SHORT REVIEW

# Electro stimulation of the nerves and muscles of the body, veins and lymphatics

Can we make a difference to oedema/lymphoedemas in immobile and mobile patients, and can we overcome senescence associated with venous and lymphatic drainage function as we age?

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Abstract Veins and lymphatics are a side-by-side dual drainage system responsible for the wellbeing of the body systems, their cells and tissues. There are a range of intrinsic and extrinsic factors which affect their vaso-motoricity and we often deal with the significant health impacts of the failure of this dual drainage system though poor knowledge of how we might better influence them. In this paper we cover the range of strategies we can use to stimulate the nerves and muscles of these systems as well as the skeletal musculature using Transcutaneous Electrical Nerve Stimulation (TENS) and Electrical Muscle Stimulation (EMS) to gain improved outcomes for those with lymphoedemas when used alone or in addition

to lymphatic drainage massage, compression, skin care, exercise, and general activity. I hope the information in this paper stimulates more evidence gathering and further trials considering these infrequent forms of treatment to stimulate our side by side dual drainage systems the veins and lymphatics for better management of lymph and other oedemas.

**Keywords** Electro stimulation, History of electrostimulation, Skeletal and smooth muscles, Veins, Lymphatics

#### Introduction

The earliest reports of the use of electrical muscle stimulation date back to the first century. Interestingly, apparently a Roman doctor helped reduce pain in patients with <u>gout</u> when they were given an electrical shock from an

electric ray<sup>1</sup>. Much later in the <u>18th century</u>, "doctors" used devices to deliver electrical shocks to treat a wide range of conditions<sup>2</sup>. This was the beginning but where have we taken it and how can we improve it?

### **Background**

Veins and lymphatics are a side-by-side dual drainage system responsible for the health and wellbeing of the cells, the tissues and in fact, the whole body. Flow into and along these two systems is determined by a wide range of factors including arterial and venous pressures, protein content of the tissues, the patency of valves and pressure variations in the surrounding tissues facilitated by skeletal muscle contractions. But the factors we often forget or gloss over are those linked to the intrinsic and extrinsic factors which influence their vaso-motoricity. We must remember that both veins and lymphatics have layers of muscular cells within their walls, these layers generally being dependent on the size of the vessel and its proximity to its emptying point. These are or can be stimulated by intrinsic and



extrinsic factors, the former by electrical impulses coming along the nerves which innovate them and the latter by the state of stretch of the walls and thus muscles of these vessels with stronger contractions generally being linked to greater filling and more forceful emptying.

What does this all mean? If these combined neurogenic and myogenic mechanisms are not working or poorly working, can we improve their function by using electrical stimulation of the muscles directly or indirectly by stimulating the nerves which supply them.

We know we can do exactly that in the skeletal musculature of the surrounding tissues, removing the need to be dependent on movement/exercise induced improvements in lymphovenous outflow.

This can be especially important in those who are inactive, are obese, or who for one reason or another are bed bound, immobile, paralysed etc such as often occurs in aged care facilities.

Keeping it simple, basically what we can do is stimulate the nerves using ENS – Transcutaneous Electrical Nerve Stimulation, (commonly called TENS) as well as stimulating the muscles to partially contract<sup>3</sup> it is able to block pain receptors. Or EMS – Electrical Muscle Stimulation which can be used which works by delivering electrical pulses that directly or indirectly activate muscles to contract and relax once the stimulating current is stopped.

#### The muscles of the lymphatics

A review of lymphatic musculature in 2010 by Bridenbaugh (2010)<sup>5</sup> showed more research and information was needed about them. Scallan et al (2016)<sup>6</sup> indicated that our general understanding of lymphatic muscle cell biology was still poor.

But we know the collecting lymphatics contain muscular walls capable of both tonic and phasic contractions, which both generate and regulate lymph flow. So it's critical they are functioning properly and appropriately. As we know and Scallan et al (2016)<sup>6</sup> indicate in their review the effectiveness of the lymph pump system has an impact not only on the interstitial fluid balance but overall homeostasis.

They and others from the very early days of research in this area<sup>7</sup> emphasise that lymph propulsion requires not only strong contractions of lymphatic muscle cells, but perhaps more importantly contraction waves that are synchronized over the length of a lymphangion and properly functioning intraluminal valves. So, we can see the extreme importance of the contractions of the musculature no matter its location or form! Thus if we have skeletal muscle paralysis or sub optimal contractions and in addition

Piller, et al (2010)<sup>4</sup> undertook a placebo-controlled study of mild electrical stimulation of participants with leg lymphoedemas. The active group received 13 treatments over 4 weeks, while the control group (the self-maintenance group) received none. The active treatment group showed reductions in leg fluids of 200mls compared to the self-maintenance group (P<.001) over the treatment period. This was our first evidence for the benefit of mild electrical stimulation to improve lymphatic drainage! At that stage we were unsure as to its exact mechanism of action although information about the unit suggested a targeted action on the smooth muscles of the lymphangion and a lesser but perhaps important impact on the skeletal musculature.

In terms of stimulating our skeletal muscle to contract (using the legs as an example) we can benefit acute or chronic oedema and lymphoedema through the range of contractions that can be facilitated by it. These being Isotonic contractions which generate force by changing the length of the muscle, which can be a concentric contraction in which the muscles shorten, or Eccentric contractions in which the muscles elongate in response to a greater opposing force. Remember though that when under tension, a muscle cell or whole muscle group can lengthen, shorten, or remain the same. We know that the term "contraction" implies a shortening in the narrower sense of the word but broadly it means the generation of tension within a muscle fibre or group!

Lymphatic contractile dysfunction, we have a big problem, not only of the optimisation of the roles but other issues in which the lymphatic system is involved including obesity and metabolic syndrome, inflammation, and inflammatory bowel disease.

More recently, Solari et al (2023)<sup>8</sup> have shown exposure to a hyper- or hypo-osmolar environment can deeply affect the intrinsic contraction rate of lymph vessels and thus have an impact on lymph flow. They showed the normal response to a hyperosmolar environment to be a steady decrease in the contraction rate and lymph flow, but that it could be prevented by blocking transient receptor potential cation channel, subfamily V member 1 (TRPV1) channels with capsazepine.

In contrast to this, the response to a hyposmolar environment was an early phase of increasing contraction rate, followed by a decrease. In this case the early phase could be abolished by blocking Volume regulated anion channels (VRAC)'s with 4-(2-Butyl-6,7-dichloro-2-cyclopentyl-indan-1-on-5-yl) oxobutyric acid (DCPIB), while blocking transient receptor potential cation channel, subfamily V member 4 (TRPV4) only resulted in a delay

of the early response. Their data suggested a cooperation of the three channels can determine the response of lymphatic vessels in terms of contraction frequency and lymph flow with a prominent role of the TRPV1 and the VRAC's.

But what if it's not optimal or not working as expected is electro stimulation able to override it and lead to an appropriate response?

Another issue to face is lymphatic senescence <sup>9</sup> It's linked with alterations in the muscles of the lymph collectors and the nerves supplying them, the lymphatic glycocalyx function of lymphatic endothelial cells, the effects of UV light exposure and oxidative stress. Acute and Chronic inflammation is likely also to have an impact. A

## The basics behind lymph movement

What follows is a summary or our understanding based on an excellent article by Scallan et al (2016)<sup>6</sup> and I suggest for more details you check it out. Basically though, a combination of extrinsic and intrinsic forces move our lymph against a hydrostatic pressure gradient (at least in the lower parts of the body). In a resting individual about 1/3 of lymph from the lower extremities is a consequence of compression by skeletal muscle contractions (called the extrinsic pump mechanism) and about 2/3 to active pumping (intrinsic pump) of the collecting lymph vessels. The original work leading to this understanding was undertaken by Engeset and others in the late 70's (Olszewski and Engeset 1980)<sup>12</sup>. It's the

#### Conclusion

It may be as Scallan et al (2016)<sup>6</sup> suggest that many of our current therapies for lymphoedema only promote passive lymph transport through our various forms of massage and specific lymphatic drainage, exercises and activity. It may just be that electro stimulation focusing on them, and/or veins and surrounding skeletal musculature may help us improve outcomes! But most important of all

#### References

- 1) Francis J, Dingley J. Electroanaesthesia from torpedo fish to TENS. Anaesthesia. 2014 Oct 28;70(1):93-103. DOI:  $\underline{10.1111/anae.12887}$
- 2) Heidland A, Fazeli G, Klassen A, Sebekova K, Hennemann H, Bahner U, et al. Neuromuscular electrostimulation techniques: historical aspects and current possibilities in treatment of pain and muscle waisting. Clinical Nephrology 2013, 79 (suppl 1: S12-23. DOI: 10.5414/cnx77s106
- 3) Doucet B, Lam A and Griffin L. Neuromuscular Electrical Stimulation for Skeletal Muscle Function. Yale J Biol Med. 2012 Jun; 85(2):201–215. PMCID: PMC3375668 PMID: 22737049
- 4) Piller N, Douglass J, Heidenreich B, Mosley A. Placebo controlled trial of mild electrical stimulation. Journal of Lymphoedema 2010;5(1):15-19.

question again can be asked - can Transcutaneous Electrical Stimulation (TENS) or Electrical Muscle Stimulation (EMS) overcome this issue of senescence or at least minimise it?

Apart from this electrical stimulation may have other benefits. Katz et al 1987<sup>10</sup> and others since have indicated electrical stimulation may improve some functional outcomes in terms of its effect on fibrinolysis thereby perhaps reducing deep vein thrombosis (DVT) risk and Vance et al (2014)<sup>11</sup> in their review indicated some analgesia and supported the need for further research to see if it can also improve activity levels, function and perhaps quality of life.

strong contractions of the muscle cells in the walls of the lymphangions which are the driving force for active lymph propulsion against pressure gradients, which as we know can be large when a limb (or other body part) is in a dependent position. Unlike the veins (which have valves about 3-5 cm apart generally), lymphatic collectors have one way valves at the end of each lymphangion meaning each is only about 1 mm from the next one!

While not always indicated, there is a failure or weakening of the active lymphatic collector muscle contractions, thus a chronic distension of these collecting vessels and thus incompetence of the valves.

is undertaking it in a partnership with a communicative group of health, scientific and clinical experts to get the best outcome for the patient we are trying to help!<sup>13</sup> and remember they are all individuals and as such have individual needs which must be addressed when attempting to gain the best outcome!<sup>14</sup>

- 6) Scallan J, Zawieja S, Castorena-Gonzalez J, Davis M. Lymphatic pumping: mechanics, mechanisms and malfunction. J Physiol 2016 Oct 15;594(20):5749-5768. DOI: 10.1113/JP272088.
- 5) Bridenbaugh EA, Gashev AA, Zawieja DC. Lymphatic Muscle: A Review of Contractile Function. Lymphatic Research and Biology. 2003 Apr;1(2):147–58. DOI: 10.1089/153968503321642633
- 7) Mislin H. Active contractility of the lymphangion and coordination of lymphangion chains. Experientia 1976;32(7):820-2 DOI: 10.1007/BF02003701
- 8) Solari E, Marcozzi C, Negrini D, Moriondo A. Fluid Osmolarity Modulates the Rate of Spontaneous Contraction of Lymphatic Vessels and Lymph Flow by Means of a Cooperation between TRPV and VRAC Channels. Biology 2023 Jul 23;12(7):1039. DOI: 10.3390/biology12071039.



- 9) Filelfi SL, Onorato A, Brix B, Goswami N. Lymphatic Senescence: Current Updates and Perspectives. Biology. 2021 Apr 3;10(4):293. DOI: 10.3390/biology10040293
- 10) Katz R, Green D, Sullivan T, Yarkony G. Functional electric stimulation to enhance systemic fibrinolytic activity in spinal cord injury patients Arch Phys Med Rehabil. 1987 Jul;68(7):423-6. PMID: 2955771
- 11) Vance CG, Dailey DL, Rakel BA, Sluka KA. Using TENS for pain control: the state of the evidence. Pain Management. 2014 May;4(3):197–209. DOI: 10.2217/pmt.14.13
- 12) Olszewski WL, Engeset A. Intrinsic contractility of prenodal lymph vessels and lymph flow in human leg. American Journal of Physiology-Heart and Circulatory Physiology. 1980 Dec 1;239(6):H775–83. DOI: 10.1152/ajpheart.1980.239.6.h775
- 13) Piller N. Recognition of those at risk of lymphedema, benefits of subclinical detection, and the importance of targeted treatment and management. Indian Journal of Vascular and Endovascular Surgery. 2022;9(3):215-222. DOI: 10.4103/ijves.ijves.33 22
- 14) Piller N. What about us The patient perspective. Journal of Lymphoedema 2020;15(1):5-7.

