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The effect of calf neuromuscular electrical stimulation and intermittent pneumatic compression on thigh microcirculation

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ABSTRACT

Objective: This study compares the effectiveness of a neuromuscular electrical stimulation (NMES) device and an intermittent pneumatic compression (IPC) device on enhancing microcirculatory blood flow in the thigh of healthy individuals, when stimulation is carried out peripherally at the calf.
Materials and methods: Blood microcirculation of ten healthy individuals was recorded using laser speckle contrast imaging (LSCI) technique. A region of interest (ROI) was marked on each participant thigh. The mean flux within the ROI was calculated at four states: rest, NMES device with visible muscle actuation (VMA), NMES device with no visible muscle actuation (NVMA) and IPC device.
Results: Both NMES and IPC devices increased blood flow in the thigh when stimulation was carried out peripherally at the calf. The NMES device increased mean blood perfusion from baseline by 399.8% at the VMA state and 150.6% at the NVMA state, IPC device increased the mean blood perfusion by 117.3% from baseline.
Conclusion: The NMES device at VMA state increased microcirculation by more than a factor of 3 in contrast to the IPC device. Even at the NVMA state, the NMES device increased blood flow by 23% more than the IPC device. Given the association between increased microcirculation and reduced oedema, NMES may be a more effective modality than IPC at reducing oedema, therefore further research is needed to explore this.

1. Introduction

Neuromuscular electrical stimulation (NMES) devices and intermittent pneumatic compression (IPC) devices have been shown to be effective in improving blood flow (Tucker et al., 2010, Currier et al., 1986, Kaplan et al., 2002). They are often used post-surgery to prevent deep vein thrombosis (DVT) (Goldhaber and Morrison, 2002), in procedures such as total hip replacement (Doran and White, 1976); and have been found to reduce oedema in the thigh of total hip replacement patients post-surgery (Faghri et al., 1997).

The geko™ is an NMES device (Firstkind Ltd., High Wycombe, UK. http://www.gekodevices.com/en-uk/) and the VenaPro an IPC system (DJO Global, Centerville, US. http://www.djoglobal.com/products/venaflow/venapro). Both are used to increase blood flow circulation. The geko™ is a small, self-adhesive, disposable device, which is battery-powered and applied posterior to the fibula head over the common peroneal nerve. It has seven stimulation modes and a frequency rate of 1 Hz, with a maximum charge of 20 μC per pulse. The VenaPro consists of a calf cuff that holds an electronically controlled pump. This pump delivers air to the calf cuff, applying 50 mm Hg once per minute, so that the calf experiences graduated and asymmetric compression. It is rechargeable and designed for single patient use (Summers et al., 2015).

A previous study on the geko™ device found that it performed better in increasing both venous and arterial blood flow by around 30%, when compared to two IPC devices (Jawad et al., 2014), without the discomfort which can be associated with traditional NMES technology.

Laser speckle contrast imaging (LSCI) (moorFLPI Full-Field, Devon, United Kingdom) has become an increasingly popular equipment for measuring microcirculatory blood flow (Draijer et al., 2009; Wu et al., 2015) as it offers a high spatial and temporal resolution (Roustit and Cracowski, 2013). Using LSCI, this study compares the effectiveness of an NMES device and an IPC device on enhancing microcirculatory blood flow in the thigh of healthy individuals, when stimulation is carried out peripherally at the calf.

2. Materials and methods

2.1. Study population

Ten healthy participants consented to take part in the study. Participants were excluded from taking part if they had taken low-molecular-

Abbreviations: ARTm, artefact movement; AOS, adhesive opaque surfaces; BMI, body mass index; CBF, cutaneous blood flow; DVT, deep vein thrombosis; IFU, indication for use; IPC, intermittent pneumatic compression; LMWH, low-molecular-weight heparin; LSCI, laser speckle contrast imaging; $LS_{(SK)}$, laser speckle skin signal; LSPU, laser speckle perfusion unit; NMES, neuromuscular electrical stimulation; NVMA, no visible muscle activation; ROI, region of interest; VMA, visible muscle activation.

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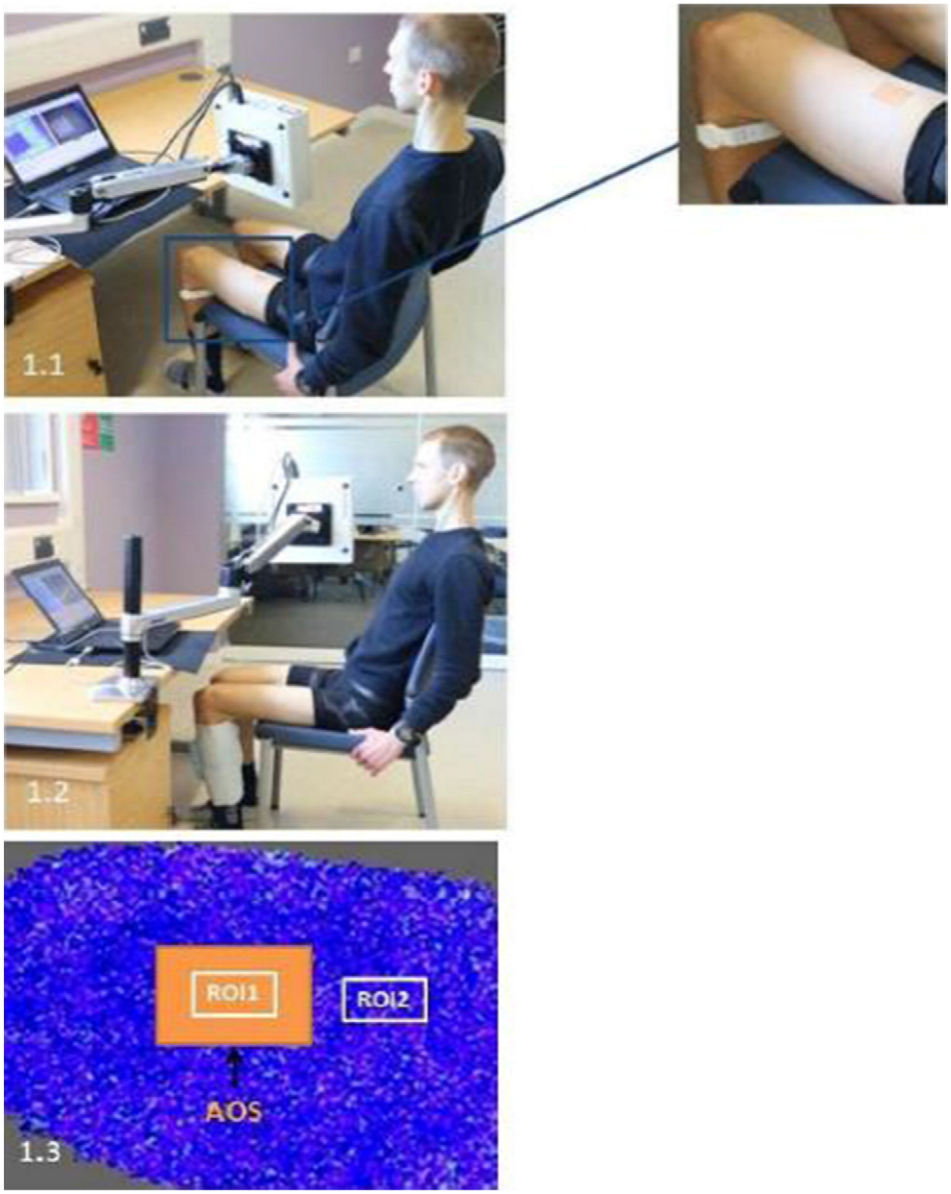

Fig. 1. Set up of LSCI for analysis of effects of NMES and IPC devices on an area of the anterior thigh. 1.1) NMES device placed just below the level of the knee simulating the common peroneal nerve behind the knee, which in turn, activates the calf and foot muscle pumps of the lower leg. 1.2) IPC cuff wrapped around the calf and secured using the Velcro. Wrap was secure, but not restrictively tight. 1.3) LSCI image recorded with graphical representation of the ROI 1, ROI 2 and AOS on an area of the thigh.

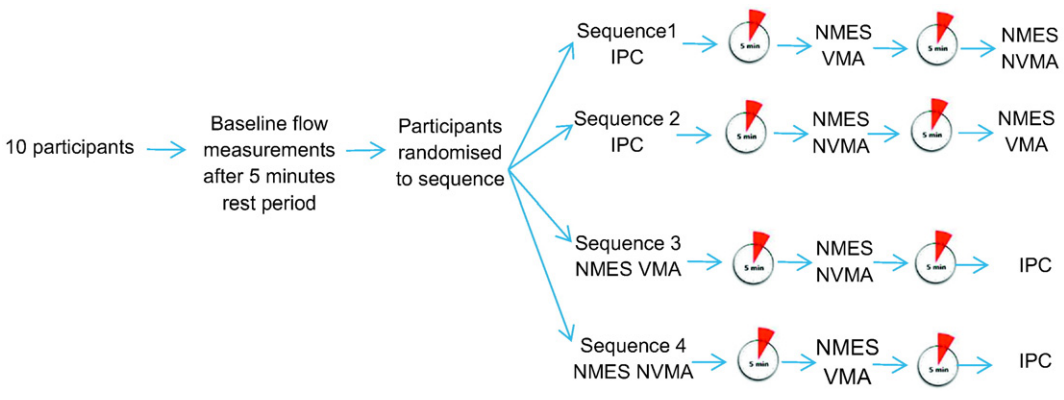

Fig. 2. Sequences of assessment using Sealed Envelope Randomization method with 5 min washout in between each test.

Table 1
Mean flux mean (SD) at baseline and by device.

n = 10	Baseline mean flux	NMES with NVMA mean flux	NMES with VMA mean flux	IPC mean flux
Mean (SD)	165.2 (86.7)	232.0 (104.0)	605.7 (321.4)	187.7 (91.6)

weight heparin (LMWH), Heparin or Warfarin; had a neuromuscular, haematological and/or cardiovascular disorder; had a pulmonary embolism; or previous history of DVT. Participants were all asked to complete a pre-test health questionnaire to ensure they met the inclusion criteria, and were requested to not smoke or consume any caffeine 2 h prior to testing.

2.2. Study design

The study received ethical approval from the Bournemouth University Research Ethics Committee on 9th February 2016 (Reference 10571).

The study was designed to compare the effects of NMES and IPC devices on microcirculation by assessing cutaneous blood flow at depth of around 300 μm on an area of the anterior thigh (approx. 77cm^2) using moorFLPI Full-Field Laser Speckle Contrast Imager (LSCI). LSCI is a non-invasive instrument designed for the measurement of blood flow within the microvasculature. The 780 nm infra-red laser beam is expanded over an area, illuminating the biological tissue and diverged to create so called 'speckles'. These speckles are imaged with a CCD camera and processed on the PC to generate a colour coded map of tissue perfusion. Rapid variation of red blood cells cause the speckles pattern to appear blurred resulting in a low contrast image, conversely, high contrast indicates low flow and the contrast image generated is quantified as a low blood perfusion image within specific region of interest (Senarathna et al., 2013; O'Doherty et al., 2009).

All assessments were performed in a temperature controlled room (22 ± 1 °C), and participants were seated for 10 min prior to testing in order to adapt to the room temperature. Participants were sitting throughout the assessments, with their feet flat on the ground. The experimental setup is outlined in Fig. 1.

To measure the blood flow perfusion, the moorFLPI Full-Field LSCI device was set with the following settings: An exposure time of 20 ms to allow for low flux measure with higher sensitivity to small changes. A display rate of 25 Hz, and a time constant of 0.3 s was used to account for rapid blood flow changes and achieve optimum contrast through reducing the image noise. The camera was placed 25–30 cm from the skin as advised by the manufacturer's instructional manual, with the camera resolution set at 152 × 113 pixels/cm^2 for spatial processing and directed perpendicular to the thigh (Bezemer et al., 2010; Kazmi et al., 2014). Resulting images were digitized and analysed off-line using the moorFLPI software (Full Field Laser Perfusion Imager Review v4.0, Moor Instruments, Devon, United Kingdom).

The mean flux within the ROI was calculated as the mean blood flow amplitude in skin area perfusion for the ten participants. Given the high sensitivity of LSCI to artefact movement (ARTm), we used adhesive opaque patch (AOS) medical tape (Leukotape®, BDF Germany) to mask the cutaneous blood flow (CBF) (Mahe et al., 2011). A proportion of the backscattered signal AOS can be subtracted from the laser speckle skin signal ($LS_{(SK)}$) to allow for a satisfactory recording of the cutaneous blood flow (CBF). "Leukotape®" was used as it was found to be effective in reducing physiological signal and accounting for skin and signal proportionality, acting as an AOS (Mahe et al., 2012, 2013).

A 6 cm^2 of AOS tape was placed to measure the ARTm and an area of 1.5 cm^2 overlaid the AOS as a marked ROI and named ROI 1(Omarjee et al., 2015; Humeau-Heurtier et al., 2014). An area of thigh was marked as a second ROI, with the same area size as ROI 1 (1.5 cm^2) and named ROI 2 which measured the $LS_{(SK)}$ (Fig. 1).

Care was taken so that ROI 1 and ROI 2 did not interchange, but kept close within 2–4 cm to reduce the need for re-centring if any mechanical movement resulted in the ROI 1 no longer being in the AOS area. Thus Eq. (1) was used for measurement of CBF (Mahe et al., 2011).

$$LS_{(SK)} = (CBF + ARTm)$$

If ROI 2 account for $LS_{(SK)}$ and ROI 1 account for ARTm, then:

$$ROI\ 2 - ROI\ 1 = CBF \tag{1}$$

Measurements were made of microvascular blood flow in the following states:

- At rest.
- Using the NMES device as per the manufacturing indication for use (IFU), so that there was a Visible Muscle Actuation (VMA).
- Using the NMES device as per IFU, so that there was No Visible Muscle Actuation (NVMA).
- Using the IPC device in accordance with the device IFU.

Image recordings of each assessment were carried out for 3 min, whilst the participant and investigator were immobile and remained silent throughout. A five minute washout period was allocated between assessments. Participants were randomised as per the groups in Fig. 2, using Sealed Envelope randomisation database (https://www.sealedenvelope.com/) to allocate participants to the sequence in which the devices were used.

2.3. Data analysis

SPSS statistics for Windows was used in the analysis (IBM, 2010). Skin blood flow was expressed in laser speckle perfusion units (LSPU). Data are expressed as the mean and standard deviation in parenthesis. Non-parametric analysis was used as the sample size was small, and therefore not normally distributed. A repeated-measured ANOVA (Friedman 2-way by rank) was used to compare the data between the four groups (baseline, NMES in NVMA state, NMES with VMA, IPC) and then post hoc tests (related samples Wilcoxon Signed Rank test) were performed to compare differences between the groups.

Table 2
Mean (SD) of percentage increase in mean flux from baseline by device.

n = 10	NMES with NVMA % increase from baseline	NMES with VMA % increase from baseline	IPC device % increase from baseline
Mean (SD)	150.6 (48.8)	399.8 (210.1)	117.3 (17.0)

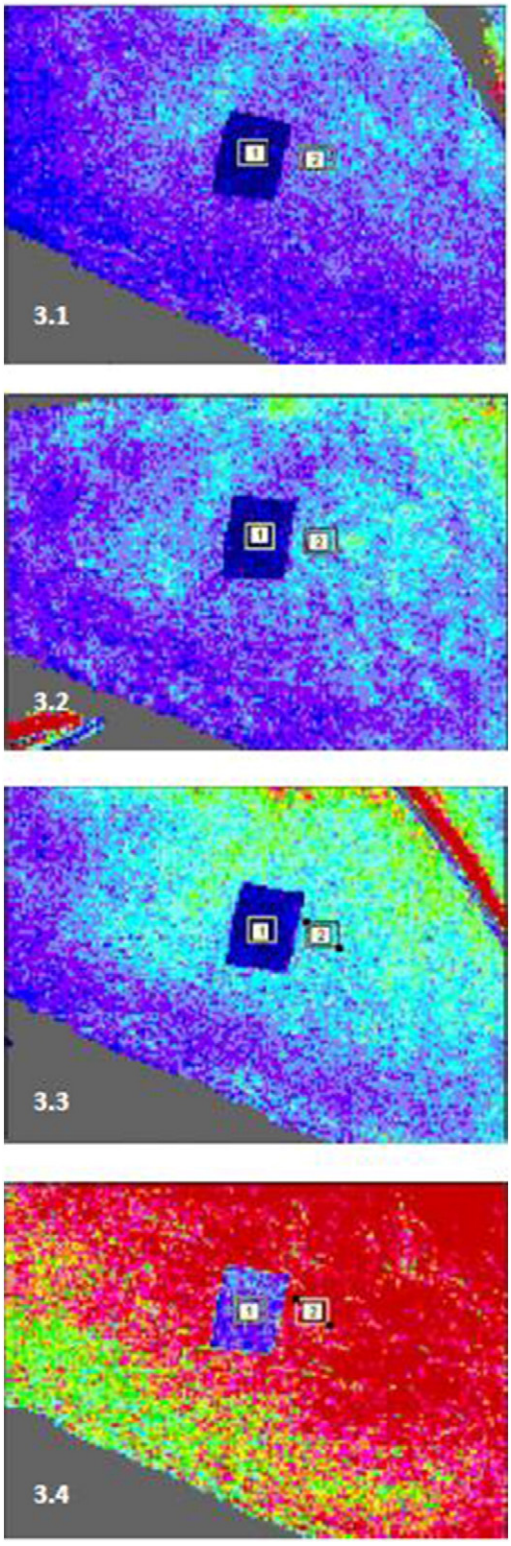

Fig. 3. Example of ROI 1 and ROI 2 positioning on the thigh in one subject. The different colour in the picture indicate different levels of perfusion; blue indicates low levels of skin perfusion, green and yellow indicates intermediate levels of skin perfusion and red indicates high levels of skin perfusion. Skin blood perfusion at 3.1) rest state, 3.2) IPC, 3.3) NMES NVMA and 3.4) NMES VMA. The taped region (AOS) is used as a marker to determine which images are affected by tissue movement, and the scale of that movement.

3. Results

Data were analysed from all ten of the participants. All participants were male, aged between 25 and 46 years, and their BMI ranged from 23 to 30 kg/m^2.

The mean flux for ROI 1 and ROI 2, and the resulting mean flux was calculated for each participant using Eq. (1), whilst the participant was at rest (baseline), when the NMES (VMA and NVMA) and IPC devices were being used. The baseline mean flux was 165.2 (SD 86.7), the mean flux for NMES with NVMA was 232.0 (SD 104.0), the mean flux for NMES with VMA was 605.7 (SD 321.4), and the median mean flux for the IPC device was 187.7 (SD91.6) (Table 1).

The percentage increase in mean flux from the baseline by participant when the NMES (VMA and NVMA) and IPC were used was calculated, and Table 2 compares the data. The mean percentage increase from baseline for the NMES with NVMA was 150.6% (SD 48.8), for the NMES with VMA was 399.8% (SD 210.1), and for the IPC device was 117.3% (SD 17.0) (Fig. 4).

The related samples Friedman's two-way ANOVA showed a statistical significant difference ($p \leq 0.001$), and post-hoc tests (related-samples Wilcoxon signed rank test) found a statistically significant difference ($p = 0.005$) when comparing baseline with NMES at NVMA state, baseline with NMES at VMA state, baseline with IPC, NMES at NVMA with NMES at VMA, NMES at NVMA with IPC and NMES at VMA with IPC device.

4. Discussion

The findings of this study suggest that the NMES device is superior to the IPC device in increasing the blood microcirculation in the thigh.

The NMES with visible muscle actuation increased the blood microcirculation by 399.8% from baseline flux perfusion which is a substantial increase when compared to IPC device with 117.3% from baseline flux perfusion. The effect of NMES with no visible muscle actuation also recorded a 150.6% increase in flux from baseline which again suggests superiority of the NMES over IPC.

An obvious limitation in relation to applying the results of this study to relevant clinical populations (for example, hip replacement patients) is the small number of participants who were all male, and aged 25 to 46 years. Major surgery, such as hip replacement is likely to affect blood flow in the rehabilitation period, and it is likely that as age plays a major role in the deterioration of micro vessels, results may differ

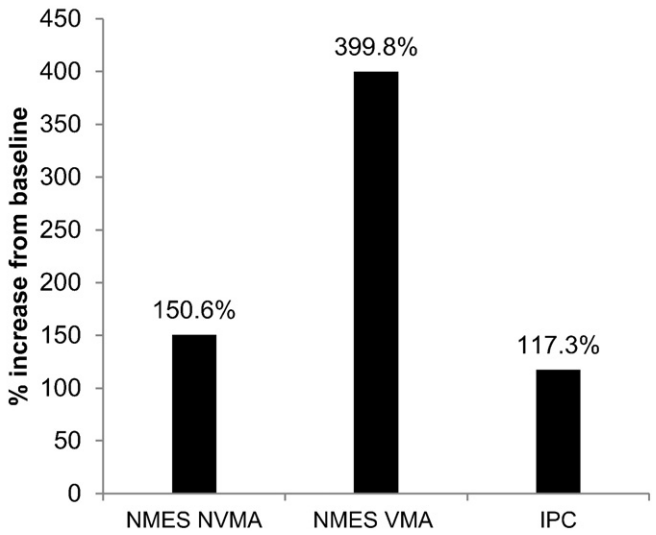

Fig. 4. Mean percentage increase in blood flow from baseline for NMES with NVMA, NMES with VMA and IPC device.

between age groups (Khalil et al., 2016). This may also be true for gender (Richter et al., 2014), although studies on the effect of the phase of the menstrual cycle on microvascular function have had conflicting results (Millet et al., 2011). The wide range of standard deviations observed in the study can be explained by the heterogeneous nature of microcirculatory blood (Pries and Secomb, 2009).

A bespoke setting was used to account for the low flux measure encountered during the recording of the IPC and baseline states, in line with manufacturer's recommendations. This setting therefore increased the visual contrast of the taped region of NMES VMA as seen in Fig. 3. Nevertheless AOS was an accurate mark to determine the artefact movement effect given both ROI 1 and ROI 2 were reviewed in real-time and recorded images were analysed offline.

This pilot study is valid, as its intention was to not only test a hypothesis that the devices would increase microcirculation, but also to develop a methodology that could in future studies be used for testing clinical populations.

Oedema in the thigh is a common post-operative problem in hip replacement surgeries that can effect rehabilitation. Therefore, modalities that increase microcirculation in the thigh may be helpful in reducing oedema and therefore accelerate recovery. Future work is planned that will examine this relationship and this is why microcirculation was measured specifically in the thigh. Enhanced recovery after surgery (ERAS) protocols now enable patients following hip replacement to walk on the day of surgery and go home 1–3 days post-operatively (Husted, 2012; Wainwright and Middleton, 2010). Therefore, the sitting testing position has relevance in clinical populations, as patients no longer convalesce in bed. The sitting position also helped to standardise and increase accuracy of the LSCI, this is because movement of the lower leg was prevented due to the foot being in contact with the floor. This ensured minimal movement of the region of interest and therefore accurate readings.

A larger ROI and longer test period could also have reduced any variability of CBF measured both at the baseline and also during the use of the NMES and IPC devices (Rousseau et al., 2011). The method of subtracting the LSCI signal from the Leukotape as the adhesive opaque patch (ROI 1) from the signal of cutaneous blood movement flux (ROI 2) allowed a simple method to account for artefact (Mahe et al., 2011). However (Omarjee et al., 2015), further enhanced the accuracy of the Eq. (1) coefficient factors by creating a bespoke bilayer adhesive to optimize the removal of artefact movement.

5. Conclusions

In comparison to the IPC device, the NMES device significantly increases cutaneous blood flow in the thigh with healthy individuals. Given the dynamics of venous flow and its direct effect on microcirculation, NMES may be a more efficient solution to reduce oedema, improve healing and the prevention of wound complications in comparison to the IPC device in clinical populations such as total hip replacement patients. LSCI is a convenient, non-invasive and accurate method for measuring microcirculation and comparative effect of mechanical devices designed to increase blood flow.

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