# 12 weeks daily gluteal and hamstring electrical stimulation improves vascular structure and function, limb volume and sitting pressure in spinal cord injury: A pilot feasibility study

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**ABSTRACT**

Objective: We examined the long-term effects of low-intensity electrical stimulation (ES) on (micro)vasculature and sitting pressure of a home-based, wearable ES device in a pilot feasibility study. Design: In a cohort observation before-after trial, 9 middle-aged male (n=8) and female (n=1) individuals (48±15 y) with ASIA A-C classified chronic (1-24y) SCI underwent 12-wk of self-administered daily, low-intensity gluteal and hamstring ES [50Hz, 6 hrs (30min ES, 15min rest)]. Common femoral artery (CFA) diameter and blood blow were determined with ultrasound, skin vascular function during local heating was assessed using Laser-Doppler flowmetry, thigh volume was estimated using leg circumferences and skinfolds, and interface sitting pressure was measured using pressure-mapping. Results: Resting CFA diameter increased (0.73±0.20 to 0.79±0.22cm, $P<0.001$), baseline CFA blood flow increased (0.28±0.12 to 0.40±0.15 L/min, $P<0.002$). Gluteal cutaneous vascular conductance showed a time*temperature interaction ($P=0.01$) with higher conductance at 42°C after 12 weeks. Ischial peak pressure decreased ($P=0.003$) by 32±23mmHg and pressure gradient decreased (23±7 to 16±6 mmHg, $P=0.007$). Thigh volume increased (+19%, $P=0.01$). Conclusion: Twelve weeks daily, home-based gluteal and hamstring ES is feasible and effective to improve (micro)vasculature and sitting pressure and ES may have clinical implications for ameliorating pressure ulcers and (micro)vascular complications in SCI.

*Key words:* Spinal cord injury, electrical stimulation, vascular function, pressure ulcers

**What is Known:**

SCI increases skin ulcer risk via poor microvascular perfusion and prolonged sitting pressure. Acute electrical stimulation (ES) improves microvascular perfusion and reduces sitting pressure. Specialist equipment, facilities and trained staff make regular ES application impractical.

**What is New:**

12 weeks of daily home-based low-intensity ES using a wearable device were examined. ES increased common femoral artery diameter and blood flow and gluteal skin blood flow. Ischial peak pressure and pressure gradient decreased and thigh volume increased after ES. These findings have clinical implications for ameliorating pressure ulcers and (micro)vascular complications in SCI.

## INTRODUCTION

A motor complete spinal cord injury (SCI) results in the immediate loss of voluntary muscle contractions and paralysis below the spinal cord lesion. Individuals with an SCI are subject to a wheelchair user (sedentary) lifestyle and as a consequence, a myriad of complications which have profound consequences for psychological and physiological health.[1 2] The (re)occurrence of pressure ulcers is one of the most frequently observed and extremely concerning complications amongst individuals with SCI. In the United Kingdom, the average cost to treat one stage 4 pressure ulcer is estimated at £14,108.[3] Considering that 85% of the SCI population will develop at least one pressure wound at some stage in their life,[4] health and social care systems are exposed to a significant cost burden. This emphasises the need for immediate and effective risk reducing interventions for the development of pressure ulcers for individuals with SCI.

Physical deconditioning resulting from lower-limb paralysis causes changes in micro- and macro-vascular structure and function which, when combined with prolonged sitting pressure and loss of muscle mass covering bony structures, contributes to subcutaneous tissue ischemia and the development of pressure ulcers.[5-7] Reactivating the paralyzed muscles by electrically stimulated muscle contractions (partly) reverses many of these complications in SCI individuals. For example, electrical stimulation (ES) has been found to increase artery diameter,[8] improve arterial compliance,[9] restore contractility in denervated muscle fibers and increase muscle mass,[10 11] improve muscle oxidative capacity,[12] enhance capillary supply,[13] and improve cutaneous microcirculation.[14] Collectively, ES is an effective and clinically significant tool for improving the health of individuals with SCI.

Despite the many reported benefits, the need for specialist equipment, facilities and trained staff for ES interventions make regular application expensive and impractical for many individuals with SCI. In an attempt to overcome such limitations, wearable clothing garments with embedded surface electrodes to provide long-term, low-intensity muscle activation have been introduced. This type of ES activates muscle tissue, but without the concomitant joint movement, and has the advantage to be applied for prolonged periods. Using an acute bout of ES, this method has demonstrated many important benefits relevant to pressure ulcer prevention, such as reducing sitting pressure over the ischial tuberosity and an increase in transcutaneous oxygen levels.[15 16] Additionally, previous work has shown that applying acute bouts of low intensity ES using a wearable clothing garment leads to incremental increases in blood flow in the conduit and skin microcirculation, an effect that is sustained in the minutes after ES[14]. Currently, however, no study has examined the effects of long-term, daily home based low intensity ES in individuals with SCI.

The purpose of this study was to examine the effects of 12 weeks, daily gluteal and hamstring ES using a wearable clothing garment on skin and conduit artery vascular function, limb volume and sitting pressure in people with SCI. It is expected that the cumulative effects of 12 weeks, daily ES would result in an increase in femoral artery diameter, improved skin vasculature function, increased limb volume and reduced sitting pressure.

## METHOD

### Design

Participants with a SCI underwent 12-wk of self-administered daily, low-intensity gluteal and hamstring ES as part of a pilot feasibility study. Participants visited Amsterdam Rehabilitation Research Center on 3 occasions. The initial visit was used to administer ES, ensure all inclusion criteria were met and to explain the study in detail. The following two visits were before and after the 12-week intervention and consisted of the experimental measures.

### Participants

Twelve middle-aged male (n=10) and female (n=2) individuals (48±14 y) with ASIA A-C classified SCI were recruited (see Table 1). Time since injury was at least 1 year (7.1±7.8 y) prior to the study. Current smokers were excluded and none of the participants had any known cardiovascular diseases (does not indicate the absence of occult peripheral vascular disease) nor had any current pressure ulcers/injuries. All procedures conformed to the Declaration of Helsinki and all participants provided informed verbal and written consent. The study was approved by the local institutional medical ethical board and conformed to all STROBE guidelines and reports the required information accordingly (see Supplementary Checklist).

### Electrical Stimulation Intervention

ES was applied with an adapted wearable clothing garment[14] connected to a portable battery operated stimulator (Neuropro, Berkelbike, Nijmegen, the Netherlands). The clothing garment was a pair of specially developed elasticated velcro shorts with embedded surface electrodes (Axiobionics, Ann Arbor, MI, U.S.A). Shorts were applied so that surface electrodes were positioned bilaterally with one electrode at the upper side of the gluteal muscle and one halfway along the hamstring muscle. ES was applied to both limbs using 50-Hz biphasic impulse frequency and was individualized (prior to the start of the 12-week intervention) to a level that did not cause discomfort but elicited a strong visible tetanic contraction (without limb movements that disturbed normal sitting). Stimulation amplitude was progressively increased every 3 weeks to minimise muscular fatigue in the early stages and to compensate for training adaptations. The stimulation protocol ran for 6 hrs and comprised of blocks of 30 min stimulation followed by 15 min rest. A duty cycle consisting of 4 s rest for every 1-s contraction was used.[15] For the 12-week duration, each participant was instructed to use the shorts as much as possible (with a minimum of 6-hours daily) and to record their daily usage using a diary.

**Outcome Measures**

Prior to arrival on the visits before and after the 12-week intervention all participants refrained from consuming alcohol and caffeine for at least 24 hours due to their vasoactive effects. No participants were taking vasoactive medications. All experimental measures were performed in the same order and at same time of day pre and post intervention.

*Femoral Artery Diameter and Blood Flow:* Participants were transferred from their wheelchair and comfortably placed onto a bed in the supine position. After a 20-min resting period, a 10-MHz multi-frequency linear array probe, attached to a high resolution ultrasound machine (T3000, Terason, Burlington, MA, U.S.A) was used to image the common femoral artery (CFA) 2 cm proximal to the femoral bifurcation. Continuous Doppler velocity assessments were recorded for 1 minute using the lowest possible insonation angle (always <60°) for later offline analysis. Data were analysed using custom-designed edge detection and wall tracking software which is largely independent of researcher bias.[17]

*Skin Vascular Function:* Laser Doppler flowmetry was used to examine skin vascular function. The participant rested comfortably lying in a prone or partial prone/side position. Two heating disks (Perimed 355, Perimed AB, Järfälla, Stockholm, Sweden) were instrumented on the same gluteal and hamstring skin positions as the electrodes in the clothing garment using adhesive stickers. A 7-laser array probe (PF 413, Perimed AB Järfälla, Stockholm, Sweden) was placed into each heater. The heating discs were connected to a heating unit (PeriTemp 4005 heater, Perimed AB, Järfälla, Stockholm, Sweden) and manually set to 33°C. Baseline cutaneous blood flow was then measured as red blood cell flux using a laser Doppler flowmeter (Periflux system 5000, Perimed AB, Järfälla, Stockholm, Sweden) for 10 min at 33°C. Subsequently, local skin temperature was increased by 1°C per 5 min up to 42°C.[18] Thereafter, the heating probes were held at 42°C for 30 min and finally at 44°C for a remaining 20 min.[19] Heart rate and mean arterial pressure (MAP) were recorded using an automated sphygmomanometer (Dinamap Vital Signs Monitor, GE Healthcare, Hoevelaken, Netherlands) at 5-min intervals throughout the protocol. This slow heating protocol induces a largely nitric oxide (NO)-mediated, microvascular response.[20] Red blood cell flux was collected and stored using dedicated software (PeriSoft for Windows, Perimed AB, Järfälla, Stockholm, Sweden). Skin blood flow was expressed as cutaneous vascular conductance (CVC=red blood cell flux/mean arterial pressure) to account for potential variations in skin blood flow due to blood pressure. Baseline CVC was averaged during the 10-min baseline recording. Subsequently, CVC was calculated over a stable 60s period for the final minute of each local temperature increment and over the last 5-minutes of each plateau phase at 42°C and 44°C. Data were presented as absolute values, but also normalised to maximal CVC at 44°C (%$CVC_{max=}$[CVC/$CVC_{max}$] 100).

*Limb Volume:* Thigh muscle volume was estimated based on a calculation using anthropometric measures of leg circumferences, leg length (Seca 201 Ergonomic measuring tape, Seca, Birmingham, U.K) and skin folds (Harpenden Skinfold Calipers, Cranlea Human Performance Ltd, Birmingham, U.K). This approach has been validated against the gold standard H-MRI as a reliable and accurate method of measuring skeletal muscle volume in people with SCI.[21] All measurements were taken by the same experimenter with the participant lying on a bed in the supine position.

*Sitting Pressure:* Interface sitting pressure was measured using a force sensitive array (FSA, mFlex, Vista Medical, Vancouver, Canada) pressure-mapping device. The device was a 42x42cm, 2mm thick, soft flexible mat consisting of 256 pressure sensors (1.82cm$^2$ per sensor). Each participant was transferred from their wheelchair to a standardized table chair and sat in a normal position for 2 min whist values were recorded. The ischial tuberosities were defined from the FSA profile as the 3x3 sensors with the highest pressure values. The nine sensors were averaged to give a mean IT pressure value for the left and right IT area. Peak IT pressure was defined as the value of the sensor with the highest pressure within the IT area. Pressure gradient, which is indicative of shear forces within the tissue and is associated with the risk of developing pressure ulcers[22] was calculated by subtracting the average of the 16 surrounding sensor values from the mean IT pressure.

**Data Analysis**

Statistical analyses were performed using SPSS 25.0 software (SPSS Inc, Chicago, IL, USA). Data were expressed as mean±SD and statistical significance was set at $P$ <0.05. The effects of 12 weeks ES on gluteal and hamstring skin vascular function was examined using two-way ANOVA with repeated measures (main effects for time (of the heating protocol) and intervention (pre and post)). Paired *t*-tests were used to assess differences in sitting pressure, limb volume, femoral artery diameter and femoral artery resting blood flow before and after the 12-week ES intervention. All data were tested for normal distribution and Wilcoxon signed rank test was used where appropriate.

**RESULTS**

There were no adverse events during the intervention. One individual was unable to continue due to hospital admission (for an issue unrelated to the intervention). Two individuals were in full time employment and found the device too time consuming or difficult to apply on a daily basis. Of the remaining participants, eight indicated that they adhered to the minimum requirement of 6 hours per day 7 days a week with one participant choosing to use it in excess of 10 hours per day. Eight of the nine participants chose to wear the shorts during the night when sleeping and one individual used them both day and night.

*Femoral Artery Diameter and Blood Flow:* Mean baseline CFA blood flow significantly increased by 43% from pre (0.28±0.12 $L \cdot min^{-1}$) to post 12 weeks ES (0.40±0.15 $L \cdot min^{-1}$; $P$ <0.001; Figure 1A). Resting diameter of the CFA increased significantly by 8.3% from pre (0.73±0.20 cm) to post 12 weeks ES training (0.79±0.22 cm; $P$<0.001; Figure 1B).

*Skin Vascular Function:* There was no difference in MAP from pre to post 12-weeks ES ($P$=0.21). Local heating induced a gradual, slow heating response (main effect for time for both gluteal and hamstring skin blood flow, $P$<0.001; Figure 2). There was no significant difference in the gluteal skin blood flow response to local heating when expressed as either, absolute CVC ($P$=0.17; Figure 2A) or percentage of maximum CVC (%$CVC_{max}$, $P$=0.19) after 12 weeks of ES. There was a significant time×intervention interaction for absolute CVC ($P$=0.02) and %$CVC_{max}$ ($P$ <0.001) indicating that the change in skin blood flow during local heating from baseline to maximal levels was higher after 12 weeks ES. There was no significant difference in hamstring skin absolute CVC ($P$=0.47; Figure 2B) or %$CVC_{max}$ ($P$=0.41) after 12 weeks of ES. There was also no significant time×intervention-interaction for absolute CVC ($P$=0.86), or %$CVC_{max}$ ($P$=0.41).

*Sitting Pressure:* Peak IT pressure significantly decreased by 32±23 mmHg (*P*=0.003; Figure 3A) with 12 weeks of ES. IT interface pressure reduced by 19% from 37±9 mmHg to 30±6 mmHg, although this did not reach statistical significance (*P*=0.06; Figure 3B). IT Pressure gradient significantly decreased by 30% from 23±7 mmHg to 16±6 mmHg with 12 weeks of ES (*P*=0.007; Figure 3C).

*Limb Volume:* Skin fold measures could not be obtained in two individuals, so analyses were performed on thigh circumference as well as overall limb volume. When taking into consideration upper, mid and lower girth measurements, average thigh circumference significantly increased from pre to post 12 weeks of ES (478±40 vs. 482±41 mm, *P*=0.008). There was a significant overall increase in thigh volume (4.7±1.2 vs. 5.3±1.2 L, *P*=0.01).

## DISCUSSION

The primary aim of this study was to examine the effects of 12 weeks low-level ES using a wearable clothing garment on (micro)vascular function and sitting pressure in areas at risk of pressure ulcers. The main findings are that 12 weeks of ES increased femoral artery diameter, basal blood flow and limb volume, and reduced peak ischial tuberosity sitting pressure and pressure gradient. Conversely, despite improved skin responses to local heating at the gluteal area, ES did not appear to cause significant alterations in hamstring cutaneous circulation during localised heating. Collectively, these findings indicate that regular, low-level ES using a wearable garment induce beneficial effects on (micro)vasculature and sitting pressure that may help safeguard against pressure ulcers and confer similar cardiovascular health benefits. Given the relative simplicity of low-intensity ES, future studies are warranted on whether such a garment can ultimately reduce risks for clinically relevant health problems in this vulnerable population

This study is the first to explore the effects of prolonged daily, low-level ES utilising a clothing garment on micro- and macrovascular structure and function in persons with a SCI. In the present study, there was an 8.3% and 43% increase in femoral artery diameter and basal blood flow, respectively. These observations are in line with previous ES training studies that report a 30-50% increase in blood flow and a 6-8% increase in diameter after 4 to 12 weeks of ES-induced cycling or ES-assisted Odstock standing in SCI.[8 23-25] An important difference between our work and these previous ES-based studies, however, is that these previous studies adopted significantly higher levels of ES with the more demanding and time-consuming ES-type exercise. In healthy individuals, conduit artery structural modification is dependent on repeated changes in blood flow.[26] In a previous study, ES induced an acute increase in femoral artery blood flow.[14] The repeated exposure to this increase in flow (and therefore shear stress), may contribute to vessel remodeling, whereby the increased levels of shear are normalised by an increase in luminal diameter. Taken together, the findings of our study suggest that daily ES using this practical, home-based method is effective in improving (macro)vasculature structure, most likely through repeated exposure to elevations in blood flow and shear stress.

Contrary to the original hypothesis, cutaneous microvascular function covering the hamstring muscles did not change, whereas the change in gluteal CVC throughout local heating increased after 12 weeks of ES. Gradual local heating of skin leads to the production of nitric oxide and smooth muscle relaxation via hyperpolarisation from EDHFs and heating the skin to 42°C, the vasodilation that occurs is largely endothelial and NO mediated.[20] Therefore, the interaction effect and the small increase in gluteal cutaneous microcirculation at 42°C suggests that cutaneous endothelial function, potentially via upregulation of NO, is improved after 12 weeks ES. Another potential explanation relates to the presence of structural changes in the skin. However, blood flow at 44°C, which causes maximal cutaneous vasodilation and may be used to assess structural differences,[27] did not change after 12-weeks ES. Thus, the improvement in gluteal skin microvasculature was not accompanied with changes in cutaneous vessel architecture. The finding that these changes in skin (micro)circulation were not evident in the hamstring area may relate to regional differences in the acute (skin) blood flow responses to ES and/or (susceptibility for) the increase in blood flow in the hamstring skin area.

Whilst previous studies have highlighted the potency of ES to improve sitting pressure during ES,[22] these studies are limited in that it is not known whether these effects remain during periods of non-stimulation. The results from the current study indicate that the acute pressure reduction during ES is maintained after continued long-term usage when measured under resting conditions *without* active muscle stimulation. This suggests presence of structural and/or chronic adaptations that improve sitting pressure, rather than short-term, muscle activity-induced changes in sitting pressure. Moreover, we also examined the interface pressure gradient, which reflects the pressure distribution of the area directly surrounding and containing the area of the tuberosity. We found improved pressure distribution, meaning that 12 weeks ES caused a relatively larger part of the interface pressure supporting the surface area of the buttock, which is associated with smaller shear forces and lower risk of skin trauma.[28] It is likely that hypertrophy of the gluteal and hamstring muscles over the 12 weeks ES intervention increased the seated contact area and improved pressure distribution to areas away from the ischial tuberosity. Indeed, we found a significant increase in limb volume and thigh circumference after 12 weeks of ES. Although this does not provide direct evidence for muscle hypertrophy, our findings match previous long-term ES-studies in SCI that adopted more sophisticated measures (e.g., CT-scans[29] and DEXA[30]). Due to the extensive time individuals with an SCI spend sitting, these findings are potentially clinically relevant for pressure ulcer prevention.

**STUDY LIMITATIONS**

There are some limitations to this study that require consideration. Firstly, no control group was included. Despite this, the positive alterations recorded across a range of outcomes (micro- and macrovascular, sitting pressure and anthropometric) strongly suggest that the ES intervention resulted in favorable adjustments for SCI but the low number of participants in this pilot feasibility study limits generalizability of the results at this time; future larger randomized controlled studies are therefore required. Three participants dropped out of the study due to hospital admission or the intervention being too time consuming. Although not ideal, these events are expected for chronic interventions and given that this study is designed as a pilot feasibility study this information provides important data on likely drop-out rates and the community feasibility of future larger randomized controlled studies. Similarly, as part of the study’s pilot feasibility approach, 6 hours of stimulation was chosen because we wanted to examine the effect of as much as stimulation as was possible during the day or overnight, within the limits of practicality. Less stimulation can still produce beneficial results [15] but it is not yet clear what the required minimum level of stimulation is, therefore, future work should identify the lowest dose of stimulation possible for inducing favorable outcomes.

## CONCLUSION

In summary, this study demonstrates that 12 weeks of low-intensity gluteal and hamstring ES induces marked structural changes in the femoral artery, most likely through repeated increases in hyperaemic shear stress during ES. Secondly, ES causes a decrease in peak sitting pressure, pressure gradient and an increase in limb volume, which all may result from increases in (gluteal) muscle mass. Thirdly, nitric oxide-mediated function of the cutaneous microvessels covering the gluteal muscles, but not hamstrings, is improved. This highlights the potency for low-intensity ES in SCI rehabilitation and disease prevention. Future work should focus on the potential impact of low-intensity ES in the prevention (and/or treatment) of co-morbidities related to peripheral deconditioning of muscle and vasculature.

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**Figure Legends**

Figure 1. A) Individual and group mean common femoral artery resting blood flow and B) resting diameter pre and post 12-week electrical stimulation. The red line depicts overall mean. *Main effect of 12 weeks of electrical stimulation (P <0.05).

Figure 2. Cutaneous vascular conductance (CVC) responses across time points from baseline at 33°C to maximal plateau at 44°C of the A) gluteal and B) hamstring before and after 12 weeks of electrical stimulation. *Significant interaction of time and temperature.

Figure 3. Individual and group mean A) peak IT pressure of a single sensor in the IT area, B) average IT pressure and C) IT pressure gradient before and after 12 weeks of electrical stimulation. Red bar indicates group mean. *Main effect of 12 weeks of electrical stimulation (P <0.05).