Simulated Manual Lymph Drainage Therapy for In-Home Treatment of Acute/Chronic Pain

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ABSTRACT

The treatment approach for pain depends first and foremost on whether the pain being experienced by the patient is acute or chronic. Acute pain, which most commonly arises from a surgical procedure, inflammation, or an injury, typically heals in 3-6 months. Chronic pain such as headaches, nerve damage pain, low back pain, arthritis, and/or fibromyalgia can be persistent, lasting far beyond the usual course of injury healing. The intensity and persistence of chronic pain adversely affects a person's well-being, functional capacity, and quality of life.

Current treatment options for chronic pain sometimes have limited effectiveness because it may not be feasible or affordable for regularly scheduled treatment; may require the motivation and patience of the individuals to adhere to exercises, physical therapies, and/or other regimens that are part of a multimodal approach; and, in the case of many pain medications, patients often experience unpleasant side effects.

Manual lymphatic drainage therapy (MLD) has been a well-established treatment and much research in Australia, Europe and North America has proven its efficacy as a stand-alone treatment and in combination with other therapies. MLD has been used for lymphedema, edema, traumatic injuries, hematoma and post-fracture treatment. Lymphedema is a progressive disease of the lymphatic system arising from impaired lymphatic drainage, accumulation of interstitial fluid, and fibroadipose deposition. Secondary lymphedema resulting from cancer treatment is the most common form of the disease in developed countries, affecting 15% to 40% of patients with breast cancer after lymph node dissection. Despite recent advances in microsurgery, outcomes remain variable and, in some cases, inadequate. Thus, development of novel treatment strategies is an important goal. Research over the past decade suggests that lymphatic injury initiates a chronic inflammatory response that regulates the pathophysiology of lymphedema. T-cell inflammation plays a key role in this response. In this review, the authors highlight the cellular and molecular mechanisms of lymphedema and discuss promising preclinical therapies[1].

Moreover, the pain-relieving effect of MLD can also be put to use when treating distortions and dislocations, CRPS - complex regional pain syndrome, scar therapy, various soft-tissue rheumatic disorders such as tendinitis and carpal tunnel syndrome. Additionally, MLD may even be included in the treatment of pathological conditions associated with local edema in the brain region (stroke, craniocerebral trauma). More recent experience with MLD includes: mastodynia, so-called "cellulite", fibromyalgia, scleroderma[2]. MLD is indicated for a variety of conditions as it both affects and acts upon the diverse physiological functions of the human body and, in particular, the parasympathetic system.

However, the historical drawback with MLD is that it is an expensive and time-consuming therapy that has only ever been offered in a clinical setting by a trained therapist. MLD requires an exacting regimen of manual manipulation and pressures to achieve the desired effect.

This paper introduces a new type of automated manual lymph drainage (MLD) over-the-counter medical device that provides many of the same benefits as MLD given by a trained therapist. The device was developed using the same basic principles of MLD and its development required a thorough understanding of the anatomy of the body's circulatory systems (i.e. arterial, venous and the lymphatic system).

Pain Background

Chronic pain can cause the nervous system to respond to persistent irritation by undergoing maladaptive structural reorganization which in turn causes more pain and stress. Like any long-term health condition, chronic pain often leads to complications beyond physical symptoms, such as new or worsened depression, anxiety, and/or difficulty sleeping.

Chronic pain can also make it more difficult to perform job duties in the workplace (sometimes leading to financial instability), manage tasks at home, and attend social gatherings, leading to relational problems. Some research suggests that the more severe the pain, the more serious these problems may become. Moreover, stress that often accompanies chronic pain can cause or exacerbate many serious health problems such as depression, anxiety, personality disorders, cardiovascular diseases, high blood pressure, heart attack and even stroke.

It is well known that managing chronic pain can be difficult. Long-term management generally requires in-clinic treatment followed by daily home maintenance therapy for the duration of the patient's life. However, the serious and often compounding consequences of chronic pain make finding and administering effective treatment a critical goal. Unfortunately, this process is complex and often uniquely personal. Treatment of pain varies from patient to patient according to how long, how severe, and how debilitating it is within individual experience and circumstance, which of course is dynamic across a lifespan and therefore inherently subject to change.

The universal response of tissue to injury, whether traumatically or surgically induced is inflammation. If left unchecked, a swelling tsunami can ensue. Increased vascular permeability enables extravasation of fluid into the extracellular tissue spaces. Much of the fluid becomes displaced to the subcutaneous tissue. Increases in vascular permeability are believed to be the result of histamine and histamine-like permeability factors released because of the surgical intervention[3]. Additional theories adhere to the belief that increased vascular permeability is directly due to overt vascular or cellular injury[3]. Extensive surgical dissection results in endothelial cell disruption and may take several days to months for repair and regeneration to occur. The more extensive the procedure, the more damage the cells sustain, and the more prolonged the edema.

Lymphatic vessels play a key role in removing the protein-rich fluid from the extracellular spaces and rapidly dilate to several times their normal caliber early in the inflammatory phase[3,4-7]. Increased tissue edema is often associated with lymphatic stasis. Normal functioning lymphatic mechanisms and venous drainage are required for the body to remove inflammatory mediators from the subcutaneous tissues[4-5]. Impaired vascular perfusion at the microvascular level may result from impaired lymphatic drainage[4,5,6] and cause accumulation of pro-inflammatory substances that can create continuous nociceptor

activation and related pathophysiological states including central nervous system sensitization and neuroinflammation[3]. It is well-established that persistent, peripheral nociceptive sources can initiate, maintain, and perpetuate chronic pain states, with tissue injury and inflammation leading to the local release of substances including glutamate, serotonin, bradykinin, Substance P, nerve growth factor (NGF), and norepinephrine (NE)[3]. These substances are transmitted to the central nervous system by primary afferent nociceptors resulting in lower nociceptor activation thresholds in the periphery contributing to chronic pain[3].

MLD Background

The lymphatic system responds to muscle activity as well as to specific hand pressure techniques used by MLD. There are a variety of conditions MLD can effectively treat as it both affects and acts upon the *diverse physiological functions* of the human body[5]. MLD is also an effective method to activate the parasympathetic nervous system, which in turn relaxes the mind and body[1].

There are two primary functions of the lymphatic system; it helps protect the body from infections and disease and helps to maintain the balance of fluid between the blood and bodily tissues, a process also known as fluid homeostasis. It forms a crucial part of the body's immune system, providing an important defense against bacteria and other intruders. The lymphatic system also facilitates the absorption of fats and fat-soluble nutrients within the digestive system.

The lymphatic system performs these functions by collecting the lymph fluid (i.e. proteins, bacteria, viruses, and other waste) and carrying it through the lymph vessels to the lymph nodes, where the materials making up the fluid are filtered[5]. The filtered lymph fluid then rejoins the circulatory system at the venous angles just below the collar bones.

Danish massage practitioner Emil Vodder (1896-1986) was one of the first to practice MLD, “intuitively” manipulating swollen lymph nodes with a technique he developed and named “lymph drainage massage”. Several years later, a German physician, Johannes Asdonk (1910-2003), further developed Vodder’s techniques and established them as manual lymphatic drainage (MLD). Since that time, extensive research and clinical evidence has been well documented to establish MLD techniques as an evidence-based and effective treatment practice for a variety of conditions.

Renowned medical scholar Bruno Chikly suggests the importance of both draining and stimulating the lymphatic system as preventative medicine before it is inhibited by surgery and medications. He goes on to report that post-surgical effects of lymphatic drainage include prevention of infection, alleviations of muscle spasms and pain, reduced scarring complications, detoxification, and the reduction/alleviation of edema[2].

With an understanding of the importance of the nervous system in pain identification and treatment, a breakthrough 1994 study illustrated the influence of MLD therapy on the central nervous system (CNS), showing how when properly applied, it can dramatically reduce intracranial pressure.

Main Action of Manual Lymph Drainage Therapy (MLD)

MLD works to create lymph fluid balance by accelerating lymph absorption and circulation (i.e., excess water, proteins, bacteria, viruses, and waste) that have escaped from cells and interstitial tissues[5].

Dr. Vodder's technique is characterized by gentle, pumping, circular hand movements using pressures of around 30 mmHg, combined with a 'zero' pressure (resting) phase. When MLD massage pressures are applied to the body, lymph flow increases, antigens are carried to the lymph nodes, and pain is subsequently relieved (known as an analgesic effect). As a result, MLD techniques have a relaxing effect on the body, decreasing muscle hypertonicity and spasms. Additionally, there is an analgesic effect as a result of absorbing the nociceptive substances[5].

Each stroke uses both a working and a resting pressure phase. In the working pressure of the stroke, the skin is stretched such that lymph capillaries and smooth musculature of the lymphangions are manipulated to activate the mechanoreceptors. This working pressure of each stroke lasts about 3 seconds and is then released immediately to allow the tissues to relax and expand. The greater the stroke stretch, the greater the increase of the frequency and amplitude of lymphangion contraction.

The resting pressure, then works as a doorway to a deeper healing. The work-and-release process is repeated a number of times in the same area of the body. The directional pressure during the work-and-release phase helps absorb lymph fluid and moves the fluid toward the heart where it can enter the venous system. The pressure should be enough to stretch the skin to its elastic capacity. To deliver these techniques effectively, MLD therapy has traditionally required specialized training[5].

MLD activates lymph function and circulation. It indirectly stimulates the fluid circulation of the body (e.g., dilates blood capillaries and activates venous return). Lymph drainage reduces edemas through some of these mechanisms. The passage of lymph in the lymph nodes stimulates the immune system (humoral as well as cellular immunity). MLD decreases sympathetic and increases parasympathetic response (sympatholytic action). By stimulating parasympathetic tone, MLD can cause relaxation, antispastic and antalgic effects.

The nociceptors are structures in the body that generate pain signals. As proposed in the "gate control theory" of Ronald Melzack and Patrick Wall (Melzack 1996; Melzack and Wall 1968), stimulation of the large-diameter non-nociceptive nerve fibers measurably decreases pain responses as well[2]. The rhythmic, intermittent pressure of MLD therapy techniques works to stimulate these large diameter non-nociceptive fibers. This can be very helpful in restoring the body's energy resources, regenerating injured tissues, and dealing with pain[5].

Table 1: Evidence summary: reported effects of MLD	
Hutzschenreuter and Brummer, 1988; Hutzschenreuter and Herpertz, 1993	Stretching effect on lymph collectors and local smooth muscle increased the frequency of contraction of lymphangions/lymph vessels and increased lymphatic transport capacity.
Francois et al, 1989	Lymph flow increased (as measured by lymphoscintigraphy) possibly owing to increased rate of contraction of lymphatics.
Casely-Smith and Bjorlin	Variations in interstitial pressures led to enhanced filling and emptying of initial lymphatics.

Leduc, 1988	'Call-up' technique propelled lymph in the collecting lymphatics and exerted a suction effect on distal lymphatics; the 'reabsorption' technique moved proteins from a subcutaneous tissue injection site.
Hutzschenreuter and Ehlers, 1988	The influence of MLD on the autonomic nervous system produced a calming effect.
Hutzschenreuter et al, 1989	Blood flow increased in superficial blood circulation and peripheral arteries.
Williams et al, 2002	Breathlessness decreased and sleep improved.
Mayrovitz 2007	Greater lymph flow is generated with a greater stretch, increasing the frequency and amplitude of the lymphangion contraction[6].
Keser 2019	MLD increased pain threshold and pain tolerance, which may be important for pain control and other components of complex decongestive therapy[7]

Any prolonged pain, such as pain generated by a migraine, acute injuries, rheumatoid arthritis, complex regional pain syndrome, fibromyalgia, is therefore among the indications for needed lymphatic drainage[8].

The receptors in the skin react only when there are stimulation changes. The ideal pressures of 33 mmHg or 1 oz./cm, which is about 8 oz./in properly applied MLD (stretching and releasing pressures), work to constantly stimulate these skin receptors, tending to cancel messages of pain to the central nervous system delivered by nociceptor nerve fibers (pain sensors)[5].

Consequently, proper manual lymphatic drainage can produce positive effects such as decongesting, calming, pain reduction and even immunologic enhancement due to the resulting increased exposure of antigens to lymphocytes[5].

MLD also helps accelerate the transportation of bacteria and allergens to the body's defense systems (i.e., the lymph nodes) and to where the increased rate of lymphatic drainage heightens the sensitization of lymphocytes and macrophage. The latter can travel more rapidly via the blood flow to reach the "scene of action" and intervene by phagocytosis, which in turn works to strengthen the immune system[5].

MLD impact on fluid shifts and endothelial cell function

Lymph is a complex fluid with biological functions and varies in composition depending on the organ from which it originated (skin, cerebral, renal, hepatic, ect). Lymph plays a significant role in immunological function; potential pathogen tolerance, inflammation, autoimmunity, metabolic disorders, cardiovascular and cancer metastasis[9]. Lymphatic endothelial cells line lymphatic vessels, composed of both smooth and striated muscle that provide for maintance of lymphatic vessel tone and contractility. Forward flow is maintained by competent bicuspid lymphatic valves. The segment of lymphatic vasculature between 2 valve sets is defined as a lymphangion, the basic unit of the lymphatic system. Flow rate under typical physiologic conditions is 1-5 ml/hour, though lymphatic collectors are able to compensate for up to 20x normal lymph flow volume before failure of contractile capacity.

Pathological lymphangiogenesis is associated with multiple conditions (inflammation, primary and secondary lymphedema, cancer), resulting in increased vascular endothelial growth factors (VEGF-A, VEGF-C, VEGF-D, VEGFR-3) and Prox1 that promotes lymphatic endothelial cell proliferation[9]. The lymph proteome demonstrates protein markers and immune mediator factors that will vary with tissue and organ homeostasis and reflect biologic function or dysfunction. Ideally, MLD can assist in re-establishment of normal lymphangion function, reduction in interstial edema and clearance of inflammatory factors to restore tissue homeostasis. Lymphedema of venous etiology (phlebolymphedema) is a commonly encountered condition and recognized to be associated with venous hypertension, inflammation, endothelial dysfunction and shedding of the endothelial glycocalyx resulting in furtherer inflammation and elevation of pro-inflammatory mediators (IL-6, IL-1, TNF-alpha, elevated MMPs and reactive oxygen species/ROS)[10]. Standard of care for lymphedema of venous etiology includes compression stockings and lymphedema pumps that replicate MLD-like therapy to decrease leg volume and to decrease pain and discomfort. As part of and in conjunction with Complete Decongestive Physiotherapy (CDP), MLD has been shown to mobilize fluid and reduce limb volume with associated decreases in both extracellular and intracellular fluid[11], many changes occurring within the first week of consistent daily therapy.

In a 3-week study of 13 patients with lymphedema undergoing 30 minutes of daily MLD as a part of CDP (with gradient compression), vascular function via flow-mediated dilatation (FMD), carotid-femoral pulse wave velocity (PWVcf), retinal microvascular changes (optic disc imaging) and blood biomarkers (plasma ADMA – Asymmetric dimethylarginine) were determined[12]. MLD caused significant decreases in plasma ADMA (a gold standard for endothelial cell function, decreased values indicating improved endothelial function), and significant positive correlations in PWVcf and FMD, indicative of vasodilation. No changes were noted in the retinal vasculature. As this is the first study to report such findings, the authors advise further research in various stages of lymphedema be performed with more patients. Additional further studies may involve Near InfraRed Fluorescence Imaging[13] (NIRFLI; see 2011 Tan and Sevick-Muraca report on MLD positive impact on lymphangion contractility with MLD) and the non-invasive imaging modalities Near InfraRed Spectroscopy (NIRS) and thermography, both of which have early case reports in peer reviewed literature for the potential of assessing fluid shifts related to lymphedema management with compression and CDP though not MLD specific.

In-Clinic Manual Lymph Drainage (MLD) Therapy

The clinician's understanding of the impact of pain disorders on the physical, emotional, and social aspects of their patient's life is critical to making the best possible symptom management and treatment decisions. Manual lymphatic drainage does have evidence for use in orthopedics in the peri-operative period[14].

Clinical treatments for acute and/or chronic pain are available, including the latest in interventional and injection therapies, medication evaluation and recommendation, rehabilitative approaches, implantable pain management devices, and regenerative therapies, such as platelet rich plasma and stem cell injections. Unfortunately, many new treatments are not FDA approved, not reimbursed by insurance, can be very costly, and in too many cases, may not work at all.

The most significant drawback to providing clinical MLD therapy is the cost and inconvenience to the patient. Ongoing MLD therapy can be very effective in managing chronic pain, but many private health insurance plans do not yet provide coverage.

Compression Pumps
All traditional pumps use non-stretch air pressure chambers to squeeze and hold high pressures over a significantly large surface area. These pressure are measured in the internal air chambers via a PSI (pressure per square inch) gauge. The drawback with traditional compressions pumps is the internal pressure measures significantly higher inside the chamber than the pressure that is measured against the human body.

The exception is the Flexitouch® system which Irene Waldridge invented to treat lymphedema and venous insufficiency. The therapy pressures were measured with a pressure mapping system which demonstrated the device followed MLD therapy pressure principles for treating lymphedema and venous insufficiency. It is considered the gold standard for managing lymphedema and non-healing venous leg ulcers as published in the **Journal of the American Medical Association (JAMA)** Dermatology[15], among other peer reviewed publications. This lymphedema pump represented a major advancement and improvement in lower extremity lymphedema, and phlebolymphedema cares[16]. In a 2015 study, the Flexitouch System showed an improved quality of life and reduced cellulitis in lower-extremity lymphedema patients[17]. Although this pump specifically treats lymphedema and venous insufficiency, it remains costly and is not indicated for use to alleviate acute and or chronic pain.

Features and Benefits of the new Neuroglide™ System
The Neuroglide system is a new technology that was developed for personal in-home use as part of a long-term *treatment plan intended for relieving pain and increasing circulation*. The system consists of a controller unit and a Back/Neck Pad. Additionally, future therapy attachments (i.e. lumbar pad, calf-foot wrap, knee wrap, and a scalp wrap) will be sold separately.

All Neuroglide therapy attachments use a unique proprietary stretchable fabric and air channel technology to mimic the stretch and release type pressures that more accurately emulates MLD pressures against the body. To accurately measure the pressures against the human body, a calibrated Tekscan pressure mapping system was used to measure the Neuroglide system. The Tekscan system measured the pressures distributed between the human body and support surfaces such as seats, massage therapy table, mattresses, cushions, and backrests.

There are 3 pressure settings, we measured all three pressures. For this White Paper, we only show the pressures for the Intense setting. A pressure mapping sensor mat was positioned on top of the back/neck pad, then a test subject was weighed, and their height measured before the individual laid on the pad. The pad consists of 16 air channels that sequentially inflate and deflate from distal to proximal one at a time. The air channel pressures in each air channel were measured in mmHg pressures over time against the body. The results show the Neuroglide intense pressures mimic MLD therapy by applying specific amounts of gradual, stretching pressure, variable and sequentially timed to inflate and deflate against a small surface area of the body. The pressures are shown below. This pressure mapping test verifies the Neuroglide system pressures mimic MLD therapy principles.

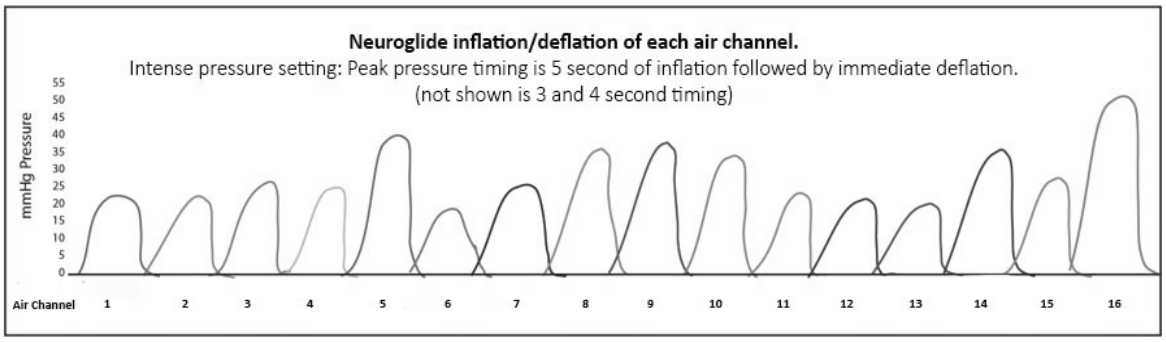

Table 2: Neuroglide™ Simulates Manual Lymphatic Drainage Principles		
Neuroglide™	**Neuroglide™ System**	**Manual Lymphatic Drainage (MLD)[2]**
Inflation / Deflation Time in Seconds	"Working phase": Inflates 3, 4, or 5 seconds, then deflates immediately to allow a "1 second resting phase" for emptying of the lymphatics. When an air channel is inflated, each air channel provides a gentle, slow stretch working pressure against the body. When an air channel deflates, it provides a resting phase.	Each hand stroke uses both a working and a resting pressure phase. The working phase applies mild, medium or intense pressures, while the resting phase does not apply pressure. Variations in interstitial pressures led to enhanced filling and emptying of initial lymphatics. Casely-Smith and Bjorlin.
Repetitive / Repeatable	Treatment sessions include 15, or 30 minutes	2 hours
Gradual / Variable Stretch	Ultra-stretch air channels inflate a stretch action (variable pressure) against the body like a balloon to enhance the initial lymph capillaries to fill with lymph fluid. As shown in the chart above, the Neuroglide™ pressure profile is based on inflation pressure timing over the body's surface area.	Stretching effect on lymph collectors and local smooth muscle, increased the frequency of contraction of lymphangions/lymph vessels and increased lymphatic transport capacity. Hutzschenreuter and Brummer, 1988; Hutzschenreuter and Herpertz, 1993. Greater lymph flow is generated with a greater stretch, increasing the frequency and amplitude of the lymphangion contraction. Mayrovitz 2007[6].
Sequential distal to proximal	Each air channel sequentially inflates and deflates from distal to proximal part of the body. Increases the rate of contraction of the lymphatics.	Increases the rate of contraction of the lymphatics.
Optimal Pressures <45 mmHg	Optimization of the initial lymph capillaries which allow filling of the excess water, proteins, bacteria, viruses, and waste products.	Optimization of the initial lymph capillaries which allow filling of the excess water, proteins, bacteria, viruses, and waste products.

In Clinic Pilot Study

To validate the indications for use of pain relief and to increase circulation, the Neuroglide Pain Relief & Recovery System was used on several patients in a clinical setting under the supervision of a Doctor of Physical Therapy. Patients and clinicians who suffered from myalgia pain, fibromyalgia, headaches, and chronic pain tried the Back/Neck Pad.

The following are comments from the clinician who conducted the pilot study:

"I am a physical therapist who is a Board-Certified Clinical Specialist in Oncologic Physical Therapy. I have worked in the practice of cancer rehabilitation since 1995. I enjoy working with this population because my therapeutic interventions have a significant impact on improving the quality of life for cancer survivors. I have recently had the opportunity to try the Eva Medtec, Inc. device for those patients experiencing pain and anxiety. Here are my observations:"

- "A patient who was recently diagnosed with metastatic breast cancer to the spine was unable to lie flat due to pain. She found narcotic medication to cloud her head and disliked the side effects. She found the use of the back/neck pad reduced her need for narcotic medication and allowed her to sleep in a reclined position. This resulted in a significant improvement to her daily life."
- "A patient who had experienced a thoracic spine compression fracture due to decreased bone mineral density (which can be a side effect of aromatase inhibitors) found the use of the device to reduce muscle spasm pain in the upper back."
- "A survivor of endometrial cancer who also had lower extremity lymphedema and chronic back pain found the machine to reduce her back pain symptoms while providing a comforting massage to her swollen hip area."
- "For anyone who tried this device, the overwhelming feedback was a sense of relaxation and improved sense of well-being. The relaxation response improves venous and lymphatic return, slows and deepens breathing, and reduces muscle tension."
- "The Neuroglide has been very helpful for treating stress-related headaches. As a therapist, we are moving all day and often find ourselves in stressful situations. The device has allowed a few of us to relax during down time so that we were able to return to work and finish our day."

Conclusion

The Neuroglide System, is a revolutionary and innovative automated manual lymphatic drainage device to alleviate pain. It is a recently developed technology that administers a gentle therapeutic pressure against the neck and or back using the well-established methods and principles of manual lymph drainage pressures (MLD). Neuroglide offers consumers and patients a consistent, accessible, and effective in-home alternative to clinical MLD therapy as part of their daily routine to temporarily relieve pain and increase circulation.

References

[1] The Vicious Circle of Stasis, Inflammation, and Fibrosis in Lymphedema. Plast. Reconstr. Surg. 151: 330e, 2023.

[2] Wittlinger Lymphedema Clinic, Friday, May 2020, (Online). (accessed Friday, May 2020.)

[3] Tuckey B, Srbely J, Rigney G, Vythilingam M, Shah J. Impaired Lymphatic Drainage and Interstitial Inflammatory Stasis in Chronic Musculoskeletal and Idiopathic Pain Syndromes: Exploring a Novel Mechanism. Front Pain Res (Lausanne). 2021 Aug 23;2:691740. doi: 10.3389/fpain.2021.691740. PMID: 35295453; PMCID: PMC8915610.

[4] Stav Brown, MD Joseph H. Dayan, MD, MBA Raghu P. Kataru, PhD Babak J. Mehrara, MD
[5] Silent Waves, Theory and Practice of Lymph Drainage Therapy. Chikly, MD, DO, LMT. 2nd ed. Scottsdale: International Health & Healing Inc Publishing.

[6] Mayrovitz HN. Interface pressures produced by two different types of lymphedema therapy devices. Phys Ther. 2007;87:1379–1388.

[7] Keser I. et al. Does Manual Lymphatic Drainage Have Any Effect on Pain Threshold and Tolerance of Different Body Parts? LYMPHATIC RESEARCH AND BIOLOGY 2019 Volume 17, Number 6:651-654.

[8] Pertaining to manual lymphatic techniques, much research and clinical evidence has been well documented to establish that these techniques are evidence-based. (Foldi, Foldi, and Kubik 2003; Zuther and Norton 2013; Chikly 2004), wound care (Chikly 2004; Zuther and Norton 2013; Azoubel et al. 2010), rheumatoid arthritis (Joos, Bourgeois, and Famaey 1993; Zuther and Norton 2013; Foldi et al. 2003), and complex regional pain syndrome (CRPS) (AK et al. 2009; Santamato et al. 2019; Chikly 2004).

[9] Hansen KC, et al. Lymph formation, composition and circulation: a proteomics perspective. International Immunology 2015;27(5):219-227.

[10] Castro-Ferreira R, et al. The role of endothelial dysfunction and inflammation in chronic venous disease. Ann Vasc Surg 2018;46:380-393.

[11] Brix B, et al. Fluid shifts induced by physical therapy in lower limb lymphedema patients. J Clin Med 2020;9:3678(1-15).

[12] Brix B, et al. Physical Therapy affects endothelial function in lymphedema patients. Lymphology 2020;53:109-117.

[13] Tan IC, et al. Assessment of Lymphatic Contractile Function After Manual Lymphatic Drainage Using Near-Infrared Fluorescence Imaging. Arch Phys Med Rehabil 2011;92:756-64.

[14] David Doubblestein, PT, PhD(ABD), OCS, CLT-LANA, Cert. MDT1 Sandy Sublett, PT, DPT, OCS, CLT, Min Huang, PT, PhD, NCS. Effects of Manual Lymphatic Drainage Techniques on Conditions Affecting the Musculoskeletal System: A Systematic Review. Orthopaedic Practice volume 32 / number 2 / 2020

[15] The Cutaneous, Net Clinical, and Health Economic Benefits of Advanced Pneumatic Compression Devices in Patients with Lymphedema Pinar Karaca-Mandic, PhD, Alan T. Hirsch, MD, Stanley G. Rockson, MD, Sheila H. Ridner, PhD, RN. JAMA Dermatol 2015 Nov;151(11):1187-93. doi: 10.1001/jamadermatol.2015.1895.

[16] Pneumatic Compression Device Treatment of Lower Extremity Lymphedema Elicits Improved Limb Volume and Patient-Reported Outcomes Authors: Satish C. Muluk, MD; Alan T. Hirsch, MD; Elisa C. Taffe, MD. European Journal of Vascular and Endovascular Surgery Publication Date: 2013 (Volume 46, Number 4) Oct;46(4):480–7.

[17] Pneumatic Compression Improves Quality of Life in Patients with Lower-Extremity Lymphedema Sheila N. Blumberg, MD, MS, Todd Berland, MD, Caron Rockman, MD, Firas Mussa, MD, Allison Brooks, MSN, RN-BC, Neal Cayne, MD, Thomas Maldonado, MD Annals of Vascular Surgery May, 2015 Vol. 29(4):628–629.