A comparison of customized strategies to manage muscle fatigue in isometric artificially elicited muscle contractions for incomplete SCI subjects

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Abstract— Muscle fatigue due to functional electrical stimulation still prevents its widespread use as a gait rehabilitation tool for spinal cord injured subjects. Although there is an active research towards optimization of pulse parameters to delay muscle fatigue, changes in stimulated muscle's performance during repeated contractions due to fatigue have not been yet determined. In this work, a study conducted in two phases with a sample of incomplete spinal cord injured patients is presented. In the first phase, a fatigue protocol based on submaximal isometric contractions allowed to obtain an objective criterion for estimation of fatigue of knee muscles from initial changes in muscle performance. The criterion is incorporated in the fatigue protocol in the second phase of the study, to compare two novel customized fatigue management strategies. Results showed that knee flexor muscles develop less force and lower fatigue than extensor muscles. Muscle fatigue management strategies based on customized modulations of stimulation frequency are valid to delay muscle fatigue.

Key Words: FES, fatigue, isometric, model, walking, estimation.

I. INTRODUCTION

FUNCTIONAL ELECTRICAL STIMULATION (FES) has the capacity to produce movement in denervated, paralyzed, or spastic muscles or persons with spinal cord injury (SCI) [1]. However, a significant limitation of non-physiologically induced muscle activation is the overall decreased efficiency of contraction and propensity for development of muscular fatigue. The purpose of muscle fatigue management strategies is to achieve a more efficient stimulation, similar to healthy voluntary activation, throughout the study of the effects on muscle response of the stimulation parameters: pulse amplitude (PA), duration (PD), frequency (Freq), and train configuration.

The effect of pulse amplitude and duration on muscle fatigue is not as predominant as the effects of frequency. A study showed that, for the same amount of electrical charge, which directly correlates with muscle force generated, the combination of lower frequencies with longer pulse durations reduces fatigue compared to higher frequencies and shorter pulse durations [2]. In general, train frequencies around 100 Hz will produce more muscle fatigue than lower frequencies, although this relation is not straightforward [3]. Conversely, low frequencies have been reported to induce higher fatigue rate than high frequency stimulation [4], with excessively low frequencies, typically under 30 Hz, have been shown to induce a long-lasting type of muscle fatigue [5].

The effect of the number and distribution of the pulses within stimulation train has also been investigated [6], [7], [8]. Although this strategy holds potential to delay muscle fatigue, optimal choice of the number of pulses seemed to be subject-dependent [6]. Besides, random modulation of the inter-pulse interval within stimulation trains decrease fatigue rate compared to stimulation at constant inter-pulse interval [7], but other experiments have shown that random modulation of inter-pulse interval did not affect muscle fatigue compared to constant frequency [8]. These results suggest that there may be several optimal stimulation trains, dependent on the task, muscle group and population being studied.

A further constituent of FES that also affects muscle force generation, fatigue and comfort during stimulation is electrode type and placement. The use of array electrodes for muscle stimulation have been proposed recently [9], which has shown to greatly decrease rate of fatigue [9], [10]. However, this novel method posses several challenges that need to be solved prior to implement these devices in functional rehabilitation devices, as the configuration of the electrodes within the matrix [11], and the need for specific multi-channel stimulator and control strategies.

As shown, research in the area of FES-related muscle fatigue pursues optimizing stimulation parameters. As result, muscle fatigue is delayed due to decreased stimulation intensity. However, muscle fatigue would eventually be developed as consequence of the artificial contractions made over the muscle. The use of FES for rehabilitation demands a criterion for monitoring muscular performance to adapt therapy intensity. Furthermore, in the case of FES-driven walking, this criterion could prevent danger situations due to diminished muscle performance. Besides, monitoring muscle performance allows tailoring fatigue management strategies to the specific muscle fatigue response of the patient. This is of the utmost importance because the stimulation parameters are highly demanding, in order to elicit suitable muscle force to mobilize and/or stabilize the lower limb joints. In this sense, the choice of the stimulation parameters and the decremental stepwise strategies to investigate (see material and methods for description), responded to the final
application of the results from this study, which is framed within research projects that aims to develop hybrid robot-FES walking exoskeletons (Rehabot and Hyper projects) [12]. Thus, the stimulation parameters were set aiming to obtain the maximum force at the initial steps during the hybrid walking therapy.

Some studies have introduced a criteria to customize stimulation strategies to the fatigue response [8], [13]. However, those criteria were not associated with the actual fatigue response of the muscles. Some research groups have explored the use of the evoked electromyographical signal (eEMG) of the muscle under stimulation as indicator of muscle performance. However, the correlation between eEMG and muscle fatigue of SCI is still controversial [14], [15], [16]. Furthermore, the complexity of recording eEMG during stimulation still remains problematic. It requires specific and custom-made equipment for rejecting artifacts from the stimulation [15]. In conclusion, new methods for estimation of muscle fatigue are needed.

The objective of this article is to investigate the muscle fatigue response of two customized strategies conducted in a sample of SCI subjects. These strategies are defined based on compatibility with FES -driven walking, which typically features high stimulation modulation of stimulation frequency and pulse amplitude to elicit muscle contraction, pulse train duration 14 sec, duty cycle 43%). After completing the warming period, a resting period of 5 min. was then followed (step 2; Fig. 1). Hip joint was flexed 100 degrees and knee joint was flexed 45 degrees with the dynamometer axis aligned with the knee joint. Three 5 X 5 cm electrodes (Alexgaard, Pals-platinum) were placed over the motor points of Vastus Lateralis, Rectus Femoris and Vastus Medialis knee extension muscles, and two electrodes over the motor points of Semitendinosus and Biceps Femoris knee flexion muscles. A PC-controlled stimulator was used (Rehastim, Hasomed GmbH) which delivers biphasic current-controlled rectangular pulses. Dynamometer force was feed into a data acquisition card (NI PCI-6602, National Instruments) at 1kHz sampling rate. Stimulator control and data acquisition was implemented on Simulink Real-Time Windows Target.

The experimental protocol is showed in Fig. 2. After obtaining informed consent, the patient was seated and secured on the dynamometer (Chattanooga Group Inc.) with the lower leg securely attached to the rotating lever arm just above ankle. Trunk, pelvis and tight of the dominant leg tested were stabilized using straps (Fig. 1). Hip joint was flexed 100 degrees and knee joint was flexed 45 degrees with the dynamometer axis aligned with the knee joint. Three 5 X 5 cm electrodes (Alexgaard, Pals-platinum) were placed over the motor points of Semitendinosus and Biceps Femoris knee flexion muscles. A PC-controlled stimulator was used (Rehastim, Hasomed GmbH) which delivers biphasic current-controlled rectangular pulses. Dynamometer force was feed into a data acquisition card (NI PCI-6602, National Instruments) at 1kHz sampling rate. Stimulator control and data acquisition was implemented on Simulink Real-Time Windows Target.

During experiments, subjects were seated on a KinCom dynamometer (Chattanooga Group Inc.) with the lower leg securely attached to the rotating lever arm just above ankle. Trunk, pelvis and tight of the dominant leg tested were stabilized using straps (Fig. 1). Hip joint was flexed 100 degrees and knee joint was flexed 45 degrees with the dynamometer axis aligned with the knee joint. Three 5 X 5 cm electrodes (Alexgaard, Pals-platinum) were placed over the motor points of Semitendinosus and Biceps Femoris knee flexion muscles. A PC-controlled stimulator was used (Rehastim, Hasomed GmbH) which delivers biphasic current-controlled rectangular pulses. Dynamometer force was feed into a data acquisition card (NI PCI-6602, National Instruments) at 1kHz sampling rate. Stimulator control and data acquisition was implemented on Simulink Real-Time Windows Target.

Ten motor incomplete SCI subjects volunteered for participating in this study (age: 47±14 y.o., weight: 79±12 Kg, height: 1.74±0.08 m, injury level from C4 to D7, ASIA C and D). The patients participating in both phases were the same, although there was four drop-outs for the second phase. Incomplete patients were targeted to ensure preserved partial muscle innervation, therefore muscle contraction. To homogenize the group of subjects regarding muscle functional, inclusion criteria were knee muscular balance score between 2 and 3 (International Muscle Balance Score [17]) and spasticity index lower than 3 (Asworth scale [18]). All subjects were previously involved in a therapeutic FES training program for 2 to 4 months. The local Ethics Review Board approved the study and informed consent was obtained from all subjects.
Finally, a relaxation period was carried out following same procedure as for warming (step 6). The procedure was repeated then for the remaining muscle group.

Figure 2: Experimental protocol, based on submaximal isometric contractions

A. Procedure

1) Phase I: muscle fatigue criteria. For this phase, the muscle fatigue test (step 5 in Fig. 2) consisted of delivering stimulation trains with constant current, pulse width, frequency and duty cycle 43%. Once this phase was completed, the data were analyzed following the procedure described in Data Analysis section.

2) Phase II: muscle fatigue criteria. Once the first phase was completed and the data analyzed, the second phase was undergone three weeks after the first phase. The same patients were contacted again for participating in this phase. Four patients were not available for this phase, so the study group for this phase was comprised by six motor incomplete SCI subjects (age: 51±15 years of age, weight: 83±14 Kg, height: 1.74±0.05 m, injury level from C4 to D7, ASIA C and D).

Two customized stepwise decremental modulation strategies were compared in this phase: frequency modulation (FM) and pulse amplitude modulation (AM). The modulation consisted of a stepwise decrease on frequency and pulse amplitude respectively, made upon detection of muscle fatigue. A third constant frequency and amplitude (CFA) strategy, were no changes on the stimulation parameters were made, was included for control condition. The experimental procedure for this phase was equal to the first phase procedure (Figs. 1 and 2), but for the muscle fatigue test period (step 5), which differed slightly depending on the strategy tested, as shown below. Each muscle fatigue management strategy was evaluated in a day with at least 48 hours between evaluations. Thus the experimental protocol was completed in three different days, one for each strategy. The strategies were randomly sorted for each patient. Similarly to the first phase, stimulation was delivered for 15 minutes while the generated force was recorded through the dynamometer force sensor. Regarding the strategy tested, stimulation parameters were modulated as follows.

Force-time integral (FTI) was calculated immediately after each stimulation pulse, (see Data Analysis section for more details). Muscle fatigue was estimated by monitoring the time-evolution of the FTI values for each stimulation train and comparing with the fatigue criteria obtained in phase I (see Results section and Fig. 3 for more details). Once the FTI decreased below the criteria, fatigue is estimated and then changes on the stimulation parameters were done depending on the strategy being studied.

For all three FM, AM and CFA strategies, initial stimulation parameters were as follows: pulse width 350µs, frequency 70Hz, current amplitude set at 90% of the maximum tolerable value, pulse train duration 14 sec., and duty cycle 43%. For FM strategy, stimulation frequency was decreased 10 Hz after fatigue detection, while pulse amplitude, pulse width train duration and duty cycle remained constant. In the case of AM strategy, stimulation amplitude was decreased 2mA after fatigue detection, while frequency, pulse width, train duration and duty cycle remained constant. Finally, for CFA strategy, stimulation parameters frequency, pulse amplitude, pulse width, train duration and duty cycle remained constant during the experiment. A customized program was developed in Simulink to implement the muscle fatigue criteria and the stimulation control, and a graphical user interface (GUI) was designed to set and change in real-time stimulator parameters upon fatigue detection: once muscle fatigue was detected, the pulse amplitude or frequency was changed through the GUI and feed in real-time to the stimulator control, setting the stimulation parameters for the next stimulation trains on which fatigue was estimated.

B. Data analysis

Data analysis conducted in both phases was as follows. FTI values were calculated for each stimulation pulse, removing gravitational torque and normalizing by subjects’ leg length. Normalization was performed to account for the position of the force sensor. The FTI corresponding to the first stimulation pulse (hereinafter initial and last FTI) were group averaged for each muscular group. For each stimulation train, the FTI was normalized to the initial FTI, obtaining a normalized time-evolution of the FTI (NFTI). The NFTI of all patients were averaged, obtaining a NFTI curve representative of each muscle group. The number of pulses needed for the FTI to decay 15, 20 and 50% of the initial FTI was also obtained. Friedman and Wilcoxon post-hoc test with Bonferroni correction was used to determine changes in FTI. Also a regression analysis was performed for FTI versus time data. SPSS was used for all analyses.
III. RESULTS

A. Phase I: muscle fatigue criteria

Figure 3: Subject-averaged NFTI for flexor and extensor muscles. Mean normalized FTI values for all subjects (N=10). Vertical bars mean standard deviation. Coefficient of determination (R²) for each regression curve: extensor muscles=0.98, Flexor muscles=0.95. * denotes p<0.05.

Fig. 3 shows the NFTI for extensors and flexors muscles representative of the group of patients. It should be noted that time and pulse number are equivalent since train length and duty cycle are held constant. The regression analysis showed an exponential relationship between FTI VS cycle, which is consistent with previous data found in literature [2], [19], [20], [21]. It can be observed that FTI decay for flexors muscles shows a slower decay than extensors muscles. Statistical analysis of differences among NFTI mean values between consecutive pulses showed a significant decay in FTI (11%, p<0.05) for extensor muscles at second stimulation train, whereas for flexors the significant decay in FTI occurs in the ninth pulse (19%, p<0.05). Given that the stimulation parameters remained fixed, this significant drop in NFTI can be assumed to be due to a decline in muscular performance. Thus, within the population analyzed, a decrease of 11% in extensor muscles NTFI, or 19% for flexor muscles denote the minimum change in this variable that indicates the appearance of muscle fatigue. These values were used in the phase II to customize the strategies as it is described in the next section.

Figure 4: Left: absolute values for FTI at the initial and last stimulation trains. Right: Number of pulses to decrease 15%, 20% and 50% of the initial FTI. Flexor and extensor muscle groups. * denotes p<0.05; ** denotes p<0.01.

Further differences were found in non-normalized FTI (Fig. 4, left): 79 N for extensors and 41 N for flexors (p=0.05), although at the end of the experiments FTI values were similar between muscles (p=0.80). FTI at the end of the experiment was significantly lower compared to the beginning of the experiment for both muscle group (p<0.01). Fig. 4 right depicts NFTI reduction in relation with number of applied stimulation pulses. Decays of 15, 20 and 50% showed differences within muscle groups. However no differences in pulses to decay were found between muscle groups.

B. Phase II: customized strategies for fatigue management

Fig. 5 left, shows the group average results of NFTI for each strategy tested of the knee extensor muscles. Here it can be noticed the different evolution of NFTI for each strategy, which is more noticeable in Fig. 5 right, where the adjusted data to an exponential decay function for the three strategies tested is showed. It can be noticed a higher NFTI for AM strategy than CFA and FM. Fig. 6 left, shows the absolute values for FTI at the initial and last stimulation trains for extensor muscles. Statistical analysis showed no differences among all three strategies at the initial FTI. Last values of FTI showed also no differences among strategies, although last FTI value for FM strategy showed a tendency to be higher than AM (p=0.173) and CFA (p=0.075) strategies.

Figure 5: Comparison of extensor muscles FTI for the three strategies tested (N=6). Right: NTFI group average for each strategy (vertical bars means standard deviation). Left: fitted data. Coefficient of determination (R²) for each strategy: FM=0.96, CFA=0.97, AM=0.98.

Fig. 6 right, shows the number of stimulation trains to the initial FTI to decay 15%, 20%, and 50% for extensor muscles. Within strategies, the comparison among values showed that there were statistical differences between 15% to 20% of decay for FM (*1), AM (*2) and CFA (*3) strategies, and between 20% to 50% of decay for FM (*4), AM (*5) and CFA (*6) strategies respectively. No differences were found across strategies for the same decay percentage. In the case of 50% of decay, FM showed a tendency to need a higher number of pulses than AM (p=0.345) and CFA (p=0.500) strategies to decay a 50% of the initial FTI.

Figure 6: Left: Absolute values for FTI at the initial and last stimulation trains. Right: Number of pulses to decrease 15%, 20% and 50% of the initial FTI for each strategy, extensor muscles. * denotes p<0.05.

Fig. 7 left, shows the group average results of NFTI for each strategy tested of the knee flexor muscles. Here it can be noticed the different evolution of NFTI for each strategy, which is more noticeable in Fig. 7 right, where the adjusted data for the three strategies tested is showed. Comparing Figs. 5 and 7, it can be noticed that extensor muscles have a
more pronounced decay overall for three strategies than the flexor muscles. We first noticed that on the data of the first phase of the study (Fig. 3).

![Graph showing comparison of flexor muscles FTI for the three strategies tested (N=6). Right: NTFI group average for each strategy (vertical bars means standard deviation). Left: fitted data. Coefficient of determination (R²) for each strategy: FM=0.93, CFA=0.98, AM=0.90.](image)

Fig. 8 left, shows the absolute values for FTI at the initial and last stimulation trains for flexor muscles. The FTI for the last train for FM strategy was higher than AM and CFA strategies (p<0.05). No differences among all three strategies at the initial FTI were found. Fig. 8 right, shows the number of stimulation trains to decay 15%, 20%, and 50% of the initial FTI for flexor muscles. Within strategies, the comparison among values showed that there were statistical differences between 15% to 20% of decay for FM (*1), AM (*2) and CFA (*3) strategies, and between 20% to 50% of decay for FM (*4), AM (*5) and CFA (*6) strategies respectively. No differences were found across strategies for the same decay percentage. In the case of 50% of decay, FM showed a tendency to higher number of pulses than AM (p=0.075) and CFA (p=0.225) strategies.

![Graph showing comparison of flexor muscles FTI at the initial and last stimulation trains. * denotes p<0.05.](image)

IV. DISCUSSION

The objective of this study was to compare two strategies for muscle fatigue management compatible with high stimulation parameters, customized to the specific muscle response. The first phase aimed to propose an objective criterion to estimate muscle fatigue from changes in muscular performance. Obtained results confirm that changes in muscle performance can be detected by monitoring the FTI of the generated muscle force. Either FTI or peak force developed during stimulation train have been used without distinction for assessing muscle fatigue [21], [22], [23], [24], [25]. However, peak force can be easily affected by stochastic phenomena related with spasm. FTI on the other hand, represents the mean force value developed by the muscle during the stimulation train, thus is more robust and representative than peak force.

The work presented here analyzes the fatigue of knee flexor muscles and compares it versus extensor knee muscles. The study of the fatigue of knee flexor muscle group is of the utmost importance for walking-related functional activities, since this muscle group plays a fundamental role in achieving adequate toe-clearance during the swing phase. Results show that the relative decay for flexor muscles is slower than for extensor muscles which indicates that flexor muscles develop less fatigue in this protocol (Fig. 3 and 4, left). However, this slower decay in muscle performance was not confirmed by the analysis of the number of pulses to decay (Fig. 4, right). On the other hand, the force developed by the flexor muscles was notably lower than extensor muscle force (Fig. 4, left). These results suggest that stimulation of flexor muscles is less efficient than for the extensor muscles.

The obtained fatigue models are similar to the models presented in the literature [2], [19], [20], [21], exhibiting an exponential decay. Total FTI decay in the work presented here differs between extensor and flexor muscles, towards a 75% for flexor and 50% for extensor. The variety on stimulation protocols found in the literature difficult direct comparison and discussion of these results, but is in general in line with the trends reported. The progress of the NFTI for flexor muscles exhibits a greater variability than extensor muscles, mainly at the beginning of the curve (Fig. 3). This can be attributed to the fact that the potentiation effect [26] was not controlled in the experimental protocol. Whilst there is not a specific criteria for establishing the number and configuration of the stimulation trains to account for potentiation, it was assumed that potentiation was overcome during the iterative search of the pain threshold (Fig. 2, step 3), which took 5 to 10 pulses in average, similar to the number of pulses delivered in the protocols that accounted for muscle potentiation [2], [13], [24], [25], [27]. It is noticeable that in the case of quadriceps, potentiation was not detected. Nevertheless, performance of extensors muscles seems to be more affected by non-controlled factors than extensor muscles.

Up to the best of the authors’ knowledge, this is the first work that addressed the establishment of a criterion to discriminate muscle fatigue from changes in muscular performance. The minimum statistically significant change in NFTI was 89% for extensor muscles and 81% for flexor muscles. Given that the stimulation parameters remained fixed, this significant drop in NFTI can be assumed to be due to a decline in muscular performance. In other words, within the population analyzed, a decrease of 11% in extensor muscles NTFI, or 19% for flexor muscles denote the minimum change in this variable that indicates the appearance of muscle fatigue. Some studies have tested stepwise modulation of stimulation parameters for management of muscle fatigue based on estimates of decreased muscle performance. For example, Chou [13] used a drop of 10% in peak force to estimate muscle fatigue and thus change stimulation parameters. A rationale for this value was however not given. Thrasher [8] stated that a drop of 3 dB (70.8%) in peak force was a criteria for estimate muscle fatigue. The work presented here represents an effort to discriminate muscle performance drop from stochastic effects, assuming this change as a fatigue criterion. It should be noticed here that the fatigue criteria for the extensor muscles, a drop in FTI of 11%, is similar to the 10% drop in peak force proposed by Chou [13]. Nevertheless, the latter
was performed in a population of 12 healthy subjects, which limits the comparison between studies.

The muscle fatigue criteria were applied to comparatively analyze the effects on muscle fatigue of two customized strategies for muscle fatigue management. These strategies were selected regarding compatibility with FES-driven walking, which typically features high stimulation parameters (frequency, pulse amplitude and amplitude). FM strategy showed that discrete decrements on stimulation frequency of flexor muscles delays muscle fatigue compared to CFA and AM strategies, which was statistically significant for flexor muscles. In the case of extensor muscles, a similar trend was observed, although statistical significance was not obtained. The superior performance showed by FM strategy agrees with general results from other studies, where frequency modulation is shown that delays muscle fatigue [6], [13], [28], and stimulation intensity modulation leads to a decreased muscular performance [13]. Differences in the metabolic energy expenditure or on the recovery of force-generating ability could constitute and explanation of these results. However, we do not have adequate data to further investigate the mechanisms underlying muscle performance in the protocols presented here. Measuring the electrophysiological activity of motor units and/or the metabolic energy expenditure will shed light on these mechanisms.

The effects of high versus low stimulation frequency in muscle fatigue are still controversial, although recent studies have shown that stepwise increments on stimulation frequency can delay muscle fatigue [13]. A limitation of the work presented here is that the reverse FM strategy (stepwise increments in stimulation frequency) was not considered to compare its effects on fatigue. We only designed two strategies in order to not complicate the design of the study. Furthermore, comparison with other criteria for modulation of stimulation parameters (like the proposed by [13] or others) would shed light into the suitability of the criteria utilized in this work for tailoring fatigue strategies.

The results from this work are applicable to the generation of force through isometric muscle contractions. Quadriceps muscles work in isometric conditions during the stance phase of walking, thus the results from this work can be directly applied to the actual control of quadriceps muscles during walking. On the contrary, the swing phase is a dynamic movement, thus the results from this work can differ from the actual flexor muscle fatigue during hybrid walking. An experimental design based on isokinetic muscle contractions matching leg's weight could better resemble the real stimulation conditions and requirements during walking. However, inability of SCI patients to develop enough force for this procedure would impede setting such isokinetic experiment with this type of patient sample.

V. CONCLUSION

An objective criterion for early detection of muscle fatigue of electrically stimulated muscles in individuals with incomplete SCI has been presented, using FTI to model muscle performance in time. Force characteristics and fatigue trend differs between flexor and extensor muscles. Flexor muscles develop less force and also lower fatigue than extensor muscles.

The muscle fatigue detection criteria allowed implementing tailored muscle fatigue management strategies between stimulation trains. The fatigue-adapted modulation strategy presented in this work can be combined with other muscle fatigue management strategies.

The results showed that the FM strategy leads to higher NFTI values for both muscle groups thus delaying fatigue, and the worst results were obtained with AM modulation strategy. The approach presented here can be considered for monitoring and delaying muscle fatigue during assisted walking, despite the high stimulation parameters needed to elicit muscle contractions suitable for walking. These results provide the basis for online application of fatigue management strategies for assistance of human gait with neuroprostheses or hybrid exoskeletons, exploiting the inherent capabilities of lower limb muscles after a SCI.

Further work is needed to investigate if tailoring muscle fatigue strategies to the specific muscle response of the patient leads to better outcomes than other proposed criteria.

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