geko^{TM} Mechanism of Action summary

Electrical stimulation has been used for many decades to reduce venous stasis in the legs. [i] Historically, these devices used a substantial current applied transcutaneous to the muscles, to induce intermittent tetanic contractions in the gastrocnemius muscles, so squeezing blood out of the rear compartment of the leg. The substantial currents and duty cycles (e.g. on 1 s, off 1s) required to stimulate muscle directly caused considerable pain, and meant that it was generally only possible to use these devices under anaesthetic. Additionally, the power requirements were so large that either mains electricity supply or a substantial battery box were required, necessitating electrode leads trailing to the patient.

Work done previously to optimise the patterns, waveforms, and parameters of stimulation [ii] had all been done in quite different contexts. In the field of Functional Electrical Stimulation (FES) – the application of electrical stimulation to actuate function in paralysed muscles (for example paraplegic cycling) – the aim was to generate stable, controllable, sustained contractions. In the case of stimulation to build muscle and strength training, the aim was to minimise discomfort, while bringing about muscle fatigue. Generally, these devices used burst of pulse trains: “Russian current” to achieve sustained contractions. Variations on the theme consisted of sinusoidal vs square waves, or asymmetrical waveforms, but generally all in bursts of multiple waves at high frequency (>10Hz).

By making several departures from the approach above, we have been able to produce a compact, wearable, integrally-powered device which delivered effective blood pumping in the leg without causing discomfort.

Momentary contraction

In contrast to FES, for activating the venous muscle pumps sustained muscle contraction is not needed or indeed desirable. The body’s own venous pump system consists of a system of blood-filled reservoirs (veins) with in-built unidirectional valves. In essence, it operates much like a hand sphygmomanometer bulb pump: once the bulb is squeezed to empty, sustained further squeezing delivers no benefit. The optimal pumping pattern is a series of very short squeezes, releasing in between to allow the bulb to re-fill. Similarly, we discovered that the optimal stimulation regimen for activating the leg pump was a single pulse to elicit a momentary twitch of the leg muscles, followed by a (e.g. 1 second) pause for venous re-fill, followed by another single pulse, and so on.

Single pulse

A single momentary pulse represents a tiny fraction of the total charge delivered by a train of 100 pulses over a 1 second period, required to sustain tetanic contraction. Less charge meant not only that the stimulus was many times more comfortable, but also needed a much smaller power supply.

Optimal activation of the leg pump: Dorsiflexion vs Plantarflexion

The conventional wisdom previously had it that, since the venous pumps are predominantly contained in the posterior chamber of the leg, it is necessary to stimulate contraction in the gastrocnemius and soleus muscles in order to activate the pump. We challenged this wisdom. Initially noting that the standard clinical test for venous sufficiency uses 10 x dorsiflexions (toe lifts) rather than plantarflexions to empty the veins, we posited that contraction of muscles in the anterior chamber must also be effective in actuating the pump. Analysis of the fluid mechanics, system dynamics, and anatomy of the system led us to a better understanding of the pumping mechanism.

Blood is pumped from the leg by a combination of the following mechanisms:

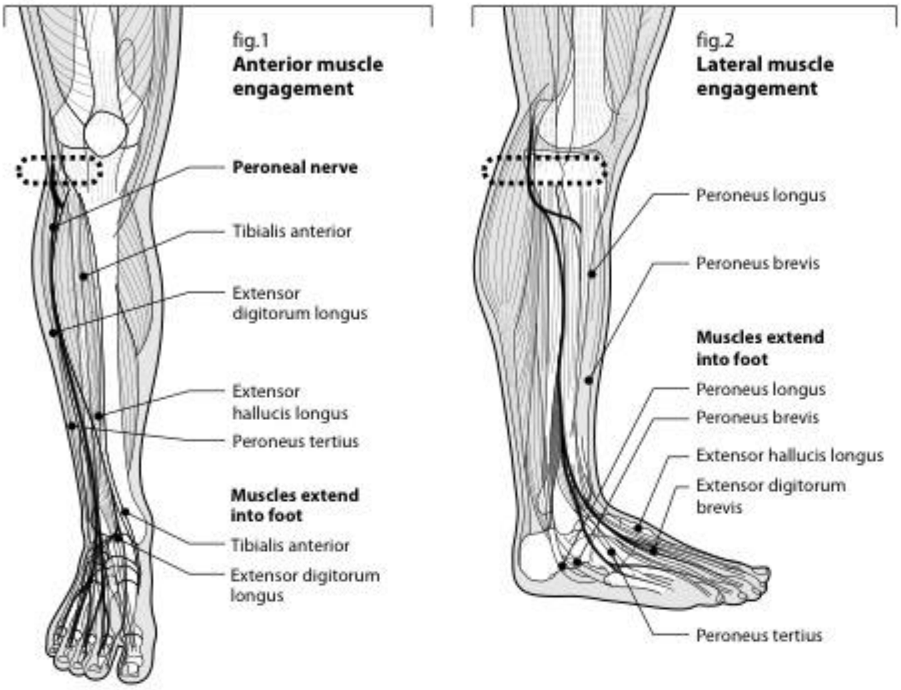
1) **Distention**
   As muscle is extended, its cross-sectional area (CSA) reduces in approximate inverse proportion to its length. In so doing, the vessels contained within the muscle complex also reduce in CSA, thus evacuating blood.
2) **Compression**
   Since the leg is contained within relatively inextensible fascia, its circumference is of approximately fixed length. Any contraction of muscles within the fascia leads to an increase in cross-sectional area of those muscles, now acting against the constraint of the inextensible fascia. This creates circumferential tension In the fascia, which effectively applies compression to the whole leg. It will be appreciated that this occurs regardless of which set of muscles (anterior chamber or posterior chamber) contracts.
3) **Inertia**
   Because of the mass of the blood, it has a tendency to remain stationary when surrounding structures move, unless actively propelled. Since the valves are unidirectional, there is a tendency for an eccentric movement to leave the blood where it is, whereas a concentric movement will force the blood centrally. This may be analogised to the party trick of snatching a table-cloth out from underneath the crockery on a table setting.
4) **Reciprocation**
   Considering once again the bulb pump mentioned above, or indeed a bicycle pump (which also operates on the basis of a unidirectional valve): regardless of whether the up-stroke or the down-stroke of the pump is responsible for the pumping, it is necessary to have a reciprocating action. Continuous pressure in one direction achieves nothing, as the reservoir never refills. So, dorsiflexion alone will not cause pumping, and plantarflexion alone will not cause pumping. Effective pumping requires an on-going alternating sequence of contraction and relaxation in opposing muscle groups, and it matters little which comes first in the sequence. However, referring to 3 above, when we consider the inertial component in the system, there is a benefit to a dynamic asymmetry in the sequence. Considering again the crockery on the table cloth, a 'snatch' (a fast twitch) is required to move the cloth from underneath the crockery, whereas a slow movement will tend to take the crockery with it. Similarly, there is an inertial advantage in having the 'fast twitch' on the eccentric movement of the rear chamber of the leg (extending gastrocnemius/soleus), which the blood overcomes the valve closing pressure and moves centrally relative to the compartment. The return stroke, where the whole structure returns.

The 4 points above led us to the conclusion that a cycle consisting of a twitch of the muscles of the anterior chamber of the leg, followed by relaxation/refill, would optimise pumping. This, we subsequently verified experimentally[iii].

Common peroneal nerve

Rather than directly stimulating the muscle, we identified a suitable location for accessing the common peroneal nerve where it passes superficially near the skin. By accessing this nerve prior to its deep-superficial branch, we are able to stimulate two separate complexes of muscles, as per figs 1 & 2 below.

figs. 1 & 2: **Stimulated muscles** / Muscles stimulés / Stimulierte Muskeln



Stimulation of the nerve requires less current and is considerably more comfortable than directly stimulating the muscle, to achieve the same degree of muscle contraction. This, again, reduces our power requirements.

Fixed electrode spacing

It was noted that FES applications of electrostimulation frequently entail much trial and error in terms of electrode placement. This process is frequently complicated by the fact that 2 different properties are simultaneously being varied: stimulus location, and electrode spacing. It greatly simplified electrode placement if both positive and negative electrode were provided on a single substrate in fixed spacing. This also contributed to the feasibility of producing the device a single integral unit.

Initial geko Clinical Development

Existing modalities for DVT prevention and edema management tend to be divided between:

- **Pharmaceutical** interventions which aim to reduce coagulability of the blood, or
- **Mechanical** interventions which aim to reduce stasis (i.e. promote blood flow).

The latter group includes graduated compression stockings, which aim to increase venous velocity by Bernoulli Effect, whereby reducing the diameter of the vessel (by squeezing) increases flow speed, assuming constant flow volume. Although this mechanism may increase velocity[iv], it provides no active augmentation of flow volume (without the patient's own ambulation), and indeed may actually reduce flow volume by occlusion.[v]

The other common mechanical prophylaxis is Intermittent Pneumatic Compression (IPC), which intermittently squeezes the leg to evacuate blood from the venous system, effectively making 'passive' use of the venous valve pumps. Problems with this system are the need for a bulky pump unit, trailing tubes, and inflatable sleeves on the legs, which are all inconvenient and contribute to poor patient tolerance.

In the initial study [iii], data acquired from 30 healthy volunteers demonstrated that electrical stimulation of the common peroneal nerve significantly enhances both venous volume and venous velocity in the lower limb compared with baseline. Venous volume blood flow increases seen in the superficial femoral vein were exceptionally high (up to100%).

In a further study [vi] it was established that the geko™ device is superior to IPC Huntleigh Flowtron™ and IPC Kendall SCD™ devices in enhancing blood flow in the lower limbs. At higher geko™ settings increases in the femoral venous and arterial blood volume flow of ~30% was seen over the other two devices. Microcirculatory blood velocity in the skin, increased substantially by ~ 370% following the use of the geko™ device compared to a modest 59% and 44% increase following the use of the IPC-HF and the IPC-Kendall devices respectively. The study also showed the geko™ to be safe and well tolerated by the participants.

Warwick et al [vii]found that stimulation of the common peroneal nerve using the geko™ device increased blood flow in the femoral vein, with the lower leg in a cast thus offering a viable means of thromboprophylaxis for patients in a plaster casts for whom other modes of mechanical prophylaxis are unsuitable.

Williams et al[viii] confirmed geko's superiority over IPC, finding IPC caused 51% (p=0.002), 5% (ns) and 3% (ns) median increases in venous peak velocity, time-averaged maximum velocity and volume flow, respectively; geko™ stimulation caused a 103%, 101% and 101% median increases in the same parameters (all p=0.002). Intermittent pneumatic compression did not improve arterial haemodynamics, however geko™ caused 11%, 84% and 75% increase in arterial parameters (p<0.01).

Khanbai [ix] found that geko™ reduced venous transit time, ambulatory venous pressure and leg volumes with the greatest effect in the lying position.

Zhang [x] observed an increase in muscle blood oxygenation using geko™.

In a randomised controlled trial[xi], 30 consecutive patients undergoing total knee replacement were allocated to receive geko™ plus low molecular weight heparin and below-knee compression stockings (Group 1) or low molecular weight heparin and below-knee compression stockings alone (Group 2). Electrostimulation was performed for 1 h in every 4 h after the operation. Peak blood velocity in the femoral vein was evaluated with Duplex ultrasonography in supine position in the absence of the study devices to blind the radiologist.

Postoperative peak blood flow velocity in the femoral vein was significantly higher in the geko™ group compared to control group (17.462.86 cm/s vs. 13.843.58 cm/s, $p<0.02$). The geko™ group achieved a significant increase in peak blood flow velocity in the femoral vein after the operation (mean increase 67.4817.38%, $p<0.001$). It was concluded that the geko™ enhanced venous flow in the lower limb and may be of use as a supplementary technique in deep venous prophylaxis following lower limb orthopaedic operations.

Nicolaides et al [xii] succeeded in measuring flow in the deep veins of the lower limb, and found that peak velocity (PV) increased 216% in the peroneal vein, by 112% in the posterior tibial vein and by 137% in the gastrocnemial vein ($P<0.001$). Ejected volume per stimulus increased by 113% in the peroneal vein, by 38% in the posterior tibial vein and by 50% in the gastrocnemial vein ($P<0.003$). Associated volume flows during the muscle contraction were increased by 36%, 25% and 17%, respectively ($P=0.05$).

A substantial body of published evidence gives a convincing case for geko's effectiveness in addressing the Stasis corner of Virchow's Triad, both in healthy subjects and in a variety of patient groups. However, studies have also pointed to geko's potential to reduce coagulability of the blood. In a study[xiii] of 70 vascular patients (30 claudicants, 25 patients postoperative infra-inguinal bypass grafts and 22 patients with varicose veins) randomly assigned to geko™ or control groups, a statistically significant reduction in plasma PAI-1 was demonstrated following peroneal nerve stimulation with geko™. This indicates that geko™ Increases fibrinolytic activity, further supporting its role in DVT prophylaxis.

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