				
Left	Pre SS	3.46E-05	3.30E-05	-1.98E-06
Left	Post SS	3.26E-05	5.09E-06	
Left	Pre Imp	2.49E-05	3.99E-05	-9.26E-06
Left	Post Imp	1.57E-05	2.48E-05	
Right	Pre SS	2.42E-05	1.34E-05	-1.90E-05
Right	Post SS	5.24E-06	3.50E-06	
Right	Pre Imp	1.37E-05	7.74E-06	-3.68E-06
Right	Post Imp	1.00E-05	4.58E-06	

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Table E.1: Continued from previous page

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
EMGITB006				
Medial Gastrocnemius				
Left	Post SS	2.54E-05	1.10E-05	
Right	Pre SS	2.14E-05	9.61E-06	-9.14E-06
Right	Post SS	1.22E-05	4.21E-06	
Rectus Femoris				
Left	Post SS	3.38E-05	1.45E-05	
Right	Pre SS	1.41E-05	9.84E-06	-3.71E-06
Right	Post SS	1.04E-05	5.52E-06	
Semitendinosus				
Left	Post SS	2.76E-05	6.20E-06	
Right	Pre SS	3.84E-05	1.38E-05	-2.89E-06
Right	Post SS	3.55E-05	8.95E-06	
Tibialis Anterior				
Left	Post SS	2.58E-05	7.92E-06	
Right	Pre SS	3.28E-05	1.39E-05	-3.10E-06
Right	Post SS	2.97E-05	2.02E-05	
EMGITB007				
Medial Gastrocnemius				
Left	Pre Imp	8.59E-06	2.19E-06	1.43E-05
Left	Post Imp	2.29E-05	1.58E-05	
Right	Pre Imp	1.25E-05	4.74E-06	1.46E-05
Right	Post Imp	2.71E-05	2.49E-05	
Rectus Femoris				
Right	Pre Imp	6.90E-05	9.48E-06	6.74E-06
Right	Post Imp	7.57E-05	7.20E-06	
Semitendinosus				
Left	Pre Imp	4.71E-05	5.54E-06	5.78E-06
Left	Post Imp	5.28E-05	5.03E-06	
Right	Pre Imp	5.80E-05	5.80E-06	-4.21E-06
Right	Post Imp	5.38E-05	1.03E-05	
Tibialis Anterior				
Left	Pre Imp	1.96E-05	2.45E-06	2.68E-05
Left	Post Imp	4.65E-05	1.47E-05	
Right	Pre Imp	2.59E-05	1.20E-05	-1.21E-06
Right	Post Imp	2.47E-05	1.86E-05	
EMGITB008				
Medial Gastrocnemius				
Left	Pre SS	1.03E-05	3.43E-06	5.22E-06
Left	Post SS	1.55E-05	2.53E-06	
Right	Pre SS	1.81E-05	5.67E-06	8.83E-06
Right	Post SS	2.69E-05	1.67E-05	
Rectus Femoris				
Left	Pre SS	1.05E-05	6.08E-06	1.18E-05
Left	Post SS	2.23E-05	7.02E-06	
Right	Pre SS	3.52E-05	1.23E-05	-1.19E-05
Right	Post SS	2.33E-05	2.86E-06	
Semitendinosus				

Continued on next page

Table E.1: Continued from previous page

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
Left	Pre SS	1.85E-05	6.15E-06	2.37E-06
Left	Post SS	2.08E-05	2.29E-06	
Right	Pre SS	4.22E-05	1.33E-05	-2.54E-05
Right	Post SS	1.68E-05	1.10E-06	
Tibialis Anterior				
Left	Pre SS	8.20E-06	4.65E-06	1.38E-06
Left	Post SS	9.58E-06	6.33E-06	
Right	Pre SS	3.43E-05	1.29E-05	-1.62E-05
Right	Post SS	1.81E-05	1.19E-06	
EMGITB009				
Medial Gastrocnemius				
Left	Pre SS	1.05E-05	2.22E-06	-5.81E-06
Left	Post SS	4.73E-06	1.47E-06	
Right	Pre SS	2.17E-05	1.21E-05	-4.98E-06
Right	Post SS	1.67E-05	1.00E-05	
Rectus Femoris				
Left	Pre SS	1.49E-05	4.56E-06	-4.16E-06
Left	Post SS	1.07E-05	2.92E-06	
Right	Pre SS	8.69E-06	4.10E-06	-4.20E-06
Right	Post SS	4.48E-06	1.63E-06	
Semitendinosus				
Left	Pre SS	1.88E-05	6.31E-06	-1.12E-05
Left	Post SS	7.53E-06	3.67E-06	
Right	Pre SS	2.05E-05	5.42E-06	-2.54E-06
Right	Post SS	1.79E-05	1.22E-05	
Tibialis Anterior				
Left	Pre SS	1.08E-05	3.99E-06	-2.09E-06
Left	Post SS	8.73E-06	1.33E-05	
Right	Pre SS	2.15E-05	1.24E-05	-1.50E-05
Right	Post SS	6.51E-06	2.25E-06	
EMGITB010				
Medial Gastrocnemius				
Left	Pre SS	1.55E-05	9.29E-06	4.07E-07
Left	Post SS	1.59E-05	1.42E-05	
Left	Pre Imp	6.09E-06	4.19E-06	-3.25E-06
Left	Post Imp	2.84E-06	1.25E-06	
Right	Pre SS	2.14E-05	1.94E-05	-9.51E-06
Right	Post SS	1.19E-05	5.50E-06	
Right	Pre Imp	4.18E-06	2.97E-06	-1.07E-06
Right	Post Imp	3.12E-06	1.93E-06	
Rectus Femoris				
Left	Pre SS	1.98E-05	1.34E-05	-1.06E-05
Left	Post SS	9.15E-06	1.91E-06	
Left	Pre Imp	3.42E-06	1.00E-06	-5.85E-07
Left	Post Imp	2.84E-06	1.23E-06	
Right	Pre SS	1.10E-05	8.77E-06	2.83E-06
Right	Post SS	1.38E-05	8.70E-06	
Right	Pre Imp	4.33E-06	3.41E-06	-1.43E-06

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Table E.1: Continued from previous page

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
Right	Post Imp	2.90E-06	1.32E-06	
Semitendinosus				
Left	Pre SS	1.09E-05	4.99E-06	1.28E-06
Left	Post SS	1.21E-05	9.50E-06	
Left	Pre Imp	3.52E-06	1.62E-06	1.53E-06
Left	Post Imp	5.05E-06	2.81E-06	
Right	Pre SS	8.22E-06	6.63E-06	-3.42E-06
Right	Post SS	4.79E-06	2.63E-06	
Right	Pre Imp	4.43E-06	2.42E-06	1.70E-06
Right	Post Imp	6.13E-06	4.90E-06	
Tibialis Anterior				
Left	Pre SS	1.56E-05	7.67E-06	7.54E-06
Left	Post SS	2.32E-05	1.37E-05	
Left	Pre Imp	5.08E-06	2.96E-06	-1.32E-06
Left	Post Imp	3.76E-06	2.67E-06	
Right	Pre SS	5.03E-05	3.15E-05	-3.16E-05
Right	Post SS	1.87E-05	1.25E-05	
Right	Pre Imp	4.76E-06	3.54E-06	-1.08E-06
Right	Post Imp	3.68E-06	3.47E-06	
EMGITB011				
Medial Gastrocnemius				
Left	Pre SS	1.54E-05	9.13E-06	-4.11E-06
Left	Post SS	1.13E-05	7.96E-06	
Right	Pre SS	4.69E-05	2.32E-05	7.77E-06
Right	Post SS	5.46E-05	3.86E-05	
Rectus Femoris				
Left	Pre SS	1.40E-05	6.34E-06	-9.49E-06
Left	Post SS	4.48E-06	1.34E-06	
Right	Pre SS	2.49E-05	1.56E-05	-6.34E-06
Right	Post SS	1.85E-05	1.19E-05	
Semitendinosus				
Left	Pre SS	1.28E-05	4.38E-06	1.13E-06
Left	Post SS	1.40E-05	9.05E-06	
Right	Pre SS	1.71E-05	9.65E-06	-1.90E-06
Right	Post SS	1.52E-05	6.43E-06	
Tibialis Anterior				
Left	Pre SS	1.60E-05	9.61E-06	8.37E-06
Left	Post SS	2.43E-05	1.43E-05	
Right	Pre SS	1.23E-05	2.48E-06	-1.70E-06
Right	Post SS	1.06E-05	6.10E-06	
EMGITB012				
Medial Gastrocnemius				
Left	Pre SS	2.06E-05	7.04E-06	-9.83E-06
Left	Post SS	1.08E-05	1.00E-05	
Right	Pre SS	1.90E-05	9.47E-06	-1.43E-05
Right	Post SS	4.69E-06	4.60E-06	
Rectus Femoris				
Left	Pre SS	2.95E-05	1.32E-05	-2.68E-05

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Table E.1: Continued from previous page

Patient	Event	Mean RMS of all MAS repetitions	SD	Absolute Difference
Left	Post SS	2.71E-06	1.09E-06	
Right	Pre SS	1.54E-05	8.44E-06	-8.61E-06
Right	Post SS	6.77E-06	7.58E-06	
Semitendinosus				
Left	Pre SS	3.50E-05	5.74E-06	-3.12E-05
Left	Post SS	3.78E-06	1.91E-06	
Right	Pre SS	1.87E-05	3.33E-06	5.65E-05
Right	Post SS	7.51E-05	0.000189	
Tibialis Anterior				
Left	Pre SS	2.72E-05	9.52E-06	-2.27E-05
Left	Post SS	4.43E-06	2.39E-06	
Right	Pre SS	2.18E-05	7.92E-06	-1.67E-05
Right	Post SS	5.10E-06	1.70E-06	

F

PAV and ITB

Table F.1: Mean PAV value, standard deviation and absolute difference for each muscle, per patient. The mean (SD) is calculated over all MAS repetitions for each muscle. The absolute difference is the difference in mean PAV pre- an post treatment.

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
EMGITB001				
Medial Gastrocnemius				
Left	Pre SS	86.98	67.81	-46.04
Left	Post SS	40.95	48.27	
Left	Pre Imp	72.85	83.10	-58.98
Left	Post Imp	13.86	14.73	
Right	Pre SS	9.94	3.93	-4.95
Right	Post SS	4.93	3.15	
Right	Pre Imp	106.83	77.44	328.24
Right	Post Imp	9.12	4.52	
Rectus Femoris				
Left	Pre SS	105.65	70.12	48.50
Left	Post SS	154.14	164.18	
Left	Pre Imp	106.29	74.07	-79.11
Left	Post Imp	27.18	47.34	
Right	Pre SS	47.78	41.20	-37.26
Right	Post SS	10.52	7.52	
Right	Pre Imp	16.29	18.00	477.49
Right	Post Imp	24.00	20.53	
Semitendinosus				
Left	Pre SS	41.33	36.11	-22.82
Left	Post SS	18.51	13.42	
Left	Pre Imp	125.08	118.11	-121.78
Left	Post Imp	3.29	4.91	
Right	Pre SS	11.12	5.64	7.04
Right	Post SS	18.16	25.96	
Right	Pre Imp	139.77	97.33	-75.57
Right	Post Imp	16.66	15.80	
Tibialis Anterior				
Left	Pre SS	69.38	73.33	-42.30
Left	Post SS	27.07	43.30	
Left	Pre Imp	452.91	1283.73	-438.66
Left	Post Imp	14.24	23.07	
Right	Pre SS	27.93	17.54	-23.42

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Table F.1: Continued from previous page

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
Right	Post SS	34.79	59.91	
Right	Pre Imp	47.79	34.57	239.63
Right	Post Imp	13.36	10.88	
EMGITB002				
Medial Gastrocnemius				
Left	Pre SS	6.74	3.97	-1.80
Left	Post SS	26.64	12.41	
Right	Pre SS	33.47	11.85	13.76
Right	Post SS	13.75	3.25	
Rectus Femoris				
Left	Pre SS	7.06	4.83	37.68
Left	Post SS	44.75	18.39	
Right	Pre SS	4.99	1.66	17.69
Right	Post SS	22.68	6.91	
Semitendinosus				
Left	Pre SS	7.22	4.98	36.69
Left	Post SS	43.91	31.88	
Right	Pre SS	24.12	6.64	81.87
Right	Post SS	105.99	250.16	
Tibialis Anterior				
Left	Pre SS	1.93	4.09	32.87
Left	Post SS	22.29	10.06	
Right	Pre SS	8.55	3.50	-3.28
Right	Post SS	4.70	3.84	
EMGITB003				
Medial Gastrocnemius				
Left	Pre SS	195.92	151.39	-169.28
Left	Post SS	14.88	9.18	
Right	Post SS	9.95	10.30	
Rectus Femoris				
Left	Pre SS	69.80	79.15	-19.17
Left	Post SS	50.63	61.34	
Right	Post SS	18.69	17.00	
Semitendinosus				
Left	Pre SS	189.27	85.17	-177.62
Left	Post SS	11.65	11.66	
Right	Post SS	13.60	6.48	
Tibialis Anterior				
Left	Pre SS	91.26	77.78	-68.97
Left	Post SS	8.00	3.90	
Right	Post SS	11.38	7.56	
EMGITB004				
Medial Gastrocnemius				
Left	Pre SS	36.47	41.52	-22.72
Left	Post SS	42.29	29.97	
Right	Pre SS	133.46	150.61	-76.91
Right	Post SS	31.61	25.53	

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Table F.1: Continued from previous page

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
Rectus Femoris				
Left	Pre SS	2.78	2.76	77.59
Left	Post SS	80.36	27.89	
Right	Pre SS	269.82	231.84	-212.15
Right	Post SS	57.67	51.99	
Semitendinosus				
Left	Pre SS	60.98	48.97	88.26
Left	Post SS	149.24	125.95	
Right	Pre SS	355.40	303.41	-219.18
Right	Post SS	136.22	108.30	
Tibialis Anterior				
Left	Pre SS	74.43	73.56	-69.73
Left	Post SS	11.42	5.71	
Right	Pre SS	38.56	28.41	11.09
Right	Post SS	67.90	76.49	
EMGITB005				
Medial Gastrocnemius				
Left	Pre SS	18.60	14.88	-3.72
Left	Post SS	16.50	9.46	
Left	Pre Imp	7.29	6.20	1.83
Left	Post Imp	40.64	72.12	
Right	Pre SS	31.18	29.74	31.36
Right	Post SS	8.34	2.50	
Right	Pre Imp	14.09	13.23	26.01
Right	Post Imp	10.73	2.80	
Rectus Femoris				
Left	Pre SS	240.55	260.30	-174.01
Left	Post SS	66.54	60.70	
Left	Pre Imp	66.66	59.54	-42.66
Left	Post Imp	31.08	65.08	
Right	Pre SS	102.06	234.22	-65.26
Right	Post SS	36.80	44.37	
Right	Pre Imp	11.43	4.29	31.51
Right	Post Imp	20.30	23.00	
Semitendinosus				
Left	Pre SS	49.24	49.31	-31.03
Left	Post SS	18.21	13.37	
Left	Pre Imp	28.46	24.32	-11.80
Left	Post Imp	8.69	9.72	
Tibialis Anterior				
Left	Pre SS	108.68	85.13	-100.68
Left	Post SS	1.82	0.71	
Left	Pre Imp	68.78	73.35	-55.42
Left	Post Imp	5.40	12.57	
Right	Pre SS	92.75	53.71	28.98
Right	Post SS	3.56	4.68	
Right	Pre Imp	6.07	2.80	137.98
Right	Post Imp	18.79	9.22	

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Table F.1: Continued from previous page

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
EMGITB006				
Medial Gastrocnemius				
Left	Post SS	22.26	10.85	
Right	Pre SS	110.82	61.94	-40.77
Right	Post SS	27.38	16.63	
Rectus Femoris				
Left	Post SS	54.40	19.48	
Right	Pre SS	119.97	176.04	-80.39
Right	Post SS	39.57	19.19	
Semitendinosus				
Left	Post SS	66.03	19.55	
Right	Pre SS	104.43	34.38	-20.22
Right	Post SS	84.21	14.96	
Tibialis Anterior				
Left	Post SS	101.51	35.15	
Right	Pre SS	117.04	52.27	-75.81
Right	Post SS	169.76	88.26	
EMGITB007				
Medial Gastrocnemius				
Left	Pre Imp	50.03	23.33	-9.38
Left	Post Imp	435.07	340.43	
Right	Pre Imp	37.72	12.34	-21.17
Right	Post Imp	40.10	38.30	
Rectus Femoris				
Right	Pre Imp	12.69	2.62	2.89
Right	Post Imp	42.94	6.58	
Semitendinosus				
Left	Pre Imp	68.91	25.36	-60.22
Left	Post Imp	64.20	7.89	
Right	Pre Imp	22.31	6.21	-2.49
Right	Post Imp	31.18	7.48	
Tibialis Anterior				
Left	Pre Imp	219.65	91.09	-214.25
Left	Post Imp	287.42	63.76	
Right	Pre Imp	12.82	6.39	-8.23
Right	Post Imp	144.05	83.56	
EMGITB008				
Medial Gastrocnemius				
Left	Pre SS	23.30	16.01	18.99
Left	Post SS	4.99	2.30	
Right	Pre SS	16.86	10.47	2.85
Right	Post SS	47.23	40.91	
Rectus Femoris				
Left	Pre SS	4.33	3.21	-2.63
Left	Post SS	1.70	0.95	
Right	Pre SS	14.14	4.61	-9.91
Right	Post SS	4.23	0.97	
Semitendinosus				

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Table F.1: Continued from previous page

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
Left	Pre SS	64.67	31.57	-58.89
Left	Post SS	5.78	1.18	
Right	Pre SS	10.82	4.86	-5.71
Right	Post SS	5.11	1.11	
Tibialis Anterior				
Left	Pre SS	49.88	35.98	-38.46
Left	Post SS	4.50	5.44	
Right	Pre SS	87.81	31.51	-13.71
Right	Post SS	5.27	1.08	
EMGITB009				
Medial Gastrocnemius				
Left	Pre SS	38.69	13.97	-7.08
Left	Post SS	56.55	29.18	
Right	Pre SS	36.85	18.63	60.61
Right	Post SS	62.54	43.23	
Rectus Femoris				
Left	Pre SS	129.05	39.55	66.19
Left	Post SS	195.24	61.40	
Right	Pre SS	22.14	11.69	-4.27
Right	Post SS	17.87	10.67	
Semitendinosus				
Left	Pre SS	88.96	19.44	49.85
Left	Post SS	138.81	84.96	
Right	Pre SS	31.54	10.13	90.79
Right	Post SS	122.33	128.62	
Tibialis Anterior				
Left	Pre SS	33.59	21.05	34.31
Left	Post SS	49.65	116.93	
Right	Pre SS	52.43	27.00	-8.97
Right	Post SS	121.73	66.41	
EMGITB010				
Medial Gastrocnemius				
Left	Pre SS	23.93	24.96	-7.43
Left	Post SS	70.04	95.27	
Left	Pre Imp	2.86	2.38	7.88
Left	Post Imp	16.55	14.30	
Right	Pre SS	216.20	301.80	-31.67
Right	Post SS	19.71	10.09	
Right	Pre Imp	0.17	1.24	18.95
Right	Post Imp	19.12	14.86	
Rectus Femoris				
Left	Pre SS	61.79	76.86	-42.18
Left	Post SS	19.61	7.02	
Left	Pre Imp	13.89	11.13	6.41
Left	Post Imp	15.58	8.45	
Right	Pre SS	25.74	20.35	93.06
Right	Post SS	118.80	86.95	
Right	Pre Imp	1.77	3.16	16.50

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Table F.1: Continued from previous page

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
Right	Post Imp	18.27	8.95	
Semitendinosus				
Left	Pre SS	93.83	61.56	-43.75
Left	Post SS	50.08	49.77	
Left	Pre Imp	7.74	6.49	11.42
Left	Post Imp	19.82	15.16	
Right	Pre SS	12.64	10.27	37.10
Right	Post SS	49.74	50.28	
Right	Pre Imp	3.11	5.60	18.70
Right	Post Imp	21.81	22.50	
Tibialis Anterior				
Left	Pre SS	6.99	3.87	-5.17
Left	Post SS	41.23	33.16	
Left	Pre Imp	4.72	3.67	14.07
Left	Post Imp	4.59	3.28	
Right	Pre SS	445.34	272.88	-425.50
Right	Post SS	74.10	55.56	
Right	Pre Imp	5.24	5.58	23.78
Right	Post Imp	29.01	28.15	
EMGITB011				
Medial Gastrocnemius				
Left	Pre SS	35.92	32.65	-27.57
Left	Post SS	97.47	100.31	
Right	Pre SS	68.34	44.92	41.91
Right	Post SS	184.54	151.63	
Rectus Femoris				
Left	Pre SS	22.81	15.69	5.92
Left	Post SS	28.73	14.73	
Right	Pre SS	17.56	14.16	114.13
Right	Post SS	131.69	91.37	
Semitendinosus				
Left	Pre SS	7.70	6.63	58.09
Left	Post SS	65.79	57.64	
Right	Pre SS	4.68	2.37	53.17
Right	Post SS	57.85	40.20	
Tibialis Anterior				
Left	Pre SS	18.90	14.06	-15.35
Left	Post SS	43.46	27.53	
Right	Pre SS	14.00	8.81	-4.49
Right	Post SS	19.84	14.25	
EMGITB012				
Medial Gastrocnemius				
Left	Pre SS	120.27	74.14	-92.89
Left	Post SS	110.25	121.44	
Right	Pre SS	13.61	7.48	21.28
Right	Post SS	34.89	54.51	
Rectus Femoris				
Left	Pre SS	99.56	36.48	-96.15

Continued on next page

Table F.1: Continued from previous page

Patient	Event	Mean PAV of all MAS repetitions	SD	Absolute Difference
Left	Post SS	3.40	2.38	
Right	Pre SS	6.37	3.90	28.35
Right	Post SS	34.73	53.33	
Semitendinosus				
Left	Pre SS	34.44	8.03	3.12
Left	Post SS	37.56	31.55	
Right	Pre SS	8.59	1.91	7.23
Right	Post SS	15.82	47.85	
Tibialis Anterior				
Left	Pre SS	205.86	76.01	-36.10
Left	Post SS	9.50	9.82	
Right	Pre SS	19.84	6.91	-11.22
Right	Post SS	8.62	6.46	

G

Median Frequency and ITB

Table G.1: Mean Median Frequency, standard deviation and absolute difference for each muscle, per patient. The mean (SD) is calculated over all MAS repetitions for each muscle. The absolute difference is the difference in mean Median Frequency pre- an post treatment.

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
EMGITB001				
Medial Gastrocnemius				
Left	Pre SS	38.08	12.72	22.53
Left	Post SS	60.61	29.67	
Left	Pre Imp	82.58	28.73	-31.01
Left	Post Imp	51.57	23.07	
Right	Pre SS	98.63	22.60	1.23
Right	Post SS	99.87	22.52	
Right	Pre Imp	76.81	24.53	25.62
Right	Post Imp	102.43	22.80	
Rectus Femoris				
Left	Pre SS	33.84	10.99	39.18
Left	Post SS	73.02	54.57	
Left	Pre Imp	28.74	4.12	63.74
Left	Post Imp	92.48	20.58	
Right	Pre SS	82.81	26.61	53.14
Right	Post SS	135.95	29.50	
Right	Pre Imp	94.63	30.64	-8.56
Right	Post Imp	86.07	23.65	
Semitendinosus				
Left	Pre SS	38.93	21.00	29.69
Left	Post SS	68.62	45.70	
Left	Pre Imp	54.10	30.43	22.16
Left	Post Imp	76.26	22.59	
Right	Pre SS	84.43	17.50	32.27
Right	Post SS	116.71	37.23	
Right	Pre Imp	45.40	19.53	29.10
Right	Post Imp	74.49	16.60	
Tibialis Anterior				
Left	Pre SS	40.37	12.35	32.65
Left	Post SS	73.02	43.51	
Left	Pre Imp	45.59	8.69	37.00
Left	Post Imp	82.59	29.61	
Right	Pre SS	59.97	13.93	1.07

Continued on next page

Table G.1: Continued from previous page

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
Right	Post SS	61.04	16.08	
Right	Pre Imp	56.63	25.84	44.86
Right	Post Imp	101.49	36.82	
EMGITB002				
Medial Gastrocnemius				
Left	Pre SS	145.49	10.71	28.14
Left	Post SS	173.63	14.13	
Right	Pre SS	127.65	8.23	39.92
Right	Post SS	167.57	6.36	
Rectus Femoris				
Left	Pre SS	75.36	11.12	21.68
Left	Post SS	97.04	7.67	
Right	Pre SS	79.91	6.35	14.27
Right	Post SS	94.18	6.59	
Semitendinosus				
Left	Pre SS	85.86	9.82	18.66
Left	Post SS	104.52	13.40	
Right	Pre SS	101.65	14.38	-47.63
Right	Post SS	54.01	3.02	
Tibialis Anterior				
Left	Pre SS	124.48	22.12	-7.09
Left	Post SS	117.39	10.91	
Right	Pre SS	163.71	13.81	-31.72
Right	Post SS	131.99	20.36	
EMGITB003				
Medial Gastrocnemius				
Left	Pre SS	87.59	32.19	-8.17
Left	Post SS	79.42	24.43	
Right	Post SS	116.60	44.00	
Rectus Femoris				
Left	Pre SS	88.74	31.83	70.97
Left	Post SS	159.71	95.59	
Right	Post SS	119.94	63.06	
Semitendinosus				
Left	Pre SS	131.27	13.54	30.02
Left	Post SS	161.29	85.68	
Right	Post SS	64.04	7.64	
Tibialis Anterior				
Left	Pre SS	123.16	45.91	-52.41
Left	Post SS	70.75	12.57	
Right	Post SS	86.39	13.33	
EMGITB004				
Medial Gastrocnemius				
Left	Pre SS	49.13	20.84	12.34
Left	Post SS	61.48	23.15	
Right	Pre SS	78.08	37.06	-3.64
Right	Post SS	74.44	23.03	

Continued on next page

Table G.1: Continued from previous page

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
Rectus Femoris				
Left	Pre SS	56.90	20.03	9.15
Left	Post SS	66.05	18.59	
Right	Pre SS	62.09	12.18	-6.41
Right	Post SS	55.68	13.54	
Semitendinosus				
Left	Pre SS	46.19	6.06	10.83
Left	Post SS	57.02	11.58	
Right	Pre SS	61.06	9.64	-5.06
Right	Post SS	55.99	12.57	
Tibialis Anterior				
Left	Pre SS	59.67	17.80	20.02
Left	Post SS	79.70	9.21	
Right	Pre SS	69.73	17.21	-10.17
Right	Post SS	59.56	18.15	
EMGITB005				
Medial Gastrocnemius				
Left	Pre SS	85.48	28.33	13.33
Left	Post SS	98.81	24.54	
Left	Pre Imp	110.96	21.38	21.58
Left	Post Imp	132.54	25.32	
Right	Pre SS	89.01	28.46	25.09
Right	Post SS	114.10	22.07	
Right	Pre Imp	120.54	27.41	5.42
Right	Post Imp	125.97	14.99	
Rectus Femoris				
Left	Pre SS	59.70	13.28	0.36
Left	Post SS	60.05	17.90	
Left	Pre Imp	76.75	18.37	14.28
Left	Post Imp	91.03	14.22	
Right	Pre SS	60.22	21.53	-12.71
Right	Post SS	47.51	17.18	
Right	Pre Imp	69.29	11.80	22.29
Right	Post Imp	91.58	25.76	
Semitendinosus				
Left	Pre SS	92.43	17.51	-28.17
Left	Post SS	64.26	13.16	
Left	Pre Imp	82.97	11.90	-6.28
Left	Post Imp	76.69	6.20	
Tibialis Anterior				
Left	Pre SS	82.60	16.08	-29.36
Left	Post SS	53.24	3.50	
Left	Pre Imp	72.43	7.59	6.65
Left	Post Imp	79.08	27.61	
Right	Pre SS	75.31	18.54	8.87
Right	Post SS	84.18	18.73	
Right	Pre Imp	112.69	7.34	-11.07
Right	Post Imp	101.61	14.47	

Continued on next page

Table G.1: Continued from previous page

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
EMGITB006				
Medial Gastrocnemius				
Left	Post SS	149.16	15.04	
Right	Pre SS	80.52	21.31	35.30
Right	Post SS	115.82	26.40	
Rectus Femoris				
Left	Post SS	61.42	4.25	
Right	Pre SS	56.46	9.40	7.61
Right	Post SS	64.08	11.01	
Semitendinosus				
Left	Post SS	64.63	8.37	
Right	Pre SS	66.75	6.92	-2.40
Right	Post SS	64.35	4.10	
Tibialis Anterior				
Left	Post SS	84.04	13.80	
Right	Pre SS	68.15	14.96	-0.61
Right	Post SS	67.54	10.39	
EMGITB007				
Medial Gastrocnemius				
Left	Pre Imp	55.07	4.57	42.65
Left	Post Imp	97.72	18.08	
Right	Pre Imp	67.50	4.80	27.82
Right	Post Imp	95.32	10.02	
Rectus Femoris				
Left	Pre Imp	68.52	10.19	-8.02
Left	Post Imp	60.50	8.02	
Right	Pre Imp	58.12	2.71	4.46
Right	Post Imp	62.59	4.36	
Semitendinosus				
Left	Pre Imp	53.81	0.88	2.80
Left	Post Imp	56.61	2.64	
Right	Pre Imp	54.52	2.28	-0.74
Right	Post Imp	53.78	2.55	
Tibialis Anterior				
Left	Pre Imp	81.57	15.07	62.61
Left	Post Imp	144.18	18.04	
Right	Pre Imp	75.46	5.31	19.26
Right	Post Imp	94.72	10.36	
EMGITB008				
Medial Gastrocnemius				
Left	Pre SS	78.96	35.97	62.49
Left	Post SS	141.45	15.78	
Right	Pre SS	120.69	31.56	-39.39
Right	Post SS	81.30	29.20	
Rectus Femoris				
Left	Pre SS	65.75	18.91	-5.20
Left	Post SS	60.55	2.57	

Continued on next page

Table G.1: Continued from previous page

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
Right	Pre SS	78.26	7.15	-12.95
Right	Post SS	65.31	9.29	
Semitendinosus				
Left	Pre SS	64.09	11.32	28.94
Left	Post SS	93.03	6.05	
Right	Pre SS	152.25	10.36	-22.39
Right	Post SS	129.86	5.47	
Tibialis Anterior				
Left	Pre SS	62.22	35.34	20.67
Left	Post SS	82.89	40.53	
Right	Pre SS	91.79	11.85	-12.03
Right	Post SS	79.76	2.22	
EMGITB009				
Medial Gastrocnemius				
Left	Pre SS	130.61	18.78	-2.63
Left	Post SS	127.98	23.14	
Right	Pre SS	124.68	16.28	-46.02
Right	Post SS	78.66	35.05	
Rectus Femoris				
Left	Pre SS	76.70	16.86	-7.14
Left	Post SS	69.56	8.63	
Right	Pre SS	58.51	7.33	-4.58
Right	Post SS	53.94	4.23	
Semitendinosus				
Left	Pre SS	54.91	10.69	3.32
Left	Post SS	58.23	13.20	
Right	Pre SS	54.03	5.72	0.71
Right	Post SS	54.74	12.07	
Tibialis Anterior				
Left	Pre SS	123.20	25.49	-30.09
Left	Post SS	93.11	34.00	
Right	Pre SS	107.52	11.49	-32.64
Right	Post SS	74.88	25.10	
EMGITB010				
Medial Gastrocnemius				
Left	Pre SS	48.89	14.90	12.97
Left	Post SS	61.86	31.91	
Left	Pre Imp	87.69	37.39	22.04
Left	Post Imp	109.73	31.33	
Right	Pre SS	108.92	33.49	14.21
Right	Post SS	123.13	31.55	
Right	Pre Imp	128.58	19.43	-9.41
Right	Post Imp	119.17	30.00	
Rectus Femoris				
Left	Pre SS	76.82	19.91	3.86
Left	Post SS	80.67	8.87	
Left	Pre Imp	83.42	11.82	-1.67
Left	Post Imp	81.74	19.20	

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Table G.1: Continued from previous page

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
Right	Pre SS	83.21	10.20	7.29
Right	Post SS	90.49	13.15	
Right	Pre Imp	87.41	11.39	-5.97
Right	Post Imp	81.43	8.14	
Semitendinosus				
Left	Pre SS	65.97	19.26	4.77
Left	Post SS	70.74	29.77	
Left	Pre Imp	69.55	15.58	-6.60
Left	Post Imp	62.95	14.55	
Right	Pre SS	65.43	13.63	24.40
Right	Post SS	89.83	31.64	
Right	Pre Imp	60.79	11.28	-11.07
Right	Post Imp	49.72	18.62	
Tibialis Anterior				
Left	Pre SS	79.96	24.03	-2.40
Left	Post SS	77.56	15.52	
Left	Pre Imp	90.96	29.89	-0.32
Left	Post Imp	90.64	38.84	
Right	Pre SS	89.28	20.53	4.63
Right	Post SS	93.91	40.82	
Right	Pre Imp	132.22	20.91	-11.22
Right	Post Imp	120.99	25.47	
EMGITB011				
Medial Gastrocnemius				
Left	Pre SS	155.10	51.37	-26.26
Left	Post SS	128.84	61.97	
Right	Pre SS	76.37	19.74	-15.99
Right	Post SS	60.39	19.65	
Rectus Femoris				
Left	Pre SS	100.98	38.04	2.99
Left	Post SS	103.97	27.39	
Right	Pre SS	73.60	36.45	-20.93
Right	Post SS	52.68	18.20	
Semitendinosus				
Left	Pre SS	127.49	26.75	-29.01
Left	Post SS	98.48	37.04	
Right	Pre SS	138.97	37.48	-55.15
Right	Post SS	83.83	31.24	
Tibialis Anterior				
Left	Pre SS	120.12	53.94	-38.40
Left	Post SS	81.72	47.81	
Right	Pre SS	116.94	21.06	-52.16
Right	Post SS	64.78	31.24	
EMGITB012				
Medial Gastrocnemius				
Left	Pre SS	126.80	14.21	-56.56
Left	Post SS	70.24	30.20	
Right	Pre SS	100.28	16.65	-24.79

Continued on next page

Table G.1: Continued from previous page

Patient	Event	Mean Median Frequency of all MAS repetitions	SD	Absolute Difference
Right	Post SS	75.49	23.85	
Rectus Femoris				
Left	Pre SS	54.10	4.74	1.14
Left	Post SS	55.24	12.33	
Right	Pre SS	52.58	8.89	2.95
Right	Post SS	55.53	18.47	
Semitendinosus				
Left	Pre SS	69.91	8.39	-20.18
Left	Post SS	49.73	15.29	
Right	Pre SS	109.57	17.82	-59.00
Right	Post SS	50.57	3.78	
Tibialis Anterior				
Left	Pre SS	96.94	9.62	-26.09
Left	Post SS	70.84	12.34	
Right	Pre SS	92.73	8.50	-25.34
Right	Post SS	67.39	14.78	

H

CCR and ITB

Table H.1: Mean CCR, standard deviation and absolute difference for each muscle, per patient. The mean (SD) is calculated over all MAS repetitions for each muscle. The absolute difference is the difference in mean Median Frequency pre- an post treatment.

Patient	Event	Mean CCR of all MAS repetitions	SD	Absolute Difference
EMGITB001				
Medial Gastrocnemius				
Left	Pre SS	1.19	0.09	
Left	Post SS	1.29		
Left	Pre Imp	0.36	0.70	
Left	Post Imp	1.06		
Right	Pre SS	2.58	0.46	
Right	Post SS	3.04		
Right	Pre Imp	0.46	2.25	
Right	Post Imp	2.72		
Rectus Femoris				
Left	Pre SS	0.56	-0.20	
Left	Post SS	0.37		
Left	Pre Imp	1.45	0.18	
Left	Post Imp	1.63		
Right	Pre SS	0.90	0.11	
Right	Post SS	1.00		
Right	Pre Imp	0.13	0.83	
Right	Post Imp	0.96		
Semitendinosus				
Left	Pre SS	0.81	-0.44	
Left	Post SS	0.37		
Left	Pre Imp	0.59	0.02	
Left	Post Imp	0.61		
Right	Pre SS	1.56	0.35	
Right	Post SS	1.91		
Right	Pre Imp	3.31	-2.23	
Right	Post Imp	1.08		
EMGITB002				
Medial Gastrocnemius				
Left	Pre SS	3.48	-3.05	
Left	Post SS	0.43		
Right	Pre SS	0.61	-0.28	

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Table H.1: Continued from previous page

Patient	Event	Mean CCR of all MAS repetitions	SD	Absolute Difference
Right	Post SS	0.34		
Rectus Femoris				
Left	Pre SS	2.78	-0.52	
Left	Post SS	2.26		
Right	Pre SS	1.79	-1.74	
Right	Post SS	0.05		
Semitendinosus				
Left	Pre SS	0.71	-0.24	
Left	Post SS	0.47		
Right	Pre SS	0.67	0.96	
Right	Post SS	1.63		
EMGITB003				
Medial Gastrocnemius				
Left	Pre SS	6.19	-5.23	
Left	Post SS	0.97		
Right	Post SS	0.87		
Rectus Femoris				
Left	Pre SS	0.20	0.61	
Left	Post SS	0.81		
Right	Post SS	0.42		
Semitendinosus				
Left	Pre SS	2.43	-1.46	
Left	Post SS	0.97		
Right	Post SS	2.43		
EMGITB004				
Medial Gastrocnemius				
Left	Pre SS	1.09	-0.99	
Left	Post SS	0.11		
Right	Pre SS	0.79	4.50	
Right	Post SS	5.29		
Rectus Femoris				
Left	Pre SS	0.44	0.33	
Left	Post SS	0.77		
Right	Pre SS	0.92	-0.25	
Right	Post SS	0.67		
Semitendinosus				
Left	Pre SS	2.87	-2.11	
Left	Post SS	0.76		
Right	Pre SS	1.55	1.30	
Right	Post SS	2.85		
EMGITB005				
Medial Gastrocnemius				
Left	Pre SS	0.50	-0.14	
Left	Post SS	0.37		
Left	Pre Imp	1.81	-0.51	
Left	Post Imp	1.29		
Right	Pre SS	0.29	6.06	

Continued on next page

Table H.1: Continued from previous page

Patient	Event	Mean CCR of all MAS repetitions	SD	Absolute Difference
Right	Post SS	6.35		
Right	Pre Imp	2.14	0.91	
Right	Post Imp	3.05		
Rectus Femoris				
Left	Pre SS	0.51	-0.22	
Left	Post SS	0.29		
Left	Pre Imp	0.31	-0.12	
Left	Post Imp	0.19		
Right	Pre SS	0.96	2.10	
Right	Post SS	3.06		
Right	Pre Imp	0.49	-0.18	
Right	Post Imp	0.31		
Semitendinosus				
Left	Pre SS	2.30	1.43	
Left	Post SS	3.73		
Left	Pre Imp	3.85	-0.34	
Left	Post Imp	3.51		
EMGITB006				
Medial Gastrocnemius				
Left	Post SS	0.79		
Right	Pre SS	1.05	-0.12	
Right	Post SS	0.93		
Rectus Femoris				
Left	Post SS	0.71		
Right	Pre SS	0.19	0.03	
Right	Post SS	0.22		
Semitendinosus				
Left	Post SS	0.54		
Right	Pre SS	1.66	1.36	
Right	Post SS	3.02		
EMGITB007				
Medial Gastrocnemius				
Left	Pre Imp	0.55	-0.35	
Left	Post Imp	0.19		
Right	Pre Imp	0.26	-0.06	
Right	Post Imp	0.20		
Rectus Femoris				
Right	Pre Imp	1.00	0.19	
Right	Post Imp	1.19		
Semitendinosus				
Left	Pre Imp	1.83	-0.68	
Left	Post Imp	1.15		
Right	Pre Imp	0.86	-0.28	
Right	Post Imp	0.58		
EMGITB008				
Medial Gastrocnemius				
Left	Pre SS	1.83	1.24	

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Table H.1: Continued from previous page

Patient	Event	Mean CCR of all MAS repetitions	SD	Absolute Difference
Left	Post SS	3.07		
Right	Pre SS	0.38	0.64	
Right	Post SS	1.02		
Rectus Femoris				
Left	Pre SS	0.97	-0.20	
Left	Post SS	0.77		
Right	Pre SS	1.31	0.13	
Right	Post SS	1.45		
Semitendinosus				
Left	Pre SS	2.71	-1.58	
Left	Post SS	1.14		
Right	Pre SS	2.01	-1.31	
Right	Post SS	0.70		
EMGITB009				
Medial Gastrocnemius				
Left	Pre SS	0.62	0.08	
Left	Post SS	0.70		
Right	Pre SS	3.39	-1.47	
Right	Post SS	1.92		
Rectus Femoris				
Left	Pre SS	1.27	0.98	
Left	Post SS	2.25		
Right	Pre SS	0.30	-0.16	
Right	Post SS	0.13		
Semitendinosus				
Left	Pre SS	1.39	-0.95	
Left	Post SS	0.44		
Right	Pre SS	3.35	3.20	
Right	Post SS	6.54		
EMGITB010				
Medial Gastrocnemius				
Left	Pre SS	1.16	-0.80	
Left	Post SS	0.36		
Left	Pre Imp	1.36	-0.45	
Left	Post Imp	0.91		
Right	Pre SS	1.78	-0.99	
Right	Post SS	0.79		
Right	Pre Imp	0.28	0.06	
Right	Post Imp	0.34		
Rectus Femoris				
Left	Pre SS	2.89	-2.61	
Left	Post SS	0.28		
Left	Pre Imp	0.99	-0.30	
Left	Post Imp	0.69		
Right	Pre SS	2.03	0.87	
Right	Post SS	2.91		
Right	Pre Imp	0.41	0.12	
Right	Post Imp	0.52		

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Table H.1: Continued from previous page

Patient	Event	Mean CCR of all MAS repetitions	SD	Absolute Difference
Semitendinosus				
Left	Pre SS	0.47	1.16	
Left	Post SS	1.62		
Left	Pre Imp	1.42	1.01	
Left	Post Imp	2.43		
Right	Pre SS	1.05	-0.70	
Right	Post SS	0.36		
Right	Pre Imp	0.80	3.68	
Right	Post Imp	4.47		
EMGITB011				
Medial Gastrocnemius				
Left	Pre SS	2.81	-2.27	
Left	Post SS	0.54		
Right	Pre SS	3.34	2.68	
Right	Post SS	6.01		
Rectus Femoris				
Left	Pre SS	1.94	-1.30	
Left	Post SS	0.64		
Right	Pre SS	2.05	-0.78	
Right	Post SS	1.27		
Semitendinosus				
Left	Pre SS	1.23	3.99	
Left	Post SS	5.22		
Right	Pre SS	0.54	0.14	
Right	Post SS	0.68		
EMGITB012				
Medial Gastrocnemius				
Left	Pre SS	0.33	0.03	
Left	Post SS	0.35		
Right	Pre SS	0.47	0.16	
Right	Post SS	0.63		
Rectus Femoris				
Left	Pre SS	1.69	-1.19	
Left	Post SS	0.50		
Right	Pre SS	0.44	-0.17	
Right	Post SS	0.26		
Semitendinosus				
Left	Pre SS	1.79	0.17	
Left	Post SS	1.96		
Right	Pre SS	0.70	2.94	
Right	Post SS	3.64		

I

Statistical Analysis

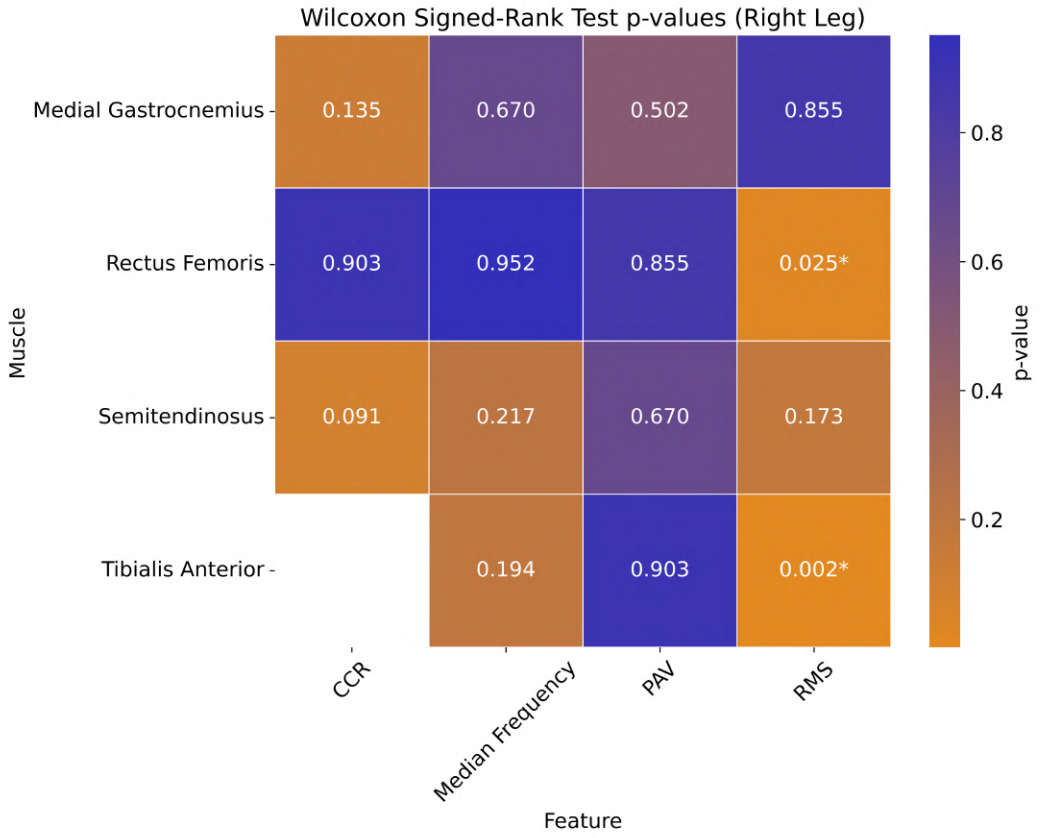

Figure I.1: Right leg: Heatmap of the p-values from the Wilcoxon Signed-Rank test to evaluate for what feature and what event a significant change is seen. * Denotes statistical difference after Benjamini-Hochberg correction.

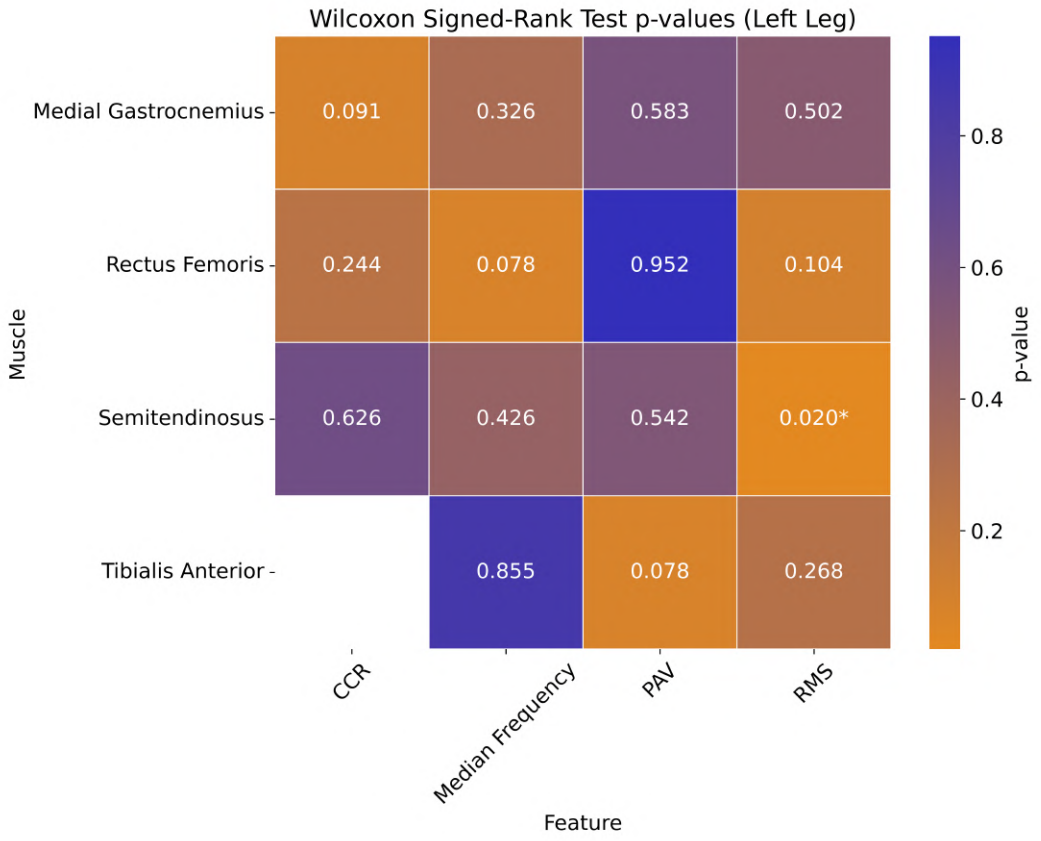

Figure I.2: Left leg: Heatmap of the p-values from the Wilcoxon Signed-Rank test to evaluate for what feature and what event a significant change is seen. * Denotes statistical difference after Benjamini-Hochberg correction.

J

MAS vs. RMS

Table J.1: Overview of percentage differences of the RMS and the differences in MAS scores for each muscle of each individual patient.

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB001						
Left SS	-55.69	0	-37.70	0	-68.70	-2
Right SS	5.29	0	72.68	0	-16.45	-1
Left Imp	-47.31	0	-74.23	1	78.50	1
Right Imp	18.84	0	-71.40	1	106.31	0
EMGITB002						
Left SS	-35.10	-3	-41.71	-2	-55.26	0
Right SS	-0.80	-2	140.49	-2	-58.73	0
EMGITB003						
Left SS	37.98	-3	-45.75	-3	-73.00	-3
EMGITB004						
Left SS	-21.67	-1	-66.61	-1	-52.22	-1
Right SS	-41.45	-1	-76.94	-1	316.42	-1
EMGITB005						
Left SS	-77.31	-3	-62.30	-3	11.39	-1
Right SS	-14.20	-3			346.08	-1
Left Imp	-56.28	0	-68.26	-3	-45.98	0
Right Imp	-52.53	0			-39.07	-1
EMGITB006						
Right SS	-21.55	0	-4.97	-1	-26.61	0
EMGITB007						
Left Imp			-25.79	1	-6.16	1
Right Imp	15.37	1	0.66	0	4.13	-1
EMGITB008						
Left SS	-12.10	-2	-8.99	1	29.89	0
Right SS	-56.47	-3	-71.65	-1	29.50	0

Continued on next page

Table J.1: Continued from previous page

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB009						
Left SS	-10.41	-3	-72.01	-3	-38.09	0
Right SS	-18.64	-1	31.86	-3	-82.22	0
EMGITB010						
Left SS	-73.77	0	4.92	-2	-69.07	-4
Right SS	-18.23	-1	-52.73	1	3.78	0
Left Imp	-38.90	-1	53.66	-2	-72.79	-4
Right Imp	-14.31	-1	202.98	1	44.76	0
EMGITB011						
Left SS	-57.16	-4	97.29	-3	-87.44	0
Right SS	-35.28	-2	-9.40	-3	82.37	0
EMGITB012						
Left SS	-96.79	0	-89.81	-4	-91.48	-4
Right SS	-57.77	-2	-20.42	-3	-86.83	-4

K

MAS vs. PAV

Table K.1: Overview of percentage differences of the PAV and the differences in MAS scores for each muscle of each individual patient.

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB001						
Left SS	-58.31	0	-27.09	0	-96.61	-2
Right SS	-87.71	0	250.99	0	-63.67	-1
Left Imp	40.66	0	-98.78	1	-93.18	1
Right Imp	79.79	0	-87.37	1	-55.24	0
EMGITB002						
Left SS	1055.86	-3	585.59	-2	9.86	0
Right SS	420.71	-2	-34.19	-2	-75.24	0
EMGITB003						
Left SS	-7.13	-3	-89.18	-3	-97.74	-3
EMGITB004						
Left SS	2293.09	-1	19.16	-1	229.79	-1
Right SS	-60.93	-1	-80.85	-1	108.68	-1
EMGITB005						
Left SS	-74.02	-3	-56.63	-3	-1.45	-1
Right SS	-2.67	-3			-54.60	-1
Left Imp	-62.14	0	-79.09	-3	-41.95	0
Right Imp	238.40	0			-29.66	-1
EMGITB006						
Right SS	-30.26	0	-22.02	-1	-40.54	0
EMGITB007						
Left Imp			-36.46	1	252.73	1
Right Imp	281.82	1	1.07	0	-66.26	-1
EMGITB008						
Left SS	-86.99	-2	-94.07	1	-85.80	0
Right SS	-81.37	-3	-64.97	-1	42.54	0

Continued on next page

Table K.1: Continued from previous page

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB009						
Left SS	62.03	-3	-18.53	-3	93.42	0
Right SS	14.53	-1	519.18	-3	-68.15	0
EMGITB010						
Left SS	-86.12	0	-45.92	-2	-32.62	-4
Right SS	242.73	-1	316.57	1	-74.05	0
Left Imp	-50.79	-1	176.48	-2	329.12	-4
Right Imp	12937.94	-1	2177.51	1	-1653.79	0
EMGITB011						
Left SS	204.42	-4	1258.81	-3	-75.64	0
Right SS	618.38	-2	1594.46	-3	183.43	0
EMGITB012						
Left SS	-99.12	0	6.78	-4	-93.26	-4
Right SS	203.86	-2	-88.82	-3	-0.59	-4

L

MAS vs. Median Frequency

Table L.1: Overview of percentage differences of the Median Frequency and the differences in MAS scores for each muscle of each individual patient.

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB001						
Left SS	140.98	0	86.46	0	142.18	-2
Right SS	107.45	0	-9.97	0	-13.17	-1
Left Imp	140.90	0	99.00	1	-50.12	1
Right Imp	2.98	0	105.72	1	-6.69	0
EMGITB002						
Left SS	17.68	-3	15.93	-2	15.28	0
Right SS	12.30	-2	-45.02	-2	24.18	0
EMGITB003						
Left SS	118.47	-3	-35.31	-3	-19.40	-3
EMGITB004						
Left SS	-8.67	-1	33.50	-1	52.07	-1
Right SS	-38.70	-1	-3.39	-1	-47.82	-1
EMGITB005						
Left SS	40.96	-3	-26.46	-3	-17.80	-1
Right SS	0.29	-3	-22.34		45.20	-1
Left Imp	31.09	0	3.05	-3	3.88	0
Right Imp	28.25	0	-25.92		-5.37	-1
EMGITB006						
Right SS	18.01	0	-2.80	-1	20.56	0
EMGITB007						
Left Imp			4.96	1	79.37	1
Right Imp	4.31	1	5.98	0	55.12	-1
EMGITB008						
Left SS	5.93	-2	49.53	1	9.05	0
Right SS	-26.40	-3	-13.98	-1	-30.43	0

Continued on next page

Table L.1: Continued from previous page

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB009						
Left SS	-7.31	-3	-19.04	-3	-9.49	0
Right SS	7.05	-1	0.58	-3	-13.37	0
EMGITB010						
Left SS	24.49	0	-7.00	-2	229.42	-4
Right SS	2.80	-1	45.34	1	2.83	0
Left Imp	7.64	-1	-2.08	-2	40.98	-4
Right Imp	10.42	-1	-53.30	1	27.52	0
EMGITB011						
Left SS	3.79	-4	-51.69	-3	42.46	0
Right SS	-23.51	-2	-63.11	-3	-55.74	0
EMGITB012						
Left SS	18.99	0	-8.87	-4	-13.47	-4
Right SS	13.39	-2	-49.89	-3	-17.22	-4

M

MAS vs. CCR

Table M.1: Overview of percentage differences of the CCR and the differences in MAS scores for each muscle of each individual patient.

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB001						
Left SS	-34.57	0	-54.10	0	7.87	-2
Right SS	11.75	0	22.49	0	17.78	-1
Left Imp	12.45	0	2.88	1	195.87	1
Right Imp	629.42	0	-67.28	1	487.05	0
EMGITB002						
Left SS	-18.57	-3	-34.36	-2	-87.64	0
Right SS	-97.04	-2	143.92	-2	-45.35	0
EMGITB003						
Left SS	302.78	-3	-60.02	-3	-84.36	-3
EMGITB004						
Left SS	75.70	-1	-73.51	-1	-90.31	-1
Right SS	-27.32	-1	83.67	-1	568.02	-1
EMGITB005						
Left SS	-42.63	-3	62.16	-3	-27.51	-1
Right SS	219.31	-3	111.30		2060.67	-1
Left Imp	-39.26	0	-8.82	-3	-28.33	0
Right Imp	-36.12	0	64.74		42.55	-1
EMGITB006						
Right SS	17.45	0	81.54	-1	-11.85	0
EMGITB007						
Left Imp			-37.09	1	-64.63	1
Right Imp	18.47	1	-32.87	0	-21.40	-1
EMGITB008						
Left SS	-20.70	-2	-58.06	1	68.15	0
Right SS	10.28	-3	-65.38	-1	170.12	0

Continued on next page

Table M.1: Continued from previous page

Patient	Rectus Femoris	MAS RF diff	Semitendinosus	MAS HAM diff	Medial Gastrocnemius	MAS GAS diff
EMGITB009						
Left SS	76.86	-3	-68.47	-3	13.48	0
Right SS	-55.72	-1	95.54	-3	-43.41	0
EMGITB010						
Left SS	-90.34	0	247.04	-2	-69.02	-4
Right SS	42.97	-1	-66.18	1	-55.77	0
Left Imp	-30.15	-1	71.05	-2	-33.13	-4
Right Imp	28.45	-1	460.87	1	21.90	0
EMGITB011						
Left SS	-67.10	-4	324.91	-3	-80.88	0
Right SS	-37.87	-2	25.46	-3	80.33	0
EMGITB012						
Left SS	-70.38	0	9.77	-4	7.82	-4
Right SS	-39.68	-2	419.33	-3	35.08	-4

N

PGIC Correlation

Table N.1: Table presenting the PGIC scores of all patients for the corresponding measurement event. The percentage differences are the mean differences of the three MAS repetitions of the corresponding muscle. Thus the Perc. Diff. RMS of the Medial Gastrocnemius is the average of MAS assessment 1, 2 and 3 of the medial gastrocnemius muscle. PGIC = Patient Global Impression of Change; SS = Single Shot. PGIC scores: 1 = very much improved; 2 = much improved; 3 = minimally improved; 4 = no change; 5 = minimally worse; 6 = much worse; 7 = very much worse. MAS = Modified Ashworth Scale; corrected values for calculation: 0 = 0; 1 = 1; 1+ = 2; 2 = 3; 3 = 4; 4 = 5

Patient	Leg, Event	Most severe muscle	Perc. Diff. RMS	PGIC	MAS
EMGITB001	Left SS	Medial Gastrocnemius	-68.70	3	-2
	Right SS	Medial Gastrocnemius	-16.45	3	-1
	Left Implant	Medial Gastrocnemius	78.50	3	1
	Right Implant	Medial Gastrocnemius	78.50	3	1
EMGITB002	Left SS	Semitendinosus	-41.71	1	-2
	Right SS	Medial Gastrocnemius	-58.73	1	-2
EMGITB004	Left SS	Rectus Femoris	-21.67	3	-1
	Right SS	Rectus Femoris	-41.45	3	-1
EMGITB005	Left Implant	Semitendinosus	-68.26	3	-3
	Right Implant	Rectus Femoris (HFHE)	-86.60	3	-2
EMGITB006	Right SS	Medial Gastrocnemius	-26.61	4	0
EMGITB007	Left Implant	Rectus Femoris (HFHE)	66.12	1	0
	Right Implant	Rectus Femoris (HFHE)	24.71	1	0
EMGITB008	Left SS	Rectus Femoris	-12.10	4	1
	Right SS	Rectus Femoris (HFHE)	-24.70	4	-1
EMGITB009	Left SS	Rectus Femoris (HFHE)	4.92	2	-4
	Right SS	Medial Gastrocnemius	-82.22	2	0
EMGITB010	Left SS	Medial Gastrocnemius	-69.07	1	-4
	Right SS	Rectus Femoris (HFHE)	-12.31	1	-1
	Left Implant	Medial Gastrocnemius	-72.79	4	-4
	Right Implant	Medial Gastrocnemius	44.76	4	0
EMGITB012	Left SS	Medial Gastrocnemius	-91.48	1	-4
	Right SS	Medial Gastrocnemius	-86.83	1	-4

0 Literature Research

Quantification of EMG signals, in patients with Upper Motor Neuron lesions to determine spasticity: a literature review

DECEMBER 6TH, 2023

CENTER FOR PAIN MEDICINE, ERASMUS MEDICAL CENTER, ROTTERDAM

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TM30003 LITERATURE REVIEW

ABSTRACT

Introduction

This literature review focuses on the analysis of electromyography (EMG) signals in patients with upper motor neuron (UMN) lesions to quantify spasticity. UMN lesions, which result from stroke, traumatic brain injury, or spinal cord injury, often lead to spasticity. This is a complex motor disorder that affects the control of muscle activity. The variability in the clinical presentation of spasticity requires objective quantification for effective monitoring of treatment effects. Current quantification methods, which include the Modified Ashworth Scale (MAS), electrophysiological methods, and biomechanical tools, have limitations in terms of objectivity and reliability.

To address these challenges, this review explores the use of surface EMG (sEMG) as a more objective and practical method of spasticity quantification. The primary objective is to provide an overview of various sEMG features used to quantify spasticity in patients with UMN lesions. Secondary objectives include distinguishing features based on time, frequency, and time-frequency domains, as well as analysing passive and active movement scenarios.

Results

The PRISMA analysis method was used for the selection of literature and resulted in 23 articles. Recommendations for sEMG features are discussed, highlighting the importance of objective, practical, and reliable measures for spasticity assessment. Features such as root mean square, stretch reflex onset, and average rectified value are discussed for their effectiveness in quantifying spasticity. The features were distinguished according to the signal analysis domain and the type of movement, active or passive.

Conclusion

The results highlight the challenge of establishing a golden standard for spasticity quantification, especially when comparing the MAS with sEMG features. Therefore, a combination of robust features is proposed, to provide a more solid framework for quantifying spasticity and evaluating treatment effects.

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1 Introduction

1.1 Upper Motor Neuron Syndromes

The motor system of the human body is divided into the upper and lower motor neuron. The Upper Motor Neuron (UMN) initiate and modulate voluntary movements, while lower motor neurons directly control the muscles that ensure the execution of these movements, see *Figure 1: Illustration of the UMN*. Damage to the UMN can result from a variety of causes, which include stroke, traumatic brain injury (TBI), cerebral palsy (CP), spinal cord injury (SCI), and inflammatory, neurodegenerative, or metabolic diseases such as multiple sclerosis (MS) (1). A positive sign of an UMN syndrome is spasticity, which is defined as *"a velocity-dependent increase in tonic stretch reflexes with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neurone (UMN) syndrome" (2).* Of the above causes, spasticity affects approximately 35% of stroke patients, more than 90% of CP patients, about 50% of the TBI patients, 40% of the SCI patients, and between 37% and 78% of the MS patients (3). Spasticity manifests through a range of symptoms, such as muscle hypertonia, overactive reflexes, involuntary movements, contractures, muscle weakness, and pain. As a result of these symptoms, patients experience limitations in caregiving, activities of daily living and participation, resulting in a reduced quality of life (4).

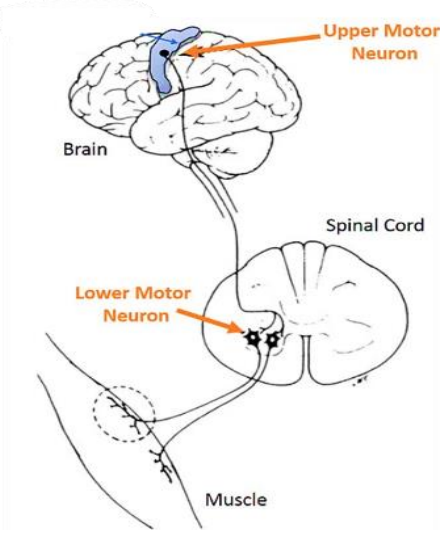

Figure 1: Illustration of the UMN

1.2 Clinical variability of spasticity

The different causes for UMN lesions make the pathophysiology of spasticity heterogeneous, meaning that various underlying mechanisms influence the clinical presentation of the patient. Although spasticity is easily identified, its quantification and accurate treatment present complex challenges. More precise quantification of spasticity allows for better monitoring and adjustment of treatment (5). Currently, different tools are used to quantify spasticity; (Modified) Ashworth Scale (MAS), different frequency scales, the Pendulum test, electrophysiological methods, and biomechanical methods (6). The most widely used clinical scale to measure increased muscle tone is the MAS, where physicians assess spasticity levels using a scoring table ranging from 0 to 4. The moderate inter- and intra-rater reliability make this method sensitive for subjectivity (7). This wide variety of tools, their subjectivity, and the difference in patient experience and actual clinically measured outcomes, make the quantification of spasticity complex and therefore also monitoring of treatment effect. A previous review of Gomez-Soriano et al. reported an agreement on the definition of spasticity and the need of training and experience for evaluators. From there they recommend identifying a measure of spasticity with the following requirements: objective, practical and reliable (8).

1.3 Electromyography

The abovementioned requirements for a new measure of spasticity, points towards a method called surface electromyography (sEMG). This diagnostic method assesses the response to passive or active movements of the muscle and the associated nerve by measuring electrical activity. Using sEMG, neuromuscular deviations can be detected to quantify the degree of spasticity (9). Compared to the MAS, sEMG is a more objective method to measure increased muscle tone. Both methods are equally non-invasive and cause a similar level of discomfort for the patient. The analysis of sEMG signals involves extracting features related to the required information. Nevertheless, the reliability of these selected features still requires evaluation.

1.4 Review objective

Improving the objectivity of spasticity measurement in individuals with different UMN lesions can enhance both monitoring and treatment adjustments. Therefore, an objective, practical, and reliable method of quantifying sEMG signals is needed. The aim of this review is to provide an overview of different features extracted from sEMG signals to determine the level of spasticity in patients with UMN lesions. Hence, the research objectives are:

Primary objective

To provide an overview of the described EMG features for quantifying spasticity in patients with UMN lesions.

Secondary objectives

- To distinguish between features described in the time, frequency, and time-frequency domain.
- To distinguish between features described for analysis of passive and active movement analysis.
- To provide an overview of the pre-processing methods used

2 Methods

2.1 Search Strategy

The Embase, Medline and Web of Science databases were searched for articles on EMG recordings in patients with spasticity. The following search term was applied on the databases, to search for articles in a time frame until August 2023.

Embase.com

('electromyography'/exp/mj OR (electromyogra* OR electroneuromyogra* OR polyelectromyogra* OR ((electr*) NEAR/3 (myogra*)) OR EMG OR sEMG):ti) AND (quantif* OR measur*):ab,ti,kw AND ('spasticity'/de/mj OR (spastic*):ab,ti) *NOT [conference abstract]/lim AND [english]/lim NOT (gait/de/mj OR (gait*):ti)*

Medline

(*Electromyography/ OR (electromyogra* OR electroneuromyogra* OR polyelectromyogra* OR ((electr*) ADJ3 (myogra*)) OR EMG OR sEMG).ti.) AND (quantif* OR measur*).ab,ti,kf. AND (*Muscle Spasticity/ OR (spastic*).ab,ti.) *NOT (news OR congres* OR abstract* OR book* OR chapter* OR dissertation abstract*).pt. AND english.lg. NOT (*Gait/ OR (gait*).ti.)*

Web of Science

TI=((electromyogra* OR electroneuromyogra* OR polyelectromyogra* OR ((electr*) NEAR/2 (myogra*)) OR EMG OR sEMG)) AND TS=(quantif* OR measur*) AND (TI=(spastic*) OR AB=(spastic*)) *NOT DT=(Meeting Abstract OR Meeting Summary) AND LA=English NOT TI=(gait*)*

2.2 In- and exclusion

The articles were screened and excluded if one of the following exclusion criteria applied:

- No patients with spasticity were included.
- No measure of muscle activity was included.
- EMG parameters used for analysis were not specified.
- Quantification of spasticity was performed without using (surface) EMG.
- Measurements were performed on animals.
- The full text version was not available (in English).
- Conference or workshop papers.

The defined search terms and the process of in- and exclusion, resulted in 23 articles. The whole selection procedure is shown in *Figure 2: PRISMA overview of article selection* and *Appendix B – Detailed search results.* During the selection process, an additional exclusion criterion was added. This stated that studies evaluating EMG signals using outdated (non-digital) techniques were also excluded. The development of the EMG techniques within the last 20 years delivered new possibilities but was not considered when defining the exclusion criteria. As there are clear differences in the muscle response to passive and active movements, the articles were divided into two separate groups: active movements and passive movements.

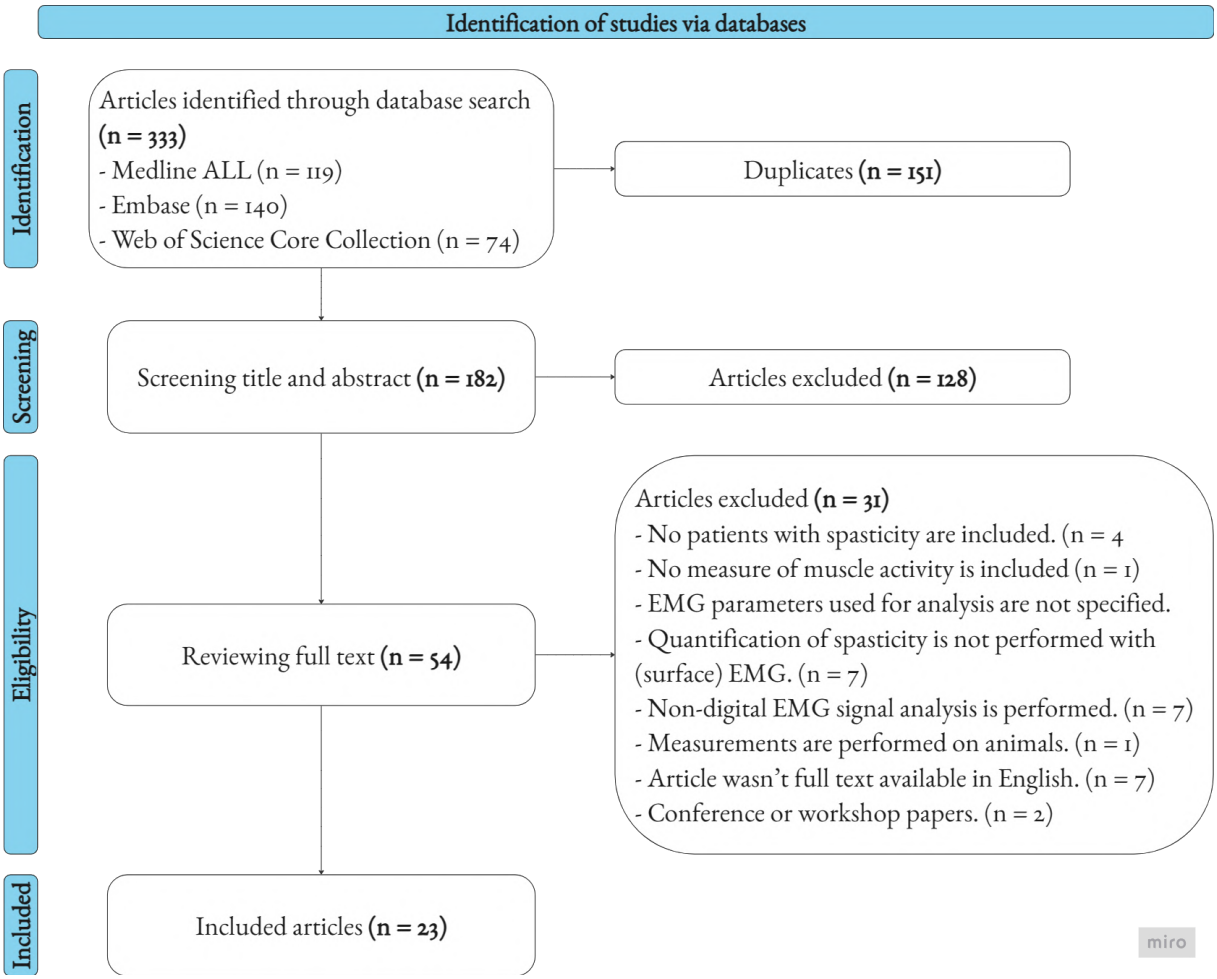

Figure 2: PRISMA overview of article selection

2.3 Data extraction

All included articles were read and (s)EMG parameters and pre-processing steps used for quantification were listed for each article. Thereafter, the different domains for signal analysis were used to categorize the (s)EMG parameters applied in each study. For the three most often described parameters, the performance and clinical relevance is evaluated. The performance of other described features in the time, frequency or time-frequency domain are shortly evaluated as well. Furthermore, the different types of pre-processing methods were summarized, see *Appendix E – Pre-processing methods*.

3 Domains for signal analysis

Before the desired feature can be extracted from the collected data for further analysis, the signals need to be processed. The first crucial step to ensure accurate analysis is pre-processing the signal by reducing noise and handle missing data. Following the pre-processing, the signals are analysed using the selected features. Three different domains for signal analysis are existing: time domain, frequency domain, and time-frequency domain (10). The choice of analysis domain depends on the specific research question, amount of data, and characteristics of the EMG signals. In the following section all three domains are clarified, and the corresponding advantages and disadvantages are outlined.

3.1 Time Domain

Within the domain, the signal variation over time is analysed using the independent value of time (t). This domain simplifies signal interpretation, making it is easier understand and to calculate relevant features. Time domain features directly measure aspects like amplitude, variability, and shape, offering a straightforward understanding of muscle activity patterns. This domain is also less computationally intensive than the more complex frequency domain. This is a definite advantage when dealing with large data sets or real-time applications where fast processing is essential (11). In addition, time domain features are known to be more robust to noise, as they often involve simple mathematical operations such as averaging, summing, or calculating slopes. These methods provide noise averaging, signal accumulation and/or noise smoothing (12).

3.2 Frequency Domain

In the frequency domain, the signal distribution across a range of frequencies is analysed. Valuable insight can be gained from the frequency domain as different muscle actions are associated with specific frequency bands. For example, identifying coordinated patterns of muscle activation can reveal muscle groups working in synergy, providing insight into neural control strategies. By applying transforms like the Fourier Transform, the signal is converted from the time domain to the frequency domain (13). Converting the signal is also applied for specific filtering tasks and helps by removing noise or interference concentrated in certain frequency bands, thereby enhancing the quality of the EMG signal (12).

3.3 Time-Frequency Domain

The time-frequency domain provides a representation of EMG signals with localised frequency information over time intervals. Short-Time Fourier or the Wavelet Transform are used to convert to the time-frequency domain. Currently EMG signal analysis is often performed in the time domain, thus detailed information of frequency components is not available. Having information on both time and frequency can be particularly useful when analysing non-stationary signals (14). In addition, muscle activation patterns caused by specific movements can be revealed in this domain. This helps to understand the dynamics behind muscle activity. Therefore, this domain is often used the in analysis of active motion (15).

4 Described features for passive movements.

The articles that were included within this literature review contained measurements of passive and active movements. Each type elictis distinct (EMG) responses, and therefore other features are relevant. *Appendix C – Features for passive movements*, provides an overview of all the EMG features described for the quantification of spasticity in passive movements. Seven distinct features were extracted in total, each with its own variances. Features that focus specifically on te time domain are individually evaluated to explain their meaning in relation to spasticity. First the three features, most described for the time domain. And in the following section the remaining features.

4.1 Three most described EMG features of the time domain

4.1.1 The Root Mean Square (RMS)

The RMS is a method of data reduction and often used for EMG analysis in the time-domain. This method reflects the activity and synchronization of motor units, like raw EMG (16). Different features can be determined when using the RMS of EMG signals. Within the current literature the following features are described.

Mean value of the RMS

Casthilo et al. (17) calculated the mean RMS for calculation of the percentage difference between EMG activity before and after treatment. This method gives one value as representation of the muscle intensity. With this certain value the effect of the treatment on muscle intensity is evaluated. The mean value is also determined by Schless et al. (18), to define EMG onset. In other words, the time of the first muscle activity. This feature is applied to evaluate the performance of a manual spasticity assessment instrument on three levels (1 intra- and (2) inter-rater reliability (3) within/between sessions. The two studies of Casthilo et al. (17) and Schless et al. (18) apply the same feature on a different study objective. The method of Casthilo et al. resulted in measuring a reduction in muscle spasticity after treatment, compared with measurements before treatment. But this method did not deliver significant differences due to limited study population size. The same accounts for how the mean RMS was applied by Schless et al. (18), they conclude that the overall performance of the mean RMS feature is sufficient when it comes to evaluating performance of the developed device by inter/intra-rater reliability. No evaluation was conducted on the performance of the feature in comparison with the MAS scores.

The main objective of the study of Sorinola et al. (19) was to investigate the reliability of the EMG response to manual stretches of the hemiplegic wrist by assessing the effect of velocity and repetition. Their second objective was to investigate the correlation of EMG with clinical assessments of spasticity and physical function such as, MVC, MAS and the Block and Box Test (BBT). The RMS was calculated for measurements of 3 cycles of 10 passive manual stretches. The mean value of each cycle was used for further evaluation. In stroke patients EMG activity increased with velocity and was not affected by repetition. RMS EMG correlated positively with the MAS only at the lowest assessed velocity. No other positive correlations were found between EMG response and clinical assessment methods for spasticity.

Amplitude of the RMS

Abraham et al. (20) calculated the RMS EMG amplitude to observe changes in sEMG activity before and after surgery to assess co-contraction in pronation and supination movements. And eventually, compare the change in amplitude value with the change in MAS score. Co-contraction is a phenomenon often seen in patients with spasticity because the inhibition of the antagonist, after activation of the agonist, is distorted. During passive movement, no significant decrease in co-contraction was seen using the RMS EMG amplitude. Patients who reported an improvement in hand function showed increased RMS EMG amplitude values. This improvement is in contrast with the MAS scores, which did not change for most of these patients.

Average Limb Response (ALR)

Two publications of Sherwood et al. (21, 22) describe the ALR for the quantification of spasticity. This feature is based on the RMS and applied in units of $uV_{RMS.}$ It is obtained by averaging the RMS EMG activity for each individual muscle over a certain timeframe. Averaging the sEMG data over different muscles leaves one single variable that represents the response of each limb, to each phase of each manoeuvre. Results show consistent and reliable data when using the ALR. This feature contains activity of each muscle that is activated during the passive movements. It is stated that this represents an expansion beyond what would be perceived by a clinical examiner evaluating the muscle resistance by stretching.

The RMS of the EMG data is used to calculate several features to quantify spasticity. All features have the overlapping characteristic of translating muscle activation intensity. When applying the RMS to EMG signals, the resulting signal is easier to interpret. From this current selection of literature, we can conclude that the RMS is an accessible method for analysing EMG data.

4.1.2 Integrated EMG activity

Integrated EMG refers to the process of summing up the raw EMG signal over a specific time frame. This gives a single value which represents the overall muscle activity during that time interval. This measure can be used in the quantification of spasticity and is also referred to as the Area Under the Curve (AUC). This feature is described in three different articles.

First, Kim et al. (23) applied the integrated EMG to determine quantification of spasticity and to characterize the EMG spasticity assessment parameters by investigating the clinical correlation with the MAS. They measured the integrated EMG activity from the full wave rectified signal, meaning that the absolute value of the signal is used for integration. EMG assessment was combined with isokinetic assessment obtaining joint resistance and angular velocities. Significantly different results were obtained using integrated EMG assessment to compare stroke patients with healthy controls. Although this feature did not correlate with the MAS score, it still provides enough valuable information to quantify spasticity, especially when combined with the features obtained from the isokinetic assessment.

Second, In the research by Winslow et al. (24) integrated EMG is used extensively to identify and classify muscle activity in EMG recordings using an automatic algorithm. The integral signal was constructed by rectifying the EMG and computing the AUC every 10 ms. Integrated EMG activity was obtained to classify types of spasms, such as unit, tonic, or clonus events. These events differ from one another by the density and intensity of peak bursts.

Classification was based on the number of above-threshold integrals within a fixed timeframe and the number of EMG bursts above the defined threshold integral (mean of highest 10% of integrals + 3SD). When this feature was applied to an automatic detection algorithm, the performance was comparable to two experts, but the execution time was reduced.

Third, the research of McGibbon et al. (25) aimed to show that wearable sensor system (angle sensor and 2-channel EMG) worn during a stretch-reflex assessment, can be used to quantify spasticity more objectively. Besides the muscle reflex intensity, the muscle reflex density was determined as well. Muscle reflex density represents the resistance against passive movement, generated from spasticity. This resistance is also referred to as muscle reflex gain: "amount of force required to extend the limb in proportion to the increasing joint angle" (26). The AUC is used as representation of muscle reflex density of the antagonist muscles. Quantification was performed using the *kinematic model* where a processed reference signal is used for comparison. It was found that the metrics correlated strongly with neurophysiological responses, and positive correlations with the MAS scores were provided. But this conclusion results from analysis of EMG signal combined with goniometry.

4.1.3 The Stretch Reflex

The Stretch Reflex Threshold (SRT) finds is based on the motor control theory (27), which states that the excitability of the SRT is related to central commands that descend to the motor neurons. With UMN lesions these commands are often disrupted (28) and therefore the threshold levels can differ. The SRT can be expressed by velocity and angular coordinates representing the joint angle at which motor neurons, and the respective muscles fibers, begin to be recruited in response to a stretch performed at a given velocity. This theory is applied in the Lambda model (29) which is a measure to quantitatively evaluate spasticity with sEMG. In patients with UMN lesions, a higher stretch velocity will result in earlier reflex responses, in other words a lower SRT measure.

Tonic Stretch Reflex Threshold (TSRT)

A study of Silva et al. described the SRT in a study with the aim to distinguish reflex EMG activity from baseline EMG. A differentiation of the SRT is used, which is called the Tonic Stretch Reflex Threshold. This measure represents the angle in which recruitment of motor neurons begins when the muscle is at rest (i.e., zero stretch velocity). This measure is obtained by linear regression of various Dynamic SRT points, since generating a stretch with zero velocity is not possible. Values of the TSRT closer to full flexion of a joint correspond to more severe spasticity cases, where values closer to full extension indicate less severe levels of spasticity. The number of calculations of the TSRT must be performed with high precision to ensure clinically relevant information. These calculations are mainly dependent on the accuracy of detection of onset of the reflex activity. Silva et al. therefore tried different approaches for this detection step and showed that their 'three-stage' method bring sufficient results when comparing it with other methods from the literature. But this research was applied on just 5 spastic subjects and no inter- or intra-rater reliability was evaluated.

The TSRT detection method of Silva et al. was also applied within research of Zhang et al., who proposed another novel regression-based framework for quantitative assessment of muscle spasticity using EMG. They developed three evaluation methods to calibrate

biomarkers into evaluation scores. These scores can be regarded as a prediction of the MAS score. The aim of the study was to validate the three models and evaluate the usability and feasibility for clinical use. The first model is based on the *Lambda model* of Levin et al. (27), the second model was based on the *Kinematic model* of McGibbon et al. (25) and the third model was a combination of both. The results showed improved performance on spasticity assessment when combining both models. About the correlation with the MAS no clear conclusions have been drawn, due to its subjectivity making it less trustable. Although no significant difference between the three models was found, the evaluation scores showed its capability of discriminating different degrees of spasticity.

Reflexive Electromyography Threshold (RET)

To quantify changes in elbow spasticity over time following botulinum injections Lee et al. (30) evaluated the MAS score and RET. This evaluation was done by analysing the velocity and length dependence of the (hyper)excitable stretch reflexes. The SRT was determined performing full flexion and full extension to define one stretch range. Eventually, the SRT was set within time range of this movement, when the EMG activity increased more than 3 SD above baseline activity. By performing several passive stretch reflexes, a mean RET value was determined for each patient and combined with the average angle value. With a decrease in angle threshold, an increase in excitability of the stretch reflex is indicated. The RET revealed changes in spasticity after treatment, that could not be observed from clinical MAS evaluations.

4.1.4 Suitable for quantification of spasticity?

In conclusion, The RMS has multiple uses, including evaluation of treatment effects, determination spasticity onset, and classifying the severity of spasticity. However, the correlation between RMS features and MAS score remains controversial.

Using the integrated EMG signal as feature, classification and quantification of spasticity can be performed. However, this feature is often used in combination with isokinetic characteristics and provides easily interpretable information. A correlation with the MAS was found when this combination of methods was applied (25).

Currently available methods for the detection of the stretch reflex onset to passive movements are accurate enough for further analysis. The analysed characteristics, such as, level of excitability and inhibition, provide insights into the intensity of spasticity and is therefore of added value when evaluating treatment.

When comparing sEMG features with MAS the subjectivity of the scale is supported (29) or it is shown that sEMG can detect smaller changes then the MAS when it comes to treatment evaluation (21, 22). Moreover, for evaluation of spasticity by passive movements, the time domain offers a wide variety in features. It is important to keep the following recommendations in mind when choosing features for extraction. Make sure that the feature translates the aspect of spasticity that the study objective requires (classification, quantification, or assessment). Furthermore, it is important to ensure that more than one feature is extracted and that they enhance each other's performance.

4.2 Other described EMG features of the time-domain

Compound Muscle Action Potential (CMAP)
A feature that is described in one single article (31) originates from the motor nerve conduction assessment. The CMAP represents the sum of the Motor Unit Action Potentials (MUAP). In other words, it signifies the overall micro voltage generated by muscle fibers in response to an electrical stimulus. From the CMAP the amplitude, latency and conduction velocity are used for further analysis. This feature represents the conduction of electrical impulses along nerves and motor-nerve transit. It is used to quantify the suppressive action of a treatment on neuromuscular transmission. Picelli et al. applied this feature to find more accurate indices that could affect decisions in spasticity treatment. Changes in the CMAP were related to changes in other indicators for spasticity severity, such as echography or muscle thickness.

Average Rectified Value (ARV)
The second feature derived from EMG data is the Average Rectified Value, performed by Campanella et al. (32). Full wave or half-wave rectification adjusts for negative amplitudes by either removing the negative voltage component or converting the negative into a positive. This amplitude measure is directly correlated with the intensity of muscle activation, where a higher ARV signifies a stronger muscle contraction. Campanella et al. calculated the ARV to assess the effect of botulinum toxins on muscle hypertonia and compared it with shear wave elastography. The ARVs for spastic dystonia exhibited a significant decrease after treatment.

Amplitude Value
As third feature, two studies describe the peak amplitude value of the EMG signal. The first study by Cooper et al. (33) applied the peak amplitude value to calculate the normalized amplitude of stretch responses. The following formula is used:

$$\frac{Peak\ sEMG - Mean\ resting\ sEMG}{SD\ of\ the\ resting\ sEMG}$$

Using this feature the magnitude of the response on passive movement can be determined. This is of added value when comparing responses of affected and unaffected muscles of hemiparetic patients. Or comparing muscle responses of healthy volunteers and muscle responses of paretic patients.
McGibbon et al. (25) used the change in EMG amplitude to ascertain the onset time of the spasticity response. Then, various time frames were established to quantify the muscle reflex *intensity* of both agonist and antagonist muscles. Quantification was performed based on the *Kinematic model,* which employs a motion reconstruction curve (reference) to identify changes. This approach relies on the assumption that a consistent pattern exists between the actual and reconstructed curve among healthy controls. Deviations from this reference pattern occur in the presence of abnormal muscle tension, caused by spasticity. This method was also applied to quantify muscle reflex *density*. Scatter plots show a slight correlation between the intensity and density measure and more measures to construct validity is recommended.

Mean baseline activity
The fourth described feature, the mean of EMG activity, is frequently used and can be applied in various contexts. Research by Skold et al. (34) applied the mean electrical activity to define EMG baseline. This mean was calculated over a 10-second duration during passive movement. Mean baseline EMG activity of antagonists and agonists

were analysed through three distinct parameters. Firstly, the individual activity of the antagonist and agonist muscles. Secondly, by evaluating the net difference between antagonist and agonist mean activity, representing the muscular resistance to the induced movement. Lastly, by summing the activity of both agonist and antagonist as representation of co-activation resulting in rigidity of the joint. Using mean EMG activity as representation of EMG baseline offers an easy to interpret impression of muscle response and does not need much calculation effort. Skold et al. applied this method to investigate whether the MAS is a valid measure of spasticity. Changes in MAS scores and EMG parameters correlated within certain limits.

Furthermore, Alcan et al. (35) aimed to realize the diagnosis of spasticity with a fuzzy logic classifier (FLC). This classifier required diverse inputs; thus, the mean calculation was employed to extract three different parameters. First, the mean value, comparable to the method used by Skold et al. (34). Second, the mean absolute value (MAV), a measure of the average absolute magnitude of a signal within a specific time window. MAV quantifies the overall amplitude of muscle activation and is valuable in determining activation levels. Third, the standard deviation of the mean value provides information on how the signal deviates around the mean, offering information on signal variability. These features resulted in sufficient performance of the FLC, in combination with other features extracted from the time-frequency domain.

The features each provide unique insights into the quantification of spasticity. Both CMAP and ARV represent the intensity of muscle activation, with different precision. CMAP, in combination with other parameters, can detect change in patients with spasticity. However, it is not yet applied independently, to quantify spasticity levels. Similarly, while ARV demonstrates the effects of spasticity treatment, it does not distinctly differentiate between spasticity levels. The amplitude feature, used in several applications, represents the magnitude of the muscle response. It is valuable for distinguishing between damaged and non-damaged muscles in patients and discerning differences in EMG responses between healthy subjects and patients. The versatile application of the amplitude feature across different studies supports its performance. Furthermore, the mean EMG, being easily interpretable, is commonly used as it provides a comprehensive overview of the muscle response. In the literature, researchers often calculate differential features from the mean, such as the MAV and the baseline EMG differences between agonist and antagonist muscles. Given the complexity of spasticity pathology, quantification methods utilizing multiple features is essential. While there is some overlap in information, these features complement and reinforce each other. Taking all into account, it is recommended to integrate multiple features to quantify spasticity effectively, enabling the demonstration of clinically relevant changes.

4.3 Described EMG features of the time-frequency domain.

In the frequency domain no features for quantification of spasticity were described. However, for the time-frequency domain four features were described. A study of Alcan et al. (35) described three features within the time-frequency domain, applied to a fuzzy logic classifier (FLC). Additionally, Hu et al. described the Stretch Reflex Onset within two publications.

Daubechies Wavelet Transfer

The first and second features were derived using Daubechies Wavelet Transform of the 10^{th} order. This method was applied to calculate the MAV and the Median Absolute Value. To obtain the original signals, a wavelet-denoising method was used before applying the Daubechies Wavelet Transform. These features are related to the wavelet analysis of the EMG signal and were integrated into their own developed model for the calculation of the third feature.

Maximum Power Value

The third feature captures the maximum power value and is determined through the application of the Short Time Fourier Transform on the wavelet-denoised signals, described earlier. This feature is related to the spectrum analysis of the EMG signal and signifies the frequency at which the highest EMG power is registered within a specific time segment. A spectrogram provides a clear overview of the power distribution within the signal and is thus suitable for analysis of maximum power value parameter. Extracting this feature offers additional information about the intensity of muscle activation and is therefore of added value within a self-developed classifier. It contributed to the performance of the FLC, obtaining high sensitivity, specificity, and accuracy.

Stretch Reflex Onset (SRO)

Hu et al. (14, 36) approached the stretch reflex from the time-frequency domain to develop a practical clinical method for objective evaluation of spasticity. The EMG signal was transformed to the time-frequency domain using the Hilbert-Huang transform and applying Marginal Spectrum Entropy (HMSEN). Using a self-developed detection algorithm, the SRO was determined as representation of the moment of (hyper)excitability of the stretch reflex. From the onset time point, excessive reflex activation is seen, which was evaluated by the RMS difference (RMSD). The developed algorithm could precisely detect the SRO. And differences in RMSD between patients was measured, but an objective reference scale to quantify these differences is missing. A comparison with the MAS was performed, and correlations between the MAS and RSMD were found. No significant differences of RMSDs values between two MAS groups was found, which supports the doubts discussed earlier about the subjectivity of the MAS.

5 Described features for active movements.

In this chapter, features applicable to the analysis of active movements will be evaluated for time and time-frequency domain, for a full overview see Appendix D – Features for active movements. Active movements bring variability due to voluntary control while passive movements provide a more controlled environment for analysing sEMG signals. Consequently, making the analysis of active movements more challenging in terms of understanding muscle activation patterns.

5.1 Described EMG features of the time domain.

Pearson Product-Moment

Within research of Cowan et al. (37) the activation patterns of agonist and antagonist muscles in the lower limbs are assessed using the Pearson Product-Moment correlation. This method measures the degree of association between the two muscle activation profiles, yielding a correlation coefficient known as *Pearson r*. The study concludes that this coefficient is adequate for evaluating treatment effects on the on the antagonist muscle. However, caution is needed when interpreting the correlation coefficient. Considering the relative amplitudes of the two curves is essential for accurate assessment.

$$Pearson\ r = \frac{\sum(x_i - x)(y_i - y)}{\sqrt{\sum(x_i - x)^2 (y_i - y)^2}}$$

Root Mean Square (RMS) amplitude

The amplitude of the RMS EMG is computed in the study of Abraham et al. (20) to observe changes in sEMG activity before and after surgery in pronation and supination movements. They then compared the amplitude changes with the alterations in MAS scores. During active movement, a significant reduction in co-contraction was seen using the RMS EMG amplitude. This reduction was observed even in individuals whose MAS scores remained unchanged after surgery.

Co-Contraction Ratio (CCR)

A different approach of the RMS is applied in research of Ohn. et al. (38). Their main objective was to investigate upper-limb movements using EMG to determine the degree of co-contraction and latency between agonist and antagonist. For the evaluation of degree of co-contraction, the CCR was determined by dividing the RMS of the agonist muscle, by the RMS of the antagonist muscle. Co-contraction is an important factor of recovery of upper limb function. A correlation between functional recovery and CCR was seen for the upper limbs which supports the negative effect of high co-contraction on functional outcome. Furthermore, results showed a positive correlation between the CCR and the MAS score. The CCR feature is useful for assessing spasticity in terms of functional performance of patients with spasticity.

Maximum Voluntary Induced Contraction (MVIC)

Schless et al. (18) primarily focused passive movements in their study, see section 4.1.1. with the analysis augmented by a the MVIC. The peak muscle contraction achievable is signified by the MVIC and is often employed in rehabilitation settings, although not directly for quantifying spasticity levels.

Similarly, in the study conducted by Sarcher et al. (39) MVIC was used to calculate three different amplitude normalisation methods. The normalized amplitudes were applied to assess upper limb EMG pattern variations during elbow movements in both healthy subjects and

cerebral palsy (CP) patients. A secondary objective was to detect changes after treatment aimed at reducing muscle activation. One of the three methods effectively identified deviations of upper limb muscle activation, both between healthy controls and patients, as wel as after treatment. Here the MVIC is more applied as a pre-processing step, not as the feature that is directly used for quantification.

The EMG amplitude normalization methods were chosen for to identify the method that resulted in EMG patterns where changes between subjects are easily to identify. It is concluded that this method can be applied to detect changes between healthy subject and patients in sEMG patterns during upper limb movements. But it is not yet clear what changes are clinically relevant.

5.2 Described EMG features of the time-frequency domain.

In the time-frequency domain only one feature is described, by R.T. Lauer et al. (40). Their objective was to develop an assessment methodology using sEMG time and frequency characteristics, to provide clinically relevant information in children with CP. The sEMG signals were acquired during gait analysis and processed in five different steps. The Continuous Wavelet Transform (CWT) was used because it preserves original time information and operates over all frequencies, thus preserving both the time and frequency aspects of the sEMG signal. However, the trade-off between preserving detailed information and computational speed is recognised.

To assess changes in motor activity further analysis is performed using a self-developed EMG index. This starts by calculating the mean frequency for each gait cycle interval. This value is used to examine muscle characteristics between the left and right sides, and to compare agonist and antagonist muscle activity across a joint. Finally, principal component analysis is used to find correlations and variations between subjects. This output was used to calculate an EMG index, representing the deviation in muscle activation patterns during gait between patients and controls. This method can be used to quantify both typical and atypical changes in muscle activation patterns, allowing the observation of asymmetry in left and right function, as well as the activity of agonist and antagonist muscles. This suggests that it may provide insight into abnormal muscle activity such as co-contraction in muscle spasticity, but further refinement of this index is needed.

6 Conclusion

Recommended features and their meaning in spasticity

The RMS is easy to compute and applicable for multiple research objectives. It is particularly suitable for the evaluation of treatment effects. The Stretch Reflex method accurately determines the onset of reflexes, allowing precise analysis of muscle activity within the correct time frame. It enhances the accuracy of determining spasticity levels. Often used in analyses, especially in the form of the TSRT applied in the kinematic model and Lambda model, it has shown promising results. Significant differences after treatment were measured with the ARV feature and amplitude value. The CCR is a clear, easy-to-calculate, and interpretable parameter to identify co-contractions, a common phenomenon in patients with spasticity. However, it is crucial to be critical and consider combining it with other features. Calculating a ratio between two responses, it's essential to examine individual responses separately to avoid misinterpretation.

Analysis domain

The time component was consistent across all studies, which led to in analysis only in the time domain or time-frequency domain. Focusing only on the frequency domain neglects the signal's representation over time, crucial as movements occur over specific durations. Despite the relevance of the frequency to muscle activation patterns, analysis often shifts to the time-frequency domain due to the temporal nature of movements.

When evaluating the performance of patients with spasticity, particularly during gait, the time-frequency domain offers a comprehensive analysis. Although more computationally intensive, it retains all relevant time and frequency information, providing a more complete analysis. Time domain analysis ensures ease of interpretation and calculation, which is critical for both clinical applicability and real-time monitoring.

Type of movement

Analysing passive movements is preferred due to minimal interference from voluntary actions, ensuring reliable sEMG signals. Manual passive movements offer patient comfort and align with the clinical context, allowing simultaneous MAS assessment. Mechanical equipment enhances data collection, measuring speed and joint mobility, but its clinical use is limited to patient discomfort and clinical applicability constraints.

Golden Standard

Currently most of the features are compared with the MAS resulting in divergent results on correlation between both. For some features, such as the SRO, and AUC, correlation with the MAS was found. But no convincing results were found, and the subjectivity of the MAS is often mentioned as explanation. Furthermore, the comparison between MAS and sEMG is made in terms of the amount of information obtained about the patient (22). sEMG offers much more information on muscle condition and responses, then one physician measuring the joint stiffness.

Concluding, a combination of features offers a robust framework for quantifying spasticity and effect of treatment. Preferably this is measured by performing passive movements, since more features can be derived, and less noise distortion is present. The combination of features for the quantification of spasticity could contain the RMS, SR threshold/onset detection, ARV and CCR.

Appendix A – List of Abbreviations

Abbreviation	Definition
AVR	Average Rectified Value
ALR	Average Limb Response
CP	Cerebral Palsy
CCR	Co-Contraction Ratio
CMAP	Compound Muscle Action Potential
CVA	Cerebral Vascular Accident
CWT	Continuous Wavelet Transform
HHT	Hilbert-Huang Transform
ITB	Intrathecal Baclofen
MVIC	Maximum Voluntary Induced Contraction
MAV	Mean Absolute Value
MAS	Modified Ashworth Scale
PPM	Pearson Product Moment
RMS	Root Mean Square
STFT	Short Time Fourier Transform
SD	Standard Deviation
SRO	Stretch Reflex Onset
SRT	Stretch Reflex Threshold
sEMG	Surface Electromyography
TSRT	Tonic Stretch Reflex Threshold
UMN	Upper Motor Neuron

Table 1: List of Abbreviations

Appendix B – Detailed search results

Database searched	Platform	Years of coverage	Records	Records after duplicates removed
Medline ALL	Ovid	1946 - Present	119	119
Embase	Embase.com	1971 - Present	140	55
Web of Science Core Collection*	Web of Knowledge	1975 - Present	74	7
Total			**333**	**182**

Table 2: Detailed search results

Appendix C – Features for passive movements

Passive movements			
Analysis Domain	**Specified**	**Representation**	**Used by**
Time Domain	CMAP	Analysis of the conduction of electrical impulses along nerves. Used to quantify the suppressive action of treatment on neuromuscular transmission. Evaluation based on signal amplitude, latency, and conduction velocity.	A.Picelli et al. (31)
	RMS	Amplitude of the RMS EMG signal	A.P. Abraham et al.(20)
		Mean for calculation of percentage difference before and after treatment.	J. Castilho et al. (17)
		Mean and SD used to define EMG onset. Single largest value of RMS EMG amplitude to define MVIC (maximum voluntary isometric contraction)	S.H. Schless et al. (18)
		RMS used to calculate the Average Limb Response, in units of $uV_{RMS.}$	A.M. Sherwood et al. (2000) (22) A.M. Sherwood et al. (1997) (21)
		Linear envelope used to perform Phase-Amplitude Coupling evaluation.	C. H. Yeh et al. (41)
		Mean RMS EMG value used to assess influence of velocity and speed on manual passive stretches.	Sorinola et al. (19)
	Integrated EMG activity	Activity for the passive movement at each velocity (amplitude units/sampling rate)	D.Y. Kim et al. (23)
		AUC calculated for windows of 10 ms, after rectification, for indication of muscle activity.	J. Winslow et al. (24)
		AUC determined to represent das density measurement of EMG amplitude over the trial duration for antagonist muscles.	C. McGibbon et al. (25)
	Average Rectified Value	Measure of the amplitude and intensity of muscle activation, after rectification and averaging. It's directly proportional to the intensity of muscle activity. A higher value indicates stronger muscle contractions.	W. Campanella et al. (32)
	Peak amplitude	(Peak SEMG – Mean resting SEMG) / SD of resting SEMG After analysis if a response was present and short or sustained.	A. Cooper et al. (33)
		EMG amplitude change is used to determine onset time. The change in EMG amplitude was used to represent the discrete change in EMG intensity of the antagonist.	C. McGibbon et al. (25)
	Tonic/Dynamic Stretch Reflex Threshold (D/TSRT)	SRT (also referred to as Dynamic Stretch Reflex Threshold - DSRT) can be expressed by means of velocity and angular coordinates representing the joint angle at which motor neurons, and the respective muscles fibers, begin to be recruited in response to a stretch performed at a given velocity.	M.B. Silva et al. (42)
		Two evaluation models were developed to quantitatively evaluate spasticity. First, Lambda model that evaluates the SRT that refers to the joint angle when the EMG signal is induced. Second, the kinematic model where a reference motion pattern is constructed for each patient. Based on the assumption of a consistent pattern between the actual and reconstructed motion curve.	X. Zhang et al. (29)
	Reflexive Electromyography Threshold (RET)	Reflexive Electromyography Threshold (RET): where baseline activity exceeds 3 standard deviations from the baseline, within the 100 ms before eliciting the stretch.	H. Lee et al. (30)

	Mean	Mean electrical activity before and after the movement-associated electrical activity during 10 sec recording period.	C. Skold et al. (34)
		Mean value is related to the EMG signal amplitude	V. Alcan et al. (35)
	Absolute Mean	Mean absolute value is related to the EMG signal amplitude	
	Standard Deviation of mean	Standard deviation of mean value is related to the EMG signal amplitude	
Time-Frequency domain	Max. Power	Maximum power value is related to spectrum analysis of the EMG signal	
	Absolute D_mean	10th level detailed coefficient mean absolute value is related to wavelet analysis of the EMG signal	
	Absolute D_median	10th level detailed coefficient median absolute value is related to wavelet analysis of the EMG signal and obtained by using Daubechies WT	
	Stretch Reflex Onset (SRO)	Based on the Hilbert-Huang transform Marginal Spectrum Entropy (HMSEN) and the RMS of sEMG signals. The HMSEN is used to detect the SRO and the spasticity is quantified based on difference between the RMS of a fixed length sEMG signals, obtained after the SRO and the RMS of a baseline signal.	B. Hu et al. (Feb 2018) (36) B. Hu et al. (Jul 2018) (14)

Appendix D – Features for active movements

Active Movements			
Analysis Domain	**Specified**	**Representation**	**Used by**
Time Domain	Pearson Product-Moment	The Pearson r correlation coefficient measures the degree of association between the two muscle activation profiles. Calculated mathematically with the linear envelope of muscle x and y at time *i*, and the mean of the discretized EMG profile of muscle x and y.	M.M. Cowan et al. (37)
	Co-contraction Ratio	To determine Co-contraction Ratio: RMS target muscle/RMS reference muscle	S.H. Ohn et al. (38)
	Maximum Voluntary Induced Contraction	Mean and SD used to define EMG onset. Single largest value of RMS EMG amplitude to define MVIC (maximum voluntary isometric contraction)	S.H. Schless et al. (18)
	Normalized signal	Normalization of the signal amplitude so datasets acquired with different hardware can be compared. Normalization performed with three methods: 1) peak value measured over the averaged E/F and the average P/S movements, 2) peak value in all movement trials, and 3) peak value using a 200 ms plateau of the MVIC against manual resistance. Averaged = average of 5 EF or PS cycles.	A. Sarcher et al. (39)
Time-Frequency Domain	Instantaneous Mean Frequency	Calculated by the Continuous Wavelet Transform, presenting a scalogram (3D graph with frequency (scale), amplitude (magnitude/power) and gait cycle (%)	R.T. Lauer et al. (40)

Appendix E – Pre-processing methods

Reference	Types of filters	Bandwidth (Hz)	Sampling frequency fs (Hz)	Conversion Resolution (Bit)
Abraham et al. (20)	**Band pass**	**15-1.5k**	**1k**	**14**
Alcan et al. (35)	Wavelet denoising filter	0-1.5k	10k	12
Campanella et al. (32)	Band pass	20-500	-	-
Castilho et al. (17)	Band pass	20-500	2k	-
Cooper et al. (33)	Low pass Butterworth	100 Hz	1k	-
Cowan et al. (37)	**High and low pass**	**15-30**	**100**	**-**
Hu et al. (14, 36)	Low pass	500	1k	12
	Notch	10		
Kim et al. (23)	Band pass	10-5k	-	16
Lauer et al. (40)	**Low pass**	**2k**	**1k**	**-**
	Extra low pass	**350**		
Lee et al. (30)	-	-	1k	12
McGibbon et al. (25)	Band pass	20-400		
	Zero-lag 4th order Butterworth low pass	10	-	-
Ohn et al. (38)	**Band pass**	**20-450**	**1k**	**-**
Picelli et al. (31)	-	-	-	-
Sarcher et al. (39)	**4th order Butterworth Band pass**	**10-450**	**1k**	
	2nd order Butterworth zero lag	**50**		
Schless et al. (18)	3rd order Low pass	30-50	2k	-
Sherwood et al. (22)	Band pass	40-600	1.8k	12
Silva et al. (42)	Band pass	20-1k	2k	16
Skold et al. (34)	Band pass	20-1k	100	12
Sorinola et al. (19)	Band pass	10-1k	5k	-
Winslow et al. (24)	Hardware	30-1k	1k	-
	Nonlinearly scaled Morlet Wavelet	74.8-193.9		
Yeh et al. (41)	Notch band	50/60	256	
Zhang et al. (29)	Zero-lag 4th order band pass	20-450	-	-

Bold = study on active movements
Green = Most used filter type is band pass filter
Yellow = Most used bandwidth is from 20 Hz up to 500/600 or 1k Hz
Orange = Most used sample frequency is 1k Hz

Pre-processing of EMG signals usually involve amplification, band pass filtering, full wave rectification and subsequent low-pass filtering, see Figure 3: Flowchart of Pre-Processing steps of sEMG signals (42). When reviewing the literature on the bandwidth of the band pass filter, it is recommended that a high-pass filter of approximately 10-30 Hz is used to improve muscle force estimates (43). This corresponds to the average applied high-pass levels of the band pass filters in the selected literature. For the low pass level of the band pass filter often a value of approximately 500 Hz is recommended (43), here some outliers towards 1k Hz are seen. The low-pass cutoff values are recommended to use since it removes noise and therefore returns the informative part of the EMG signal. No clear trend in used bandwidth is seen within the studies assessing active movements. This can be clarified by the difference in study objectives, proof of concept, performance analysis of a new parameter or evaluation of new classification method. Note, the literature used as reference evaluated the pre-processing of sEMG data in terms of estimating muscle force, no specific recommendations on spasticity evaluation were found.

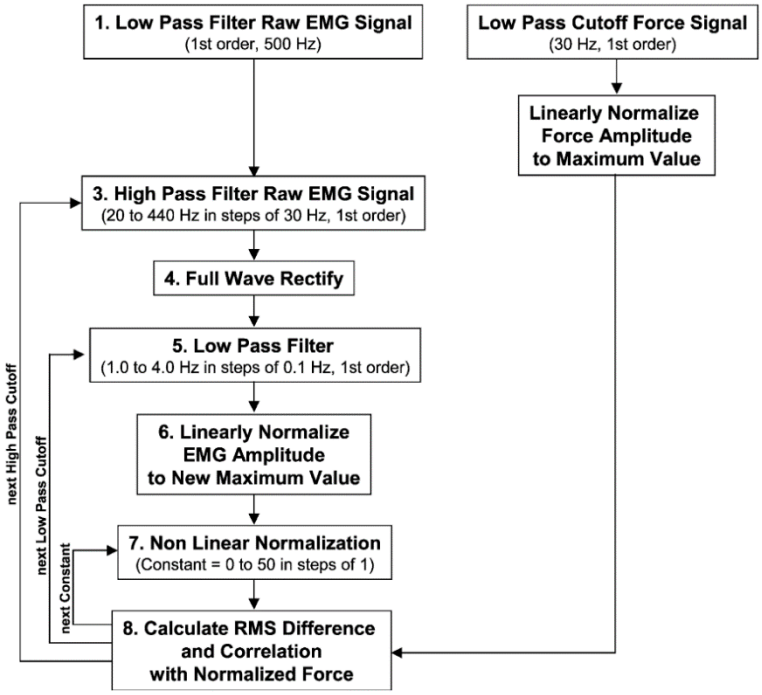

Figure 3: Flowchart of Pre-Processing steps of sEMG signals (42).

The subsequent low-pass filters used studies determine the linear envelope of the EMG signal, which replicates the second-order response of the muscles and the electromechanical delay within the neuromuscular crossbridge mechanism (44).

Commonly used sampling frequencies are close to 2000 samples/s, meaning fs = 2k Hz. Some studies applied higher sampling frequencies resulting in more specific representations of the EMG signal and its fast variations. However, increasing the sample frequency brings the risk of aliasing. To avoid aliasing the Nyquist theory should be applied, where fs is twice the highest frequency of interest (45). Sample frequencies below 1k Hz are not recommended since the loss of information is too high (46).

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