Annotated Bibliography

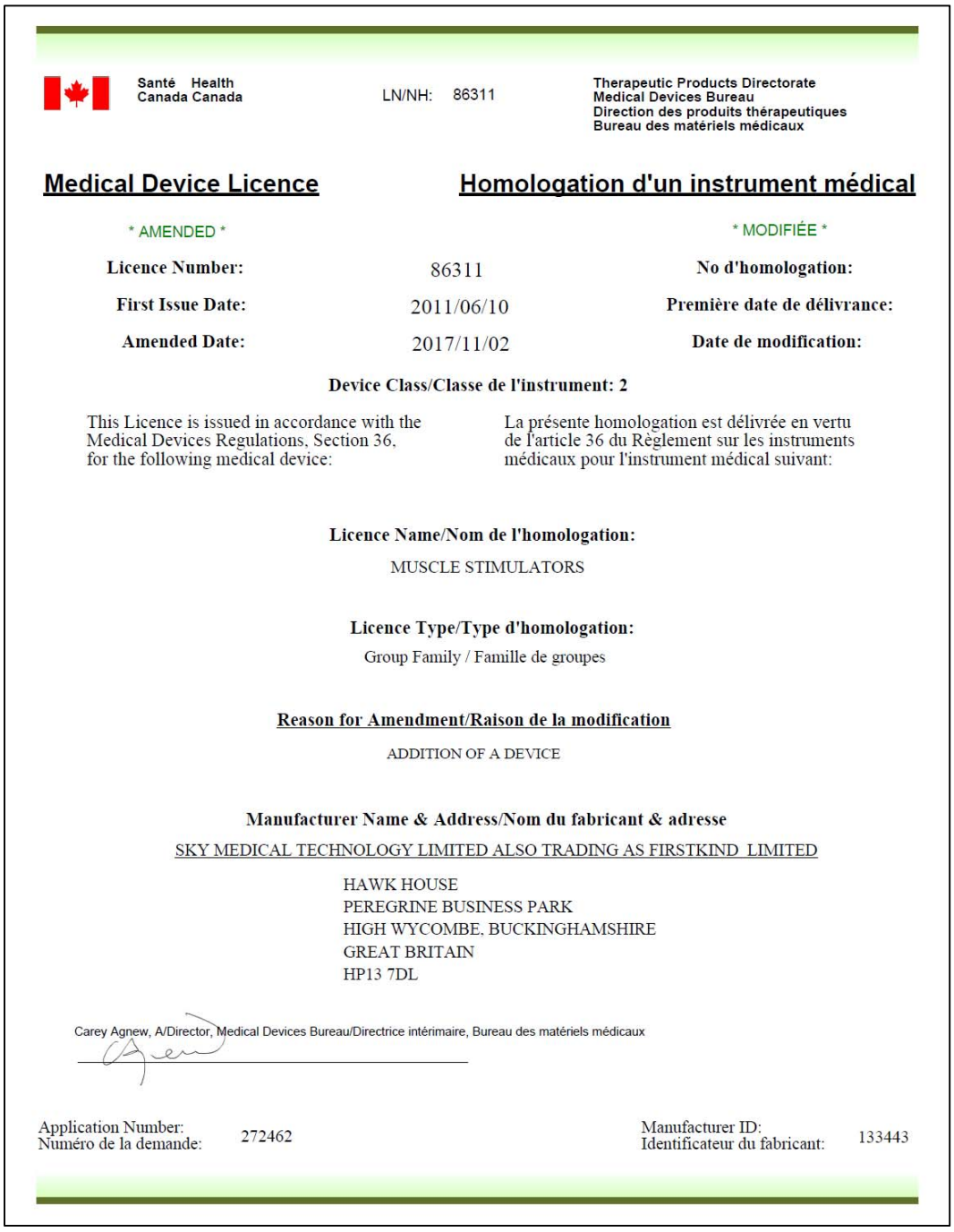
The geko™ Device

Purpose: To provide a brief 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Exclusion: Published or Unpublished Case Studies with subjects <3 which can be viewed on geko™ website http://gekodevices.com/en-uk/studies/studies-trials/

Health Canada Registration:



Santé Canada Health Canada

LN/NH: 86311

Therapeutic Products Directorate
Medical Devices Bureau
Direction des produits thérapeutiques
Bureau des matériels médicaux

Medical Device Licence — **Homologation d'un instrument médical**

* AMENDED * — * MODIFIÉE *

Licence Number:	86311	**No d'homologation:**
First Issue Date:	2011/06/10	**Première date de délivrance:**
Amended Date:	2017/11/02	**Date de modification:**

Device Class/Classe de l'instrument: 2

This Licence is issued in accordance with the Medical Devices Regulations, Section 36, for the following medical device:

La présente homologation est délivrée en vertu de l'article 36 du Règlement sur les instruments médicaux pour l'instrument médical suivant:

Licence Name/Nom de l'homologation:

MUSCLE STIMULATORS

Licence Type/Type d'homologation:

Group Family / Famille de groupes

Reason for Amendment/Raison de la modification

ADDITION OF A DEVICE

Manufacturer Name & Address/Nom du fabricant & adresse

SKY MEDICAL TECHNOLOGY LIMITED ALSO TRADING AS FIRSTKIND LIMITED

HAWK HOUSE
PEREGRINE BUSINESS PARK
HIGH WYCOMBE, BUCKINGHAMSHIRE
GREAT BRITAIN
HP13 7DL

Carey Agnew, A/Director, Medical Devices Bureau/Directrice intérimaire, Bureau des matériels médicaux

Application Number: / Numéro de la demande: 272462

Manufacturer ID: / Identificateur du fabricant: 133443

Table of Contents:

The geko™ Device Product Specifications				
Product name	geko™			geko™ plus
Model reference	T-1	T-2	Wound Therapy	R-2
Product type	Powered muscle stimulator			
Class	BF (The entire device is considered to be a patient applied part)			
Dimensions	149mm x 42mm x 11mm	186mm x 31mm x 11mm		
Weight	16g (device only)	10g (device only)		
Power source	Internally powered equipment, battery not replaceable			
Battery	Primary lithium coin cell - removable for disposal			
Utilization	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	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	Affected leg (local response) 6-hour wear time; Battery lasts 6 hours and shuts off; 2-day use & discard; 6-days per week (Canada)	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
Operation	Continuous operation - equipment not suitable for use in presence of flammable anaesthetic mixture with air or with oxygen or nitrous oxide			
Stimulation modes	7 (selected pulse widths)		10 (selected pulse widths)- settings 1 and 2 are lower than in R-2	8 (selected pulse widths)
Pulse current	27mA	27mA	54mA	54mA
Load impedance	200Ω to 3kΩ for 27mA output	200Ω to 3k Ω for 27mA output	200Ω to 3k Ω for 54mA output	200Ω to 3kΩ for 54mA output
Pulse voltage	Set by current and load			
Pulse width ±10%	70, 100, 140, 200, 280, 400,560µs	50, 70, 100, 140, 200, 280, 400µs	25, 35, 50, 70, 100, 140, 200, 280, 400,560µs	50, 70, 100, 140, 200, 280, 400, 560µs
Repetition rate	1HZ (±5%)			
Max charge	20µC per pulse	20µC per pulse	40µC per pulse	40µC per pulse
Net charge output	zero per cycle			
Output coupling	Ceramic capacitor			

1. **Initial Research Stimulation of Common Peroneal Nerve and Haemodynamic Effects**

2a. Augmentation of venous, arterial and microvascular blood supply (Pre- development of geko™ device).
Paper: Tucker AT, Maass A, Bain DS, et al. Augmentation of venous, arterial and microvascular blood supply in the leg by isometric neuromuscular stimulation via the peroneal nerve. *Int J Angiol* 2010;19:e31–e37.

Methods: Thirty healthy volunteers received modified neuromuscular stimulation to the common peroneal nerve with a range of 1 mA to 40mA, 1Hz 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.
Results:

Test	Location and Results (Increases)
Photophlesmography (PPG)	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. *P=0.0004* *60% for geko™ parameters*
Strain gauge phlesmography (SPG)	Change in mid-calf circumference: 55 to 70% of that achieved with full dorsiflexion *P<0.001*
Duplex ultrasound	Femoral vein venous volume flow range ~160% to 380% of baseline *P<0.01* *Superficial femoral vein 100% increase in volumetric flow and peak velocity* for geko™ parameters Femoral vein mean peak venous velocity range ~150 to 360% of baseline *P<0.01*
Transcutaneous oxygen tension (TCP02) on dorsum of foot	Tissue oxygen in the leg decreased from baseline during the evaluation, but stimulated values (~92 to 97%) were consistently significantly higher than unstimulated values *P=0.03*
Laser Doppler Fluxmetry	Skin dorsum of foot microcirculatory flux range of ~400 to 2500% *P<0.01* *400% for geko™ parameters*
Heart rate	No change
Pulse oximetry	No change to oxygen saturation
Blood Pressure	No change

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. *no change in the length of the contracting muscle

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2b. Cardiac Output and Improved lower leg blood flow (Pre- development of geko™ device)
Paper: Jawad, Huda**.** The effect of a novel electrical stimulation method for improving lower limb blood flow in healthy volunteers. PhD dissertation. Queen Mary University of London/ St. Bart's. 2012.
https://qmro.qmul.ac.uk/jspui/handle/123456789/3120 (266 pages)
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.

Test	Baseline Mean and SD	400 µs Stimulation Mean and SD	600 µs Stimulation Mean and SD	Summary/ Significance
Femoral Arterial Flow	174.1 ± 39.2 ml/min	258.8 ± 65.6 ml/min 55% increase	273.1 ± 97.1 ml/min 54% increase	$p \leq 0.05$
Cardiac Arterial Peak Velocity	81.19 ± 13.62 cm/sec	101.6 ± 22.43 cm/sec Increased x 24%	100.9 ± 26.37 cm/sec Increased x 24%	$p \leq 0.05$
Vessel Diameter and Cross-sectional Area	0.64 ± 0.10 mm	0.63 ± 0.12 mm	0.64 ± 0.11 mm	p>0.05 no real change
Skin Microcirculation (foot) (Laser Doppler Flowmetry)	7.71 ± 3.39	107.5 ± 68.1 1186% increase	117.9 ± 67.8 1552% increase	$p \leq 0.05$
Left ventricular outflow tract velocity time integral (LVOT VTI)	21.96 ± 3.23	23.27 ± 3.37 6% increase	22.79 ± 3.06 4% increase	$p \leq 0.05$
Ejection Fraction	59.9 ± 3.72 %	60.3 ± 7.44 %	62.6 ± 4.80 %	p=0.09 no real change
Left Ventricular Diastolic Volume	117.7 ± 37.10ml	120.2 ± 32.30 ml	121.1 ± 27.86 ml	p=0.61 no real change
E' Velocity	0.80 ± 0.16 m/s	0.77 ± 0.12 m/s	0.76 ± 0.08 m/s	P=0.29 no real change
Deceleration Time	187.4 ± 24.82 ms	194.1 ± 31.4 ms	187.9 ± 20.28 ms	P= 0.59 no real change
E' Lateral	3.76 ± 5.53 m/s	3.79 ± 5.58 m/s	3.89 ± 5.79 m/s	P=0.75 no real change

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

Test	Arterial Velocity (cm/sec) Mean (SD)	Signifi-cance	Venous Velocity (cm/sec) Mean (SD)	Signifi-cance	Arterial Flow (ml/min) Mean (SD)	Signifi-cance	Venous Flow (ml/min) Mean (SD)	Signifi-cance	Microcirc-ulation Dorsum of both feet
Baseline	69.92 ± 21.32	P>0.05 No significance	10.7 ± 4.32	P<0.001 21% increase	176.6 ± 65.6	P≤0.05	59.4 ± 41	P<0.001 81% increase	4.66 flux units
1 hour	70.47 ± 28.5		24.09 ± 8.30 (158% increase)		288. 7 ± 127.2 (125% increase)		233.76 ± 114.5 (489% increase)		73.59 flux units
2 hours	76.04 ± 16.47		26.82 ± 6.57 (169% increase)		237.3 ± 81.7 (62% increase)		223.6 ± 76.3 (374% increase)		Not provided
3 hours	83.69 ± 13.03		30.07 ± 13.32 (221% increase)		259.4 ± 71.9 (99% increase)		253 ± 86.8 (471% increase)		
4 hours	82.23 ± 15.56		25.67 ± 5.54 (162% increase)		253 ± 100.1 (87% increase)		223 ± 76.9 (405% increase)		75.85 flux units (p<0.001)
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."*

2c. Sensory Nerve Stimulation and Compression Bandaging; TCP02 and Healing of Chronic VLUs (Pre- development of geko™ device).

Paper: Ogrin R, Darzins P, Khalil Z. The use of sensory nerve stimulation and compression bandaging to improve sensory nerve function and healing of chronic venous leg ulcers. *Current Aging Science*. 2009;2(1):72–80.

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.

Measure	**Sham**			**Activation**		**Statistical significance**
Wound Healed by 12 weeks	10/15 (66%)			8/14 (57%)		none
Average weekly Wound Healing Rate	0.6 ± 0.2 cm^2/week			1.1 ± 0.3 cm^2/week		P=0.18 (not significant)
All patients	**Control**	**Sham Stim**	**Statistical significance**	**Control**	**Activated Stim**	
Microvascular Blood Flow(cm^2)	-15.4 ± 60.1	16.9 ± 42.1	P=0.47	0.4 ± 5.3	25.8 ± 23.9	P=0.29(not significant)
TCp02 @ 39°C (mmHg)	-4.49 ± 9.1	5.5 ± 3.6	P=0.31(not significant)	2.6 ± 4.9	5.1 ± 2.0	P=0.15 (not significant)
TCp02 @ 44°C (mmHg)	18.7 ± 7.3	13.9 ± 5.7	P<0.05	0.9 ± 4.8	7.5 ± 3.7	P=0.21 (not significant)
Flare Response to hot red pepper (cm^2) (C-fiber activation)	2.4 ± 5.0	1.7 ± 2.0	P=0.45(not significant)	5.6 ± 1.9	9.1 ± 4.1	P=0.32 (not significant)

Nerve Sensation Threshold 5Hz ECPT (mA) (C-fiber activation)	-0.4 ± 0.4	-0.4 ± 0.3	P=0.77(not significant)	-0.2 ± 0.3	-0.3 ± 0.5	P=0.86(not significant)
Only Patients who healed	**Control**	**Sham Stim**	**Statistical significance**	**Control**	**Activated Stim**	
Microvascular Blood Flow(cm^2)	-23.6 ± 31.1	39.8 ± 60.1	P=0.33	-2.3 ± 5.5	-1.9 ± 33.9	P=0.99(not significant)
TCp02 @ 39°C (mmHg)	-5.33 ± 5.86	3.33 ± 4.23	P=0.32 (not significant)	4.8 ± 5.9	4.8 ± 1.7	P=1.00 (not significant)
TCp02 @ 44°C (mmHg)	-0.1 ± 5.4	18.7 ± 7.3	P=0.05	6.6 ± 6.2	5.9 ± 6.1	P=0.94 (not significant)
Flare Response to hot red pepper (cm^2) (C-fiber activation)	2.4 ± 1.8	1.7 ± 5.0	P=0.99(not significant)	6.0 ± 3.4	11.8 ± 8.1	P=0.24 (not significant)
Nerve Sensation Threshold 5Hz ECPT (mA) (C-fiber activation)	-0.7 ± 0.5	-0.4 ± 0.4	P=0.44(not significant)	-0.2 ± 0.2	-0.9 ± 0.6	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."*

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2. The geko™ Device and Haemodynamics

The effects of the geko™ device to (1) produce force during isometric ankle joint dorsiflexion, and (2) alter muscle oxygenation and blood volume/ velocity in the resting human leg.

3a.i Paper: Zhang Q, Styf J, Ekström L, Holm AK. Effects of electrical nerve stimulation on force generation, oxygenation and blood volume in muscles of the immobilized human leg. Scand J Clin Lab Invest. 2014 Aug;74(5):369-77.

Methods: The geko™ device 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.**

3a.ii. Paper: Yilmaz S, Calbiyik M, Yilmaz BK, Askoy E. Potential role of electrostimulation in augmentation of venous blood flow after total knee replacement: A pilot study. Phlebology. 2016 May;31(4):251-6. doi: 10.1177/0268355515580473. Epub 2015 Apr 6.
http://gekodevices.com/media/118659/potential_role_of_electrostimulation_in_augmentation_of_venous_blood_flow_after_total_knee_replacement_a_pilot_study.pdf

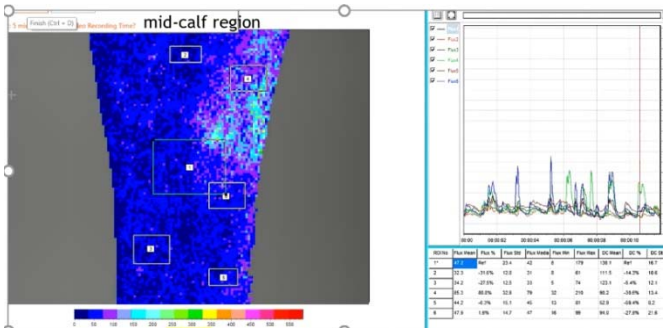
Methods: Thirty consecutive patients undergoing total knee replacements were randomized to either receive peroneal nerve electrostimulation plus low molecular weight heparin and below-knee compression stockings or low molecular weight heparin and below-knee compression stockings alone. The device (assume 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 postion, 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.

Results:

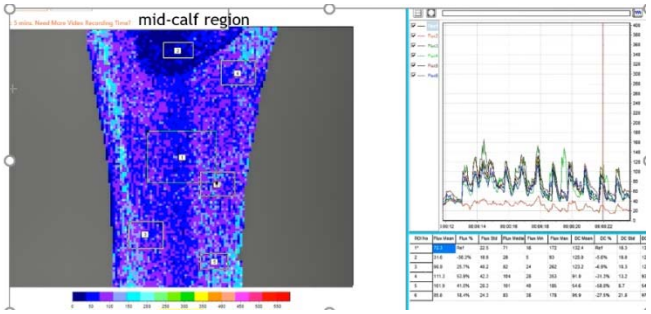
Test	Control (no device + stockings + heparin)	Estim Group (device + stockings + heparin)	Summary/ Significance
Peak Velocity Femoral Vein "Post-operative"	13.84 ± 3.58 cm/s	17.46 ± 2.86 cm/s	P<0.02
Peak Velocity Increase Femoral Vein "After the surgery"	Not provided	67.48 ± 17.38 cm/s 67.5% increase	P<0.001

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*

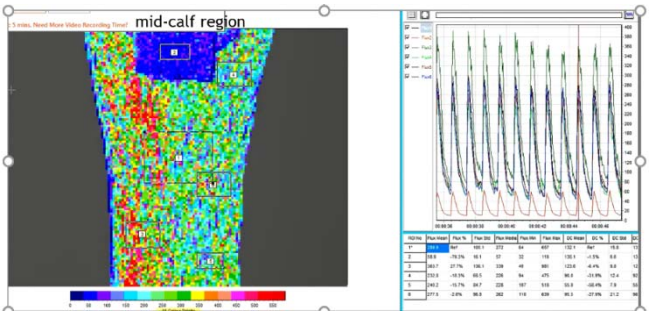
3a. iii. Hemodynamic Testing: Using Speckle contrast optical spectroscopy to measure microcirculatory tissue perfusion in a healthy leg with geko™ device off, activated with no foot twitch and activated with foot twitch. Courtesy Firstkind, High Wycombe, UK, part of ongoing research.



First 0-15 seconds - baseline measurement. The geko™ device is not activated. The increase in colour is due to normal systolic heart beat.



15-30 seconds - the geko™ device is activated, before a foot twitch is achieved; resulting in a 100% - 200% increase in microcirculatory flux



30-45 seconds - 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, 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.

3b. Intermittent Pneumatic Compression (IPC) vs. geko™
Five Papers:

3b.i. Paper: 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

Baseline measurements were taken of superficial femoral venous velocity and volume flow, then the subjects received bilateral therapy with the two devices 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.

Test	IPC Venous	Summary/ Significance	geko™ Venous	Summary/ Significance
Peak Velocity	19%	Not provided	42%	Not provided
Time Averaged Peak Velocity (TAMV)	12%	Not provided	27%	Not provided
Volume Flow	7%	Not provided	46%	Not provided

3b. ii. **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 2015, Vol. 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 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°.

Results:

Test	IPC Venous	Summary/ Significance	IPC Arterial	Summary/ Significance	geko™ Venous	Summary/ Significance	geko™ Arterial	Summary/ Significance
Peak Velocity	51%	p=0.002	-8%	No signifi-cance	103% increase	p=0.002	11% increase	p<0.01
Time Averaged Peak Velocity (TAMV)	5%	p=0.002	-12%	No signifi-cance	101% increase	p=0.002	84%	p<0.01
Volume Flow	3%	p=0.002	-13%	No signifi-cance	101%	p=0.002	75% increase	p<0.01
Microcirculatory Flux	~ 10% increase				~240 % increase in paper but data actually shows 152% (First Kind analysis)			

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.*

3b.iii. Paper: Jawad, Huda**.** The effect of a novel electrical stimulation method for improving lower limb blood flow in healthy volunteers. PhD dissertation. Queen Mary University of London/ St. Bart's. 2012. Chapter 7. The Effectiveness of the geko ™ Medical Device versus Intermittent Pneumatic Compression: A Comparative Study. https://qmro.qmul.ac.uk/jspui/handle/123456789/3120 (266 pages). (This paper also appears in section 2b.)
Methods: Ten healthy volunteers lay supine on a padded table that could be tilted manually, with their heads supported by a pillow and tilted upwards to 45°. After 30 minutes of supine rest, baseline measurements were recorded. The geko™ devices were then fitted bilaterally. Each device was active for a period of 30 minutes followed by 10 minutes recovery phase, to allow vascular re-equilibration prior to switching on the next device. Changes in blood flow and volume, together with microcirculatory velocity were measured using laser Doppler flowmetry and colour flow duplex ultrasound.

Results: Superficial Femoral Vein and Femoral Artery

Test	Baseline with no device	geko™ T-1 High Pulse Width	Geko™ T-1 Low Pulse Width	Significance	IPCHF	IPC Kendall
Venous Volume Flow mL/min Median (IQR)	123.5 ± 73.4	163 ± 105.3 33% increase	129 ± 42.7 13% increase	$p \leq 0.001$	118 ± 72.7 4% decrease	115 ± 60.2 4% decrease
Arterial Volume Flow mL/min Median (IQR)	197.5 ± 135.8	244.5 ± 125 30% increase	170 ± 107.5 7% decrease	$p \leq 0.001$	181.5 ± 70.5 9% decrease	158 ± 73 16% decrease
Venous Velocity		174% increase	73% increase	$p \leq 0.001$	166% increase during inflation only	143% increase during inflation only
Arterial velocity		24% increase	2% increase	$p \leq 0.001$	1% decrease during inflation only	4% decrease during inflation only
Microcirculatory flux		394% increase	345% increase	$p \leq 0.001$	59% increase	44% increase

No significant difference in mean femoral vessel diameter was reported between the devices studied $p > 0.05$. Blood velocity increases every second with the geko™ 1 Hz device, opposed to IPC where acceleration occurs only with the inflation cycle. No significant difference was reported between the devices following the measurement of blood pressure, transcutaneous tissue oxygen (TcPO2), tissue oxygen saturation (SPO2) as well as heart rate, $p > 0.05$. All measurements remained equally stable throughout the study.
Key Learning Points: The geko™ T-1 set with a higher pulse width (a higher setting) was more effective than with a lower pulse width, and both were significantly better than both IPC devices in all measures ($p \leq 0.001$)

3b. iv Paper: Jawad H, Bain DS, Dawson H, Crawford K, Johnston A, Tucker AT. The effectiveness of a novel neuromuscular electrostimulation method versus intermittent pneumatic compression in enhancing lower limb blood flow. *J Vasc Surg*: Venous Lymphat Disord. 2014;2(2):160-5.

Methods: 10 healthy volunteers. For each subject, the geko™ T-1 device 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.

Results:

Test	IPC Venous	IPC Arterial	geko™ Venous "Threshold"	geko™ Venous "Normal Clinical"	Summary/ Significance	geko™ Arterial "Threshold"	geko™ Arterial "Normal Clinical"	Summary/ Significance
Mean Blood Flow Volume	-4%	-9 to -16% (2 devices)	14%	32% increase	$p \leq 0.001$	-7%	30% increase	$p \leq 0.001$
Mean Blood Flow Velocity	143% - 166%	-1% to -4%	73%	174% increase		2%	24% increase	$p \leq 0.001$
Micro-circulation	44-59%		394% (Normal Clinical) and 345% (Threshold) in paper, but data actually showed 270% increase (First Kind analysis)					$p \leq 0.001$
Mean vessel diameter	No significant difference in femoral vessel diameter between the devices							$p>0.05$

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.

3b.v. Bahadori S, Immins T, Wainwright TW. The effect of calf neuromuscular electrical stimulation and intermittent pneumatic compression on thigh microcirculation. Microvascular Research 2017; 111: 37–41.

Methods: *Blood microcirculation of ten healthy individuals was recorded using laser speckle contrast imaging (LSCI) technique*. A region of interest (ROI) was marked on each participant thigh. The mean flux within the ROI was calculated at four states: rest, NMES device with visible muscle actuation (VMA), NMES device with no visible muscle actuation (NVMA) and IPC device.*
*** Speckle contrast optical spectroscopy, a non-invasive, diffuse optical method for measuring microvascular blood flow in tissue

Test	geko™ with no visible muscle activation	geko™ with visible muscle activation	IPC Device	Significance
Mean (SD) of Percentage increased in mean flux from baseline with device.	150.6 $\pm$ 48.8	399.8 $\pm$ 210.1	117.3 $\pm$ 17	P=0.005

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.*

3c. Effect of geko™ Device with Patients with Chronic Venous Disease

3c.i. Poster: Williams KJ, Babber A., Ravikumar R, Ellis M, Davies AH. Pilot Trial of neuromuscular stimulation in the management of chronic venous disease1. Poster VEINS Conference, UK. 2014

3c.ii. Poster: Williams KJ, Babber A., Ravikumar R, Davies AH. Pilot Trial of neuromuscular stimulation in the management of chronic venous disease2. Poster VEINS Conference, UK. 2014

3c.iii. 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.

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 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, 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 7a).

Results: At baseline after 20 minutes of geko™ stimulation

Haemodynamic changes in Femoral Vein	Healthy	Superficial Venous Insufficiency	Deep Venous Insufficiency	Deep Venous Obstruction	Significance
Peak Velocity %	46.7 ± 71*	72.2 ± 64**	69.3 ± 131	25.3 ± 44	*p<0.05 **p<0.01
Time Averaged Peak Velocity (TAMV) [blood flow] %	8.2 ± 55	48.4 ± 64*	421.1 ± 75	-0.5 ± 31	
Volume Flow %	9.7 ± 80	90.3 ± 141*	39.3 ± 108	2.8± 24	
Leg Fluximetry	275**	265*	69	47*	
Arm Fluximetry	84**	71*	24	107*	

After 6 weeks of geko™ use

Haemodynamic changes in Femoral Vein	geko™ Baseline Healthy	geko™ after 6 weeks Healthy	Paired *t*-test	geko™ Venous CVI Disease (combined) Baseline	geko™ Venous CVI Disease (combined) after 6 weeks	Paired *t*-test
Peak Velocity	24.3 ± 63	71.6 + 75* *53% increase*	P=0.16	30.8 ± 55 *p<0.05*	104.2 +/-117 *60% increase***	P=0.05

Haemodynamic changes in Femoral Vein	geko™ Baseline Healthy	geko™ after 6 weeks Healthy	Paired *t*-test	geko™ Venous CVI Disease (combined) Baseline	geko™ Venous CVI Disease (combined) after 6 weeks	Paired *t*-test
Time Averaged Peak Velocity (TAMV) [blood flow]	-15.9 ± 41	35 ± 59 *13% increase*	P=0.05	9.7 ± 57	52.6 +/- 67 *27% increase**	P=0.07
Volume Flow	-19.8 ± 27	42.4 ± 106 *8% increase*	P=0.12	24.3 ± 84	90.8 +/- 142 *51% increase**	P=0.15

Haemodynamic change from baseline with bilateral NMES (-p<0.05, ** -p<0.01, single/paired t-test)*

Key Learning Points: Regular use over 6 weeks increased all venous parameters, although less so in patients with deep venous disease. Leg swelling was reduced by 16% (p<0.05) in patients with venous disease. No mention is made of any of these patients also having open venous leg ulcers. Note that a paper is in process that will provide further analysis and statistical significance.

3c iv. PAPER: *Pilot Randomised Control Trial: Neuromuscular Electrical Stimulation in Treating Venous Disease R. Ravikumar, K.J. Williams, A. Babber, T.R. Lane, H.M. Moore, A.H. Davies European Journal of Vascular and Endovascular Surgery Volume 50 Issue 3 p. 390e404 September/2015*

Abstract from the document:

Introduction: *Chronic venous disease (CVD) is a common and potentially costly condition affecting a significant proportion of the population. This pilot randomised control trial investigates the effect of a neuromuscular electrical stimulation (NMES) device that causes sequential contraction of the foot and calf muscles in patients with CVD.*

Methods: *Twenty-two patients with CEAP C2-C4 venous disease were randomised to a sham or test device. 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 ¼ 0.0623). There was no improvement in limb volume in either the sham or test group over the 6 weeks (sham +0.7%, p ¼ 0.16; test +2.3%, p ¼ 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.*

Conclusion: *This trial demonstrated a significant improvement in venous haemodynamics and reduction in limb swelling with the test device compared to the sham group following immediate usage. In addition, it had a positive effect on quality of life outcome measures. The device is safe to use as a home based adjunct in managing venous disease. Due to the small sample size, some improvements were not statistically significant and subgroup analysis was not performed. Further trials are required to determine optimal frequency of device usage and the effect on different subgroups of patients with venous disease.*

3d. Effect of geko™ and Coronary Blood Flow / Ejection Fraction

Paper: 3.d.i. (Poster) Lavi S, Alemayehu M, McLellan A, D'Alfonso S. Peripheral Muscle Stimulation Increases Coronary Blood Flow. Session Title: Peripheral and Vascular Biology Abstract Category: 36. TCT@ACC-i2: IVUS and Intravascular Physiology Presentation Number: 2102-307JACC March 17, 2015 Volume 65, Issue 10S.

3.d.ii. Camuglia AC, Alemayehu M, McLellan A, Wall S, Abu-Romeeh N, Lavi S. The impact of peripheral nerve stimulation on coronary blood flow and endothelial function. Cardiovascular Drugs Ther. 2015;29: 527-533.

Methods: Peripheral blood flow studies were measured at baseline and after one hour of exposure to geko™ 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.

Results:

Test		Results with geko™ (Increase)			Summary/ Significance
		Baseline	**Minimal Twitch X 2 minutes**	**Maximum Setting X 2 minutes**	
Coronary Blood Flow-stenosed vessel	Average Peak Velocity (APV)	21.9 ± 12 cm/s	23.9 ± 12.9 cm/s (unclear which setting)		No significant difference p=0.23
	Coronary Flow Reserve (CFR)	2.2 ± 0.9 cm/s	1.9 ± 0.3 cm/s (unclear which setting)		No significant difference p=0.4
Coronary Blood Flow-Control (undiseased vessel)	Average Peak Velocity (APV)	20.3 ± 7.7 cm/s	21.0 ± 8.3 cm/s	23.5 ± 10 cm/s	Statistically Significant increase (15.8%) P=0.03, perhaps r/t increased venous return
	Coronary Flow Reserve (CFR)	2.2 ± 0.6 cm/s	2.4 ± 0.6 cm/s (unclear which setting)		No significant increase P=0.4, think that longer duration
	geko™ x 1 hour at Separate Appointment				
Systemic Endothelial Function	Rh-PAT* index	2.28 ± 0.39		2.67 ± 0.6	Statistically significant increase with geko™ activation P=0.045 "Represents a potentially disease-modifying mechanism"
Peripheral Blood Flow		Increased in all patients except 1			No significant increase P=0.13; thought to be a Type 2 error r/t small sample size

***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.

3dii. 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.

Property of Firstkind Ltd. William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University, London, UK.

Abstract

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 two different pulse widths (Box 1: 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.

3e. Effect of geko™ on Patients With Lower Limb Vascular Disease

3ei. Effect of geko™ Device on People with Intermittent Claudication

Paper: Barnes R, Shahin Y, Tucker AT, Chetter IC. Haemodynamic efficacy of the geko™ electrical neuromuscular stimulation device in claudicants. Oral presentation at Society of Academic & Research Surgery, 2014 Annual Meeting (January 8/9, 2014), Cambridge University, England.http://www.surgicalresearch.org.uk/wp-content/uploads/2013/10/1A_Vascular_Surgery_1.pdf

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™ 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 ABPI 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 ABPI of the active limbs was 0.68(SD 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).

Test	Baseline	Control (no geko™) Amount of change	Activated geko™ Amount of Increase	Summary/ Significance
Arterial Volume Flow		0.003 L/min	0.65 L/min 29% increase	p=0.026
Venous Volume Flow		0.0005L/min	0.041L/min 23% increase	p=0.023
Microcirculatory Flow		Decrease of 6.21 flux units	21.16 flux units	P<0.01

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 effects appear to be local and not systemic.

3eii.Paper: 0161 Short Paper Prize Section: Barnes R, Shahin Y, Tucker A, Chetter I. Haemodynamic augmentation in patients with peripheral arterial disease with the geko™ transcutaneous neuromuscular electrical stimulation device. Abstracts / International Journal of Surgery. 2015;18:239.

Methods: After 30 minutes to acclimatize, bilateral baseline arterial, venous and microcirculatory flow was measured by laser doppler. The 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.

Haemodynamic Tests	geko™ Baseline	Increase passive leg after 60 minutes activation	Increase geko™ leg after 60 minutes activation	Paired *t*-test
Arterial Volume Flow		-0.004L/min (mean)	0.68 L/min (mean)	p<0.001
Venous Volume Flow		0.002 L/min (mean)	0.034 L/min (mean)	p<0.001
Microcirculatory Flux		0.39 flux units	22.25 flux units (mean)	p<0.001

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).

3eiii. Paper: Barnes R, Madden LA, Chetter IC. Fibrinolytic effects of peroneal nerve stimulation in patients with lower limb vascular disease. Blood Coagulation and Fibrinolysis. 2016; 27:275-280.

Methods: 75 participants:

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

Tested with geko™ 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.

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

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.

3e.iv. Paper: Yilmaz S, Mermi EU, Zobaci E, Aksoy E, Yastı C. Augmentation of arterial blood velocity with electrostimulation in patients with critical limb ischemia unsuitable for revascularization. Vascular. 2017;25(2):137-141. Article first published online: May 6, 2016 DOI: https://doi.org/10.1177/1708538116649317

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 ¼ 11, mean age: 65.3 4.2 years, received iloprost infusion protocol alone) or Group 2 (n ¼ 11, mean age: 62.9 6.7, received iloprost infusion plus standardized protocol of peroneal nerve electrostimulation). Electrostimulation was delivered with 1 Hz frequency, 27 mA current, and 200 ms pulse width, for one hour in every four, monitored by nurses. The device was operated only while the patients were resting in bed lying in supine position. 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 ¼ 0.57), whereas the increase in Group 2 was marked (from 23.8 18.3 to 32.2 19.7, p ¼ 0.01). Blood velocity in posterior tibialis artery also increased in both groups, but not of statistical significance. No significant difference was found in 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 between Group 1 and Group 2 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 as an adjunct to medical therapy in patients with critical limb ischemia.

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3 e.v. Poster: Barnes R, Barakat H, Tucker A, Chetter A. ASiT 2014 Conference Poster Abstracts: Prospective observational series to evaluate the efficacy of the geko™ neuromuscular electrical stimulation device to produce muscle contraction in vascular patients. International Journal of Surgery 2014: 12 (Supplement 3): s110.
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 geko™ 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 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 (p5 (OR:17.831, 95%CI 2.713- 117.193; P¼0.003) 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 Learnings: 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 3a.iii) and wound healing is occurring (6b, c, d and h). It may be that length of time to healing may be increased with those patients. Further evaluation and research is needed.

3f. The geko™ Effect on Deep Veins

3f.i. Paper: Griffin M, Bond D, Nicolaides A. Measurement of blood flow in the deep veins of the lower limb using the geko™ neuromuscular electrostimulation device. Poster.
3f.ii. Paper: Griffin M, Bond D, Nicolaides A. Measurement of blood flow in the deep veins of the lower limb using the geko™ neuromuscular electro-stimulation device. International Angiology 2016; 35(4):406-10.

Methods: The aim was to determine the effect of the geko™ 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 calf 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.

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

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.

3g.i. The geko™ device effect on Venous Blood Flow with Casting
Paper: Warwick DJ, Shaikh A, Gadola S, Stokes M, Worsley P, Bain D, Tucker AT, Gadola SD. Use of the geko™ device in below knee cast patients. Neuromuscular electrostimulation via the common peroneal nerve promotes lower limb blood flow in a below-knee cast. Bone Joint Res 2013;2:179–85.

Methods: Ten healthy volunteers were tested with geko™ 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.

Results: Increase in Venous Blood Flow at the Superficial Femoral Vein

Position	geko™ activated No cast Mean ± SD	Summary/ Significance	Plaster Cast non-activated geko™ Mean ± SD	Plaster cast geko™ activated Mean ± SD	Summary/ Significance
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 (venous flow is already high in this position)	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.*

3g.ii. The geko™ device effect on Microcirculation with Casting

Paper: Warwick D, Shaikh A, Worsley P, Gadola S, Bain D, Tucker A, Gadola SD, Stokes M. *Microcirculation in the foot is augmented by neuromuscular stimulation via the common peroneal nerve in different lower limb postures: a potential treatment for leg ulcers*. Int Angiol. 2015 Apr;34(2):158-65.

Methods: Ten healthy volunteers were tested with geko™ 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.

Results:

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

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.

3h. The geko™ Device Reduces Venous Blood Sludging

3hi. Poster Abstract: Lattimer C, Azzam M , Kalodiki E. Common peroneal nerve stimulation reduces blood sludging in the popliteal vein standing and lying. 2016. http://www.gekodevices.com/media/128135/acp_2016_geko.pdf See videos for dynamic view.

Methods: The aim was to determine whether the Common Peroneal Nerve Stimulation (CPNS) 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. 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, p=0.0005.

Key Learning Points: The CPNS device significantly reduces the Venous Sludge Index irrespective of whether the subject is standing or lying down. The relationship between erythrocyte aggregation, stasis and VTE risk requires more investigation.

3hii. Lattimer CR, Azzam M, Papaconstandinou JA, Villasin M, Ash S, Kalodiki E. Neuromuscular electrical stimulation reduces sludge in the popliteal vein. J Vasc Surg Venous Lymphat Disord. 2018 Mar;6(2):154-162. doi: 10.1016/j.jvsv.2017.09.008. Epub 2017 Dec 29.

ABSTRACT

Background: *The common peroneal nerve stimulator (CPNS) is a UK-approved device for reducing venous thromboembolism (VTE) risk. It resembles a wrist watch and is placed over the common peroneal nerve, discharging electricity at a rate of 1 impulse/s. It has been presumed that as blood flow slows, erythrocytes aggregate into ultrasound-detectable echogenic particles, described as venous sludge. The aim of the study was to determine whether the CPNS reduces venous sludge by using an ultrasound-derived gray-scale (0-255) venous sludge index (VSI).*

Methods: *Twenty-five healthy volunteers had their right popliteal vein video recorded using B-mode ultrasound at 22 frames/s in longitudinal and transverse views, standing and lying. This was performed first with the CPNS off and then with the CPNS on. The CPNS impulse intensity used was set from 1 to 7 for each individual, and the level was sufficient to cause an outward jerking movement of the foot. A single frame of the possible 154 frames, lasting 7 seconds, was selected using a random number generator for the image analysis. The "brightness" of the erythrocyte aggregates (pixels) within a circular sampling area was quantified using the VSI. The brighter the sample, the greater the sludge.*

Results: *Values are expressed as median (interquartile range). On standing with the device off, there was a significantly higher VSI (P < .0005) compared with lying (longitudinal view, 27.7 [18.8-41.4] vs 11.7 [5.5-17.5]; transverse view, 20.7 [13.6-32.2] vs 11.4 [6.3-15.9]). 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]).*

Conclusions: *The CPNS device significantly reduces venous sludge within the popliteal vein irrespective of whether the subject is standing or lying down or of the longitudinal or transverse position of the ultrasound transducer. 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. However, the relationship between erythrocyte aggregation, venous stasis, and venous thromboembolism risk requires more investigation.*

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

Paper: Poster Abstract: O15 Khanbhai M, Hansrani V, Sultan J, Burke J, McCollum CN. The effect of neuromuscular electrostimulation on lower limb venous physiology. Academic Surgery Unit, Institute of Cardiovascular Sciences, Manchester Academic Health Science Centre. Society of Academic & Research Surgery, VASCULAR 1 Wednesday 7 January, 2015 09.45-11.20 http://www.surgicalresearch.org.uk/sars-2015/

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.

Mean Venous Transit Time (VTT) from dorsal foot to Popliteal Vein	**Baseline No Device**	**geko™ @100 µs**	**geko™ @200 µs**	**geko™ @400 µs**	**Statistical Significance**
VTT Patient Standing	37 ± 3.0	31.3 ± 3.8 (15% reduction)	25.2 ± 4.0 (31% reduction)	19.8 3.6 (46% reduction)	P< 0.001
VTT Patient Sitting	35.0 ± 2.8	27.6 ± 3.5 (21% reduction)	22.2 ± 4.1 (36% reduction)	16.3 ± 3.6 (53% reduction)	P< 0.001
VTT Patient Lying (Supine)	31.4 ± 2.4	21.3 ± 3.3 (32% reduction)	15.7 ± 3.1 (50% reduction)	11.3 ± 2.6 (64% reduction)	P< 0.001
Mean fall in Ambulatory Venous Pressure (AVP)	17.7 ± 2.1	15.2 ± 2.7 (14% fall)	9.3 ± 5.4 (47% fall)	5.7 ± 1.9 (67% fall)	P< 0.001
Mean Leg Volumes	3414 ± 148.6	3312 ± 146.1 (2.9% reduction)	3122 ± 143.7 (8.5% reduction)	2820 ± 302.8 (17% reduction)	P< 0.001

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:
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.

3.j. **Guidance:** The geko device for reducing the risk of venous thromboembolism. Medical technologies guidance. Published: 25 June 2014 nice.org.uk/guidance/mtg19 https://www.nice.org.uk/Guidance/mtg19
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.*

3k. **Costing statement:** 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.

3l. Research paper: Pelech N. Acupuncture at Urinary Bladder 40 (UB-40) and neuromuscular stimulation (geko™ device) effecting short-term lower limb blood flow in healthy subjects: a comparative study. Barts and the London School of Medicine and Dentistry. Paper submitted in part fulfilment of the intercalated BSc in Sports & Exercise Medicine. 2012. Firstkind Archives.

To our knowledge, this study is the first to investigate the effect of the geko™ on Achilles tendon and foot blood flow.

Abstract

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™ 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 Achillies 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.

3m. Williams K. Section 6.4 Concomitant use of common peroneal nerve stimulation and graduated compression stockings Neuromuscular Stimulation of the Leg. PhD Thesis, Imperial College London for the degree of Doctor of Philosophy. April 2017. https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf

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[1]. A high stiffness compression system causes fluctuations in the lower leg during walking compared to a low stiffness or elastic system[2], producing the greatest improvements in venous blood flow, e.g. in ejection volume and ejection fraction, from the lower leg[3]. 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[1]. At this time we consider the geko™ device to be an adjunctive therapy combined with a compression system.

1. O'Meara S, CullumN, Nelson EA, Dumville JC. Compression for venous leg ulcers. Cochrane Database of Systematic Reviews 2012, Issue 11.
2. Partsch H, Clark M, Mosti G, et al. Classification of compression bandages: practical aspects. *Dermatol Surg* 2008; 34(5): 600–9.65.
3. Mosti G, Mattaliano V, Partsch H. Inelastic compression increases venous ejection fraction more than elastic bandages in patients with superficial venous reflux. *Phlebology* 2008; 23(6): 287–94.)

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4. The geko™ Device and Oedema Reduction

Also see 3.b.iv. paper for hypothetical link with effect on microcirculation and oedema.

4a. Post-operative oedema

Paper: 4a.i. (Poster) Wainwright TW, Immins T, Middleton RG. An RCT comparing the effect of the geko™ device and TED stockings on post-operative oedema in Total Hip Replacement patients. Physiotherapy UK, October 2014, Birmingham.

Methods: 40 patients undergoing hip surgery were randomized to either geko™ or Thrombo Embolitic Deterrent stockings (TEDS) prior to the surgery. They were used continually on bilateral legs post-surgery until discharge. Circumference measures were taken of the ankle, knee and thigh pre-operatively, immediately post-operatively and on every hospital day. 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: Between pre-operation and discharge, at the thigh on the operated leg, geko™ users had a mean change in swelling of +1.5 cm (±0.3cm) and TEDS users had a mean change of +2.9 cm (±0.6cm), or about double for the TEDS group. 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.

Key Learning Points: The geko™ device appears to have been twice as effective in managing post-operative oedema following Total Hip Arthroses compared to use of TED stockings, in both the operative and non-operative limb.

4a.ii. Kocialkowski C, Pickford N, Bhosale A, Pillai A. The geko device: a novel treatment for the reduction of post-operative swelling following forefoot surgery**.** Research 2014;1:1272. Available at: https://www.labome.org/research/The-geko-device-a-novel-treatment-for-the-reduction-of-post-operative-swelling-following-forefoot-su.html

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 patients pain score using the Visual Analogue Scale.

4aiii. Poster: (Paper in development) Alharbi B, Aquil S, Ali O, Saha M, May M, Luke P, Sener A. Neuromuscular stimulation leads to improved lower limb oedema, urine output and blood flow compared to standard TED stockings and compression devices following kidney transplantation: A randomized controlled trial. Departments of Surgery[1] and Microbiology and Immunology[2;] Matthew Mailing Center for Translational Transplant Studies[3]. Western University, London, Ontario, Canada

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.

Results:

Measurement	Group 1 IPC	Group 2 geko™	Statistical Significance
Increase in calf circumference from baseline	+7.5% (2.3 $\pm$ -2 cm)	No change 0.34% (0.05 $\pm$ -0.95 cm)	p<0.0001
Increase in thigh circumference from baseline	+6% 2.4 $\pm$ -2 cm	No change	p<0.001
Increase in mean flow velocity	12 cm/sec	21 cm/sec	p<0.0005
Total Urine output in 6 days	8,800 cc's	17,900 cc's	P<0.5
Serum Creatinine	No differences	No differences	-
Patient Satisfaction	Less satisfied	More satisfied	-

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.

4b. Chronic Oedema

Paper: Ingves MV, Power AH. Two Cases of Transcutaneous Electrical Nerve Stimulation of the Common Peroneal Nerve Successfully Treating Refractory, Multifactorial Leg Oedema. Journal of Investigative Medicine High Impact Case Reports. October-December 2014: 1–4. Available at: http://journals.sagepub.com/doi/abs/10.1177/2324709614559839

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.

4c. The geko™ Device in management of occupational leg oedema

Paper: Poster Wou J, Williams KJ, Davies AH, 2015, A comparative study of the effect of graduated compression stockings and neuromuscular stimulation devices in the management of occupational leg oedema. Annual Meeting of the Society-of-Academic-and-Research-Surgery (SARS(, Publisher: WILEY-BLACKWELL, Pages: 28-28, ISSN: 0007-1323http://www.surgicalresearch.org.uk/wp-content/uploads/2014/12/PosterOfDistinction.pdf

Paper: Wou J, Williams KJ, Davies AH. Compression Stockings versus Neuromuscular Electrical Stimulation Devices in the Management of Occupational Leg Swelling
International Journal of Angiology 2016; 25(02):104-109.

Abstract

Method: *10 subjects (10 legs) were recruited from a clinical workspace. They had their right leg volume and great saphenous vein (GSV) diameter at the knee measured in the morning, six hours later scans were repeated. On subsequent separate days, Grade 2 graduated compression stockings (GCS; medi, UK), peroneal nerve neuromuscular stimulation (NMES) device gekoTM (Firstkind, UK), and footplate NMES device RevitiveTM (Actegy, UK) were used bilaterally according to manufacturer's instructions.*

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.*

4d. The geko™ device and orthopedic edema

Poster: Baker P, Mahmood I, Chandler H, Anwar S, Eardley W, Rangan A. A Pilot Clinical Study Comparing the geko™ Neuromuscular Electrostimulation Device, With Current Standard of Care to Evaluate Oedema Reduction And Readiness For Theatre In Patients Requiring Open Reduction Internal Fixation Following Ankle Fracture. Trauma / Foot & Ankle Trauma / Surgical Treatment South Tees NHS Trust, Middlesbrough, United Kingdom. Submitted to European Federation of National Associations of Orthopaedics and Traumatology (EFORT) 2018.

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 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.

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5. The geko™ Device and Systemic Responses
Sports recovery and effect on serum cortisol and Creatine Kinase (CK)
5a. Paper: Beaven CM, Cook C, Gray D, Downes P, Murphy I, Drawer S, Ingram JR, Kilduff LP, Gill N. Electrostimulation's Enhancement of Recovery During a Rugby Preseason. International Journal of Sports Physiology and Performance, 2013, 8, 92-98.

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.

5b. Poster: Pilot Trial of Neuromuscular Stimulation in The Management Of Chronic Venous Disease. KJ Williams, A Babber, R Ravikumar, AH Davies. VEINS Conference.
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.
Please see Section 3c for the Hemodynamic results of this study testing for geko™ effect in people with Chronic Venous Insufficiency (CVI), 7 a. for QoL results and 8d. 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.

Change in Laser Doppler Fluximetry Reading with bilateral geko™ devices

Percentage Change	Healthy	Superficial CVI	Deep Insufficiency	Deep Obstruction
Left Leg Flux	275**	265*	69	47*
Left Hand Flux	84**	71*	24	107*

*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 in 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.

5c. The geko™ Device and Neuropathy
Paper: Williams K. Section 7.4 NMES in the management of diabetic peripheral neuropathy (NERVES). Neuromuscular Stimulation of the Leg. PhD Thesis, Imperial College London for the degree of Doctor of Philosophy. April 2017. https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf

Methods: Subjects using the geko™ 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™)
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
After week 10, all subjects filled out quality of life questionnaires: 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. *Haemodynamic measurements of velocity and volume flow, taken at the level of the femoral vessels, were increased with bilateral device action. When compared to those figures achieved in healthy subjects, percentage increase from baseline in arterial parameters were comparable, whilst venous parameters were much reduced (e.g. venous TAMV increase of 15%/0.6cm/s versus 185%/2.4cm/s in healthy individuals) (*See Table 46 from the thesis 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). Laser doppler data from the foot support the lack of microcirculatory changes with the device, with fluximetry values in the foot resistant (16% increase, not statistically significant).*

Table 46 - Absolute and percentage changes in haemodynamic variables from baseline with use of NMES

Parameter change from baseline	Mean	SD	% change from baseline
Arterial PV (cm/s)	11.53	9.2	14.15
Arterial TAMV (cm/s)	2.82	1.9	222.17
Arterial VF (ml/min)	92.14	74.0	209.60
Venous PV (cm/s)	4.09	9.8	31.19
Venous TAMV (cm/s)	0.63	2.8	15.41
Venous VF (ml/min)	36.89	67.4	32.82

N=5; PV – peak velocity; TAMV – time averaged maximum velocity; VF – volume flow; SD – standard deviation

Conclusion: *It is impossible to say whether increasing the statistical power would have allowed separation of the groups, but the data gathered here would go someway to allowing a power calculation. There is evidence to suggest that in this group of people the psychological effects of using such a device are positive, and lead to a perceived improvement in disease severity. The device is able to produce an increase in local blood flow in the ipsilateral femoral vessels, but its microcirculatory effects are attenuated compared to healthy subjects.*
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.

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6. The geko™ Device and Wound Healing

6a. Paper: Williams KJ, Davies AH. The use of a novel neuromuscular electrical stimulation device in peripheral vascular disease. Int J Case Rep Images 2014;5(11):744–747.

Methods: Three cases include the management of recalcitrant ulcers, non-reconstructable 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 are 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.*

6b. *Poster 0012:* Wounds Canada Conference: Stimulating Non-healing Venous Leg Ulcers: Evaluation of Innovative New Muscle Pump Activator. May 2017. (same authors as paper below).
Paper: Harris, C, Loney, A, Brooke, J, Charlebois, A, Coppola, L, Mehta, S, Flett, N. Refractory venous leg ulcers: observational evaluation of innovative new technology. International Wound Journal. 2017. 14;6: 1100-1107. Available at: http://onlinelibrary.wiley.com/doi/10.1111/iwj.12766/epdf
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. 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.

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.

6c. Poster 011: Evaluation of an Exciting Neuromuscular Electrical Stimulation Device for Non-Healing Venous Leg Ulcers. May 2017 Wounds Canada Conference: (same authors as paper below)
Paper: Harris, C, Duong, R, van der Heyden, G, Byrnes, B, Cattryse, R, Orr, A, Keast. Evaluation of a muscle pump-activating device for non-healing venous leg ulcers. International Wound Journal. 2017. 14;6: 1189-1198. Available at: http://onlinelibrary.wiley.com/doi/10.1111/iwj.12784/epdf

Methods: Twelve patients with eighteen VLUs recalcitrant to treatment, cared for in in two Community Care Access Centres in Ontario, consented to evaluate the 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.

6d. Poster 010: Harris C, Ramage D, Boloorchi A, Vaughn L, Kuilder G, Sandcroft W. Using a Neuromuscular Electrostimulation Device for Non-healing Lower Leg Wounds in Long Term Care Residents. May 2017. Wounds Canada Conference: (Manuscript in preparation for submission to International Wound Journal).

Methods: In the Long Term Care 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. One resident with Diabetes had a three-month history of ++ pain and an infected below-knee amputation incision on the stump; geko™ was tried for compassionate reasons as staff had prepared patient to participate**.** One resident developed wounds as she approached end of life with associated skin changes. The geko™ was started before her palliative situation was understood, and stopped at that point. She developed several wounds before passing away within 6 weeks of starting the geko™. 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 = cm^2) 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). Nursing staff found the geko™ devices easy to use, and residents/ families were generally pleased to participate in the evaluation.

Key Learning Points:

The geko™ training was effective for nursing staff. A weekly mean decrease in size of 10.9% for non-healing wounds in residents who were adherent to geko™ and best practices in this aged, complex population was considered a success.

6e. Poster: Suitor M. Adjunctive application of a muscle pump activator to improve blood flow in patients with lower limb ulcerations related to chronic venous insufficiency. Alberta Health Services. Moving Forward in Wound Management Conference: Engaging Learners, Motivating Change, and Inspiring Action. September 8, 2016.

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.

6f. Poster: Ivins NM, Jones NJ, Hagelstein SM, Walkley NA, Harding KG. An evaluation of a neuromuscular electro-stimulation (NMES) device* on patients with differing lower limb wound aetiologies
CBE Welsh Wound Innovation Centre. Presented at EWMA 2016.

Methods: All patients had hard to heal wounds of 3 mixed venous arterial, 4 venous and 3 diabetic aetiology without clinical features of infection at baseline. All cases received geko™ plus standard of care.
Results: A serial decease in mean wound size (6.23 cm2) was achieved over the eight-week evaluation period. None of the patients included in the case series evaluation achieved complete re-epitheliailisation between baseline and endpoint but a significant reduction in subjective wound pain was reported in a high proportion (90%) of the cases recruited. In respect of the patients with diabetic foot ulceration no improvement was observed over the duration of the case series evaluation.
Key Learning Points: The device was easy to apply and was well tolerated by 90% of patients which suggests that neuromuscular electro-stimulation (NMES) may be a suitable therapy in the treatment of venous and mixed aetiology leg ulceration in conjunction with compression therapy.

6g. Poster: Aquil S, AlHarbi B, Sharma H, Pacoli K, Luke P, Sener A. The impact of a muscle pump activator on incisional wound healing compared to standard TED stockings and compression devices in kidney and kidney-pancreatic transplant recipients: A randomized controlled trial. Abstract submitted to Wounds Canada and CAET Conferences May 2017.
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 (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.*

6.h. Waterloo Wellington CCAC/ LHIN evaluation January 2018 Manuscript underway.

Methods: Two streams of patients were used to evaluate the effect of the geko™ 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 cm^2 (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

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 6.75cm^2 (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.

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%).

6i. The geko™ device and Diabetic Foot Ulcers

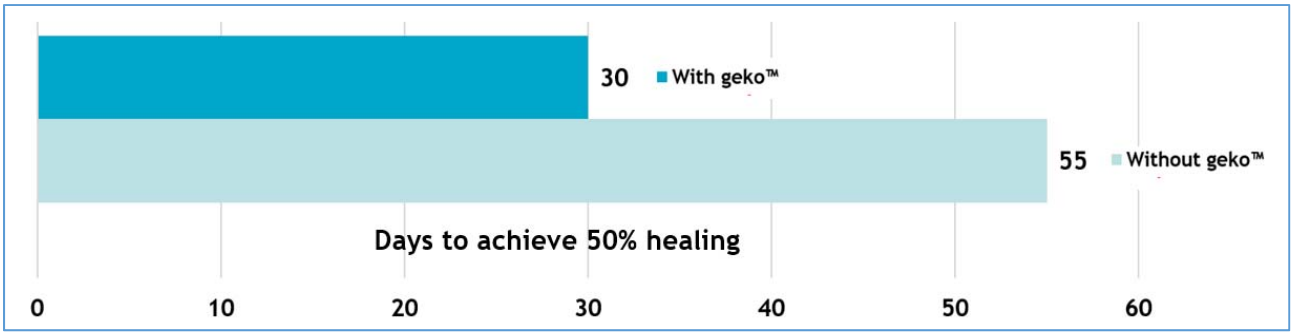
Paper: Williams K. Section 7.3 NMES in the management of diabetic foot ulcers (ULCERS). Neuromuscular Stimulation of the Leg. PhD Thesis, Imperial College London for the degree of Doctor of Philosophy. April 2017.
https://spiral.imperial.ac.uk/bitstream/10044/1/49202/1/Williams-K-PhD-Thesis.pdf

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™ 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 x W x D=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.

7. The geko™ Device and Quality of Life (two papers)

Examining the QoL with the geko™ device over 8 weeks in patients with CVI

7a. Poster: Williams KJ, Ravikumar R, Babber A, Davies AH. Can neuromuscular stimulation relieve symptoms of chronic venous disease, and improve quality of life? Annual Meeting of the Society-of-Academic-and-Research-Surgery (SARS) 2015, Publisher: WILEY-BLACKWELL, Pages: 9-9, ISSN: 0007-1323.

Methods: Please see Section 3c for the Hemodynamic results of this study testing for geko™ effect in people with CVI. 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 ($p<0.01$). When the geko™ devices were stopped for this group, quality of life continued to improve with the AVVQ scale.

		CEAP 0-3 disease			CEAP 4-6 disease			
		Week 0	**Week 6**	**Week 8**	**Week 0**	**Week 6 (end of geko™)**	**Week 8 (no geko™)**	**Significance for those with CEAP 4-6**
Disease-specific	**VCCS***	2.8	2.7	3.4	10.4	7.2	7.5	Improved by Wk 6, Deteriorating by Wk 8
	VDS*	0.65	0.7	0.8	1.9	1.0***	1.1	Improved Wk by 6, Deteriorating by Wk 8
	AVVQ*	9.0	7.5	9.2	26.4	20.8	19.3	Improved Wk 6, Continued by Wk 8
Generic	**EQ5D****	0.8	0.9	0.8	0.7	0.7	0.7	No Change
	VAS*	82.9	82.8	78.1	63.4	72.7	70.9	Increased by Wk 6 then decreased by Wk 8
	CES-D*	8.8	7.9	10.6	13.8	11.8	13.4	Improved by Wk 6 then worsened by Wk 8
	SF-12**	99.7	95.5	76.6	83.1	93.5	67.4	Improved Wk by 6, Deteriorating by Wk 8

***-$p<0.01$, 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. The results for the healthy volunteers are not included in this poster. It does not mention that any of these volunteers had existing venous leg ulcers.

7b. (This paper also appears in Section 6d.) Revera Long Term Care Evaluation (evaluation finished – writing underway) 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).

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8. The geko™ Device Tolerability

Paper 8a. (This paper also appears in Section 3b) 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

Results: Ten patients used a Verbal Rating Score (VRS). Both devices were tolerated well, VRS was statistically lower for IPC than NMES (1.5 and 2.8, p¼0.006) but both scored less discomfort than a standard blood pressure measurement.

Paper 8b. (This paper also appears in Section 3b) 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 (p¼0.006, paired Student's t-test).

Paper 8c. (This paper also appears in Section 3b) Jawad H, Bain DS, Dawson H, Crawford K, Johnston A, Tucker AT. The effectiveness of a novel neuromuscular electrostimulation method versus intermittent pneumatic compression in enhancing lower limb blood flow. *J Vasc Surg*: Venous Lymphat Disord. 2014;2(2):160-5.

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: 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, $p \leq 0.05$. 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.

Paper 8d. (This paper also appears in Section 3h) Warwick DJ, Shaikh A, Gadola S, Stokes M, Worsley P, Bain D, Tucker AT, Gadola SD. Use of the geko™ device in below knee cast patients. Neuromuscular electrostimulation via the common peroneal nerve promotes lower limb blood flow in a below-knee cast. Bone Joint Res 2013;2:179–85.

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'.

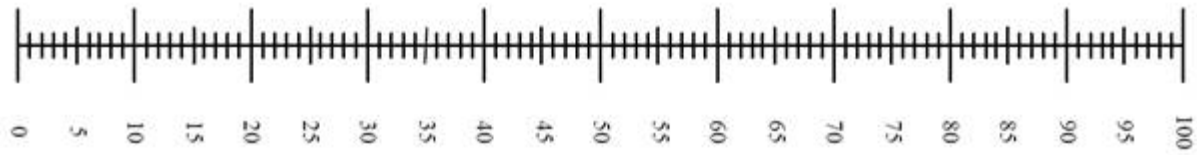
Results: *The median level of discomfort measured on the VRS across all postural positions using the geko device was 2, denoting 'minimal discomfort'. The median level of discomfort was slightly higher without casting compared with discomfort when casting was applied. The VRS showed that in the supine 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.

8e. Poster: Williams KJ, Ravikumar R, Babber A, Davies AH. Can neuromuscular stimulation relieve symptoms of chronic venous disease, and improve quality of life? Annual Meeting of the Society-of-Academic-and-Research-Surgery (SARS) 2015, Publisher: WILEY-BLACKWELL, Pages: 9-9, ISSN: 0007-1323

Methods: Please see Section 3c for the Hemodynamic results of this study testing for geko™ effect in people with CVI, 5b. for the increase in microcirculation to the hand (systemic response) and section 7a. for the QoL results. The 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.

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9. Consensus and Literature Reviews

Paper: 9a. Williams KJ, Ravikumar R, Gaweesh AS, Moore HM, Lifsitz AD, Lane TRA, Shalhoub J, Babber A, Davies AH. A Review of the Evidence to Support NMES in the Prevention and Management of Venous Disease. Chapter: Thrombosis and Embolism: from Research to Clinical Practice. Advances in Experimental Medicine and Biology. 2016. 906:377-386

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.

Paper 9b. Orsted HL, O'Sullivan-Drombolis D, Haley J, LeBlanc K, Parsons L. The effects of low frequency nerve stimulation to support the healing of venous leg ulcers. Canadian Association of Wound Care Consensus Paper - November 2016. https://www.woundscanada.ca/docman/public/health-care-professional/bpr-workshop/70-bpr-lfns-final-110316/file

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.

9c. Paper: Harding, K. An Innovative Technology for Healing Venous Leg Ulcers: geko™. Expert opinion paper. Distributed at CAWC Conference 2016, Niagara Falls, ON.

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."