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Popliteal blood flow and plantar flexion force due to neuromuscular electrical stimulation (NMES) of the calf muscle pump are strongly associated with NMES intensity.

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Abstract— **In spite of significant gains in venous flow using Neuromuscular Electrical Stimulation (NMES) of the calf muscles, little is known about the relationship between the applied electrical stimulus and the resulting venous blood flow in the deep veins of the leg. This retrospective study of repeated measures of blood flow, muscle force and NMES signals of 14 healthy subjects undergoing a week long NMES protocol aimed to determine the relationship between the applied NMES signals and the resulting muscle force and blood flow measures. Statistical analyses revealed strong correlations between NMES blood flow, NMES plantar flexion force and the applied NMES intensity.**

I. Introduction

Neuromuscular Electrical Stimulation (NMES) is the application of electrical stimuli to trigger generation of a neural action-potential-train resulting in muscle contraction [1]. NMES has been used in rehabilitation for over 40 years and applications of NMES include: restoration of upper and lower extremity function, motor re-learning, muscle strengthening and cardiovascular conditioning. Developments in this field are comprehensively discussed by Peckham et al. [2] and Sheffler et al. [3]. Understandably, NMES has found many of its applications in the treatment of spinal cord injured and stroke patients to provide an additional degree of function or to compensate for a lack of voluntary muscular activity. However, more recently NMES has been evaluated as a method for increasing venous flow via stimulation of the peripheral venous muscle pumps in the calf and foot.

The presence of a calf muscle pump in the lower limbs is critical for facilitating venous return in the presence of hydrostatic pressures (the downward force exerted by the column of blood between the foot and the heart) in the leg. Contraction of the calf muscles results in increased venous flow in the deep veins. This voluntary calf muscle pump mechanism is essential for preventing venous pooling in the deep veins which can lead to edema, venous insufficiency and subsequent deep vein thrombosis [4, 5]. Faghri et al. proposed that where voluntary calf muscle pump function is not possible (e.g. due to occupation, a sedentary lifestyle, paralysis, or during extended periods of immobility), there is an increased risk of venous pooling and an alternative form of calf pump activation, such as NMES, needs to be considered [6].

Several studies investigating NMES-based calf pump stimulation in healthy and patients populations have reported significant increases in venous return [7], arterial flow [8] and venous volume changes in the lower limbs [6, 9]. More recently NMES has been applied to the calf muscles in conjunction with compression hosiery to evaluate its possible role as a therapeutic modality for venous insufficiency [10].

In spite of significant gains in venous flow using NMES of the calf muscles, demonstrated in these healthy and patient studies, little is known about the relationship between the applied electrical stimulus and the resulting venous blood flow in the deep veins of the leg. A better understanding of this relationship would facilitate the development of effective NMES-based blood flow assist protocols for clinical applications. The objective of this study is to determine the relationship between the current applied to the calf muscles during NMES on the resulting NMES plantar flexion force and popliteal venous flow.

II. Subjects and Methods

This is a retrospective study examining the effect of changes in applied stimulation on popliteal blood flow in healthy subjects undergoing a week-long NMES and compression therapy protocol. Ethics committee approval was obtained from the Research Ethics Committee, National University of Ireland, Galway and all subjects provided written informed consent. Fourteen healthy subjects (7 male, 7 female), aged 20 - 26, were recruited. All subjects received 90 minutes of stimulation daily. Two round PALS® 5cm diameter neuro-stimulation hypoallergenic skin surface electrodes (Nidd Valley Medical Limited, England) were applied to the back of each subject's calf and NMES was applied. Knee length, Class 2 graduated compression hosiery (Scholl consumer products, UK) was worn over the electrodes and lead wires. Subjects were required to wear the electrodes, lead wires and compression stockings continuously for seven days. Subject height and weight were

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recorded and used to calculate body mass index (BMI).

A. Stimulation Protocol

A Duo-STIM muscle stimulator was used to stimulate the calf muscles [11]. The stimulation protocol was selected to maximise subject comfort, while maintaining effective contraction and was based on previous NMES endurance and comfort studies. The stimulator was programmed to provide a pulse width of 350μs, an inter-pulse interval of 100μs; a frequency of 36Hz; ramp up, contraction and ramp down times of 1s each and a relaxation time of 12s. Subjects were asked to self-administer three 30 minute NMES sessions daily for 6 days with a resting interval of at least 2 hours between each session.

One of the three daily NMES sessions was supervised and took place within a clinical measurement room, where the applied voltage, current response, popliteal venous blood flow and NMES force could be assessed throughout the week. The remaining 2 NMES sessions were independently administered by the subject at their convenience. The stimulation intensity was selected prior to each stimulation session. Subjects were asked to select the highest comfortable stimulation intensity, which was then used for the entire session. The final day of each subjects participation consisted of a single supervised stimulation session, giving each subject a total of 19 stimulation sessions over the course of the week.

III. Measurements

Each day of the 7 day protocol consisted of a testing session where various measurements were recorded before and at the onset of the 30 min stimulation session. Following selection of the maximum comfortable stimulation intensity by the subjects, isometric force (prone) and popliteal blood flow measurements (seated) were recorded immediately prior to the beginning of the 30 min stimulation session. The peak NMES voltage amplitude and peak current response to the calf muscles were recorded within the first 5 min of stimulation. Blood flow and force measurements were repeated 3 times and averaged. Subjects received a 1 min resting break between repeated measurements.

A. Blood Flow

An Ultrasound system (LOGIQ e; GE Medical Systems, Ireland) was used to measure peak venous velocity and peak resting velocity using a 10 MHz linear transducer. These velocities were automatically calculated by the LOGIQ e software and were then manually recorded by the investigators. All blood flow measurements were taken in triplicate at the popliteal vein, with the probe held at the back of the knee. The subject was in a seated position with the distal half of their thigh clear of the seat to avoid occlusion and their feet clear of the ground to facilitate a full range of motion for plantar flexion. Resting blood flow and blood flow due to NMES of the calf muscles was recorded before each supervised stimulation session. A resting period of 1 minute was given between each measurement to allow venous refilling.

B. Muscle Strength

Plantar flexor force due to NMES was assessed by a handheld dynamometer (Manual Muscle Tester, Model 01163; Lafayette Instruments Europe, Leicester, England) placed over the metatarsal heads as described by Bohannon [12]. This force measurement was taken in triplicate with the mean score calculated. Subjects were given a rest period of 1 minute between each measurement.

C. Electrical Stimulus

The applied NMES voltage and current response were measured simultaneously across the electrodes using a battery powered oscilloscope (TDS3014B; Tektronix UK, Bracknell, England). Two Tektronix P3010 passive voltage probes were used, in a differential setting, for the voltage measurements and a Tektronix TCP202 dc coupled current probe was used for the current measurements. NI Labview 8.5 software (National Instruments, Austin, Texas) was used to filter and crop the voltage and current waveforms and extract the peak voltage current and resistance values. The 3-component equivalent electrical model of the human skin, shown in Fig. 1, was used [13]. Rs represents the resistance of deep tissues (viable skin, lypodermis and muscle).

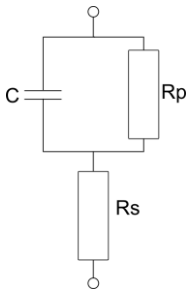

Fig. 1. Equivalent electrical model for stimulated tissue

The parallel combination of a resistor and capacitor (Rp, C) represents the electrical properties of the skin (stratum corneum). The capacitor C is uncharged at the beginning of each voltage pulse and acts as a short circuit between the electrodes and the deep tissues (Rs). As a result all of the voltage at this time will be applied over the deep tissue resistance (Rs).

D. Statistical Analysis

Statistical analyses were carried out using SPSS version 15 on grouped data from each of the seven days on all fourteen subjects. All values are expressed as means ± SE. Paired samples t-test was used to compare resting and NMES peak venous velocity values. Pearson's correlation coefficient was used for all correlations.

Multiple-regression was used to model the effect of

selected prediction variables on measures on peak venous velocity. NMES force, NMES current and BMI were selected as possible prediction variables for modeling peak venous velocity based on prior work in the area of NMES [1] and the influence of the calf muscle pump on popliteal venous flow [10, 14].

IV. Results

A. Electrical Stimulus

Peak NMES voltage averaged 23.75 ± 0.43V and had a strong linear correlation with peak NMES current ($r = .91$, $p < .001$) which averaged 54.68 ± 2.73mA. At higher voltage levels a more dispersed current response was observed (Fig. 2). The resistance of the deep tissues averaged 487 ± 13.44Ω.

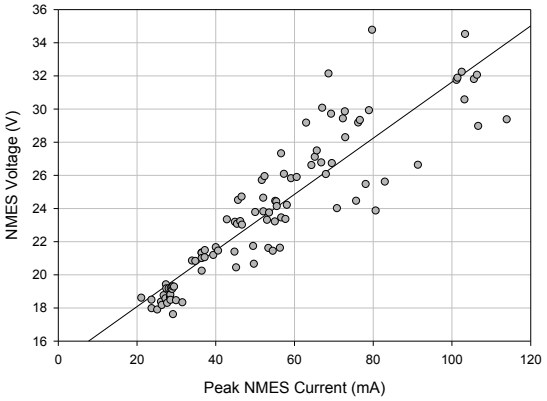

Fig. 2. NMES voltage vs. peak NMES current

B. Peak Venous Velocity and NMES Force

Plantar flexion force due to NMES averaged 7.48 ± 0.30kg. Peak venous velocities in the popliteal vein due to NMES (17.39 ± 0.84 cm/s) were significantly higher than resting peak velocities (7 ± 0.16 cm/s), $t(86) = 12.487$, $p < .001$, $r = .80$ (Fig. 3). Plantar flexion force correlated strongly with NMES peak venous velocity, $r = .67$, $p < .001$ (Fig. 4). Both NMES force and NMES peak venous velocity were also significantly related to peak NMES current, $r = .59$, $p < .001$; $r = .68$, $p < .001$ (Fig. 5).

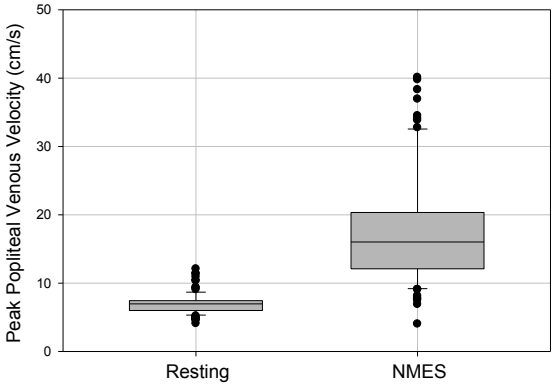

Fig. 3. Peak venous velocities due at rest and due to NMES

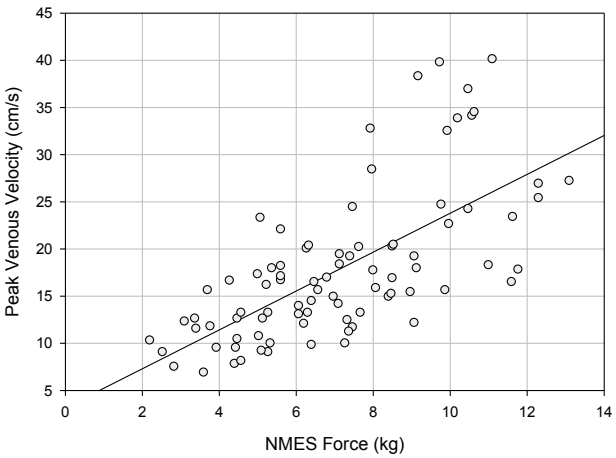

Fig. 4. NMES Force vs. NMES peak venous velocity

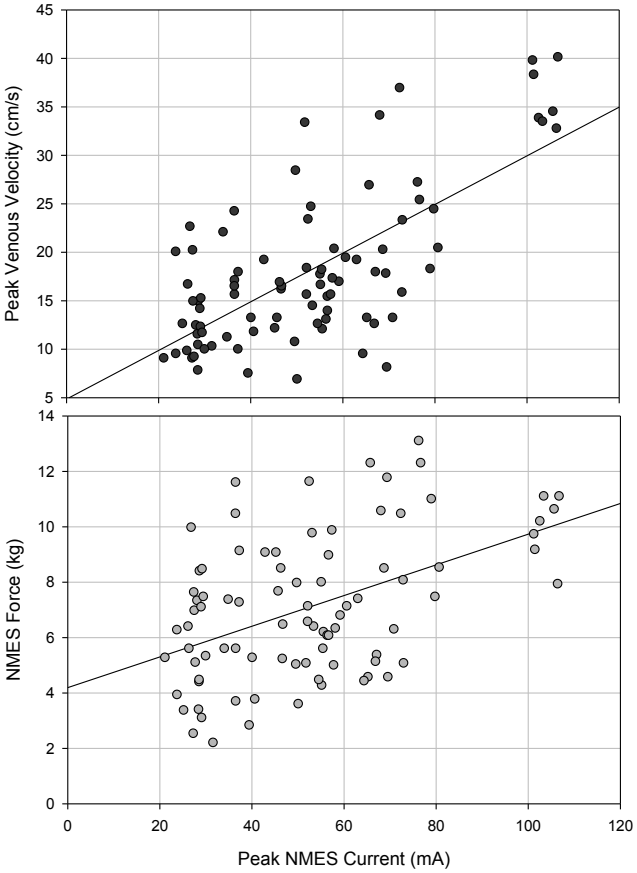

Fig. 5. Peak NMES current vs. NMES peak velocity (top panel) and NMES force (bottom panel)

C. Peak NMES venous velocity model

The linear regression model parameters are shown in Table 1. Peak NMES current, NMES force and BMI were significant predictors of peak venous velocity. Part correlations of the final model reveal that peak current and NMES force accounted for 42% of variance in the model while BMI accounted for 14% of variance in the model.

TABLE I
NMES PEAK VENOUS VELOCITY MODEL FOR SELECTED PREDICTOR VARIABLES

MODEL	PARAMETER	B	SE (B)	B'	R^2
1	(CONSTANT)	4.82	1.59		
	NMES CURRENT:	.25	.03	.69[a]	.48
2	(CONSTANT)	11.19	5.78		
	NMES CURRENT:	.17	.026	.47[a]	
	NMES Force:	1.49	.23	.49[a]	
	BMI:	-.55	.25	-.15[b]	.64*

NOTES: B = MODEL COEFFICIENTS; B' = STANDARDIZED COEFFICIENTS;
[a] $p < .001$; [b] $p < .05$; *increase in R^2 is significant $p < .001$

V. DISCUSSION

In this retrospective analysis of a week-long study of blood flow due to NMES of the calf pump, we were able to demonstrate that changes in peak venous velocity during NMES are strongly correlated with increasing NMES current and NMES plantar flexion force. Additionally, peak NMES current was strongly associated with NMES voltage. Finally an initial predictive model for peak venous velocity was determined from measures of NMES force, NMES current and Body Mass Index and was found to explain 64% of the variation in peak venous velocity measures.

The strong relationship between peak venous velocities and NMES force was clearly demonstrated in this study and signifies the importance of calf muscle contraction for promoting venous flow through the popliteal vein. Although the exact mechanism of the calf muscle pump is not fully understood it is believed that during exercise, muscular contractions increase the rate of drainage of the venous sinuses resulting in increased venous flow [15]. Though a strong relationship was demonstrated in this healthy study, this might not be true of subjects with atrophied muscles who would not be capable of producing the same force due to NMES and further research is required to investigate this.

The correlation between peak NMES current and the resulting stimulated force and peak venous velocities offers the possibility of producing significant peak venous velocities using NMES contractions with current controlled NMES. Although voltage controlled NMES, as used in this study, provides an added measure of safety [1], current controlled stimulation is preferable as the NMES current and voltage relationship becomes more variable at higher intensities (Fig. 2) and NMES peak current was found to be a better predictor of peak venous velocity and NMES force. An NMES controlled treatment strategy may have clinical significance in the prevention of deep vein thrombosis and in the treatment and management of venous disorders, such as chronic venous insufficiency.

If such a treatment were to be implemented clinically there may be some benefit to recording BMI, NMES force measures and / or peak NMES current values, as these variables accounted for 64% of the variation in peak venous velocities and are considerably easier to measure. While the current model of peak venous velocity is limited to this healthy study and falls short of a truly predictive model for blood flow, it may serve as a first step in developing an accurate model for NMES blood flow.

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