The geko™ Device
Canadian Product Specifications and Annotated Bibliography

Purpose: To provide a summary of the evidence to date for the geko™ device, particularly as it relates to haemodynamics, oedema reduction, wound healing and recovery.

Inclusion: Published papers, PhD thesis in public domain, Posters presented at Scientific Meetings and geko™ evaluations done in Canada which are currently in press or underway.

Exclusion: Unpublished Case Studies with subjects <3 which can be viewed on the geko™ website at: https://www.gekodevices.com/clinical-studies/?fwp_cs_category=3-wound-therapy

In some papers, content in italics is taken directly from the abstracts for individual papers.

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1. Health Canada Device Registration
### 2. The geko™ Device Product Output Specifications

<table>
<thead>
<tr>
<th>Product name</th>
<th>geko™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model reference and identifier</td>
<td>T-3 - 2018</td>
</tr>
<tr>
<td><strong>Product type</strong></td>
<td>Powered muscle stimulator</td>
</tr>
<tr>
<td><strong>Class</strong></td>
<td>BF (The entire device is considered to be a patient-applied part)</td>
</tr>
<tr>
<td><strong>Dimensions</strong></td>
<td>186mm x 31mm x 11mm</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>10g (device only)</td>
</tr>
<tr>
<td><strong>Power source</strong></td>
<td>Internally powered equipment, battery not replaceable</td>
</tr>
<tr>
<td><strong>Battery</strong></td>
<td>Primary lithium coin cell - removable for disposal</td>
</tr>
<tr>
<td><strong>Operation</strong></td>
<td>Continuous operation - the device is not intended for use in an oxygen rich environment such as an oxygen tent or hyperbaric chamber; or in presence of flammable anesthetic mixture with air or with oxygen or nitrous oxide</td>
</tr>
<tr>
<td><strong>Stimulation modes</strong></td>
<td>11 (selected pulse widths)</td>
</tr>
<tr>
<td><strong>Pulse current</strong></td>
<td>27, 38 or 54 mA</td>
</tr>
<tr>
<td><strong>Load impedance</strong></td>
<td>200Ω to 3kΩ for 54 mA output</td>
</tr>
<tr>
<td><strong>Pulse voltage</strong></td>
<td>Set by current and load</td>
</tr>
<tr>
<td><strong>Pulse width ±10%</strong></td>
<td>35, 50, 70, 100, 140, 200, 280 μs @27mA, 280 &amp; 400μs @38mA, 400 &amp; 560 μs @54mA,</td>
</tr>
<tr>
<td><strong>Repetition rate</strong></td>
<td>1HZ (±5%)</td>
</tr>
<tr>
<td><strong>Maximum charge</strong></td>
<td>40μC per pulse</td>
</tr>
<tr>
<td><strong>Net charge output</strong></td>
<td>Less than 0.1 μC per cycle. Charge balance is provided by return pulses of low amplitude and same the same total charge as the stimulation pulse</td>
</tr>
<tr>
<td><strong>Output coupling</strong></td>
<td>Ceramic capacitor</td>
</tr>
<tr>
<td><strong>Operating Time</strong></td>
<td>Used on Bilateral legs for systemic response but can be just one leg. 24-hour wear time single day use; battery lasts up to 30 hours</td>
</tr>
<tr>
<td><strong>Mode of Operation</strong></td>
<td>The devices are suitable for continuous operation</td>
</tr>
<tr>
<td><strong>Indicator display</strong></td>
<td>green LED, flashing to indicate operation and the setting level (pulse width): the number of flashes in the sequence</td>
</tr>
<tr>
<td><strong>Fault indication</strong></td>
<td>the stimulator device will automatically switch off for over current, under current, low battery voltage or end of operating time</td>
</tr>
</tbody>
</table>
Output voltages and currents: measured at internal outputs of the pulse generator (±15%)

<table>
<thead>
<tr>
<th>load</th>
<th>current</th>
<th>voltage</th>
<th>current</th>
<th>voltage</th>
</tr>
</thead>
<tbody>
<tr>
<td>200Ω</td>
<td>54mA</td>
<td>10.8 V</td>
<td>54mA</td>
<td>10.8 V</td>
</tr>
<tr>
<td>500Ω</td>
<td>54mA</td>
<td>27 V</td>
<td>54mA</td>
<td>27 V</td>
</tr>
<tr>
<td>1000Ω</td>
<td>54mA</td>
<td>54 V</td>
<td>54mA</td>
<td>54 V</td>
</tr>
<tr>
<td>2000Ω</td>
<td>54mA</td>
<td>108 V</td>
<td>54mA</td>
<td>108 V</td>
</tr>
<tr>
<td>3000Ω</td>
<td>54mA</td>
<td>162 V</td>
<td>54mA</td>
<td>162 V</td>
</tr>
</tbody>
</table>

Current rms (500Ω) 1.3mA rms maximum
Voltage rms (500Ω) 0.7V rms maximum

3. Annotated Bibliography

Introduction:
The common peroneal (CP) nerve is a mixed nerve; neuromuscular electrical stimulation activates motor neurons (causing muscle contraction) and both cutaneous and muscle afferents (nerve fibers carrying sensory information into the spine). Electrical stimulation (EST) and low frequency neuromuscular electrical stimulation (NMES) of the common peroneal nerve has been the subject of research in humans for several years, with citations starting around 1988. Various reported benefits of a variety of devices other than the geko™ include regional cutaneous vasodilation in subjects with peripheral vascular disease, rehabilitation of foot drop and spasticity following cerebral vascular accidents (stroke), improving gait and overactive bladder symptoms in patients with Multiple Sclerosis, intra-operative nerve conduction testing for safety, rehabilitation of hemiplegic patients regarding the effort and speed of walking, improved ankle dorsiflexion in incomplete spinal cord lesions, and lasting facilitation of cortical motor-evoked potentials suggesting that gait in patients with a weakness in the tibialis anterior muscle may be improved even after stimulation is discontinued. It is easy to see how a device that painlessly and effectively stimulates the CP nerve could have a multitude of purposes.

Research including the geko™ device focussed initially on local and then more systemic hemodynamic responses, then DVT prophylaxis, edema management, systemic responses, wound healing, quality of life and tolerability. Research continues in several streams internationally.

For the purposes of this Annotated Bibliography, only those papers using geko™, geko™ prototype development or covered in the Canadian Consensus document are included.

3-1. Pre-geko™ Research in Stimulation of Common Peroneal Nerve


Methods: Thirty healthy volunteers received modified neuromuscular stimulation to the common peroneal nerve with a range of 1 mA to 40 mA, 1 Hz to 5 Hz, 200 µs with 15 different stimulation programs. Baseline was when the patient was at rest, and testing was done while volunteer was seated in an economy airline seat. The leg was stimulated x 5 minutes, then the readings occurred with the stimulation turned off, and then the limb rested x 5 minutes before the next test was started. In the first session, settings went from 1 to 15. In the second session, the tests were repeated, but started...
with the maximum stimulation of 15 and moved down to 1. To create a baseline of what percentage of full dorsiflexion the stimulation would achieve, they used PPG over one of the dorsal foot veins and measured relative changes in optical reflectance which resulted from blood emptying from the vein during 10 sequential full dorsiflexions.

### Table of Results:

<table>
<thead>
<tr>
<th>Test</th>
<th>Location and Results (Increases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photophlebography (PPG)</td>
<td>Blood emptying from Dorsal foot veins: at least 50% of that achieved with full dorsiflexion; up to 70% with 40 mA vs 50% with 1 mA. <em>P</em>=0.0004 60% for geko™ parameters</td>
</tr>
<tr>
<td>Strain gauge phlebography (SPG)</td>
<td>Change in mid-calf circumference: 55 to 70% of that achieved with full dorsiflexion. <em>P</em>&lt;0.001</td>
</tr>
<tr>
<td>Duplex ultrasound</td>
<td>Femoral vein venous volume flow range ~160% to 380% of baseline <em>P</em>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>Superficial femoral vein 100% increase in volumetric flow and peak velocity for geko™ parameters</td>
</tr>
<tr>
<td></td>
<td>Femoral vein mean peak venous velocity range ~150 to 360% of baseline <em>P</em>&lt;0.01</td>
</tr>
<tr>
<td>Transcutaneous oxygen tension (TCP02) on dorsum of foot</td>
<td>Tissue oxygen in the leg decreased from baseline during the evaluation, but stimulated values (~92 to 97%) were consistently significantly higher than unstimulated values <em>P</em>=0.03</td>
</tr>
<tr>
<td>Laser Doppler Fluxmetry</td>
<td>Skin dorsum of foot microcirculatory flux range of ~400 to 2500% <em>P</em>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>400% for geko™ parameters</td>
</tr>
<tr>
<td>Heart rate</td>
<td>No change</td>
</tr>
<tr>
<td>Pulse oximetry</td>
<td>No change to oxygen saturation</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>No change</td>
</tr>
</tbody>
</table>

**Key Learning Points:** Note that the geko™ devices provide 27 (T1-T-2) and 54mA (R-2, W-2) and is 1 Hz; those stimulation parameters provided 60 to 70% of venous emptying response versus the 10 sequential dorsiflexions, considered to be equal to the response seen with walking (cannot do SPG/PPG when individual is ambulatory).

The technology used in the study is novel and potentially advantageous compared with similar existing muscle electrostimulation (MEST) methods – first, due to an achieved blood flow increase via indolent nerve stimulation instead of painful direct muscle stimulation, and second, due to its small size, resulting in a wide range of application possibilities. Furthermore, by stimulating the nerve proximal to the posterior/anterior bifurcation, there is simultaneous activation of the tibialis, peroneus longus and lateral gastrocnemius muscles. Together, their contraction provides a near-isometric compression* of the venous valve system within the lower leg, possibly evacuating blood more effectively than by contracting the gastrocnemius alone. No changes were observed in heart rate, blood pressure, oxygen saturation or femoral vein vessel diameter, or in the length of the contracting muscle.

### 3-1b. Paper:


*The studies outlined in this thesis were carried out on healthy adult volunteers, with the intention of investigating the efficacy of a custom built neuromuscular electrical stimulation device (THRIVE) in enhancing lower limb blood flow and supporting the development of a prototype to a commercial medical device (geko™ T-1).*

**Methods:** In ten healthy volunteers, following 30 minutes of supine rest, baseline echocardiography assessments were performed by two independently accredited echocardiographers. A custom-built electrical stimulation device (THRIVE) (pre-geko™) was fitted bilaterally to the common peroneal nerve device. Stimulation was then applied at a lower pulse width setting (400 μs), followed by a higher pulse width setting (600 μs). Each stimulation was active for a period of 30 minutes and 10 minutes resting period was used to separate each pulse width setting, to allow vascular re-equilibration. Echocardiography assessments were performed with the device still active, 5 minutes before the end of each stimulation period. To test the venous response, the THRIVE device was applied to the common peroneal nerve and stimulated for 5 minutes every 15 minutes with a low frequency (3 Hz), 25 mA and 600 μs.

### Table of Results:

<table>
<thead>
<tr>
<th>Test</th>
<th>Baseline Mean and SD</th>
<th>400 μs Stimulation Mean and SD</th>
<th>600 μs Stimulation Mean and SD</th>
<th>Summary/ Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Arterial Flow</td>
<td>174.1 ± 39.2 ml/min</td>
<td>258.8 ± 65.6 ml/min</td>
<td>273.1 ± 97.1 ml/min</td>
<td><em>P</em> ≤ 0.05</td>
</tr>
<tr>
<td>Cardiac Arterial Peak Velocity</td>
<td>81.19 ± 13.62 cm/sec</td>
<td>101.6 ± 22.43 cm/sec</td>
<td>100.9 ± 26.37 cm/sec</td>
<td><em>P</em> ≤ 0.05</td>
</tr>
</tbody>
</table>

The geko™ Device: Annotated Bibliography  Feb 7, 2019 © Perfuse Medtec Inc. 2019
Vessel Diameter and Cross-sectional Area

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Mean ± SD</th>
<th>Diameter</th>
<th>Mean ± SD</th>
<th>Diameter</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.64 ± 0.10 mm</td>
<td>0.63 ± 0.12 mm</td>
<td>0.64 ± 0.11 mm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Skin Microcirculation (foot) (Laser Doppler Flowmetry)

<table>
<thead>
<tr>
<th>Area</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Percentage Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.71 ± 3.39</td>
<td>107.5 ± 68.1</td>
<td>1186% increase</td>
</tr>
<tr>
<td></td>
<td>117.9 ± 67.8</td>
<td>1552% increase</td>
<td></td>
</tr>
</tbody>
</table>

Left ventricular outflow tract velocity time integral (LVOT VTI)

<table>
<thead>
<tr>
<th>VTI</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>21.96 ± 3.23</td>
<td>23.27 ± 3.37</td>
<td>6% increase</td>
</tr>
<tr>
<td></td>
<td>22.79 ± 3.06</td>
<td>4% increase</td>
<td></td>
</tr>
</tbody>
</table>

Ejection Fraction

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>59.9 ± 3.72 %</td>
<td>60.3 ± 7.44 %</td>
<td>62.6 ± 4.80 %</td>
</tr>
</tbody>
</table>

Left Ventricular Diastolic Volume

<table>
<thead>
<tr>
<th>Volume</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>117.7 ± 37.10 ml</td>
<td>120.2 ± 32.30 ml</td>
<td>121.1 ± 27.86 ml</td>
</tr>
</tbody>
</table>

E' Velocity

<table>
<thead>
<tr>
<th>Velocity</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.80 ± 0.16 m/s</td>
<td>0.77 ± 0.12 m/s</td>
<td>0.76 ± 0.08 m/s</td>
</tr>
</tbody>
</table>

Deceleration Time

<table>
<thead>
<tr>
<th>Time</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>187.4 ± 24.82 ms</td>
<td>194.1 ± 31.4 ms</td>
<td>187.9 ± 20.28 ms</td>
</tr>
</tbody>
</table>

E' Lateral

<table>
<thead>
<tr>
<th>Velocity</th>
<th>Mean ± SD</th>
<th>Panel</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.76 ± 5.53 m/s</td>
<td>3.79 ± 5.58 m/s</td>
<td>3.89 ± 5.79 m/s</td>
</tr>
</tbody>
</table>

The femoral artery and vein stimulation results are as follows (from pages 96-99, 110, 122):

<table>
<thead>
<tr>
<th>Test</th>
<th>Arterial Velocity (cm/sec) Mean (SD)</th>
<th>Significance</th>
<th>Venous Velocity (cm/sec) Mean (SD)</th>
<th>Significance</th>
<th>Arterial Flow (ml/min) Mean (SD)</th>
<th>Significance</th>
<th>Venous Flow (ml/min) Mean (SD)</th>
<th>Significance</th>
<th>Microcirculation Dorsum of both feet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>69.92 ± 21.32</td>
<td></td>
<td>10.7 ± 4.32</td>
<td></td>
<td>176.6 ± 65.6</td>
<td></td>
<td>59.4 ± 41</td>
<td></td>
<td>4.66 flux units</td>
</tr>
<tr>
<td>1 hour</td>
<td>70.47 ± 28.5</td>
<td>P&gt;0.05 No significance</td>
<td>24.09 ± 8.30 (158% increase)</td>
<td>P&lt;0.001 21% increase</td>
<td>288.7 ± 127.2 (125% increase)</td>
<td>P&lt;0.05</td>
<td>223.76 ± 114.5 (489% increase)</td>
<td>P&lt;0.001 81% increase</td>
<td>73.59 flux units</td>
</tr>
<tr>
<td>2 hours</td>
<td>76.04 ± 16.47</td>
<td></td>
<td>26.82 ± 6.57 (169% increase)</td>
<td>P&gt;0.05 No significance</td>
<td>237.3 ± 81.7 (62% increase)</td>
<td>P&lt;0.001 81% increase</td>
<td>223.6 ± 76.3 (374% increase)</td>
<td>P&lt;0.001 81% increase</td>
<td>Not provided</td>
</tr>
<tr>
<td>3 hours</td>
<td>83.69 ± 13.03</td>
<td></td>
<td>30.07 ± 13.32 (221% increase)</td>
<td>P&lt;0.001 21% increase</td>
<td>259.4 ± 71.9 (99% increase)</td>
<td>P&lt;0.05</td>
<td>253 ± 86.8 (471% increase)</td>
<td>P&lt;0.05</td>
<td>75.85 flux units (p&lt;0.001)</td>
</tr>
<tr>
<td>4 hours</td>
<td>82.23 ± 15.56</td>
<td></td>
<td>25.67 ± 5.54 (162% increase)</td>
<td></td>
<td>253 ± 100.1 (87% increase)</td>
<td></td>
<td>223 ± 76.9 (405% increase)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tissue Plasminogen Antigen (tPA) levels fell by 14% in the activated leg, 10% in the arm and 1% in the passive leg.

Key Learning Points: “The significant increase in cardiac output reported in our study, could be due to the direct activation of the calf muscle pump, which in turn causes the emptying of both venous beds and sinuses. Another reasoning for the increase in cardiac output, could be stress related and could be due to the exposure to a foreign sensation (electrical stimulation), which may have also resulted in an increase in heart rate. After exposure to the lower pulse width, where there was a 6% increase in LVOT VTI, the increase was only 4% following the higher pulse width, which means that the volunteer may have become accustomed to the foreign sensation applied. However, as heart rate was not monitored throughout the study it is difficult to confirm this reasoning. The study also suggests that the contractions of the calf and foot pumps effectively improve lower limb perfusion at the vascular and micro-vascular
level, improving venous return and preventing venous stasis. It enhances fibrinolytic activity. They suggest a possible systemic effect of the stimulation device, as evidenced by the increase in arterial volume flow over 3 hours. “The drop in tPA levels might suggest a fibrinolytic effect.”


Note: The devices used were not part of the geko™ development. They had an intensity of 4mA and frequency of 5Hz: lower intensity but faster frequency than geko™. However, this paper is included as it was part of the Canadian Consensus paper [3-9b] and includes venous ulcerations, so is included here.

Methods: 14 patients with chronic venous ulcers randomly allocated to active (mean age 74.8±2.3 years) and 15 to Sham nerve stimulation (mean age 76.5±2.6 years), using low frequency transcutaneous sensory nerve stimulation ™) on either the common peroneal or the saphenous nerve (depending on proximity to the wound), plus four-layer compression bandages. Patients used the devices twice daily for 5 minutes for 12 weeks or until the wounds completely healed. For the sham group, the stimulators did not deliver electrical stimulation. Participants and researchers were blinded to allocation.

Results: The activation was for a total of 10 minutes per day, compared to the current geko™ protocol for wounds, which is 6 hours per day, 5-6 days per week, or even to the 20-30 minutes of wear time seen in many geko™ investigations, but the duration of use (12 weeks) is unique and may reflect a cumulative benefit. Patients who healed, regardless of the group, were younger with ulcers of shorter duration than those who did not. Ulcers that healed in the activation group were of longer duration than those that healed in sham group; mean ulcer size in the activation group was larger at baseline than that of the sham group and healing rates in the activation group were greater than the sham: the largest and longest wounds healed more quickly with the active stimulation and compression. There was improvement, in the microvascular blood flow and TCpO2, nearly four times greater improvement in the nerve sensation and two times the flare response, (both parameters reflecting improvement in C-fiber function) in the actively stimulated leg, although none were statistically significant. C-fiber activation stimulates a release of growth factors and neuropeptides necessary for wound healing.

Table of Results:

<table>
<thead>
<tr>
<th>Measure</th>
<th>Sham</th>
<th>Activation</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Healed by 12 weeks</td>
<td>10/15 (66%)</td>
<td>8/14 (57%)</td>
<td>P=0.32 (not significant)</td>
</tr>
<tr>
<td>Average weekly Wound Healing Rate</td>
<td>0.6 ± 0.2 cm²/week</td>
<td>1.1 ± 0.3 cm²/week</td>
<td>P=0.18 (not significant)</td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sham Stim</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical significance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microvascular Blood Flow(cm³)</td>
<td>-15.4 ± 60.1</td>
<td>16.9 ± 42.1</td>
<td>P=0.47</td>
</tr>
<tr>
<td>TCpO2 @ 39°C (mmHg)</td>
<td>-4.49 ± 9.1</td>
<td>5.5 ± 3.6</td>
<td>P=0.31 (not significant)</td>
</tr>
<tr>
<td>TCpO2 @ 44°C (mmHg)</td>
<td>18.7 ± 7.3</td>
<td>13.9 ± 5.7</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Flare Response to hot red pepper (cm²) (C-fiber activation)</td>
<td>2.4 ± 5.0</td>
<td>1.7 ± 2.0</td>
<td>P=0.45 (not significant)</td>
</tr>
<tr>
<td>Nerve Sensation Threshold 5Hz ECPT (mA) (C-fiber activation)</td>
<td>-0.4 ± 0.4</td>
<td>-0.4 ± 0.3</td>
<td>P=0.77 (not significant)</td>
</tr>
<tr>
<td>Only Patients who healed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sham Stim</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical significance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microvascular Blood Flow(cm³)</td>
<td>-23.6 ± 31.1</td>
<td>39.8 ± 60.1</td>
<td>P=0.33</td>
</tr>
<tr>
<td>TCpO2 @ 39°C (mmHg)</td>
<td>-5.33 ± 5.86</td>
<td>3.33 ± 4.23</td>
<td>P=0.32 (not significant)</td>
</tr>
</tbody>
</table>
The geko™ Device: Annotated Bibliography

of leg

activated for one out of every 4 hours after the surgery. Peak blood velocity in the femoral vein was assessed with weight heparin and be
nerve electrostimulation plus low molecular weight heparin and below

Methods:

blood flow after total knee replacement: A pilo

3

in muscle

effective in reducing venous stasis and
acts as a

Key Learning Points:

statistically significant in all muscles.

(4

force generated in the muscles (r 2 _ 0.93,
approximately 2% of the force generated during voluntary MVC. The higher the stimulation intensity, the higher the

envelopes.

amplitudes.

muscles of the extensor hallucis brevis and medial gastrocnemius measured with surface EMG; however
produced muscle activation of the tib

signifi

3

2b

2a.

threshold

n

t

5Hz ECPT

mA)

(C-fiber activation)

Threshold 5Hz ECPT

(C-fiber activation)

P=0.99(not significant)

P=0.24 (not significant)

P=0.44(not significant)

P=0.18 (not significant)

P=0.05

P=0.62

P=0.18 (not significant)

Key Learning Points: In their comments on this paper, the CAWC consensus group stated: “The improvement of C-fibre activation is also an indicator of the reversal of the neuropathy that may have developed as a result of chronic oedema.”

3-2. The geko™ Device and Haemodynamics


Methods: The geko™ T-1 device (27mA) was applied to 28 legs of 14 healthy subjects. Investigations included measuring the force during voluntary isometric ankle joint dorsiflexion and the stimulation-induced myoelectric responses produced by the leg muscle contractions. Muscle oxygen saturation, blood volume and deoxygenated haemoglobin in the tibialis anterior and medial gastrocnemius muscles were measured by near-infrared spectroscopy during venous stasis (40 mmHg thigh tourniquet), with or without electrical stimulation. Myoelectric signals (EMG) were recorded by placing bipolar electrodes over the central muscle bellies of the tibialis anterior (TA), extensor hallucis brevis (EHB), peroneus longus (PL), and medial gastrocnemius (MG) muscles of the lower leg. Force generation during isometric ankle joint dorsiflexion was measured while the foot was rigidly maintained in a neutral position, i.e. 15 degrees plantar flexion, during the stimulation test period.

Results: The primary findings were the following: (1) electrical stimulation of the common peroneal nerve produced two types of muscular activity, concentric contraction of the extensor muscles that caused dorsiflexion of the ankle joint and passive stretch of the calf flexor muscles; (2) the force generation during isometric ankle joint dorsiflexion increased significantly in response to the increase in electrical stimulation intensity; and (3) electrical stimulation of the peroneal nerve counteracted the increases in muscle blood volume and deoxygenation during venous stasis. The geko device™ produced muscle activation of the tibialis anterior and peroneus longus. The stimulation also increased activation in the muscles of the extensor hallucis brevis and medial gastrocnemius measured with surface EMG; however with smaller amplitudes. The geko™ device activated the extensor muscles with an additional stretch of the antagonistic flexor muscles. These are then pulled in a distal direction during dorsiflexion, compressing the flexor muscles by the fascial envelopes. The force produced at the maximum stimulation intensity (level 7) was median 2.25 N (0.02 – 14.14), approximately 2% of the force generated during voluntary MVC. The higher the stimulation intensity, the higher the force generated in the muscles (r 2 _ 0.93, p _ 0.001). The stimulation counteracted increments in muscle blood volume (4 – 9% less increase) and deoxygenated haemoglobin (0.2 – 6% less increase) during venous stasis, although not statistically significant in all muscles. There was no effect on the systemic blood pressure of the subjects.

Key Learning Points: The passive motion of the flexor muscle caused by stimulation of the common peroneal nerve acts as a calf muscle pump, which may enhance venous return by increasing intramuscular pressure, which may be effective in reducing venous stasis and oedema, influencing muscle oxygenation, supported by the findings in this study. The results may indicate that electrical stimulation of the common peroneal nerve helps to counteract the increases in muscle blood volume and deoxygenated hemoglobin seen during venous stasis.


Methods: Thirty consecutive patients undergoing total knee replacements were randomized to either receive peroneal nerve electrostimulation plus low molecular weight heparin and below-knee compression stockings or low molecular weight heparin and below-knee compression stockings alone. The device (assume geko™ but not stated in paper) was activated for one out of every 4 hours after the surgery. Peak blood velocity in the femoral vein was assessed with Duplex ultrasonography in the supine position, but it does not state at what point the assessment was made. Presence of leg oedema and calf diameter were recorded prior to surgery and at time of discharge but are not reported.

Table of Results:

<table>
<thead>
<tr>
<th>TCp02 @ 44°C (mmHg)</th>
<th>Flare Response to hot red pepper (cm²) (C-fiber activation)</th>
<th>Nerve Sensation Threshold 5Hz ECPT (mA) (C-fiber activation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.1 ± 5.4</td>
<td>2.4 ± 1.8</td>
<td>-0.7 ± 0.5</td>
</tr>
<tr>
<td>18.7 ± 7.3</td>
<td>1.7 ± 5.0</td>
<td>-0.4 ± 0.4</td>
</tr>
<tr>
<td>P=0.05</td>
<td>P=0.99(not significant)</td>
<td>P=0.44(not significant)</td>
</tr>
<tr>
<td>6.6 ± 6.2</td>
<td>6.0 ± 3.4</td>
<td>-0.2 ± 0.2</td>
</tr>
<tr>
<td>5.9 ± 6.1</td>
<td>11.8 ± 8.1</td>
<td>-0.9 ± 0.6</td>
</tr>
<tr>
<td>P=0.94 (not significant)</td>
<td>P=0.24 (not significant)</td>
<td>P=0.18 (not significant)</td>
</tr>
</tbody>
</table>

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**Perfuse Medtec Inc. 2019**
Key Learning Points: Electrostimulation of the common peroneal nerve enhanced venous flow in the lower limb and may potentially be of use as a supplementary technique in deep venous prophylaxis following lower limb orthopaedic operations.

3-2c. Hemodynamic Testing: Speckle Spectroscopy

i) Using Speckle contrast optical spectroscopy* to measure microcirculatory tissue perfusion in a healthy leg with:
- geko™ device turned off
- geko™ device activated with no foot twitch
- geko™ activated with foot twitch.

*Speckle contrast imaging enables rapid mapping of relative blood flow distributions using camera detection of back-scattered laser light (Kazmi et al. 2015).

To view the actual video, please go to: https://www.gekodevices.com/geko-videos/speckle-imaging-video-showing-microcirculatory-blood-flow-at-baseline-and-with-the-geko-device-switched-on/
2. The geko™ device is activated at a higher setting, causing the foot to twitch, resulting in a 1,000% increase in microcirculatory flux.

Key Learning Points: While the optimal microcirculatory response is seen with the fully activated foot twitch or movement in this healthy volunteer, there is still a 100-200% increase when the foot twitch is not achieved, which is the reality with many patients with obesity or edema. This was illustrated by Williams in her 2017 PhD thesis, who described nine patients in which the NMES [geko™ T-1 device (27mA)] was unable to elicit a twitch, with a mean BMI of 35.5±5kg/m2, calf circumference 45.9±6cm, CEAP C4.1±0.6, and AVVQ 31.3±14. Although this is a healthy volunteer, these test results suggest that there may be benefit in people with lower limb disease even when a foot twitch is not obtained. Case studies series in Canada (3-6b &c) have shown that patients who did not have an initial foot twitch still benefit by a reduction in edema, pain and wound size. Our recommendation to clinicians is that they do use the device in the absence of a foot twitch and evaluate each patient individually over 1-2 weeks for indications of a positive response.

ii) When activated, the geko™ device caused a 225% increase in flux (p<0.001) in the wound bed and a 67% increase in flux (p<0.001) surrounding the peri-wound area. Increases in flux corresponds to an increase in microcirculatory blood flow, which is clearly seen in the comparison below. This results in an rise in red blood cells carrying oxygen and nutrients necessary for energy metabolism and healing. It is noted that in this example with an infected wound, hyperaemia has already occurred in response to the infection. To view the actual video, please go to: https://gekodevices.com/geko-videos/speckle-imaging-video-showing-microcirculatory-blood-flow-at-baseline-and-with-the-geko-device-switched-on-2/

3-2d-h. Hemodynamics in Intermittent Pneumatic Compression (IPC) versus geko™


Methods: Baseline measurements were taken of superficial femoral venous velocity and volume flow, then the subjects received bilateral therapy with the geko™ T-1 device (27mA) and the Intermittent Pneumatic Compression (ICP) device (SCD Express™ Compression System, Covidien, Ireland) in an interventional cross-over trial with 30 minutes of therapy,
the measurements were repeated, and finally devices were swapped for another 30 minutes and measurements taken a third time.

**Table of Results:**

<table>
<thead>
<tr>
<th>Test</th>
<th>IPC Venous</th>
<th>Summary/Significance</th>
<th>Venous</th>
<th>Summary/Significance</th>
<th>Arterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Velocity</td>
<td>19%</td>
<td>Not provided</td>
<td>42%</td>
<td>Not provided</td>
<td></td>
</tr>
<tr>
<td>Time Averaged Peak Velocity (TAMV)</td>
<td>12%</td>
<td>Not provided</td>
<td>27%</td>
<td>Not provided</td>
<td></td>
</tr>
<tr>
<td>Volume Flow</td>
<td>7%</td>
<td>Not provided</td>
<td>46%</td>
<td>Not provided</td>
<td></td>
</tr>
</tbody>
</table>

---

3-2e. **Paper:** Williams KJ, Moore HM, M Ellis and Davies AH. Haemodynamic changes with the use of a neuromuscular stimulation device compared to intermittent pneumatic compression. *Phlebology* First Published Online 10 April 2014. [http://phl.sagepub.com/content/early/2014/04/10/0268355514531255](http://phl.sagepub.com/content/early/2014/04/10/0268355514531255) 2015, 30(5): 365–372.

**Methods:** Ten healthy volunteers (mean age 27.1±3.8 years, body mass index 24.8±3.6 kg/m²) were randomized into two groups, in an interventional crossover trial. Baseline haemodynamic measurements were recorded after an equilibration rest period of 10 min, and the first geko™ T-1 device (27mA) device was applied and activated for a 20 min time period before repeat measurements were taken with the device on, off and 10 min post cessation of device. The subject was allowed to rest for a 20 min wash-out period. The second device was activated and, repeat haemodynamic measurements were taken. The patient was positioned semi-recumbent. The left superficial femoral vein and artery were used for all patients with the knee flexed and the leg externally rotated at the hip 35-40°.

**Table of Results:**

<table>
<thead>
<tr>
<th>Test</th>
<th>IPC Venous</th>
<th>Summary/Significance</th>
<th>IPC Arterial</th>
<th>Summary/Significance</th>
<th>Venous</th>
<th>Summary/Significance</th>
<th>Arterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Velocity</td>
<td>51%</td>
<td>p=0.002</td>
<td>-8%</td>
<td>No significance</td>
<td>103% increase</td>
<td>p=0.002</td>
<td>11% increase</td>
</tr>
<tr>
<td>Time Averaged Peak Velocity (TAMV)</td>
<td>5%</td>
<td>p=0.002</td>
<td>-12%</td>
<td>No significance</td>
<td>101% increase</td>
<td>p=0.002</td>
<td>84%</td>
</tr>
<tr>
<td>Volume Flow</td>
<td>3%</td>
<td>p=0.002</td>
<td>-13%</td>
<td>No significance</td>
<td>101% increase</td>
<td>p=0.002</td>
<td>75% increase</td>
</tr>
<tr>
<td>Microcirculatory Flux</td>
<td>~ 10% increase</td>
<td>~240% increase in paper but data actually shows 152% (First Kind analysis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key Learning Points:** The geko™ device seems to be operating via a modality that affects the flow properties of the vascular bed in the leg. This may be via a local pressure effect, neuronal or endogenous cytokine media, or other unknown local microvascular modification. Studies into the effect on the arterial system, and effects on subjects with vascular pathology are indicated.

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**Methods:** 10 healthy volunteers. For each subject, the geko™ T-1 device (27mA) was initially set to a threshold setting (geko™-TS) (as defined as the minimum setting to elicit a minor muscular contraction in both the calf and the foot) for a period of 30 minutes followed by 10-minutes rest. Following the 10-minute period of rest, a Normal Clinical Use (geko™-NCU) setting was selected that was characterized by 3 additional levels to the previous threshold setting-the minimum level that can achieve upward and outward twitching of the foot when raised from the ground with short duration of activation. Measurements were taken from the superficial femoral vein and artery, and microcirculation was measured on dorsum of the foot.
Table of Results:

<table>
<thead>
<tr>
<th>Test</th>
<th>IPC Venous</th>
<th>IPC Arterial</th>
<th>geko™ “Threshold” Venous</th>
<th>geko™ “Normal Clinical” Venous</th>
<th>Summary/Significance</th>
<th>geko™ “Threshold” Arterial</th>
<th>geko™ “Normal Clinical” Arterial</th>
<th>Summary/Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Blood Flow Volume</td>
<td>-4%</td>
<td>-9 to -16%</td>
<td>14%</td>
<td>32% increase</td>
<td>p≤0.001</td>
<td>-7%</td>
<td>30% increase</td>
<td>p≤0.001</td>
</tr>
<tr>
<td>Mean Blood Flow Velocity</td>
<td>143% - 166%</td>
<td>-1% to -4%</td>
<td>73%</td>
<td>174% increase</td>
<td></td>
<td>2%</td>
<td>24% increase</td>
<td>p≤0.001</td>
</tr>
<tr>
<td>Microcirculation</td>
<td>44-59%</td>
<td></td>
<td>394% (Normal Clinical) and 345% (Threshold) in paper, but data actually showed 270% increase (First Kind analysis)</td>
<td>p≤0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean vessel diameter</td>
<td>No significant difference in femoral vessel diameter between the devices</td>
<td></td>
<td></td>
<td></td>
<td>p&gt;0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key Learning Points: Although the volume flow increase after the use of the geko T-1 device at the threshold setting is less than that at the normal clinical use setting, it was still much greater than that reported after the use of the IPC devices, for which a decrease in total volume flow was observed. Measurement of arterial peak velocities demonstrated that the geko T-1 device is more effective than IPC devices in producing an increase in the femoral artery. The geko T-1 device is more effective than the IPC devices in increasing venous, arterial blood velocity and flow, and microcirculatory flux. The devices studied were safe and well tolerated by healthy subjects.


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 [geko™ T-1 or T-2 device (27mA)] with visible muscle actuation (VMA), NMES device with no visible muscle actuation (NVMA) and IPC device. * Speckle contrast optical spectroscopy, a non-invasive, diffuse optical method for measuring microvascular blood flow in tissue

Table of Results:

<table>
<thead>
<tr>
<th>Test</th>
<th>geko™ with no visible muscle activation</th>
<th>geko™ with visible muscle activation</th>
<th>IPC Device</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) of % increased in mean flux from baseline with device.</td>
<td>150.6 ± 48.8</td>
<td>399.8 ± 210.1</td>
<td>117.3 ± 17</td>
<td>P=0.005</td>
</tr>
</tbody>
</table>

Key Learning Points: 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. 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, improve healing and prevent wound complications in populations such as total hip replacements, heart therefore further research is needed to explore this.

3-2h-k. Hemodynamic Effect of geko™ Device with Patients with Chronic Venous Disease


**Methods:** Ten healthy volunteers served as the controls, with 30 individuals with Chronic Venous Disease in 3 groups: 10 with superficial venous insufficiency, 10 with deep venous insufficiency and 10 with deep venous obstruction. The geko™ T-1 device (27mA) was set to the Normal Clinical Use setting—the minimum level that can achieve upward and outward twitching of the foot when raised from the ground (dorsiflexion).

Baseline measurements were taken before activation of both devices, and 20 minutes after activation of the device, with subjects supine and semi-recumbent, and allowed to rest x 10 minutes to acclimatize. Ultrasound testing was done in the right femoral vein 3-5 cm from the saphenofemoral junction, taking 5 ultrasound measurements of venous parameters were taken from the femoral vein, and the mean was calculated. Laser doppler fluximetry was measured in the dorsum of the left hand and foot, and leg circumference measurements were taken at the calf and ankle. Bilateral geko™ devices were worn for 4-6 hours per day, 5 days per week for 6 weeks, at which time the haemodynamic measurements were repeated. Quality of life questionnaires were also taken at week 0, 6 and 8 (see Section 3-7a).

**Table of Results 1: Median Measurements taken at Femoral Vein (from Thesis Tables 24)**

<table>
<thead>
<tr>
<th></th>
<th>Healthy</th>
<th>Superficial Venous Insufficiency</th>
<th>Deep Venous Insufficiency</th>
<th>Deep Venous Obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak Velocity</strong></td>
<td>34.8**</td>
<td>62.8**</td>
<td>9.0</td>
<td>14.8</td>
</tr>
<tr>
<td><strong>Time Averaged Peak Velocity (TAMV)</strong> [blood flow]</td>
<td>-14.2</td>
<td>28.1**</td>
<td>28.2</td>
<td>-5.1</td>
</tr>
<tr>
<td><strong>Volume Flow</strong></td>
<td>-22.5</td>
<td>37.5*</td>
<td>17.4*</td>
<td>5.9</td>
</tr>
</tbody>
</table>

*p<0.05  **p<0.01 wilcoxon signed-rank

**Table of Results 2: Comparison of Hemodynamic changes in the femoral vein from baseline to week 6 (geko™ devices on in both) (from poster)**

Used with Permission.
Laser Doppler fluximetry changes in the dorsum of the left hand and foot with “device off” (baseline) compared to “device on” (from Thesis) – also covered in 3-5b.

<table>
<thead>
<tr>
<th>Percentage Change from Baseline</th>
<th>Healthy Subjects</th>
<th>Superficial Venous Insufficiency</th>
<th>Deep Venous Insufficiency</th>
<th>Deep Venous Obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg Flux</td>
<td>274.8 ± 279**</td>
<td>264.9 ± 283*</td>
<td>69.3 ± 126</td>
<td>46.9 ± 50*</td>
</tr>
<tr>
<td>Arm Flux</td>
<td>84.0 ± 126**</td>
<td>71.3 ± 76*</td>
<td>23.7 ± 57</td>
<td>106.5 ± 115*</td>
</tr>
</tbody>
</table>

(* p<0.05, ** p<0.01, Wilcoxon signed rank) These results did not change over the 6 weeks of use.
Over 6 weeks median unilateral leg volume decreased by an average of 0.2% (26.3ml, p=0.61) for healthy subjects, and 11.6% (225.4ml, p=0.03) for those with symptomatic venous disease, but this was not significant.

Key Learning Points: Regular use of 4-6 hours per day over 6 weeks increased all venous parameters, less so in patients with deep venous disease, although only peak velocity showed statistically significant improvement. The median unilateral leg volume decreased by a statistically significant average of 11.6% (225.4ml, p=0.03) for those with symptomatic venous disease. The significant changes in arm laser Doppler flux in all but the individuals with deep venous insufficiency suggests that there is a systemic benefit in using the geko™ device, similar to the systemic roles that exercise and enhanced venous return have on the circulatory system. It is not clear why the individuals with Deep Venous Insufficiency did not show significance in this.


Methods: Twenty-two patients with CEAP C2-C4 venous disease were randomised to a sham or test device (assumed to be geko™ T-1 device [27mA]). Patients were asked to use the device for 30 minutes per day for 6 weeks. Haemodynamic measurements (duplex ultrasound and laser doppler fluximetry), limb volume (perometer), venous refill time (digital photoplethysmography) and quality of life outcome measures were measured at baseline and after 6 weeks.

Results: The mean age of participants was 62 years, BMI 28.6, with a 15:7 female preponderance. At week 0, there was a significant improvement in femoral vein haemodynamics (from baseline) whilst using the device in the test compared to sham group (time averaged mean velocity (TAMV) 102.4% versus -9.1%, p < 0.0001; volume flow 107.9% versus -3.7%, p < 0.0001; peak velocity 377.7% versus -6.7%, p < 0.0001). The sham group demonstrated an increase in limb volume, which was prevented with the use of the device in the test group (sham +2.0%, p < 0.0001; test +0.8%; p = 0.0623). There was no improvement in limb volume in either the sham or test group over the 6 weeks (sham +0.7%, p = 0.16; test +2.3%, p = 0.74). A non-statistically significant improvement in disease specific quality of life outcome measures (AVVQ) was observed in the test group over the 6 weeks. Due to the small sample size, some improvements were not statistically significant and subgroup analysis was not performed.

Key Learning Points: Although this study was conducted over 6 weeks, the NMES devices were only used for 30 minutes per day. Further trials are required to determine optimal frequency and duration of device usage and the effect on different subgroups of patients with venous disease.
3-2j-o. Effect of geko™ on Patients with Peripheral Arterial Disease

3-2j. Effect of geko™ Device on People with Intermittent Claudication


**Methods:** A prospective observational series. Sixteen patients with claudication attending a structured exercise program were studied. Following a 30-minute rest period, baseline measurements of arterial, venous and microcirculatory flow (Laser Doppler) were taken bilaterally. The geko™ T-1 (27mA) device was applied for 40 minutes, unilaterally, and flow measurements repeated. The difference in flow from baseline was calculated for each measurement. The mean resting ABI of the active limbs was 0.68 ± 0.23.

**Results:** 16 patients, 11 male, 5 female, with a mean age of 67 years (SD 7.7) were recruited. The mean resting ABI of the active limbs was 0.68 ± 0.23. The mean change in arterial volume flow in the active limb was 0.65 L/min compared to control limb 0.003L/min (p=0.026). Venous volume flow increased by 0.041L/min in the active limb versus control 0.0005L/min (p=0.023). Microcirculatory flow, measured by laser Doppler, increased by a mean of 21.16 flux units in the active compared to a decrease of 6.21 in the control group (p<0.01).

**Table of Results:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Control (no geko™) Amount of change</th>
<th>Activated geko™ Amount of Increase</th>
<th>Summary/ Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial Volume Flow</td>
<td>0.003 L/min</td>
<td>0.65 L/min 29% increase</td>
<td>p=0.026</td>
</tr>
<tr>
<td>Venous Volume Flow</td>
<td>0.0005L/min</td>
<td>0.041L/min 23% increase</td>
<td>p=0.023</td>
</tr>
<tr>
<td>Microcirculatory Flow</td>
<td>Decrease of 6.21 flux units</td>
<td>21.16 flux units</td>
<td>P&lt;0.01</td>
</tr>
</tbody>
</table>

**Key Learning Points:** Transcutaneous electrical neuromuscular stimulation with the geko™ device augments arterial, venous and microcirculatory flow in patients with claudication and may prove a useful treatment adjunct in this cohort of patients. The limb that did not have the geko™ activated was not affected.


**Methods:** After 30 minutes to acclimatize, bilateral baseline arterial, venous and microcirculatory flow was measured by laser doppler. The geko™ T-1 (27mA) device was applied for 60 minutes on one leg only and the measurements were repeated, with the leg without geko™ being considered the passive limb.

**Results:** In 43 patients, 24 with claudication and 19 post-operative femoro-popliteal bypass grafts, the geko™ device was shown to be statistically significant in increasing venous and arterial volume and microcirculatory flow.

<table>
<thead>
<tr>
<th>Haemodynamic Tests</th>
<th>geko™ Baseline</th>
<th>Increase passive leg after 60 minutes activation</th>
<th>Increase geko™ leg after 60 minutes activation</th>
<th>Paired t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial Volume Flow</td>
<td>-0.004L/min (mean)</td>
<td>0.68 L/min (mean)</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Venous Volume Flow</td>
<td>0.002 L/min (mean)</td>
<td>0.034 L/min (mean)</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Microcirculatory Flux</td>
<td>0.39 flux units</td>
<td>22.25 flux units (mean)</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Key Learning Points:**

Transcutaneous electrical neuromuscular stimulation of the common peroneal nerve with the geko™ device augments arterial, venous and microcirculatory flow in peripheral arterial disease patients and may prove a useful treatment adjunct in these patients. This paper documents hemodynamic testing showing improvement due to activation of the geko™ device in ABPIs as low as 0.45 in a group of 16 claudicants (the mean resting ABPI of the active limbs was 0.68 (SD 0.23).

Methods: 75 participants:
- 30 with claudication;
- 25 post-op infra-inguinal bypass grafts, and
- 22 with varicose veins

Tested with the geko™ T-1 (27mA) device on 1 leg (active) vs none on other leg (passive), and inactive geko™ on one leg (control) x 45 minutes. Arterial flow measurements of the superficial femoral artery, and venous blood samples were taken bilaterally at baseline and following 45 minutes of stimulation. Tissue Plasminogen activator (t-PA) and plasminogen activator inhibitor 1 (PAI-1) were measured at baseline and after the 45 minutes in the passive, active and control limbs.

<table>
<thead>
<tr>
<th>Test</th>
<th>Passive (no geko™)</th>
<th>Active (activated geko™)</th>
<th>Control (inactive geko™)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in t-PA</td>
<td>-302.4 pg/ml (-5.5%)</td>
<td>-302.4 pg/ml (-7.7%)</td>
<td>-287.2 pg/ml (-6.85%)</td>
<td>No significant effect on t-PA levels</td>
</tr>
<tr>
<td>Mean change in PAI-1</td>
<td>-11.4 ng/ml (-3.6%)</td>
<td>-34 ng/ml (-16.2%)</td>
<td>-2.73ng/ml (-2.6%)</td>
<td>Statistically significant LOCAL fibrinolytic effect (not found in passive limb) P&lt;0.001</td>
</tr>
<tr>
<td>Increase in Arterial Flow</td>
<td>1.1%</td>
<td>31.5%</td>
<td>2.5%</td>
<td>Statistically significant difference between active and control P&lt;0.001</td>
</tr>
</tbody>
</table>

Key Learning Points: “Increasing fibrinolytic activity by reducing levels of plasminogen activator inhibitor 1 could have many beneficial long-term effects through the prevention of thrombosis. Increased PAI-1 levels have been shown to be implicated in the ageing-associated thrombosis and cardiovascular ageing. As such, the ability to reduce circulating levels may slow disease progression in the elderly.”

Reducing plasma levels of PAI-1 have also been shown in experiments to slow progression of chronic kidney disease and may even result in a degree of disease resolution, which has led to attempts to develop drugs and therapies, which could target its activity. It has also been shown that high levels of PAI-1 may be responsible for the development of microvascular complications associated with Type II diabetes mellitus. It can therefore be seen that peroneal nerve stimulation would be a useful treatment adjunct or prophylaxis within the vascular disease population, many of whom have multiple risk factors for thrombotic disease.


Aim: This pilot study aimed to reveal whether combination of electrostimulation with iloprost treatment achieves better results compared to iloprost alone in patients with critical limb ischemia.

Material and methods: Patients were considered eligible if they had Fontaine class III–IV symptoms with critical peripheral arterial stenosis or occlusion in arterial duplex ultrasound or computed tomography angiography and if they were not suitable candidates for surgical or endovascular revascularization due to poor distal vascular bed, failed previous grafts or stents, and high risk of operative failure. Arterial Doppler Ultrasound and pulse oximetry of the first toe or any toe without ischemic lesions were measured the day before the treatment started and the day before hospital discharge. In both groups, peak blood velocities in the anterior and posterior tibialis arteries were measured using a 7.5-MHz linear array probe with the patient laid in supine position, below the knee level and at about 5 cm proximal to the ankle. Patients were randomized into Group 1 (n= 11, mean age: 65.3 4.2 years, received iloprost infusion protocol alone) or Group 2 (n = 11, mean age: 62.9 6.7, received iloprost infusion plus standardized protocol of peroneal nerve electrostimulation). Electrostimulation was delivered with by the geko T-1 device with 1 Hz frequency, 27 mA current, and 200 ms pulse width, for one hour in every four, monitored by nurses. The device was set to a level to obtain a foot twitch, but operated only while the patients were resting in bed lying in supine position. If necessary, the level was reduced for patient tolerance. Peak blood flow velocities in the anterior and posterior tibialis arteries were measured with duplex ultrasound.
Results: There was a slight insignificant increase in blood velocity in anterior tibialis artery in Group 1 (from 17.6 13.0 to 18.6 13.1, p=0.57), whereas the increase in Group 2 was statistically significant (from 23.8 18.3 to 32.2 19.7, p= 0.01). No significant difference was seen in the increase in blood velocity in the posterior tibialis artery or the final pulse oximetry oxygen saturation levels. In both groups, mean walking distance significantly improved at the end of the treatment (increased from 86.3 79.9 to 182.7 157.6 m in Group 1, p=0.009 and from 89.0 45.9 to 300.0 80.6 m in Group 2, p=0.001). The difference in walking for Group 2 compared to Group 1 at the end of the treatment was statistically significant (p=0.03).

Conclusion: Electrostimulation of the peroneal nerve caused a substantial increase in anterior tibialis artery blood velocity when used.

Key Learning Points: Use of the geko™ device as an adjunct to medical therapy in patients with critical limb ischemia may be associated with better clinical outcomes, including longer walking distance. Walking exercise is indicated as an important part of therapy for people considered to be fit for exercise intervention suffering with intermittent claudication (Cochrane 2017 [https://www.cochrane.org/CD000990/PVD_exercise-reducing-intermittent-claudication-symptoms ])


Introduction: Transcutaneous neuromuscular stimulation (TNS) can improve micro- and macro-circulatory flow in healthy volunteers. This suggests it may be beneficial in DVT prevention and flow augmentation in vascular patients. The gekom™ device is a neuromuscular stimulation device, which stimulates the common peroneal nerve. This study aimed to establish whether the device effectively stimulates visible muscle twitch and as such may augment flow in vascular patients.

Methods: A prospective observational series. Background information, clinical examination and neuropathy scores were performed. Following gekom™ T-1 (27mA) device application, the presence of a response was recorded. Univariable and multivariable analyses were performed to compare responders with non-responders.

Results: 100 patients AAA (13%), claudication (57%), critical limb ischaemia (4%), post-op femoro-popliteal bypass graft (7%), post-angioplasty (1%), diabetic ulcers (8%), varicose veins (5%) and healthy volunteers (5%) were included. 66 males and 34 females, mean age 69 years (SD 11). Univariable analysis identified neuropathy score >5 (OR:17.831, 95%CI 2.713–117.193; P=0.003) remained significant on multivariable analysis.

Conclusions: Failure to respond to TNS devices may be predicted by greater calf circumference and neuropathy score of >5. Identifying such patients can save time and prove cost-effective.

Key Learning Points: This 2014 paper identified that patients with larger calf circumference or those with a neuropathy score of > 5 may not have a visible muscle twitch or foot movement with activation of the geko™ device. Subsequent hemodynamic testing and case series with patients of varying limb size has shown that when there is little or no visible activation, the microcirculation is still increased (see 3-2c) and wound healing is occurring (3-6b-d). It may be that length of time to healing may be increased with those patients. Further evaluation and research is needed.


Aim: This pilot study’s purpose was to evaluate the effect of NMES on patients with peripheral arterial disease.

Methods: In this controlled interventional trial, patients were recruited from a vascular outpatient clinic and randomized to either the control group, treated according to local and national guidelines (e.g. lifestyle advice, exercise class referral, smoking cessation advice, and pharmacological intervention as appropriate), or the device group, who in addition to best medical treatment, were allocated to use neuromuscular stimulation at the common peroneal nerve with the geko™ T-1 (27mA) device, 4-6 hours daily, 5 times a week. All patients completed both generic and diseasespecific quality of life questionnaires (EQ-5D, SF-12, CES-D, ICQ), and an exercise treadmill test. Arterial ultrasounds performed within 6 months were analyzed for degree of disease. Ultrasound Blood flow measurements were taken from the groin of the most symptomatic leg. At 6 weeks, all measurements were repeated and compared to baseline values.

Results: 35 subjects were recruited and randomised, with 19 in the control group, and 16 in the device group. Diary recorded device hours showed good protocol adherence, with subjects using the device for mean (SD) 5.15 (+/-1.6) hours.
Both groups increased their walking distances by statistically significant amounts, but there was no statistically significant difference. With activation of the NMES devices, the percentage increases in arterial TAMV (104%) and volume flow (118%) and venous peak velocity (43%) were all significant.

3-2p. The geko™ Effect on Deep Veins


**Methods:** The aim was to determine the effect of the geko™ T-1 (27mA) device on the velocities and volume flows in the peroneal, posterior tibial (PTV) and gastrocnemial veins in 18 healthy volunteers, and to assess the safety of the device. One leg randomly chosen; placed in sitting position with legs suspended over the couch and resting on a stool x 5 minutes to achieve baseline equilibrium. The intensity of the stimulus was dictated by each participant’s ability to comfortably tolerate the effect, using one leg per individual determined in a random selection. Blood velocity and volume flows were measured in the peroneal, posterior tibial and gastrocnemius veins in a longitudinal section using the IU22 ultrasonic scanner and a broad bandwidth L9-5 linear array transducer. Measurements were taken mid-calf for the posterior tibial and peroneal veins, gastrocnemius veins just distal to the confluence with the popliteal vein. Peak velocity (PV) (cm/sec) diameter of the vein at the point of sampling and the duration of the Doppler spectral waveform produced by the calf muscle contraction were measured. All measurements were repeated 3 times and the mean value was used.

**Table of Results:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Peroneal Vein with Activated geko™ % Increase over baseline</th>
<th>Post-Tibial Vein with Activated geko™ % Increase over baseline</th>
<th>Gastrocnemius Vein Activated geko™ % Increase over baseline</th>
<th>Summary/ Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Velocity (cm/sec)</td>
<td>216%</td>
<td>112%</td>
<td>137%</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Ejected volume per stimulus (ml)</td>
<td>113%</td>
<td>38%</td>
<td>50%</td>
<td>P&lt;0.001 to &lt;0.003</td>
</tr>
<tr>
<td>Volume Flow during Muscle Contraction</td>
<td>36%</td>
<td>25%</td>
<td>17%</td>
<td>P&lt;0.015 to &lt;0.036</td>
</tr>
</tbody>
</table>

**Key Learning Points:** Venous flow in all calf veins significantly increased during neuromuscular stimulation from the geko™ device as shown above, but this was in healthy volunteers with a short period of stimulation. The activation of the foot and calf muscle pump effect was not confined to the peroneal compartment, but extended to all the axial veins. The increases over baseline are key factors in preventing venous stasis, however the results cannot be extrapolated to patients with existing venous stasis disease or in other life situations.

3-2q-r. The geko™ device effect on Venous Blood Flow and Microcirculation with Casting


**Methods:** Ten healthy volunteers were tested with geko™ T-1 (27mA) device in 4 postures: standing (weight bearing and non-weight bearing, supine lying with lower limb horizontal and then elevated. Duplex ultrasonography of the superficial femoral vein measured venous flow and cross-sectional area before (after laying 30 minutes to achieve equilibrium) and 5 minutes after device was activated in each position. A plaster below knee cast was applied and the tests were repeated in each position, with and without the device activated.
Table of Results: Increase in Venous Blood Flow at the Superficial Femoral Vein

<table>
<thead>
<tr>
<th>Position</th>
<th>geko™ activated No cast Mean ± SD</th>
<th>Summary/Significance</th>
<th>Plaster Cast non-activated geko™ Mean ± SD</th>
<th>Plaster cast geko™ activated Mean ± SD</th>
<th>Summary/Significance</th>
</tr>
</thead>
</table>
| Supine leg horizontal     | 21.6 ± 2.2  
41% increase | p=0.04               | 15.5 ± 1.0               | 25.3 ± 3.1  
73% increase | P=0.03 |
| Supine leg elevated       | 23.4 ± 2.9  
P=0.75               | 19.5 ± 2.1               | 24.6 ± 2.8               | P=0.13 |
| Standing weight bearing   | 21.8 ± 3.4  
P=0.1               | 10.0 ± 1.6               | 22.3 ± 3.6               | P=0.02 |
| Standing non-weight bearing| 26.8 ± 3.1  
27% increase | P<0.001               | 10.7 ± 1.0               | 29.3 ± 32.8  
93% increase | P<0.001 |

No statistical change in Cross-Sectional area of the femoral vein with geko™ activation with or without casting.

Key Learning Points: The device presents a number of advantages over previous ES devices. Indirect muscle stimulation via the nerve allows muscle contraction to be affected using a much lower level of stimulus than direct muscle stimulation. This means that a given level of contraction is considerably more tolerable to the patient. The branching of the common peroneal nerve distal to the knee results in contraction of a whole complex of lower leg muscles, including those muscles responsible for foot dorsiflexion, and stabilisers. Dorsiflexion has been shown to provide more effective blood pumping than plantar flexion. This gives a more effective evacuation (by distension) of the valved vessels of the calf than by contraction of the gastrocnemius muscle.


Methods: Ten healthy volunteers were tested with geko™ T-1 (27mA) device in 4 postures: standing (weight bearing and non-weight bearing, supine lying with lower limb horizontal and then elevated). Flux was measured with laser Doppler fluxmetry on the dorsum of the foot before and 5 minutes after device was activated in each position. A plaster below knee cast was applied and the tests were repeated in each position, with and without the device activated. Measures of flux were compared to baseline levels with no cast and an inactive geko™ device.

Table of Results:

<table>
<thead>
<tr>
<th>Position</th>
<th>geko™ activated No cast</th>
<th>Plaster Cast non-activated geko™</th>
<th>Plaster cast geko™ activated</th>
<th>Summary/Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine leg horizontal</td>
<td>91.2 ± 44.1</td>
<td>24.8 ± 32.5</td>
<td>154.1 ± 35.4</td>
<td>Activated geko increased flux in all positions with and without cast p=0.001.</td>
</tr>
<tr>
<td>Supine leg elevated</td>
<td>120.7 ± 57.5</td>
<td>3.9 ± 23.7</td>
<td>278.9 ± 87.8</td>
<td>Without cast, weight bearing had least increase; with cast increases were similar in all positions</td>
</tr>
<tr>
<td>Standing weight bearing</td>
<td>30.5 ± 36.4</td>
<td>-0.7 + 19.5</td>
<td>208.5 ± 86.1</td>
<td></td>
</tr>
<tr>
<td>Standing non-weight bearing</td>
<td>99.6 ± 47.4</td>
<td>42.5 ± 42.9</td>
<td>210.7 ± 38.7</td>
<td></td>
</tr>
<tr>
<td>Microcirculatory Flux</td>
<td>41% increase</td>
<td></td>
<td>73% increase</td>
<td></td>
</tr>
</tbody>
</table>

Key Learning Points: Marked increase in flux due to plaster cast could be due to artifact with instrument or increased skin temperature. The third possibility (which is supported by short stretch compression literature) is that the rigid shell of the cast with fixed volume and cross-sectional areas (CSA) provides resistance and increases the strength of the calf muscle pump mechanism in response to the geko™ stimulation. Muscle contractions cause an increase in CSA of the muscle, and if the overall CSA of the leg is constrained, the CSA area of the vein or other fluid reservoirs (e.g. oedema) must evacuate to accommodate this.
3-2s. The geko™ Device Reduces Venous Blood Sludging


**Methods:** The aim was to determine whether the Common Peroneal Nerve Stimulation (CPNS) geko™ T-2 (27mA) device reduces stasis using the ultrasound derived venous sludge index (VSI). Twenty-five healthy volunteers had their right popliteal vein video recorded (B-mode ultrasound at 22 frames per second) in longitudinal and transverse views, standing and lying. First with the CPNS off and then with the CPNS on. A single frame out of the possible 154 frames (7 seconds) was selected at random, for the image analysis. The VSI, a grey scale index (0-255), was used to quantify the 'brightness' of the erythrocyte aggregates within the circular sampling area.

**Results:** Before the device was activated, they found a much higher VSI when the volunteers were standing, versus laying, with both views. When off, the Venous Sludge Index (VSI) was 53.5, when activated, the geko™ stimulation reduced the VSI to 7.6 in both positions and both views, which was highly significant (p=0.0005).

**Paper:** Activation of the CPNS significantly reduced all the VSI values (P < .0005) shown (longitudinal view, 2 [1.1-3.2] and 1.5 [0.5-3.1]; transverse view, 1.1 [0.6-2.7] and 0.8 [0.5-2.1]).

**Key Learning Points:** The CPNS device significantly reduces the Venous Sludge Index irrespective of whether the subject is standing or lying down. The principal mode of action of the device in the claim that it may reduce venous thromboembolism risk may be through a reduction of venous sludge. The relationship between erythrocyte aggregation, stasis and VTE risk requires more investigation.

3-2t. geko™ effect on Ambulatory Venous Pressure (AVP), Calf Venous transit time (VTT) and leg volumes


**Methods:** The geko™ device was applied over the upper lateral calf just below the knee in 19 healthy volunteers. Three power settings with pulse widths of 100, 200 and 400µs were compared with no device. Calf venous transit time (VTT) in seconds was measured using duplex to detect the time between injecting contrast into a dorsal foot vein and the arrival in the popliteal vein, standing, sitting and lying. Ambulatory venous pressure (AVP) and leg volumes were also recorded.

**Results:** The results with geko™ were statistically significant with the device at all three settings, and in all three positions. The geko™ device reduced the VTT (increased rate of blood flow) most in the laying position, where there would be no obstruction due to the knee being bent, and with the output of 400 µs. The ambulatory venous pressure and the leg volume also reduced, caused by the augmentation of the calf muscle pump function reducing venous refilling and venous volume, both implicated in venous stasis.

**Table of Results:**

<table>
<thead>
<tr>
<th>Mean Venous Transit Time (VTT) from dorsal foot to Popliteal Vein</th>
<th>Baseline No Device</th>
<th>geko™ @100 µs</th>
<th>geko™ @200 µs</th>
<th>geko™ @400 µs</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTT Patient Standing</td>
<td>37 ± 3.0</td>
<td>31.3 ± 3.8 (15% reduction)</td>
<td>25.2 ± 4.0 (31% reduction)</td>
<td>19.8 ± 3.6 (46% reduction)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>VTT Patient Sitting</td>
<td>35.0 ± 2.8</td>
<td>27.6 ± 3.5 (21% reduction)</td>
<td>22.2 ± 4.1 (36% reduction)</td>
<td>16.3 ± 3.6 (53% reduction)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>VTT Patient Lying (Supine)</td>
<td>31.4 ± 2.4</td>
<td>21.3 ± 3.3 (32% reduction)</td>
<td>15.7 ± 3.1 (50% reduction)</td>
<td>11.3 ± 2.6 (64% reduction)</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

Compression stockings of wounds involving the achilles tendon area.

Key Learning Points:
The present study provides a detailed study of venous physiology utilizing venous transit time, volumetry and ambulatory venous pressure. Neuromuscular electrostimulation independently enhances venous flow by augmenting calf muscle pump function resulting in reduced venous refilling and venous volume.

Reviewer’s comments: The T-1 was used in many of the early evaluations and has the capability to provide the following pulse widths or settings: 50, 70, 100, 140, 200, 280, 400 and 560μs. The poster does not specify how much contraction was seen with each pulse width setting, or which device was being used. Without knowing how much of a response the individuals had with each setting, it is difficult to reproduce the benefit found at 400 μs. The common peroneal nerve moves away from the fibular head by up to 18 mm when the leg is fully extended, so there tends to be less of a “twitch” seen, therefore thought to be less than therapeutic. Some patients will have a therapeutic twitch with a setting of 1 (50 μs), while others have no twitch at 8 (560 μs).

Key Learning Points: Wounds to the achilles tendon are traditionally extremely difficult to heal due to the mobility of the tendon and poor vascular response. The pain associated with wounds in this area is usually very high. With this supporting evidence; it seems appropriate to utilize the geko™ device to promote healing not only of sports injuries, but of wounds involving the achilles tendon area.


Background: Improving training and injury recovery is important in reducing disruption to athletic performance. Neuromuscular stimulation and acupuncture are both used by athletes for this purpose with benefits possibly attributed to increased blood flow. The geko™ T-1 (27mA) device, a neuromuscular stimulator, and UB-40 acupuncture are applied at the popliteal fossa and may increase lower limb blood flow.

Objectives: Ascertain and compare short-term lower limb blood flow changes during either ipsilateral neuromuscular stimulation with the geko™ or UB-40 acupuncture, in healthy subjects. Ipsilateral and contralateral legs are also to be compared. In addition, thermography, discomfort questionnaires and safety measures will be assessed.

Results: There were significant differences between the interventions (p≤0.01). The geko™ increased microcirculatory velocity by 306% in the ipsilateral Achilles peritendinous space whereas UB-40 acupuncture decreased microcirculatory volume by 36% in the ipsilateral toe pulp (p≤0.05). During geko™ the ipsilateral knee temperature increased (p≤0.05), contralateral knee and ipsilateral Achilles remained constant (p≥0.05) and both calves and contralateral ankle decreased (p≤0.05). Throughout acupuncture temperature remained constant bilaterally at all sites (p≥0.05). Discomfort data revealed no difference between the interventions (p≥0.05), rated minimal sensation/mild discomfort. No changes were detected in safety measures (p≥0.05).

Conclusion: The gekoTM considerably increased peritendinous microcirculatory velocity, which could benefit injury healing and training recovery, without significantly increasing calf muscle metabolic activity. Acupuncture at UB-40 decreased microcirculatory volume and maintained a stable temperature bilaterally. Strong evidence for the clinical use of UB-40 is still lacking. Future studies should employ larger samples sizes and use patients with pathologies.

Key Learning Points: Wounds to the achilles tendon are traditionally extremely difficult to heal due to the mobility of the tendon and poor vascular response. The pain associated with wounds in this area is usually very high. With this supporting evidence; it seems appropriate to utilize the geko™ device to promote healing not only of sports injuries, but of wounds involving the achilles tendon area.

https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf Other leg volume results from this thesis are reported in 3-2i.

**Purpose:** Neuromuscular stimulation has part of its haemodynamic effect through activation of the muscle pumps of the leg. Bench testing was performed to see if the application of compression hosiery might enhance the effect of NMES on blood flow in the lower limb.

**Methods:** 5 subjects were seated on a chair, with feet resting on the floor. Laser doppler fluximetry probes were attached to the dorsum of the left and right feet. A below-knee grade 2 graduated compression stocking (Medi, UK) (22mmHg compression) was placed on the left leg, non-compressive hosiery for warmth placed on the right. (Geko™ devices) were placed bilaterally over the common peroneal nerve according to manufacturer’s instructions. Stimulation levels used were titrated to give a definite dorsiflexion movement of the foot, whilst still ensuring comfort. Hemodynamic ultrasound measurements were taken from common femoral artery and femoral vein, and marked on the skin for repeat measurement. Baseline values were recorded after 15 minutes relaxation. Stimulation values were recorded 10 minutes after initiation of stimulation, with devices on. After 10 minutes stimulation with the NMES devices, the compression and non-compression hosiery were swapped, with devices left on. Stimulation values were compared to baseline.

**Results:** The geko™ device significantly increased arterial PV, TAMV and volume flow. The addition of grade 2 graduated compression stockings increased mean values for TAMV, and doubled volume flow compared to no compression, but did not reach statistical significance. Use of the NMES device caused mean increases in venous parameters, but did not reach statistical significance. The addition of compression hosiery reduced recorded peak velocity values compared to baseline, and percentage changes with compression were significantly more negative than without compression. Laser doppler fluximetry measurements taken from the dorsum of the foot were increased with compression (59% versus 297%). This could represent changes in the effective capacity of the arterioles, capillaries and venules; either through reflexive or neuroendocrine vasodilatation, pressure dilatation, or recruitment of more numbers of open vessels.

**Limitations:** A small study of five subjects is prone to type 2 statistical error (failure to reject the null hypothesis).

**Conclusions:** There may be changes to the microvascular system in the presence of compression. Venous ulcers are often managed with dressings and four-layer compression. There is the possibility that the use of NMES in conjunction with four-layer bandaging may enhance the blood supply to the skin of the foot, and by inference improve ulcer healing rates.

**Possible application to practice regarding use with compression bandaging:** Graduated compression stockings are recommended for prevention of Venous Ulcers and to manage chronic venous insufficiency. The theory is that graduated compression stockings are elastic in nature and will stretch with calf-muscle pump contraction. In contrast, multilayer and short stretch bandaging systems are resistant, and are described by the degree of stiffness. Multilayer systems containing one layer of elastic bandaging are more effective in treating venous leg ulcers. A high stiffness compression system causes fluctuations in the lower leg during walking compared to a low stiffness or elastic system, producing the greatest improvements in venous blood flow, e.g. in ejection volume and ejection fraction, from the lower leg. A similar study would be helpful in demonstrating what happens with patients with venous disease using the geko™ devices in combination with a multilayer bandaging system containing both elastic and inelastic components. At this time we consider the geko™ device to be an adjunctive therapy combined with a compression system.


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**3-3. The geko™ device and DVT/VTE Prophylaxis**


**Recommendation:** The case for adopting the geko™ device is supported for use in people who have a high risk of venous thromboembolism and for whom other mechanical and pharmacological methods of prophylaxis are impractical or contraindicated. Although clinical evidence is limited, the case is supported because of the plausibility that the geko device may reduce the high risk of venous thromboembolism in patients who cannot use other forms of prophylaxis, and the low risk of the device causing harm.
3-3b. Paper: Implementing the NICE guidance on the geko™ device for reducing the risk of venous thromboembolism (MTG19) [https://www.nice.org.uk/guidance/mtg19/resources/costing-statement-pdf-10461277]. The technology is recommended for patients at high risk of venous thromboembolism for whom pharmacological and mechanical prophylaxis treatment options are contraindicated. This is currently an unmet need. Venous thromboembolism – reducing the risk (NICE clinical guideline 92) recommends that patients assessed as having risk factors for bleeding should not be offered pharmacological prophylaxis, unless the risk of VTE outweighs the risk of bleeding. For a small investment in the device, savings may result from reduced rates of venous thromboembolism. Savings are anticipated for providers in secondary care as a result of lower treatment costs, and decreased bed days.


**Study characteristics and key results**

Eight studies (current until 22March 2017) enrolling a total of 904 participants that compared NMES with no treatment or with other methods for preventing blood clots, such as low-dose heparin and compression stockings. They found no clear difference in the risk of unwanted blood clots in the legs between NMES and alternative methods of blood clot prevention. They also found that NMES is associated with lower risk of formation of unwanted blood clots in the legs when compared with no treatment, but higher risk of unwanted blood clot formation when compared with heparin. Additional studies are required to obtain stronger evidence.

**Quality of the evidence**

Overall, the quality of available evidence is low and has been downgraded owing to high or unclear risk of bias, differences between studies, and imprecise effect estimates due to small numbers of studies and events.

**Authors’ conclusions**

Low-quality evidence shows no clear difference in the risk of DVT between NMES and alternative methods of prophylaxis but suggest that NMES may be associated with lower risk of DVT compared with no prophylaxis (moderate-quality evidence) and higher risk of DVT compared with low-dose heparin (low-quality evidence). The best available evidence about the effectiveness of NMES in the prevention of VTE is not adequately robust to allow definitive conclusions. Adequately powered high-quality randomised controlled trials are required to provide adequately robust evidence.


**Purpose:** To observe the clinical efficacy of GEKO Neuromuscular Electrical Stimulation (NMES) in the prevention of deep venous thrombosis (DVT) after Total Hip Arthroplasty (THA).

**Methods:** Standardized THA was the operative treatment of 72 cases of femoral head necrosis from 01-2016 to 08-2016, which were assigned to the observation group (basic prevention method plus NMES) and the control group (basic prevention method). NMES (the authors did not describe which device was utilized) was employed immediately for 24 hours/time x 3 days post-operatively. Low-intensity stimulation was advocated in early stages, then the stimulation could be gradually enhanced. DVT preventative exercises as well as instruction in rehabilitation exercises including early stage muscle relaxation and contraction, active joint movement and massage were provided to both groups. Post-operative negative pressure drainage was observed for 24 hours, with VAS scoring at day 3 post-operatively, and plasma D-dimer content measurement at day 3 pre-operatively and post-operatively. Plasma D-dime is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. Colour Doppler ultrasound DVT screening and examination were performed prior to and after the operation.

**Results:** There was no statistically significant difference (P=0.05) between the two groups in post-operative negative pressure drainage. The observation (NMES) group was superior to the control group in terms of post-operative VAS score (P=0.001), DVT incidence rate (P=0.047) and 3 days post-surgery Plasma D-dimer content (P<0.05). The differences were statistically significant (P<0.05), and no apparent adverse reactions were found in the observation group.

**Conclusions:** Application of NMES in early recovery of patients after THA could increase the lower limb venous blood flow rate and alleviate pain, serving as an effective physical therapy in the prevention of DVT.

**Key Learning Points:** Most patients reported that they were able to sleep with the device activated, and there was a statistically significant reduction in pain. The authors did not comment on a reduction in the need for narcotic analgesia.
and subsequent side-effects, or any differences in post-operative mobility. These would be important secondary outcomes in additional studies.


**Background and Aims**: Venous thromboembolism (VTE) is a common and potentially fatal complication of acute stroke. The UK National Clinical Guidelines for Stroke1 recommend intermittent pneumatic compression (IPC) as the primary method of VTE prevention after acute stroke, as the risk of symptomatic intracerebral haemorrhage outweighs the benefit from VTE prevention with routine anticoagulation with low dose heparin (including low molecular weight heparin) after stroke. Venous Thrombo Embolism (VTE) prophylaxis using Intermittent Pneumatic Compression devices (IPC) is not possible in all stroke patients. The post-stroke pathway in the Acute Stroke Unit, Stoke on Trent, United Kingdom was changed to include the geko™ device (model of device not stipulated) as an alternative to IPC for patients with acute stroke who had contradictions/not tolerate IPC. This audit was completed to assess the acceptability of this new practice for patients and staff and its impact on VTE.

**Method**: The audit included 455 patients admitted to the Acute Stroke Unit at Royal Stoke University Hospital (RSUH). All stroke patients who are immobile are given VTE prophylaxis, unless they are palliative, refusing the intervention, or fully anticoagulated. Every patient is reviewed daily on a nurse-led VTE ward round to monitor compliance with VTE prophylaxis.

**Results**: In total 6/455 (1.3%) patients developed symptomatic VTE (3 DVTs and 3 PEs) within 90 days. Of these, 4 patients (1.6%) were prescribed IPC, 1 patient (1.3%) was prescribed the gekoTM device as a secondary intervention and 1 patient (1.5%) patient was prescribed anticoagulation. There was no DVT or PE in patients treated with the gekoTM device as the primary VTE prophylaxis.

**Conclusion**: This audit shows a low incidence (1.3%) of symptomatic VTE in a high-risk population of all immobile stroke patients during the audit period. The number of patients who were contraindicated to IPC or did not tolerate IPC and were treated with the geko™ device in this project was 35.6%. Whilst limited, our data suggests that the gekoTM device may be as effective as IPC in our patient cohort.

**Key Learning Points**: Patients suffering from stroke where anticoagulant therapy is contraindicated due to risk of cerebral hemorrhage, or whom cannot have or tolerate IPC may benefit from the geko™ as part of the standard of care. A recent paper by Kim et al. (2018) found that 74-76% of patients for whom IPC was ordered for DVT prophylaxis did not receive it correctly. Use of the geko™ device may be more acceptable, and easier to administer. Further research is warranted.


**Purpose**: The aim was to quantify the claim in the NICE medical Guidance 19 document that the geko™ device “drives the venous muscle pump and imitates walking.” The NICE Guidance statement in full is: “The muscular action drives the venous muscle pump of the lower leg, facilitating the emptying of veins and increasing the return of blood to the heart. This is designed to imitate the process normally achieved by walking, without the person having to move” (page 4, 2.2).

**Method**: Twelve healthy volunteers performed 10 tip-toe maneuvers and 10 ankle dorsiflexions to imitate walking movements. The reductions in calf volume were recorded using air plethysmography (APG). The common peroneal nerve was stimulated for over 10 seconds at each of the 7 increasing electrical impulse settings (with the geko™ T-1 or T-2 device), and the volume reductions were measured for comparison. The results are expressed as median (interquartile range) absolute (ml), and percentage reduction in calf volume.

**Results**: Tip-toe and dorsiflexion pumping maneuvers were not significantly different: 59 (33.6-96.1), 81.9% vs 51.4 (34-68.5), 59.7%, respectively (P ¼ .53). However, they both outperformed the CPNS: 10.8 (7.3-18), 13.2% at P ¼ .002 and P ¼ .002, respectively. Qualitatively, the CPNS registered on the tracings as a small spike (muscle twitch) at low settings, with
larger amplitudes (ankle jerk) at higher settings. The CPNS activity spikes were discrete, lasting a median (range) of 0.24 (0.16- .3) seconds. The claim that the CPNS empties veins by pumping is supported by statistical tests which demonstrated the same significance (p=0.002) as the tip-toe and dorsiflexion maneuvers versus stationary standing. However, the amount was small with the CPNS (geko™).

Comments regarding methodology: Although the authors state that the placement of the geko™ device was positioned as recommended by the manufacturer across the common peroneal nerve, the photograph on page 447 shows the line of arrows that should be on the fibular head as being far posterior to it. This means that the device could not elicit the intended response. The recommended recovery period between each of the 11 serial controlled variable conditions (i.e. baseline, standing, tip-toes, dorsiflexions, and 7 successive settings of geko™) were omitted. The manufacturer of the Air Plethysmography system [http://acmedical.com/wp-content/uploads/2017/08/APG-advanced-course-v2.pdf] (page 5, para 3) states that to prevent exercise-induced hyperemia and engorgement of the muscles (seen in serial tests,) ensure a return to resting levels (below 2 ml/sec) prior to doing additional VFI tests, which could take 15 minutes or more. This means that in the later geko™ tests, the baseline working venous volume would be much higher than the original fill level at the beginning of the testing, so any comparison is biased in favour of the earlier tests. The authors also prematurely establish working venous volume as a reference, whereas it continues to creep up substantially throughout the study (most likely because of the exercise hyperaemia resulting from multiple activations. Again, this favours earlier tests over later tests with geko™.

3-4. The geko™ Device and Oedema Reduction

Please also see paper 3-1b for the hypothetical correlation of geko™ effect on microcirculation and oedema.

3-4a. Post-operative oedema kidney and pancreas transplant


Background: Kidney and pancreas transplant recipients undergo significant fluid shifts in the post-operative period leading to significant lower limb oedema. Intermittent compression (IPC) devices are used to reverse the oedema, however many factors may limit the use of IPC units.

Methods: prospective, randomized, controlled study where 93 patients were randomly assigned to wear IPC (Group 1, n= 50) or the geko™ device (Group 2, n=43) post-operatively until day 6 after surgery. Ultrasound Doppler of the allograft and of the lower limbs was carried out on post-operative days 1 and 5 to assess venous flow velocity in the femoral vein in addition to monitoring total urine output, serum creatinine levels, patient weight and lower leg and thigh circumferences daily, and patient satisfaction on days 3 and 6 post-op.

Table of Results:

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Group 1 IPC</th>
<th>Group 2 geko™</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in calf circumference from baseline</td>
<td>+7.5% (2.3 ± -2 cm)</td>
<td>No change 0.34% (0.05 ± -0.95 cm)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Increase in thigh circumference from baseline</td>
<td>+6% 2.4 ± -2 cm</td>
<td>No change</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Increase in mean flow velocity</td>
<td>12 cm/sec</td>
<td>21 cm/sec</td>
<td>p&lt;0.0005</td>
</tr>
<tr>
<td>Total Urine output in 6 days</td>
<td>8,800 cc's</td>
<td>17,900 cc’s</td>
<td>P= 0.003</td>
</tr>
<tr>
<td>Serum Creatinine</td>
<td>No differences</td>
<td>No differences</td>
<td>-</td>
</tr>
<tr>
<td>Patient Satisfaction</td>
<td>Less satisfied</td>
<td>More satisfied</td>
<td>-</td>
</tr>
</tbody>
</table>

The MPA device improved blood flow to the renal allograft with higher peak systolic velocity in the renal arcuate artery (p=0.001) and higher femoral vein velocity (p=0.001). This corresponded to significantly higher urine output in the MPA group (p=0.003).

Key Learning Points: Patients were more satisfied with the use of Geko Plus device than TED+IPC, and had an improved rate of oedema reduction with the geko™ device. There were no complications as a result of the study in either group.

Update January 2019: In this single center, prospective, randomized-controlled trial, 221 kidney or SPK transplant recipients (Donation after Neurological Death=109, Living Donor=52, Donation after Cardiac Death=60) were randomized as above to either wearing TED/IPC or MPAs for 7 days post-operatively. Post-operative care and discharge planning was performed by an independent nephrology team. Groups were compared with respect to days in hospital,
post-operative lower limb edema, weight, mobility, urine output, serum creatinine, delayed graft function (DGF), need for dialysis, renal blood flow and incisional wound healing.

**Results:** have been analyzed and manuscripts submitted for publishing. Once full results have been presented at conferences or published, this information can be added to this document.

3-4b. Chronic Oedema


**Methods:** the geko™ devices were offered to two patients with leg oedema that was not responding to other treatments.

Case 1: CAD, 2 previous MIs, congestive heart failure, bilateral disabling lower-extremity oedema and a right ankle ulcer for >1 year; cellulitis present on the right foot, extending to above the ankle; multiple varicosities and skin changes consistent with CVI and chronic lymphoedema in both feet. Her arterial circulation demonstrated weakly palpable lower-extremity pulses and ABPIs mildly reduced. Duplex ultrasound showed deep venous reflux but no superficial venous insufficiency. Compression wrappings, exercise, and leg elevation did not effectively improve her pain or ulceration over the past year.

Case 2: complex left leg swelling and pain; Charcot left foot deformity, foot ulcers, and peripheral neuropathy secondary to diabetes Mellitus, previous right below-knee amputation secondary to complications of DFU; lower-extremity oedema r/t significant cardiac history, renal failure, CVI and liver cirrhosis; 1-month history of left lower leg oedema below the knee and no longer able to fit into his left leg brace and orthotic boot: developed significant pain that limited his ability to ambulate and elevate his leg for prolonged periods. The swelling in his left lower leg was maximal in the ankle and foot.

**Results:** 2 cases of multifactorial and refractory leg oedema successfully reduced by 7 and 21% with the geko™ device over a period of 4 to 16 weeks.

**Key Learning Points:** In addition to helping resolve the multifactorial and refractory leg oedema, the geko™ device also appears to have improved pain and chronic wound healing; both patients were able to resume leg elevation and exercise regimes, and in case 2, return to use of brace and orthotic boot for left leg/foot.

3-4c. Occupational leg oedema


**Method:** 10 subjects (10 legs) were recruited from a clinical workspace, with no history of vascular disease. The right leg volume and great saphenous vein (GSV) diameter at the knee was measured in the morning, six hours later scans were repeated. On subsequent separate days, Grade 2 graduated compression stockings (GCS; medi, UK) for 6 hours, peroneal nerve neuromuscular stimulation (NMES 1) device geko™ T-1 (Firstkind, UK) for 4 hours, and footplate NMES 2 device RevitiveTM (Actegy, UK) for 30 minutes were used bilaterally according to manufacturer’s instructions. With the stockings and geko™ the person could be fully mobile, with the footplate they had to be stationary for

**Results:** On the first day, leg volumes increased over 6 hours by median 41ml (IQR 7.7-74.0, p<0.05) with no intervention. Percentage increase in leg volume was found to be significantly reduced by GCS compared to control (-0.52ml, p<0.01). Although NMES devices did reduce leg volumes compared to control, they were not as effective as GCS and did not reach statistical significance. Percentage changes in GSV diameter poorly correlated with percentage changes in volume.
Key Learning Points: Occupational oedema can occur in as little as 6 hours in an office environment. In this small pilot study, all devices were well tolerated and reduced leg swelling, but GCS were the only device to statistically reduce leg swelling. Lyons et al. (2002) found that the effect of NMES is augmented by a factor of 2 when used in conjunction with GCS. Further studies evaluating NMES devices with and without compression are needed to better understand the role with compression versus without compression.

3-4d-g. Orthopedic edema


Aim: The aim of this feasibility study was to investigate the potential role of a novel neuromuscular electrical stimulation (NMES) device in preventing the formation of oedema following total hip replacement (THR).

Methods: Successive primary THR patients were recruited into a randomised controlled trial to wear either the NMES (geko™ device [model not stipulated] or Thrombo Embolitic Deterrent stockings (TEDS) continually from post-surgery until discharge. They were used continually on bilateral legs post-surgery until discharge. The main outcome measure was presence of lower limb oedema, assessed by taking measurements of the circumference of the ankle, knee and thigh on the operated leg and non-operated leg, pre-operatively, post-operatively, at two days postoperatively and every day until discharge. Secondary objectives were to compare adverse events, the presence of asymptomatic and symptomatic deep vein thrombosis (DVT) and device tolerability between groups. Analysis was done by considering the leg to be a stack of two truncated conical segments (ankle to knee is one conical segment, and knee to thigh second conical segment), and assuming knee location is half-way between ankle and thigh, the volume of each conical segment was calculated.

Results: Data from 40 participants were analysed (NMES (n= 20), compression stockings (n=20)). The NMES group had significantly less oedema in the operative and non-operative limbs, and the device was found to be tolerable and safe. Although the ankle measurements increased post-operatively in the operative leg in both groups, the increase was smaller in the NMES group, but this was not statistically significant (p = 0.27). In the knee of the operated limb, there was a decrease in size for the NMES group, which alone was not significant. However, when compared to the increase in size for the compression stockings group, it was significant (p = 0.02). Similarly, in the thigh of the affected limb, the NMES group also had a non-significant decrease in size over pre-op, which became significant when compared to the increase in size experienced by the stockings group (p = 0.02). In calculations of volume, the TED group had ~ 3 times the volume increase post-operatively compared to geko™ (p=0.03). Of interest, in the unoperated limb, the change in limb volume for the TEDS group from pre-op to discharge was also ~ 3 times the volume of the geko™ group.

Conclusion: The results of this study suggest that the NMES is a safe and well tolerated alternative to compression stockings, which should be considered by clinicians seeking the additional benefit of reducing post-operative oedema. In addition, the NMES device should be considered as part of a DVT prophylaxis.
Key Learning Points: The geko™ device has been shown to be significantly effective in managing post-operative oedema in the knee and the thigh in the operative limb following Total Hip Arthroplasty compared to use of TED stockings, also benefiting the non-operative limb by reducing limb volume. There may also be a benefit with the geko™ device in reducing the risk of pressure injuries in this population, where edema causing a reduction in tissue perfusion plus reduced mobility pose a real threat to tissue integrity.


Methods: 40-year-old female diagnosed with Hallux Valgus and had a right scarf and Akin osteotomy. Device was used for 10 days with daily patient review.

Results: The device was well tolerated and at 4 days post-operatively, swelling reduced significantly and Visual Analogue Scale (VAS) pain scores showed a clinically significant improvement from 8/10 to 1/10, (VAS 1-10: 0-no pain, 10-most pain). First day post-operatively the patient reported 8/10 pain, reducing to 5/10 on the second day post-operatively and 3/10 on the third day post-operatively. Both patient and surgeon reported they thought the device was extremely beneficial.

Key Learning Points: There was no discomfort or adverse effects, no difficulty sleeping with the device switched on and no disturbance with mobility. Treatment with the geko device demonstrated a marked reduction in swelling, following three days of consecutive treatment. There was a decrease in the patient’s pain score using the Visual Analogue Scale.


Background: Ankle swelling can delay surgical fixation (up to 7 days) due to risk associated with operating on swollen tissue, including wound dehiscence (complications) and subsequent infection. “Interventions that would reduce swelling and accelerate surgical fixation could provide significant benefits to patients and healthcare providers.” Due to their unstable nature, ankle fracture patients may require open reduction internal fixation (ORIF). Typically requires up to 7 days of inpatient bed rest and elevation with a:

- Backslab plaster cast
- Backslab plaster cast + external fixation
- Backslab plaster cast + intermittent pneumatic compression.

“Sitting in a hospital bed for a week can be very frustrating and can also cause people to lose muscle mass.”

Intervention: A prospective & retrospective study investigated the use of geko™ to reduce pre-operative edema in uni-, bi- and tri-malleolar fractures. Recruited ankle fracture patients requiring surgical fixation, Fitted the geko™ device (model not stipulated) above their backslab plaster casts. Compared the results to the current standard of care, Recorded patient compliance and readiness to theatre, matched to a historical cohort for comparison.

Results: 20 patients. 2 pre-operative bed days saved on average per patient.

- 60% of patients ready for theatre in 2 days, compared to 27% in control arm, a 122% improvement.
- Current treatment = 3.66 days readiness to theatre (average).
- The geko™ device + plaster cast = 1.66 days readiness to theatre (average) (P=0.001)
- The geko™ device was well tolerated and easy to use; patients were more mobile and able to get out of bed compared to the ICP patients

Plan: the geko™ device will be their standard therapy pre-op for one year; then do further analysis.

Next Study: Hospital is looking to secure funding for another study investigating the potential for treating those with stable ankle fractures as outpatients.
3-5. The geko™ Device and Systemic Responses


Method: Twenty-five professional rugby players were assigned to 1 of 2 treatments (compression garment or a concurrent combination of electrostimulation and compression) in a crossover design over 2 × 2-wk training blocks. Each player self-selected a pulse width that was tolerable and produced visible ankle dorsiflexion and plantar flexion, which is considered to be a therapeutic response.

Results: On average, treatment duration was 11.3 ± 1.9 hours for compression and 8.4 ± 3.4 hours for the combined treatments. The combined treatment resulted in substantial benefits in self-assessed energy levels (effect size [ES] 0.86), and enthusiasm (ES 0.80) when compared with compression-garment use alone. No significant differences in salivary hormones (testosterone and cortisol) were observed between the treatments. The electrostimulation device did tend to accelerate the return of creatine kinase (CK) to baseline levels after 2 preseason rugby games when compared with the compression-garment intervention but was not statistically significant (ES 0.61; P = .08).

Key Learning Points: The combined use of an electrical stimulation device with compression garments was more effective at eliciting positive responses in self-reported energy and enthusiasm, and reduced CK levels, than the use of a compression garment alone after rugby matches. Increased CK levels are considered markers of muscle damage, so an accelerated return to baseline suggests a faster muscle recovery period.


Paper: Williams KJ, Davies AH. Pilot trial of neuromuscular stimulation in the management of chronic venous disease. VSGBI Abstracts from The Vascular Societies' Annual Scientific Meeting. British Journal of Surgery. 2015;102():20. Other results for this paper are found in: Hemodynamic results of this study testing for geko™ effect in people with Chronic Venous Insufficiency (CVI) (3-2i-j.) for QoL results and 3-8a. for tolerance to the device.

Methods: 30 subjects with venous disease and 10 healthy controls were recruited. Bilateral geko™ devices (T1, FirstKindLtd, UK) were applied to the common peroneal nerve, at a pulse width to achieve dorsiflexion of the foot (1Hz, 27mA). Laser doppler fluximetry (non-invasive measurement of microcirculation) was measured from the left hand and foot.

Table of Results: Change in Laser Doppler Fluximetry Reading with bilateral geko™ devices

<table>
<thead>
<tr>
<th>Percentage Change</th>
<th>Healthy</th>
<th>Superficial CVI</th>
<th>Deep Insufficiency</th>
<th>Deep Obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Leg Flux</td>
<td>275**</td>
<td>265*</td>
<td>69</td>
<td>47*</td>
</tr>
<tr>
<td>Left Hand Flux</td>
<td>84**</td>
<td>71*</td>
<td>24</td>
<td>107*</td>
</tr>
</tbody>
</table>

*P<0.05, ** p<0.01 single t-test

Key Learning Points:
NMES with the geko™ device to both legs improves blood supply to the skin of the foot, and has a systemic effect as evidenced by a statistically significant change to the fluximetry readings to the left hand and patients with superficial CVI and CVI with deep obstruction. There is no explanation as to why those with deep insufficiency did not also show a statistically significant improvement.

3-5c. Effect of geko™ and Coronary Blood Flow / Ejection Fraction (Also see 3-1b. paper THRIVE study results)

3-5c. Poster Abstract: Lavi S, Alemayehu M, McEllan A, D’Alfonso S. Peripheral Muscle Stimulation Increases Coronary Blood Flow. JACC 2015; 65(10S); A1841. Available at: http://www.onlinejacc.org/content/65/10_Supplement/A1841/F1

Poster available at: https://gekodevices.com/us/clinical-study/paper-2/

Method: Peripheral blood flow studies were measured at baseline and after one hour of exposure to geko™ T-1 device (27mA) with 2D and Doppler derived ultrasound estimation of popliteal artery flow (artery area and velocity). At the
same visit, endothelial function was assessed at baseline and after one hour of geko™ activation, by measuring the peripheral vasodilator response using fingertip pulse amplitude tonometry (PAT).

Coronary flow velocities were measured using a 0.014” Doppler tipped flow wire into the coronary vessel (undiseased vessel and stenosed vessel), recording average peak velocity (APV) at baseline, with geko™ T-1 on low pulse width setting (a visible muscle twitch) x 2 minutes and with geko™ on maximum setting for another 2 minutes (total of 4 minutes with geko™ activated). Sample Size was 10.

**Table of Results (from Paper):**

<table>
<thead>
<tr>
<th>Test</th>
<th>Results with geko™ (Increase)</th>
<th>Summary/ Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Minimal Twitch X 2 minutes</td>
</tr>
<tr>
<td>Coronary Blood Flow-stenosed vessel</td>
<td>Average Peak Velocity (APV)</td>
<td>21.9 ± 12 cm/s</td>
</tr>
<tr>
<td></td>
<td>Coronary Flow Reserve (CFR)</td>
<td>2.2 ± 0.9 cm/s</td>
</tr>
<tr>
<td>Coronary Blood Flow-Control (undiseased vessel)</td>
<td>Average Peak Velocity (APV)</td>
<td>20.3 ± 7.7 cm/s</td>
</tr>
<tr>
<td></td>
<td>Coronary Flow Reserve (CFR)</td>
<td>2.2 ± 0.6 cm/s</td>
</tr>
<tr>
<td>geko™ x 1 hour at Separate Appointment</td>
<td>Rh-PAT* index</td>
<td>2.28 ± 0.39</td>
</tr>
<tr>
<td></td>
<td>Peripheral Blood Flow</td>
<td>Increased in all patients except 1</td>
</tr>
</tbody>
</table>

*Rh-PAT=Reactive hyperemia-peripheral arterial tonometry

**Key Learning Points:** Compared to baseline, there was a significant increase in coronary blood flow as measured by average peak velocity (APV) in the control vessel with nerve stimulation and non-significant increase in the stenotic vessel. Coronary flow reserve did not change significantly.

Endothelial dysfunction continues to emerge as a key causative mechanism in coronary vascular disease. Patients with documented endothelial dysfunction have been demonstrated to have a higher preponderance of adverse cardiovascular events. The effect of geko™ to improve the RH-PAT index, a previously validated method of endothelial function assessment, represents a potential disease modifying mechanism given the association between endothelial dysfunction and adverse clinical outcomes. The effect on endothelial function was beyond an effect on blood pressure that was similar at baseline and following one hour of nerve stimulation. A few minutes of peripheral muscle stimulation may improve coronary blood flow. The effect of longer duration of stimulation on coronary flow and angina should be further studied.

**3-5d. Paper:** Bain DS, Jawad H, Adams K, Mathur A, Johnston A, Tucker AT. Isometric stimulation of lower leg via transdermal electro-stimulation of the common peroneal nerve improves Heart Ejection Fraction in Healthy Volunteers. Unpublished paper courtesy of Firstkind Ltd. William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University, London, UK.

**Aims:** To determine the effects on cardiac function of a device delivering painless neuromuscular stimulation of the lower leg.
**Methods:** Nine Healthy volunteers were given bilateral 3Hz transdermal electrostimulation with a custom-built stimulator (pre-geko™) with two different pulse widths (400µs & Box 2: 600µs) via the common peroneal nerve in the lower leg, causing isometric contractions of muscle structures in the lower leg surrounding the soleus valve pump.

**Results:** Echocardiogram measurements of ejection fraction (EF) using Simpson’s method showed an augmentation of 4.5%, and Left Ventricular Outflow Tract Time Integral (LVOT vti) increased by 6% relative to baseline (p=0.02). In addition, skin blood flow as measured by Laser Doppler Flowmetry (LDF) showed a 14-fold increase (p < 0.0001) relative to baseline.

**Conclusion:** The increase in ejection fraction in healthy volunteers using transdermal electro-stimulation was of a similar level to those achieved by pharmacological interventions used in the treatment of patients with heart failure. Thus, if the increase in cardiac performance seen in the healthy volunteers can be translated to patients with heart failure, isometric neuromuscular stimulation of the lower leg may well have a beneficial role to play in treating heart failure.

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**3-5e. Diabetic Peripheral Neuropathy**


**Methods:** Subjects using the geko™ T-1 (27mA) device were asked to wear the devices for 4 or more hours per day, 5 times a week, and asked to keep a diary of usage. The device was applied bilaterally with the stimulation level set to the minimum level that can achieve outward and upward twitching of the foot when raised from the ground. Subjects allocated to “no device” continued with management regimes as prescribed by their physician. Nerve conduction velocity was measured at baseline and at 10 weeks as well as Haemodynamic ultrasound measurements taken in the femoral vessels (baseline and device on), quality of life questionnaires (PAID, MNSI, NTSS-6, EQ-5D, SF-36), tolerability scores (VAS, VRS), and device usage diary.

**Results:** Small, unequal randomization: 9 individuals to geko™ device; 5 to control (no geko™). 5 subjects (56%) allocated to device were unable to elicit a twitch to stimulation.

**QoL:** Only those in the device group showed a statistically significant decrease in diabetes symptom severity (p<0.05) in 1 disease-specific QoL tool, the “Problem Areas in Diabetes” (PAID) tool. There was no significant change in either the Neuropathy Total Symptom Score-6 (NTSS-6) or the Michigan Neuropathy Screening Instrument (MNSI), or any of the generic quality of life questionnaires after the 10 weeks. Improvement in both groups functional (particularly psychological) scores suggest a confounding Hawthorne effect. Overall, no change in generic quality of life was seen in either group.

**Hemodynamics:** Velocity and volume flow increased with geko™ devices on both legs. Percentage increase from baseline in arterial parameters were comparable to healthy subjects, but venous parameters were much reduced in those with diabetic neuropathy (See Table of results below). This may represent a vastly different baseline (e.g. resting venous tone), or a physiologically different response to stimulation (e.g. differences in arteriovenous sphincter reactivity, or restricted venous inflow through calcified microcirculatory channels).

**Table of results:** Absolute and % Changes from Baseline in Subjects with Diabetic Neuropathy with geko™ T-1 device (adapted from Thesis Table 46 page 315)

<table>
<thead>
<tr>
<th>Parameter Measured in Femoral Vein and Artery</th>
<th>Mean</th>
<th>SD</th>
<th>% change from Baseline (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial Peak Velocity [PV] (cm/s)</td>
<td>11.53</td>
<td>9.2</td>
<td>14.15%</td>
</tr>
<tr>
<td>Arterial Time Averaged Maximum Velocity [TAMV] (cm/s)</td>
<td>2.82</td>
<td>1.9</td>
<td>222.17%</td>
</tr>
<tr>
<td>Arterial Volume Flow [VF] (ml/min)</td>
<td>92.14</td>
<td>74</td>
<td>209.60%</td>
</tr>
<tr>
<td>Venous Peak Velocity [PV] (cm/s)</td>
<td>4.09</td>
<td>9.8</td>
<td>31.19%</td>
</tr>
<tr>
<td>Venous Time Averaged Maximum Velocity [TAMV] (cm/s)</td>
<td>0.63</td>
<td>2.8</td>
<td>15.41%</td>
</tr>
<tr>
<td>Arterial Volume Flow [VF] (ml/min)</td>
<td>36.89</td>
<td>67.4</td>
<td>32.82%</td>
</tr>
</tbody>
</table>

There was a lack of microcirculatory changes with the device (n=6), with Laser doppler fluximetry values in the foot showing a 16% increase, and the hand a 19% increase, neither statistically significant.

**Final Nerve conduction study data missing for 6 of the 14 subjects:** Large mixed nerves and sensory nerves tested: no statistically significant difference in conduction velocities across the protocol in either group.

**Key Learning Points:**

This small study could not demonstrate any physical evidence of improvement of nerve conduction velocity with use of the geko™ device, yet we continue to hear from our patients that their neuropathic symptoms are diminished when
using the geko™ device, and their ability to feel normal touch returns. Further research using validated tools and nerve conduction studies is needed if we are to understand the effect of geko™ on Neuropathic Pain.

3-6. The geko™ Device and Wound Healing


Methods: Three cases include the management of recalcitrant ulcers, non-reconstructible critical limb ischemia, and an infected arterial bypass graft. Case 1: unilateral device to affected leg 24 hours per day x 14 days; had to stop due to rash under device. Case 2: unilateral device to remaining limb, wore it for 6–10 hours per day for six weeks. Case 3: devices were applied bilaterally and activated continuously for two weeks.

Results: Although no patients wore devices complete to healing, improvement in various dimensions were reported; improved wound appearance, decreased wound depth and a reduction in surface area of 71% in Case 1, with complete healing after 4 more weeks; Case 2 had a slight reduction in leg volume (3.4%), had improvement in 2/3 Quality of Life surveys, had increased motivation to leave the house in his wheelchair; Case 3 had reduction in oedema while device was used, healing of wounds at 6 weeks.

Key Learning Points: Neuromuscular electrical stimulation (NMES) can potentially enhance peripheral circulation in vascular patients. Difficult or recalcitrant vascular cases may benefit from it as an adjunct to best medical care. NMES has few side effects and may be especially useful where polypharmacy is an issue. The incidence of a skin reaction may necessitate device discontinuation.


Methods: Clinically challenging and complex VLU patients whose wounds had failed to heal within 24 weeks of standard therapy consented to evaluate the geko™ device as an adjunct to standard of care, in 2 Community Access Centres in Ontario, Canada. The geko™ T-2 (27 mA) devices were applied to both legs for 6 hours per day 5 days per week, during a period where the patient could be sitting some of the time in order to get the largest therapeutic response to the stimulation. During the course of the evaluation, the devices were replaced by the new generation, higher powered R-2 (54mA) devices.

Results: Eleven patients consented to the evaluation with a combined 107-year history of recalcitrant, leg ulcers. Although the pre-geko™ healing rate was unknown, all were considered non-healing. The average weekly % change in surface area (SA) for the 28 measured wounds was a 4.5% reduction (range of -3% to 40%). Two circumferential leg wounds in one patient were never measured. Six patients (54%) with 16 wounds were adherent to geko™ and best practice wound care had a 7% reduction in SA per week. In retrospect, one patient who was adherent to care was likely not healable, having been offered amputation prior to the evaluation. By removing her data, the average weekly percentage change for adherent, healable patients was 7.6% (reduction). By comparison, the average weekly percentage change for wounds in the 5 (46%) non-adherent patients with 12 measurable wounds was 1.82% (reduction). Four of the five were withdrawn from the evaluation, and returned to previous standard of care.

Key Learning Points: Provisos for success appear to include an arterial status adequate for healing, effective and prompt management of wound infections and that the patient is adherent with the treatment schedule. Importantly, patients or family members quickly mastered use of the device.

3-6c. Poster Evaluation of an Exciting Neuromuscular Electrical Stimulation Device for Non-Healing Venous Leg Ulcers. May 2017 Wounds Canada Conference: (same authors as paper below)


Methods: Twelve patients with eighteen VLUs recalcitrant to treatment, cared for in in two Community Care Access Centres in Ontario, consented to evaluate the geko™ R-2 (54mA) device, in order to determine whether it was effective for this population and should be added to the medical supplies and equipment formulary. They were followed for up to 20 weeks, until the wounds healed, they chose to discontinue the device, or the evaluation finished. Three patients
continued with the device past the 20 weeks. The geko™ devices were to be applied to both legs for 6 hours per day 5 days per week, during a period where the patient could be sitting some of the time in order to get the largest therapeutic response to the stimulation.

**Results:** Forty-four percent of the wounds healed, 39% decreased in surface area. One patient who was non-adherent with geko™ and best practices had wound deterioration in their three wounds. The average weekly wound healing rate at baseline, prior to the geko™ evaluation was 0.06%(±SD 0.10); with the device, it increased to 9.35% (±SD 0.10) P <0.01. Three patients who were not in optimal compression at baseline could start or increase the existing levels of compression therapy due to decreased pain, further enabling healing (compression therapy being the key intervention in treating VLUS).

**Key Learning Points:** This evaluation provided an opportunity to evaluate the effectiveness of the geko™ device on the hard-to-heal venous leg ulcer population. The weekly healing rate with geko™ was 9.35% (±SD 0.10) compared to 0.06% (±SD 0.10) before using geko, this result is highly significant with a P-value of <0.01.


**Paper:** Harris C, Ramage D, Boloorchi A, Vaughan L, Kuider G, Rakas S. Using a muscle pump activator device to stimulate healing for non-healing lower leg wounds in long term care residents. IWJ 2019;16(1):266-274.


**Aim:** The objective of this Long-Term Care (LTC) Innovation pilot was to test the value of a promising new neuromuscular stimulation device in elevating the experience and satisfaction of the residents; engaging and empowering the nursing staff; and improving healing and/or reducing costs.

**Methods:** Nurses in four LTC homes identified residents with non-healing lower leg wounds. Consent was obtained, and on-site training was delivered in use of the geko™ R-2 (54mA) devices.

**Results:** In the sector, eleven residents in 4 long term care homes in Ontario and Manitoba were evaluated with the geko™ device in 2016. Three residents had Diabetic Foot Ulcers (DFU), 3 had Venous Leg Ulcers (VLU) with lower leg oedema, and 2 had pressure ulcers on the heel of the foot. 2 wounds were thought to be venous by staff but had atypical wound appearances; one with a suspicious dense granular surface and one with scattered bleeding superficial wounds over much of the anterior calf. All wounds were considered non-healing. The combined duration of the wounds was 13.7 years, the mean was 1.2 years per resident prior to starting the geko™ evaluation. The Ankle Brachial Pressure Index (ABPI), an indicator of peripheral arterial circulation was not available for most residents. The initial wound measurements and date of occurrence were available for 7 residents with 10 wounds, showing an average pre-geko™ weekly change in Surface Area (SA= Length x Width = cm²) of -7.35%, an increase in size. With use of the geko™ device, the average weekly percentage change in wound size for the wounds that were measured was a statistically significant 3.2% decrease in SA (p=0.004), and 10.9% in residents who were adherent to geko™ and best practices. Nursing staff and cognizant residents can easily adjust the pulse of muscle pump activator, application and removal are simple. Most residents feel engaged with the therapy, “because they feel it working”. The LTC corporation feels that it’s a great adjunctive solution for many types of lower leg wounds (venous, mixed, diabetic, pressure) in addition to best practices in the LTC and Retirement home sectors.

**Key Learning Points:** This is the first paper that illustrates use of the geko™ device enhancing healing in recalcitrant pressure injuries and diabetic foot ulcers in the Long Term Care sector, and in residents with dementia.


**Methods:** The geko™ device was applied to three ambulatory wound clinic patients with mixed etiology lower extremity wounds and a history of chronic venous insufficiency. The device was applied to both legs over the common peroneal nerve for 6 hours per day; 5 days per week, during their daily period of greatest inactivity. This was done until wound closure was achieved and for up to one month following to help ensure a more robust healing after closure.
Results: All wounds attaining full closure and remained healed one month after the device trial was completed. Each patient demonstrated an individualized pattern of wound healing; however, healing times were expedited compared to baseline. Secondary findings included a reduced lower leg oedema, improvement in subjective pain, a softening of woody fibrosis and an improvement in skin color.

Key Learning Points: Lower extremity wounds are a challenge to the patients’ who live with them and to the health care teams developing a treatment plan. Use of NMES provides another opportunity to better address health concerns and promote positive patient outcomes.


Aims: The purpose of this case series was to evaluate the therapeutic effect of the geko™ NMES device on wound healing outcomes over an 8-week period.

Method: Thirty patients with non-healing wounds (> 3-month duration) of either venous (VLU), mixed (MLU) or diabetic foot (DFU) aetiology were recruited from a local Outpatient Wound Clinic in the South Wales area. All patients received standard of care plus geko™ (model not stipulated but thought to be R-2).

Results: During the eight-week period two participants (6%) achieved complete re-epithelialisation between baseline and endpoint. Mean wound surface area decreased over time (7.6 cm²) and an increase (21%) in the mean percentage of granulation tissue was observed in the wound bed. Pain levels reduced in 52% of patients who completed the study but the extent of oedema reduction was difficult to establish given the fact that 76% of the cohort were treated with a form of compression as part of routine standard care.

Conclusion: These findings support the use of gekoTM NMES therapy in patients with painful venous (VLU) and mixed leg ulceration (MLU) but further high-quality research needs to be conducted on the generalisability of these findings to the wider population of patients burdened with chronic wounds of differing aetiology in the lower limb.


Background: Wound infection is a serious complication in kidney and kidney pancreas (SPK) transplantation. Transplant patients are at higher risk of wound infections due to obligate immunosuppression in addition to concomitant poor wound healing risk factors including diabetes, obesity and vasculopathy. The use of muscle pump activators (MPA) has previously been shown to improve healing in patients with chronic lower leg diabetic ulcers. Its effect on wound healing in transplantation is unknown.

Methods: In a prospective, randomized, controlled, single-center, study we randomly assigned 60 patients (kidney, n=50; SPK, n=10) to wear either TED+ IPC (Group 1, n=33) or an MPA device geko™ R-2 (54mA) (Group 2, n=27) for the first 6 days following surgery. Patient demographics, postoperative outcomes and incisional wound images were taken using a HIPAA compliant application on post-operative day (POD) 3, 5 and 30 and blindly assessed using the validated Southampton wound care score. Patient satisfaction was assessed on POD 3 and 6.

Results: Recipients were 51 (24-72) years old and 66% were male with no differences in BMI or DM between groups. Although there was no difference in wound healing on POD 3 between the groups (p=0.175), the MPA group showed a significant improvement in wound healing by POD 5 (p=0.0008) which persisted till POD 30 (p=0.01). Bayesian inferential analysis revealed that the use of TED+IPC following transplantation had inferior outcomes compared to the use of a MPA with sequential moderate evidence. The rate of complex wound infections was significantly greater in the TED+IPC group compared to MPA (34% versus 22%, respectively, p<0.05). No complications were encountered in either group associated with the study.

Key Learning Points: The use of a MPA device in the immediate post-operative period leads to a significant improvement in early and late wound healing, and decreased number of complex wound infections following kidney and SPK transplantation compared to standard TED+IPC therapy.
3-6h. Waterloo Wellington CCAC/ LHIN evaluation. Perfuse Medtec Inc. data; manuscript underway December 2018 as part of a cost-benefit analysis.

**Methods:** Two streams of patients were used to evaluate the effect of the geko™ R-2 (54mA) device on lower leg wounds: Stream 1 for patients with wound which have not reduced in size by 30% with best practices within 30 days of admission (existing patients), and stream 2 for newly admitted patients with VLUs < 3 months in duration since onset. The geko™ devices were to be applied to both legs for 6 hours per day 5 days per week, during a period where the patient could be sitting some of the time in order to get the largest therapeutic response to the stimulation.

**Results:**

**Stream 1 (> 30 days on service) Demographics and Healing Rates prior to the geko™ device Evaluation:**

- 9 Evaluation positions were used by 8 patients (# 2 and 4 same patient) for an approximate total of 62 weeks of therapy.
- The 10th position was not filled
- 5 wounds with measurements present at baseline in 5 patients; three more wound measurements not available and a ninth patient evaluated for lymphedema reduction had not actual open wounds, just dermatitis and scratches. An additional wound opened during the evaluation in one patient but closed in one week.
- The largest wound was 240 cm² (SA=L x W) at baseline, circumferential around leg. That patient has been on service since 2012; first wound measurement available from March 2013
- The average length of stay prior to geko™ implementation = 42.5 weeks (range 6 weeks to 208)
- The average weekly change in wound size pre-geko™ = -3.04%/ week (increase) with a range of -36% (increase in size) to 10% reduction in size

**Stream 1 Results with the geko™ device:**

- Three wounds in 2 patients closed during the evaluation with an average of 4 weeks per wound (range of 7 days to 6 weeks)
- The average weekly change in wound size with the geko™ device for 7 measured wounds in 5 patients was a 6.5% reduction per week (Image 1).
- The patient with lymphedema had a remarkable reduction in edema measurements within the first 10 days of treatment, where there were no other changes to his compression system that would account for this.

**Stream 2 (< 30 days) Patient demographics and healing rates prior to the geko™ device:**

- 10 patients with 16 wounds on admission; at baseline: 21 wounds.
- Largest wound 6.75cm² (SA=L x W) which was also the deepest wound was 0.5 cm deep at baseline
- Average length of stay prior to geko™ implementation = 22.6 days
- Average weekly change in wound size pre-geko™ = -79.29% (increase) with a range of -618% (increase in size) to 27.7% decrease.

**Stream 2 Results with the geko™ device:**

- 16 wounds in 9 patients closed –
- Average healing time of 3.03 weeks per patient (range of 5 days to 9 weeks);
- 20% healed in 1 week, 30, 30% healed in 2 weeks, 70% healed in 4 weeks, 80% at 8 weeks, 90% at 9 weeks. One patient (10%) with recurrent infections (x 4) not healed at 17 weeks and device discontinued.
- Average weekly change in wound size with the geko™ device for all patients= 36.54% reduction SA or Volume per wound (range of 2.29 % to 100%).

3-6i. The geko™ device and Diabetic Foot Ulcers


Available at: [https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf](https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf)

**Purpose:**

To investigate the effect of NMES on the rate of healing of diabetic foot ulcers, a trial was devised which would measure wound healing, pain, and quality of life.

**Methods:** The geko™ T-1 (27 mA) devices were worn on ulcerated limb only, 4-6 hours per day, 5 days per week set to minimum level to achieve distal twitch. The two cohorts were poorly matched.

**Results:** The trial was suspended due to lack of staffing in September 2015. Eight patients were recruited. 4 patients with DFU on pressure-bearing surface and neuropathy secondary to diabetes +/- ischemic heart disease, stroke, nephropathy,
retinopathy allocated to the geko™ device tended to have a greater degree of ulceration, more severe neuropathy scores and more smokers, yet achieved endpoint of 50% reduction in volume \((L \times W \times D=\text{cm}^3)\) 25 days sooner than the control group (without geko™). Kaplan-Meier analysis was not attempted due to the low number of subjects that achieved 50% healing in area and volume measurements. Generic quality of life scores increased much more in the device group than the control group, as measured by the VAS and SF-12, but Diabetes severity scores for both groups decreased by similar amounts.

**Key Learning Points:** Further research with larger number of patients is needed to demonstrate the role of the geko™ device in healing Diabetic Foot Ulcers, and to determine statistical significance.

### 3-7. Quality of Life


**Thesis:** Williams KJ. Chapter 7.1. NMES in the management of chronic venous disease (VeINS). Neuromuscular Stimulation of the Leg. Thesis submitted to Imperial College London for the degree of Doctor of Philosophy April 2017. Pages 258-269. Available at: [https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf](https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf)

Accessed April 12, 2018. Please see Section 3-2i. for the Hemodynamic results of this study.

**Aim:** Examining the QoL with the geko™ T-1 (27mA) device over 8 weeks in patients with CVI

**Methods:** Quality of life (QoL) questionnaires were taken at week 0, 6 (end of treatment) and week 8 (2 weeks after geko™ treatment finished). Three disease-specific (Venous Clinical Severity Score [labelled as VCCS but should be VCSS], Venous Disability Score [VDS], Aberdeen Varicose Vein Questionnaire [AVVQ]) and four generic (EuroQol [EQ5D], the Visual Analog Rating Scale [VAS] of health-related quality of life, the Center for Epidemiologic Studies Depression Scale [CES-D] and the Twelve Item Short Form [SF-12] for patients with chronic conditions) QoL questionnaires were used.

**Results:** The 30 patients with CVI (no mention of existing venous leg ulcers) had improvement in some of the disease specific and generic QoL questionnaires over the 6 weeks of treatment. Those with more severe disease (C4-6) had the biggest improvement in VDS, AVVQ, and SF-12. Only VDS was statistically significant \((p<0.01)\) between week 0 to 6 \((p=0.03,\) Mann-Whitney U test). Two weeks after the geko™ devices were stopped for this group, the improvement in venous clinical scores were sustained. Healthy individuals and those with mild clinical symptoms had no change in generic quality of life over 6 weeks.

**Table of Results:**

<table>
<thead>
<tr>
<th>QoL Surveys</th>
<th>CEAP 0-3 disease</th>
<th>CEAP 4-6 disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 6</td>
</tr>
<tr>
<td><strong>Disease-specific</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCCS*</td>
<td>2.8</td>
<td>2.7</td>
</tr>
<tr>
<td>VDS*</td>
<td>0.65</td>
<td>0.7</td>
</tr>
</tbody>
</table>

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QoL Surveys

<table>
<thead>
<tr>
<th>CEAP 0-3 disease</th>
<th>CEAP 4-6 disease</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Week 0</strong></td>
<td><strong>Week 6</strong></td>
<td><strong>Week 8</strong></td>
</tr>
<tr>
<td><strong>Week 0 (end of geko™)</strong></td>
<td><strong>Week 8 (no geko™ x 2 weeks)</strong></td>
<td><strong>Significance for those with CEAP 4-6</strong></td>
</tr>
<tr>
<td>AVVQ*</td>
<td>9.0</td>
<td>7.5</td>
</tr>
<tr>
<td>EQ5D**</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>VAS*</td>
<td>82.9</td>
<td>82.8</td>
</tr>
<tr>
<td>CES-D*</td>
<td>8.8</td>
<td>7.9</td>
</tr>
<tr>
<td>SF-12**</td>
<td>99.7</td>
<td>95.5</td>
</tr>
</tbody>
</table>

***p<0.01, independent t-test

**Key Learning Points:** Further evaluations may need to be done in order to determine what specifically improved in use of the geko™ for those individuals with deep CVI, and what it was about using the device that those with superficial disease objected to. None of the volunteers found that the devices interfered with their activities of daily living or their mobility. Some chose to activate the device overnight rather than in the waking hours. The trial was underpowered to fully evaluate quality of life changes from using the device, but the results when viewed as a pilot are encouraging.

Open access on-line https://onlinelibrary.wiley.com/doi/full/10.1111/iwj.13027 (Please see wound results in paper 3-6d)

In the Long Term Care evaluation with Revera, the following feedback was received concerning use of the geko™ device:

- One resident was extremely thrilled with the wound healing progress and on numerous occasions sought the nurse out to let him know how much more enjoyable life was without the discomfort and knowledge of the wound.
- A resident with dementia whom nurses thought might not keep it on but did, and healed quite quickly. The POA was happy that the resident was chosen for the pilot.
- The son of another resident who healed was very pleased with outcome of pilot.
- Initial application of device was accepted well, throughout the process the resident was quite happy. He observed “marked improvement” in his wound healing, and stated “I know it’s the machine”. 
- Another resident was extremely happy that he does not have to have his “dressings” done. He liked how the device “feels” on his feet (he could feel it working)
- A final resident found the “strong beat” annoying, and did not like to have the devices showing below her skirts.

**Key Learning Points:** There was positive feedback as well as the one negative; this woman was of a slight build and may have been more comfortable with a lower amplitude geko™ device (this was using R-2s).


Please also see the summary of this paper in 3-6f. regarding the wound healing results.

**Pain:** 52% of patients reported a substantial reduction in wound pain during the evaluation Two patients reported an increase in subjective pain during the 8 weeks, due to increasing bioburden within the wound bed and was treated. The remaining 40% of the cohort experienced either no pain (e.g. neuropathic DFU) or no change in pain levels between baseline and endpoint.

**Patient satisfaction:** All patients who completed the evaluation reported 100% satisfaction with the device. They reported that it was easy to operate and provided minimal disruption to their daily living. These positive outcome
measures enabled patients to self-manage manage the device and take control of their symptoms while undertaking normal daily activities.

**Key Learning Points:** The results support the use of geko NMES therapy in patients with painful VLUs and Mixed venous etiology leg ulcers.

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### 3-8. Tolerability

**3-8a. Paper:** (The hemodynamic results for this paper appear in Section 3-2d-e.) Williams KJ, Moore HM, Ellis M, and Davies AH. Comparing the venous haemodynamic effect of a neuromuscular stimulation device to intermittent pneumatic compression in healthy subjects. 14th Meeting of the European Venous Forum, Belgrade, Serbia, 27–30 June 2013. Paper 1.5

**Paper:** Williams KJ, Moore HM, M Ellis and Davies AH. Haemodynamic changes with the use of a neuromuscular stimulation device compared to intermittent pneumatic compression. Phlebology. Online 10 April 2014. http://phl.sagepub.com/content/early/2014/04/10/0268355514531255

**Results** Tolerability of the device was rated by each user at the end of the protocol, using a verbal reported score (0–5; no pain, to that experienced by inflating a blood pressure cuff to 200 mmHg). All patients tolerated both devices and completed the trial. On a verbal reported score, from 0 (painless) to 5 (as painful as a sphygmomanometer cuff inflated to 200 mmHg), IPC was rated a mean of 1.5, and NMES as 2.8 (p≤0.006, paired Student’s t-test).

---


**Methods:** At the end of each program, subjects were asked to evaluate their acceptance and tolerance to each device using a discomfort questionnaire. Maximum discomfort was compared to a blood pressure cuff inflated around the upper arm. Subjects rated their discomfort levels using a visual analogue scale (VAS) by marking the level of the perceived pain along a 100 mm line, marked at one end “no sensation” and at the other end “severe discomfort”. A discrete five category verbal rating scale (VRS) was used to select the appropriate category of the perceived discomfort, where”1 = no sensation (other than muscle tensing and relaxing)”, “2 = minimal sensation”, “3 = mild discomfort”, “4 = moderate discomfort”, or “5 = severe discomfort.”

**Results:** For the geko™ T-1 device: “VAS: 35/100 geko™ set on low, 46.5/100 set on HIGH; VRS: ~2.4/5 set on LOW, 3.5/5 when set on HIGH. Analysis of the discomfort levels reported following the use of each device was not significant using the visual analogue score, p > 0.05, but showed a statistically significant difference using the verbal rating score, p ≤ 0.05. The discomfort level following the use of the geko™ T-1 device at the Normal Clinical Use setting was rated as mild discomfort as compared to the other devices studied, which were rated at a minimal sensation.

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**Methods:** Participants were asked to evaluate acceptance and tolerability of the geko device using a verbal rating score (VRS): 1, no sensation; 2, minimal discomfort; 3, mild discomfort; 4, moderate discomfort; and 5, severe discomfort. Discomfort was related to normal measurement of blood pressure, measured on the upper arm using a standard sphygmomanometer cuff, which was standardized as rating 3. Participants also indicated the level of discomfort by marking a 10 cm visual analogue scale (VAS), with 0 denoting ‘no sensation’, and 10 indicating ‘severe discomfort’.

**Results:** The median level of discomfort measured on the VRS across all postural positions using the geko device was 2, denoting ‘minimal discomfort’. The median level of discomfort was slightly higher without casting compared with discomfort when casting was applied. The VRS showed that in the supine and leg-elevated positions participants were significantly less comfortable without casting compared with the same position with casting (median difference 1, p = 0.008 to 0.02). The median VAS across all positions was 2.5 (0.9 to 6.5) with the geko™ device. Again, a lower level of discomfort was reported in the supine and leg elevated positions with casting compared with no casting (median differences 1, p ≥ 0.002 to 0.004).

**Key Learning Points (all papers):** there appears to be a trend with the VRS where individuals are aware of the sensation, with some feeling a mild discomfort. None of the participants in these papers had open wounds, which might impact their perception of the geko™ stimulation. Anecdotally, patients often say that they do not notice it after wearing for a
short while, and it would be helpful to look at the results using these evaluations over a period of time, particularly when there is an open wound. It would be important to separate discomfort from the wound and discomfort from the device.


Methods: The Visual Analogue Score (VAS) used asked: “If severe discomfort is comparative to that experienced when having your blood pressure taken, please mark the line where you place your discomfort level whilst wearing the neuromuscular device”.

No discomfort

Severe discomfort

Results: The device was well tolerated.

3-9. Consensus and Literature Reviews


Methods: A literature search of the EMBASE and Medline databases was performed, with articles up to August of 2014, and studies were included if they were full text articles, written in English, pertaining to venous disease and neuromuscular electrical stimulation (NMES).

Results: 46 articles met the inclusion criteria, although comparison between trials is hampered by variations in protocols and outcome measures, and the method of stimulation (direct muscle stimulation versus stimulation of the common peroneal nerve causing muscle innervation. NMES devices increase venous haemodynamic parameters such as peak velocity and volume flow with stimulation of the calf muscle pump compared to rest. Calf vascular resistance was significantly reduced after NMES, equivalent to that seen post-exercise, which may suggest that the benefit continues for some time after the device is stopped. Studies report them to be non-inferior to intermittent pneumatic compression (IPC), without the complications inherent to IPC. They are effective in the prevention of venous thromboembolism, though inferior to low molecular weight heparin. NMES can increase cardiac stroke volume (24%), cardiac output (26%) and reduce total peripheral resistance (21%) when compared to IPC of the calf and thigh. NMES is an important tool in the prevention and management of venous disease, and avoids the significant risks associated with heparin administration. Data explored here is heterogenous in device, protocol, and reported end-points, therefore should be interpreted with care. Long term effects of treatment with NMES have not been explored. The lack of uniformity of nomenclature impedes comparison between devices. A consensus needs to be achieved on reporting of electrical parameters such as pulse width, frequency of stimulation, intensity and waveform. Research should also investigate the effects of dosing, duration of treatment and long-term effects of electrical stimulation in treating venous disease.

Key Learning Points: NMES can reduce symptoms of chronic venous disease, causing reversal of fluid pooling in the legs (orthostatic oedema) and is augmented by a factor of 2 with the addition of graduated compression stockings. NMES may also be able to positively impact the ability of the calf muscle pump to be trained over time. Many of the geko™ articles were published after the August 2014 search date and were not included in this review.

**Methods:** A literature search was conducted (Spring 2016) to gain a better understanding of the evidence describing the physiological effects that LFNS may have on the body. Terms used included electrical stimulation, leg ulcer, NMES and TENS. The result is a narrative, not exhaustive review based on a selected sample of articles based on convenience from that initial search. Intended to provide an overview of this area of emerging research and clinical practice, using a small self-contained, portable, single-patient-use device that applies stimulation at 1 Hz over the common peroneal nerve in the lower leg (geko™).

**Results:** LFNS appears to have positive effects on blood flow in healthy volunteers. As of yet there is limited research in patients with chronic venous insufficiency. More investigation on the physiological effects that occur when the machine is applied for longer periods is warranted. Low frequency nerve stimulation causes the release of endogenous opiates and hormones within the body, thereby activating the body’s own pain-relief mechanisms. This tends to have longer-lasting effects whole-body effect compared with other methods of electrical stimulation used for pain relief. This in turn encourages an increase in patient mobility. It is also effective in reducing the symptoms of neuropathy, which is experienced in CVI. It is not clear to date what benefit it will have on patients with CVI, and they recommend further study to assess the ejection fraction and direct comparison between use of LFNS over the common peroneal nerve and full-force contraction of the gastroc and soleus calf-muscle pump to help determine the actual physiological effects behind the demonstrated improvements in oedema. The goal of LFNS is to optimize oedema reduction pain control and improved blood flow for wound healing compare to direct electrical stimulation which stimulates the wound itself. The warnings and precautions listed in this document pertain to electrical stimulation and NOT the use of the geko™ device.

**Key Learning Points:** Although current literature is inconclusive, the evidence presented above does demonstrate that this modality does have benefit in addressing pain and neuropathy, venous stasis and blood flow. These impairments have important impact on a patient’s ability to heal, particularly in patients with venous leg ulcers. Clinicians should consider the use of LFNS:

- with challenging and refractory wounds that are not responding to traditional treatments.
- to benefit patients who are at risk for developing DVT
- to manage lower leg oedema that is contributing to reported pain
- to manage stalled, chronic lower leg wounds that are not progressing along the expected healing trajectory
- in conjunction with compression or when compression cannot be tolerated
- to benefit patients who have lower leg neuropathy
- for patients with fixed ankle joints, those who are bed ridden or those who have limited mobility.

Early expert opinion would suggest that an evaluation over a four-week period, and beginning cautiously, would be a good starting point to determine if LFNS has a patient-specific benefit. The cumulative effects of using LFNS — of improving circulation (arterial and venous) as well as reducing pain and associated improved mobility — have shown to have positive effects on wound healing.


Presented as a handout at an oral podium presentation that he was doing, Dr. Keith Harding used this opinion paper to discuss new evidence that has emerged since the LFNS Consensus paper by the CAWC group commenced their efforts and his own personal experience of using the technology. In his words: “geko™ should be considered as an adjunctive therapy in the following groups of patients until the larger trials are completed:

- Fixed ankle joints or in those with limited mobility (i.e., < 200 metres per day). Blood flow is known to be compromised in these patients due to a lack of muscle pump activity.
- When wounds have become or are suspected to become (based on history/risk factors) difficult to heal. This is typically thought of as wounds that have not reduced in size by 30% at 30 days of best practice therapy.
- When compression cannot be tolerated. Without compression, blood flow is compromised. In some patients, compression could be tolerated after LFNS for a period of time.
- Where edema is present. Edema impedes healing progress and this, of course, is also tied to blood flow.
- For the management of peripheral neuropathic symptoms.
- For patients that have pain associated with their wounds.

The main danger preventing wider adoption of this technology appears to be financial consideration. However, when one considers the guiding principle of “treating the root cause” of all wounds it would seem reasonable that many wound
patients would benefit from improved blood flow. If the technology exists to deliver this, then it should be used where appropriate.”


Abstract The role and importance of compression in achieving venous return is well understood and the use of multilayer compression remains the standard of care for the patient with a Venous Ulcer. However, a range of alternative technologies have emerged which aim to reduce or overcome some of the disadvantages of bandaging. This chapter explores methods of pressure assessment under bandages to facilitate application of bandages and also discusses alternatives to bandaging including adjustable systems, Intermittent Pneumatic Compression (IPC) Systems and finally powered muscle stimulators. All these approaches, as the evidence supporting them develops, could offer useful alternatives to compression for a number of patient groups. Content regarding the geko™ device includes a summary of the method of increase to venous, arterial and microcirculation in people with chronic venous insufficiency, and the author offers it as a potential alternative to compression bandaging for patients allowing them to better achieve their treatment goals.

Reviewer’s comments: At this point in time, the idea of the geko™ device as an alternative to compression bandaging is not proven. Our experience with patients has been that as it reduces edema, and both nociceptive and neuropathic pain over a short period of time, patients are better able to tolerate therapeutic levels of compression therapy, thus optimizing their evidenced-based care. The suspected increased response by the addition of compression is supported by the work of Williams in her PhD thesis (Section 3-2y), although she used healthy volunteers and low Grade 2 stockings, and Warwick et al. (Section 3-2s-t.) who used plaster casts which provide resistance to lower leg muscle pump activity. Further research is needed to better understand the dynamics at play and the optimal therapeutic approach. In the absence of this, we continue to view the geko™ device as an adjunctive therapy for venous leg ulcers and are currently evaluating it as a first line response in addition to compression therapy (December 2018).

3-10. Fecal and Urinary Incontinence: Use of geko™ stimulating the Tibial Nerve

Background: Fecal incontinence is a socially disabling condition that affects ≤15% of adults. Neuromodulatory treatments for fecal incontinence are now well established. Less invasive, cheaper, and more ambulatory forms of neuromodulation are under exploration.

Objective: The purpose of this study was to assess the acceptability and safety of a new ambulatory tibial nerve stimulation device and to determine clinical effect size for 2 differing regimens of therapy.

Design: This was a randomized, investigator-blinded, parallel-arm, 6-week pilot trial.

Settings: The study was conducted at 7 United Kingdom trial centers. Patients were initially reviewed in the trial center, with subsequent applications of the device performed in the patients home setting.

Patients: A total of 43 eligible patients (38 women) who failed conservative management of fecal incontinence were included in the study.

Intervention: The study intervention involved twice weekly, 1- versus 4-hour transcutaneous tibial nerve stimulation for 6 weeks (total of 12 treatments). The geko™ T-1 device was utilized and the positioning over the tibial nerve is demonstrated in the article, using a vertical rather than horizontal orientation on the distal lower leg.

Main outcome measures: Standard fecal incontinence outcome tools (bowel diary, symptom severity score, and generic quality-of-life instruments) were used to collect data at baseline and at 2 weeks post treatment cessation.

Results: A total of 22 patients were randomly assigned to the 1-hour group and 21 to the 4-hour group. Improvements in fecal incontinence outcomes were observed for both groups, including median urge incontinence episodes per week at baseline and post treatment (1-hour group 2.0 to 0.5 versus 4-hour group 4.0 to 1.0) and deferment time (1-hour group 2.0 to 2.0 minutes versus 4-hour group 0.5 to 5.0 minutes). Accompanying changes were observed in physical functioning domains of quality-of-life instruments. There were no adverse events, and the treatment was highly acceptable to patients.

Limitations: Limitations included the pilot design and lack of control arm in the study. Future trials would need to address these limitations.
Conclusions: This pilot study provides evidence that transcutaneous tibial nerve stimulation with a new ambulatory device is safe and acceptable for the management of fecal incontinence. Additional study is warranted to investigate clinical effectiveness.

Key Learning Points:
Transcutaneous posterior tibial nerve stimulation using the geko™ device is safe, non-invasive and allows the patients to be fully ambulatory during treatment without requiring visits to a clinic to have the treatment.


Background: To evaluate safety, acceptability and pilot efficacy of transcutaneous low-frequency tibial nerve stimulation (TNS) using a novel device as home-based neuromodulation.

Methods: In this single-centre pilot study, 48 patients with overactive bladder (OAB) (24 with neurogenic and 24 with idiopathic OAB) were randomized to use a self-applicating ambulatory skin-adhering device stimulating transcutaneously the tibial nerve at 1 Hz for 30 minutes, either once daily or once weekly, for 12 weeks. The geko™ T-1 device was utilized and the positioning over the tibial nerve is demonstrated in the article, using a vertical rather than horizontal orientation on the distal lower leg. Changes in OAB symptoms and QoL were measured at baseline, weeks 4, 8, and 12 using validated scoring instruments (ICIQ-OAB and ICIQ-LUTSqol), 3-day bladder diary and a Global Response Assessment (GRA) at week 12.

Results: Thirty-four patients completed the study (idiopathic n=15, neurogenic n=19). No significant adverse effects were noted. Patients found the device acceptable. Eighteen patients (53%) reported a moderate or marked improvement in symptoms from the GRA. Between baseline and week-12, ICIQ-OAB part A sub-scores improved from mean (SD) 9.3 (2.5) to 7.5 (3.1), and from 9.1 (1.9) to 5.9 (1.7) in the daily and the weekly arms, respectively. ICIQ-LUTSqol part A sub-scores improved from mean (SD) 51 (12.8) to 44.2 (13.1) and 44.9 (9.0) to 35.9 (8.8) in the daily and the weekly arms, respectively. Bladder diary mean 24-hour frequency episodes improved from 11.5 to 8.8 at week 12 for both arms.

Conclusions: This novel ambulatory transcutaneous TNS (TTNS) device is safe and acceptable for use in patients reporting OAB symptoms as a form of home-based neuromodulation. A larger study however is required to confirm clinical efficacy.

Key Learning Points:
Transcutaneous posterior tibial nerve stimulation using the geko™ device is safe, non-invasive and allows the patients to be fully ambulatory during treatment without requiring visits to a clinic to have the treatment.