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PATHWAYS OF LYMPH AND TISSUE FLUID FLOW DURING INTERMITTENT PNEUMATIC MASSAGE OF LOWER LIMBS WITH OBSTRUCTIVE LYMPHEDEMA

W.L. Olszewski, J. Cwikla, M. Zaleska, A. Domaszewska-Szostek, T. Gradalski, S. Szopinska

Department of Surgical Research and Transplantology (WLO,MZ,AD-S,SS), Medical Research Center, Polish Academy of Sciences, Warsaw; Lymphedema Clinic (TG), St Lazarus Hospis, Krakow; Department of Gastrointestinal and Transplantation Surgery (WLO), Central Clinical Hospital, Ministry of Internal Affairs, Warsaw; and Department of Nuclear Medicine (JC), Central Clinical Hospital, Ministry of Internal Affairs, Warsaw, Poland

ABSTRACT

Questions remain on the use of sequential pneumatic compression including where does the fluid flow to and whether fluid can be moved to the non-swollen tissues of the hypogastrium and gluteal region? During pneumatic massage of the limb, we studied pathways of lymph and mobile tissue fluid flow using lymphoscintigraphy: a) from the calf and thigh across the inguinal region to the healthy non-swollen tissues of the hypogastrium and b) in the hypogastrium to the lateral and upper abdominal quadrants. To examine if there was effective fluid flow during pneumatic massage, plethysmographic flow measurements were also carried out. We demonstrated that: (i) pneumatic compression moved isotope in lymph remaining in functioning lymphatics and in tissue fluid in the interstitial space toward the inguinal region and femoral channel, (ii) there was no isotope crossing the inguinal crease or moving to the gluteal area, and (iii) isotope injected intradermally in the hypogastrium did not spread during manual massage to the upper and contralateral abdominal quadrants. In conclusion, intermittent pneumatic compression is effective in pushing mobile tissue fluid and relocating large fluid volumes toward the groin. However, the question that still remains is how to facilitate further flow toward the non-swollen tissues and thereby increase local absorption of fluid.

Keywords: lymphoscintigraphy, lymphedema, pneumatic compression, massage

In obstructive lymphedema of lower limbs following infections, trauma, surgery or irradiation, most or all lymphatic collectors leading to the superficial and deep inguinal lymph nodes are obstructed (1). The limited hydraulic function of damaged collecting lymphatics results in accumulation in the interstitial space of capillary filtrate containing plasma humoral and cellular components and parenchymal cell products. Impairment in transport of plasma filtered macromolecules and protein–bound ions generates high osmotic pressure. This attracts water from the vascular compartment and further increases the stagnant tissue fluid volume. Furthermore, accumulating fluid deforms the soft tissue structure and spontaneously creates fluid conducting channels in the subcutaneous tissue (2). This natural hydraulic process is insufficient for

TABLE 1
Demographic Data of Patients with Lymphedema of Lower Limb

M/F	AGE	GROUP/ STAGE	LEVEL OF EDEMA	SKIN CHANGES	LYMPHOSCINTIGRAPHY
2M,3F	28-45	II	mid calf	none	foot & lower calf tracer diffusion, few collectors and inguinal nodes
3M,2F	25-52	III	knee	foot keratosis	foot & calf tracer diffusion, single collector, inguinal node remnants
3M,2F	26-48	IV	whole limb	foot, calf keratosis	foot & calf tracer diffusion, no lymphatics and inguinal nodes
2M,3F	28-52		No lymphedema, controls		limb lymphatics normal

transporting fluid away from swollen regions and therefore requires extrinsic approaches such as massage and compression to force the mobile edema fluid toward the root of the extremity. In the calf and thigh, the natural fluid channels form along large blood vessels (e.g., saphenous, popliteal and femoral veins) and also around small unnamed vessels. These channels lead to the inguinal crease where skin is connected with the inguinal ligament and external oblique muscle by natural elastic fibers (3).

The question arises whether the accumulated tissue fluid can form natural subcutaneous channels across the inguinal crease to the hypogastrium. This would facilitate absorption of fluid in normal hypogastrium tissues, which could presumably form connections with normal lymphatics. Such newly formed flow pathways would justify the common practice of treating the core (truncal) lymphatics as a major therapy component before limb massage (4,5). The essence of this concept is that treatment must first be directed at lymphatic territories, such as the hypogastrium and trunk, so that they are adequately prepared to receive lymph (tissue fluid) from the lower limbs.

In this study, we investigated with use of lymphoscintigraphy the pathways of lymph and mobile tissue fluid flow: a) across the inguinal and gluteal regions to the healthy non-swollen tissues of hypogastrium, and b) in the hypogastrium to the lateral and upper abdominal quadrants during pneumatic massage of the limb. In addition, to prove that there was effective fluid flow produced during pneumatic massage, plethysmographic flow measurements were taken.

MATERIAL AND METHODS

Patients

The study was carried out on 15 patients, age 28-56 with mean weight of 65kg (58- 72), mean height of 168 cm (161-178) and lymphedema of one lower limb (stage II to IV) for a duration of 2 to 15 years (*Table 1*). Eleven patients reported small foot skin abrasions or light trauma of the foot in the past followed by development of foot and calf transient edema. More extensive edema developed months to years later and in 50% of cases was complicated by 1 to 3 attacks of dermato-lymphangio-adenitis. In 4 patients, edema developed without any detectable reason. Cases with acute inflammation, chronic venous insufficiency, and a systemic etiology of edema were excluded from the study. Five patients without lymphedema, but with suspicion of enlarged abdominal lymph nodes, served as controls. Lymphoscintigraphy and tissue fluid flow measurements are mandatory diagnostic procedures in our hospital for all cases with lymphedema. The consent of patients was obtained, and the study was approved by Warsaw Medical University Ethics Committee.

Clinical Staging

Staging was based on clinical evaluation including level of edema in the limb from foot to groin and degree of skin keratosis and fibrosis. Briefly, stage II pitting edema affected the foot and lower half of the calf, stage III involved the foot and calf with hard skin in foot and ankle area, and in stage IV, the whole limb was edematous with hyperkeratosis of the foot and calf skin and papillomatosis of toes (1).

Lymphoscintigraphic Staging

Evaluation of lymphatic pathways was performed using lymphoscintigraphy (*Table 1*). Stage II was defined as diffusion of tracer in the foot and lower part of calf, an interrupted outline of a single lymphatic, and few small inguinal nodes with irregular outline depicted. Stage III demonstrated no draining lymphatics with some inguinal nodes of irregular outline appearing 2 hours after isotope injection. Stage IV was characterized by diffusion of tracer in the foot and entire calf without visualization of collecting lymphatics or nodes.

Lymphoscintigraphy Technique

Lower limb lymphoscintigraphy was carried out in each patient in two sessions, the first without pneumatic compression massage and the second 7 days later following a 45 minutes limb pneumatic compression massage. Intradermal injections (0.2 ml) of ^{99m}Tc-Nanocol (3 mCi total) (Amersham, Switzerland) was made between the first, second and third toe (to visualize the superficial lymphatic system) and into the subcutis of mid- portion of the sole (to visualize the deep system). Imaging was performed using a gamma camera (Orbiter ZLC 750, Siemens, Germany) immediately after isotope injection and after 45 minutes of pneumatic massage. The images were classified according to the stage of lymphedema. In 5 of these patients (3 stage II, and 2 stage IV) additional lymphoscintigraphy of skin and subcutis of hypogastrium was performed by intradermal injection of 1/10th of the Nanocoll dose used for limb scintigraphy. The spread of isotope in the limb and its movement toward the groin were observed simultaneously with spread of isotope injected into the hypogastrium.

For semiquantitative evaluation of scintigrams, the image of lower leg and thigh lymphatics and lymph nodes was evaluated quantitatively. Lymphoscintigrams were scanned and analyzed using specialized PC software (Olympus Micro Image™ ver. 3.0.0., Olympus Optical Co., Hamburg, Germany). The surface area of the lymphatics (Lv) and inguinal lymph nodes (LN) of both extremities was evaluated in the inguinal area, thigh and calf. Data were expressed as indices obtained from the equations $I_{Lv\ or\ LN} = S_{L\ Lv\ or\ LN}/S_{C\ Lv\ or\ LN}$, where $S_{L\ Lv\ or\ LN}$ were surface of lymph vessels or lymph nodes measured on the lymphedema (L) and contralateral normal (C) extremity.

Pneumatic Compression Device

Compression massage was accomplished

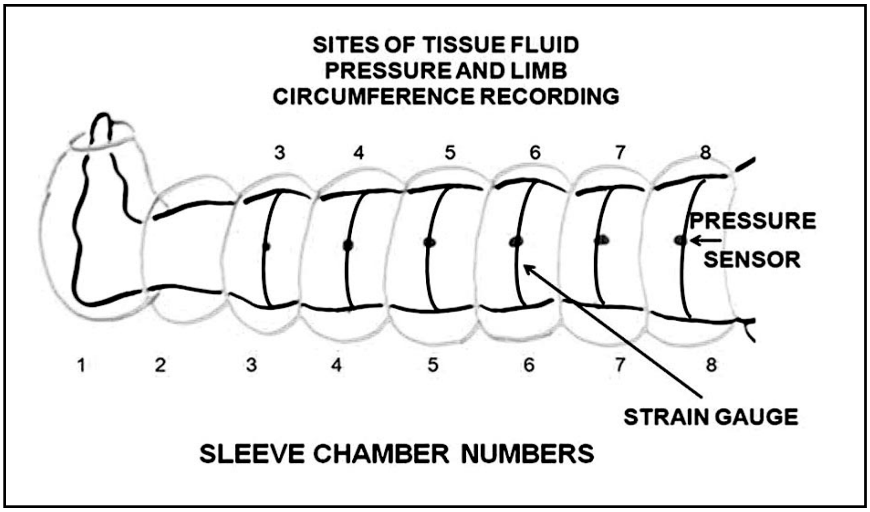

Fig. 1. Schematic presentation of lower limb in a pneumatic sleeve with eight (9cm wide) chambers. Tissue fluid pressure was measured at 6 points indicated by large dots. The lowest point in the calf was at chamber 3 level, then at levels 4 and 5. In the thigh, pressures were measured at chamber levels 6, 7 and 8. The lines encircling calf and thigh show the site of strain gauge placement for continuous measuring of circumference changes during compression.

using a device produced for us by Biocompression (Moonachie, NJ) (*Fig. 1*). The sleeve was composed of eight segments (9 cm) encasing the whole limb to the inguinal crease and which were sequentially inflated from 1 to 8. Inflation pressures were regulated from 50 to 125 mmHg with gradient pressures decreasing proximally by approximately 10% (10-15 mmHg). Inflation time of each chamber was 50 seconds, and total inflation time equaled 400 seconds. There was no deflation of the distal two chambers, and all remaining chambers were deflated for 50 seconds at the end of each cycle.

Manual Massage of Hypogastrium Prior to Pneumatic Compression of Limb

Manual massage for hypogastrium fluid clearance was performed for 10 minutes at the site of isotope injection in the upper and lateral direction just prior to pneumatic compression of the limb so that this area became adequately prepared to receive lymph (tissue fluid) from the lower limbs.

Measuring Tissue Fluid Flow Volume

Strain gauge plethysmography was used to measure changes in circumference of the calf and thigh during pneumatic compression massage (*Fig. 1*). Circumferential data was used to calculate volume changes of the limb segments. A plethysmograph (Hokanson, Bellevue, WA, type EC6) in a recording vein mode was applied. Six mercury strain gauges of a length of 22 cm to 53 cm were put around the limb at chamber levels 3 to 8 (*Fig. 1*). Increase in circumference caused elongation of the gauges, which could be read on the recorder graph scale in mm. Numerical data were used to calculate volume by multiplying cross area of limb segments by 90 mm (length of the compressing chamber). Subtracting the volume value before compression from that during compression provided data on the proximally transferred volume.

Statistical Evaluation

Numerical lymphoscintigraphy densitometry data were compared using the students t-test with significance defined at $p<0.05$.

RESULTS

TABLE 2
Comparison of Lymphoscintigraphic Images and Lymph and Tissue Fluid Flow after Intermittent Pneumatic Massage

	Lymphoscintigraphy		Calculated flow (ml/cycle) Total volume reaching groin
	Before massage	After massage	During massage
Stage II	tracer diffusion in foot and calf, single vessel, few small inguinal nodes, no iliac lymphatics	tracer diffusion in foot and calf, lymphatics up to the groin, inguinal nodes, iliac lymphatics	20-30
Stage III	tracer diffusion in foot and calf, fragments of vessels, sporadically small inguinal node no iliac lymphatics	tracer diffusion in lower thigh, lymphatics and fragments of nodes visible, no iliac lymphatics	40-60
Stage IV	tracer diffusion in foot and calf, no vessels and nodes visible	tracer diffusion in foot, calf and thigh up the inguinal crease, no lymphatics and nodes visible, tracer in femoral canal	60-120

Lymphoscintigraphic Evaluation of Lymph and Tissue Fluid Flow in the Massaged Limb

Lymphoscintigraphic and volumetric evaluation of lymph and tissue fluid flow was measured in all subjects (*Tables 2,3*). Pathways of lymph and tissue fluid flow during pneumatic compression massage were demonstrated (*Figs. 2-7*) and evaluated (*Table 2*). After massage in stage II (*Fig. 2*) and some cases in stage III (*Figs. 3,4*), tracer filled the upper parts of the thigh tissues. It then flowed along lymphatics to the femoral canal and retroperitoneal space. In stage IV, it reached the inguinal crease and accumulated in the upper thigh (*Figs. 5-7*). No tracer flow from the thigh across the inguinal crease to the lower abdominal quadrant was observed. In normal limbs, isotope flowed along the superficial and deep lymphatic system to the inguinal nodes and through the femoral canal to iliac lymph nodes.

Semiquantitative Evaluation of Lymphoscintigrams Before and After Intermittent Compression

In the total group of patients, there was increase in diffusion of tracer to the thigh and inguinal region including inguinal lymph nodes (*Table 3*). There were wide individual variations.

Lymphoscintigraphic Evaluation of Lymph Flow from Hypogastrium During Limb Massage

There was minimal radial diffusion of tracer from the site of injection in hypogastrium after manual massage of this area and

TABLE 3
Semiquantitative Densitometric Evaluation of Lymphoscintigrams Before and after Intermittent Compression (Ratio Edematous/Normal Limb)

	Limb area (including lymphatics and tissue diffusion of tracer)		Inguinal lymph nodes
	Calf	Thigh	
Before	2.4±4.5	1.2±2.5	0.3±0.4
After	2.8±5.0	2.5±3.0*	0.6±1.0*

*before vs after treatment $p<0.05$

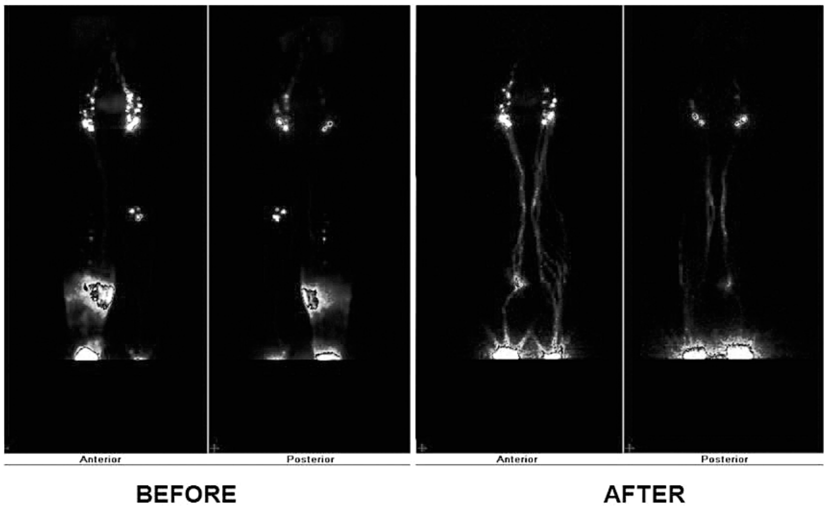

Fig. 2. Lymphoscintigrams in postinflammatory lymphedema of the right lower limb, stage II. Left) Before pneumatic compression massage (anterior and posterior), image demonstrates accumulation of tracer in the swollen calf, a weak outline of the superficial lymphatics, and visualization of inguinal and iliac lymph nodes. Right) After 1 hour of pneumatic massage, most tracer was moved along normal thigh lymphatics to the groin and iliac vessels.

also during limb massage, with no signs of its movement toward the upper or contralateral quadrants (*Fig. 7*). In two patients, flow was directed toward inguinal nodes.

Tissue Fluid Volume Transfer During Pneumatic Compression Massage

Continuous recording of circumference changes during sequential compression gave indirect insight into the volumes of fluid translocated from compressed segments into the proximal segments. The increase in circumference at each level was calculated into increase in volume, and summarized data for the 15 subjects are presented in *Fig. 8*. The tissue fluid flow ranged from 20-30 ml/cycle in the calf to 60-105 ml/cycle in the thigh.

Relationship Between the Tracer Diffusion and Tissue Fluid Flow

Pneumatic compression massage caused

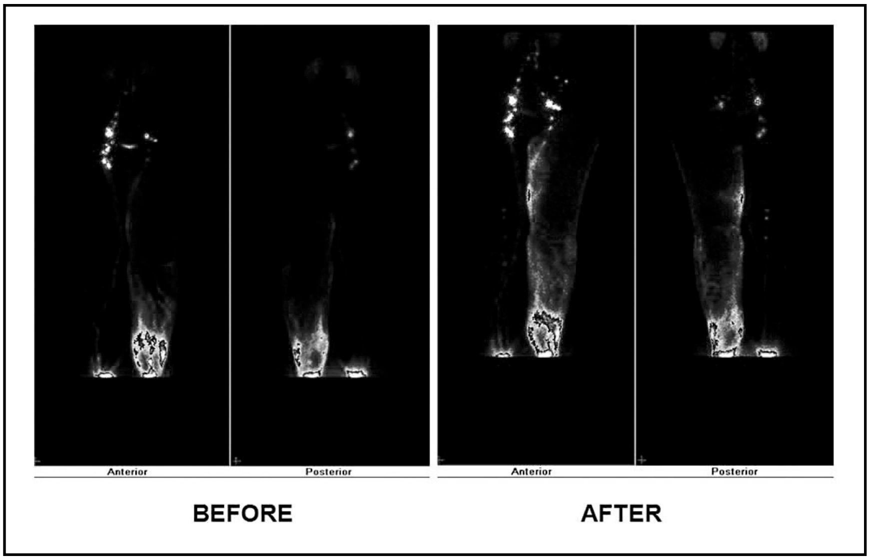

Fig. 3. Lymphoscintigrams in postinflammatory lymphedema of the left lower limb, stage III. Left) Before pneumatic compression massage (anterior and posterior), tracer accumulates in the subcutaneous space of the swollen calf, no superficial and deep lymphatics are seen, some subepidermal flow is seen in the thigh and a small inguinal lymph node, and no iliac nodes are seen. Right) After 1 hour of pneumatic massage, most tracer was moved along the subcutaneous space to the groin to visualize single small inguinal nodes. Further tracer flowed through the femoral canal along large iliac blood vessels visualizing single iliac nodes. It did not flow to the hypogastrium or gluteal region.

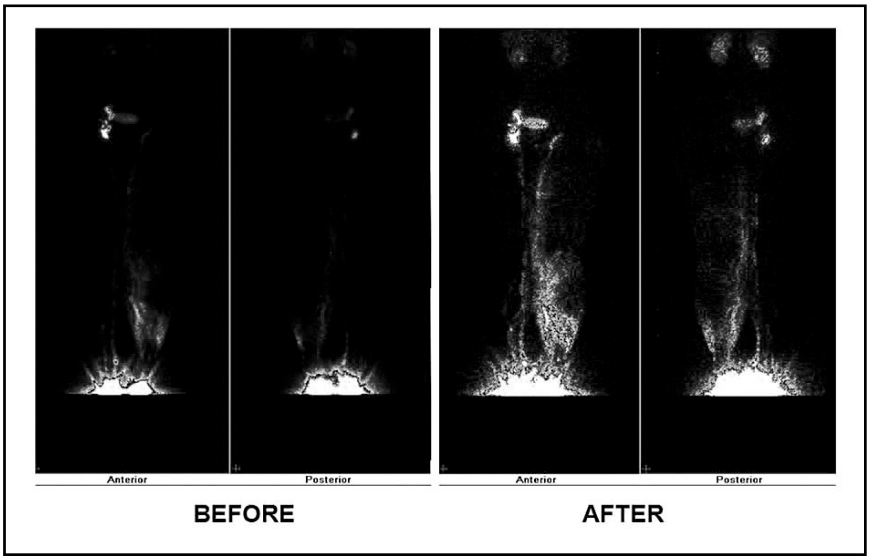

Fig. 4. Lymphoscintigrams in posttraumatic lymphedema of the left lower limb, stage IV. In this subject, lymphedema was caused by obliteration of lymphatics and fibrosis of inguinal nodes as proved by biopsy. Left) Before pneumatic compression massage (anterior and posterior), tracer accumulates in the internal aspects of the calf with a faint outline in the thigh, and no lymphatics are seen. Right) After 1 hour of pneumatic compression massage, some tracer has moved along the internal aspect of the thigh to the groin level without visualization of the inguinal nodes. There was no flow to the hypogastrium or gluteal region.

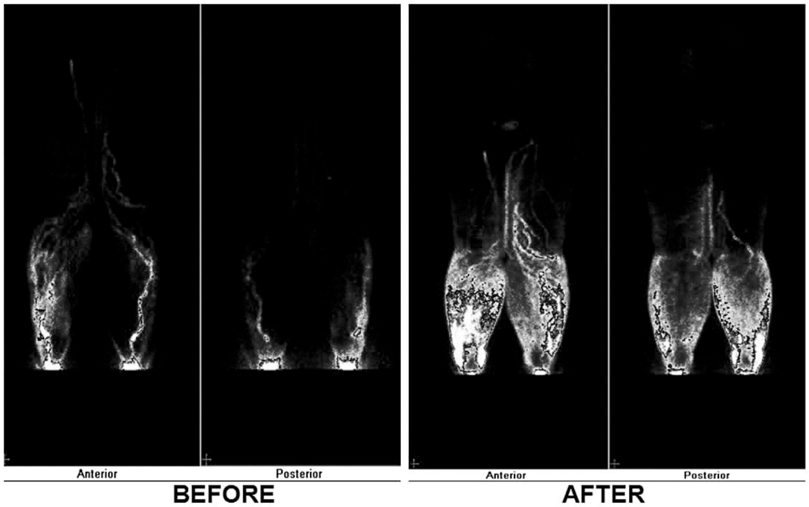

Fig. 5. Lymphoscintigrams in postinflammatory lymphedema of both lower limbs, stage IV. Left) Before pneumatic compression massage (anterior and posterior), tracer is seen in dilated calf lymphatics and tissue subcutaneous spaces reaching mid-thigh level. Right) After 1 hour of pneumatic compression massage, most tracer was moved to the thigh, but this did not reach the groin. This was presumably due to the resistance to flow in the fibrotic inguinal lymph nodes. There was no flow to the hypogastrium or gluteal region.

flow of tracer toward groin both in the lymphatics and interstitial space in subjects with stage II and III lymphedema. In stage IV lymphedema, tracer diffused into the interstitial space of the entire limb with a sharp border at the inguinal crease and it did not enter the femoral channel. Proximal flow of tracer was accompanied by tissue fluid flow (*Table 2; Fig. 8*). Most of tracer and massaged fluid accumulated in the thigh.

DISCUSSION

This study demonstrates that: (i) pneumatic compression massage of the lower limb pushed tracer in lymph in the remnant lymphatics and tissue fluid in the interstitial space toward the inguinal region and femoral canal, (ii) no tracer filling fluid channels which crossed the inguinal crease or flowed to the gluteal area were visualized, (iii) there was no tracer flow either in lymphatics or in tissue fluid to the hypogastrium, and (iv) tracer injected intradermally in the hypogastrium did not spread during both manual and pneumatic compression massage to the upper and contralateral abdominal quadrants manual massage prior to limb massage as well as during pneumatic compression of the limb in the direction of the upper and contralateral abdominal quadrants.

This study showed that sequential pneumatic compression with high inflation pressure is very effective in pushing stagnant lymph and tissue fluid in cases with obstructive lymphedema. The lymphoscintigrams demonstrated that tissue fluid finds its way toward the root of the extremity along the natural pathways with the lowest hydraulic resistance. These are the perivascular spaces and subcutaneous channels spontaneously formed by tissue deformation (2). Tracer accumulated along the great saphenous vein and internal aspect of the thigh and even if there were some flow along femoral and iliac lymphatics, tissue fluid reaching the inguinal crease did not pass through it. In advanced stage IV, tissue fluid only moved to the knee or lower thigh level.

The flow of tracer during pneumatic

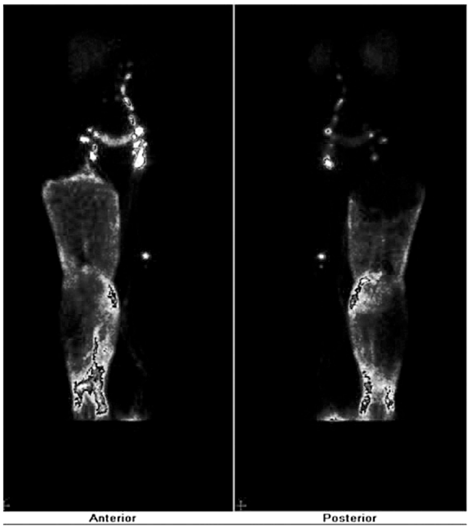

Fig. 6. Lymphoscintigrams in postinflammatory lymphedema of the right lower limb (stage IV) after one hour of pneumatic compression massage. The tracer visualized dilated subcutaneous spaces up to the inguinal level but not lymphatics. Note a sharp border for tracer flow at the inguinal ligament level. Further, tracer moved along the femoral canal to the iliac region and visualized two small lymph nodes. There was no flow to the hypogastrium or gluteal region.

compression massage followed tissue fluid flow. Large volumes of proximally moved fluid indicated that it was not only lymph in the subepidermal plexus and the remaining patent lymphatics, but also the tissue fluid accumulating in the spontaneously formed tissue spaces, where the bulk of edema fluid is usually found (2). The qualitative comparison of lymphoscintigraphic images and flow data clearly showed that sequential compression propelled lymph and stagnant tissue fluid toward the groin. Most of this fluid accumulated in the groin, as was expected. However, in contrast to the general view, it did not move toward the hypogastrium but instead moved to the femoral channel.

Results of our study revive the questions of: what is the fate of fluid accumulating in the groin? Does it find its way to the pelvis through the femoral and obturator channels? How are large portions of fluid absorbed in the upper thigh and genitalia? This cannot be absorption of water only as tissue fluid protein concentration remains at low level and at the same concentration as in the calf fluid (personal observations).

There are only few publications focused on lymph and tissue fluid flow during pneumatic compression of swollen limbs (6,7). One study using lymphatic vascular factorial analysis reported a beneficial effect of intermittent pneumatic compression in 18 of 22 limbs examined. Pneumatic compression facilitated tracer transport in the proximal portion of the limb and also pushed tracer from the injection site toward the lymphatics. The effect was evident as soon as external compression therapy began (6). In another study, pneumatic compression brought about decrease in the volume of the massaged limb, however, no flow of tracer toward the groin was observed (7). The authors concluded that water was absorbed, but that fluid proteins remained in the massaged regions. However, no data on applied pressure and inflation timing were presented which would allow analysis of tissue fluid flow. Neither of these papers addressed the problem of massaged fluid flow through the groin to the hypogastrium or pelvis through the femoral channel.

We did not include in this report a control group examining the change in the lymphoscintigraphic flow after a sham (or no treatment). Normal lymphatic contractility driven (and also tissue) flow during this time period should be able to move some tracer without the benefit of pneumatic compression massage. We also did not provide the data on the volume changes to the normal limb, as the tissue fluid flow during pneumatic compression was negligible. In addition, the pressure utilized for pneumatic compression massage in our study, while appropriate for our patients with advanced lymphedema of the legs, were higher than those used by other investigators.

There is a widely accepted notion that

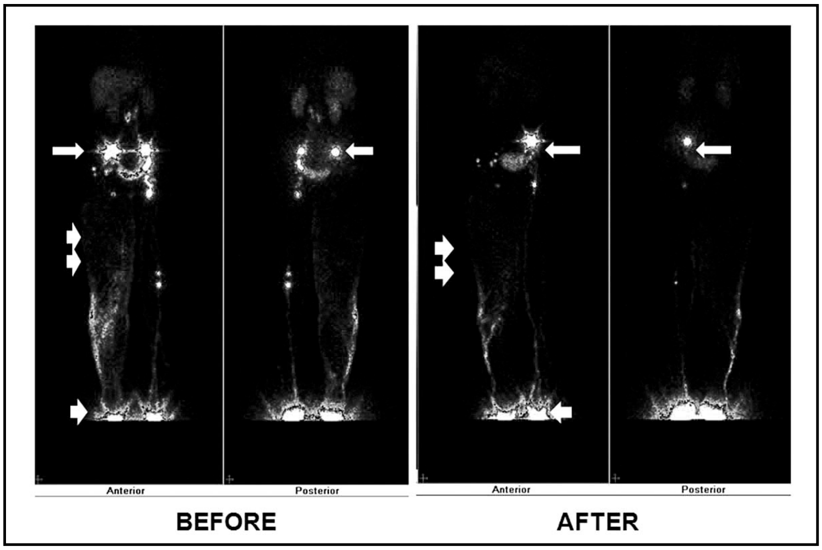

Fig. 7. Lymphoscintigrams in postinflammatory lymphedema of the right lower limb, stage III. after pneumatic compression massage (anterior and posterior). 99Tc Nanocoll was injected into the toe-web of both feet (short arrow). It visualized the superficial and deep lymphatics on the normal left side. On the right lymphedema side, Nanocoll showed few calf lymphatics (two arrows). To visualize lymph drainage from the hypogastrium, another dose of Nanocoll was injected intradermally in the right and left lower abdominal quadrant (long arrow). After 1 hour pneumatic sequential massage of the lymphedematous right limb, tracer diffused in the subcutaneous tissue of upper calf and lower thigh. It did not cross the groin level despite high pressure sequential compression. In addition, tracer injected into hypogastrium spread only slightly radially and did not flow to the upper or lateral quadrant indicating there was no inflow of fluid from the limb that would move the injected isotope.

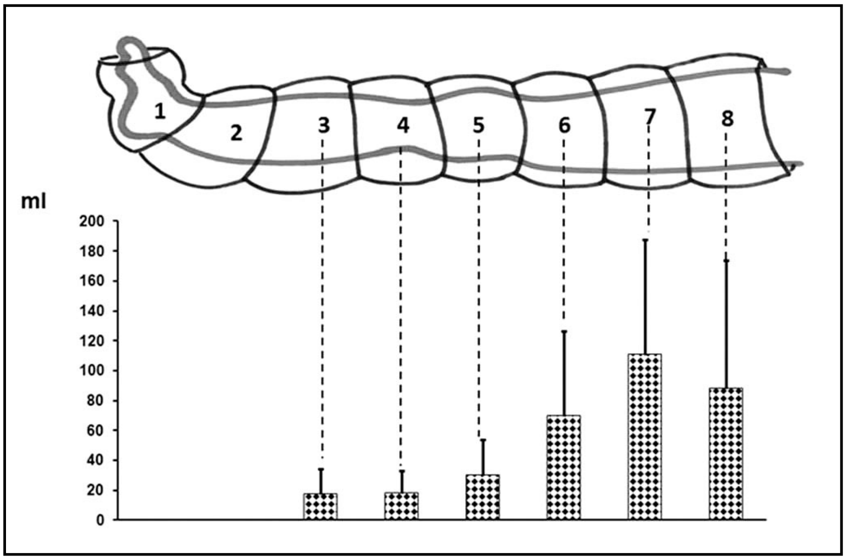

Fig. 8. The picture and graph depict the calculated tissue fluid flow during intermittent pneumatic compression in numbered sleeve segments from the calf to the groin (ml/cycle, mean ± SD of 15 patients stage II-IV). Sequential inflation of chambers 1 to 8 was set at 120mmHg for a duration of 55 seconds each with no distal deflation. The gradient between chamber 1 and 8 was 10-15 mmHg.

emptying of the hypogastrium by manual or pneumatic massage prior to limb massage creates space for lymph and tissue fluid from the massaged tissues. The essence of this concept is that treatment must first be directed at lymphatic territories, such as the trunk, so that they are adequately prepared to receive lymph from subsequently treated lymphedematous regions such as the arm or leg. This truncal clearance or decongestion approach makes intuitive sense to most intensively trained practitioners.

According to Földi (4), lymphatic tributary regions or territories are separated by lymphatic watersheds. The term *watershed* is borrowed from hydrology, where it can be thought of as a drainage basin usually bounded by ridges of higher ground. Although lymphatic watersheds are not true anatomical structures, their dividing lines delineate the direction of lymph flow (5). Even though treatment of the trunk has long been a standard MLD (manual lymphatic drainage) process, there have been no anatomical studies confirming the presence of watersheds or randomized clinical trials comparing manual lymphatic drainage with and without truncal decongestion.

In this study, we were not able to confirm lymph and tissue fluid flow to the hypogastrium and from there to the neighboring quadrants. The tracer containing lymph and tissue fluid were stopped at the inguinal crease, and flow was directed toward the femoral channel. Also tracer flow away from the hypogastric subcutaneous tissue was not observed. Manual massage of this region revealed radial spread of isotope but not flow to the upper or lateral quadrant. Accordingly, the concept of proximal clearing-hypogastrium clearance should be reevaluated based on objective physiological studies of tissue fluid hydraulics.

In summary, sequential intermittent compression massage of the lymphedematous lower limbs is effective in propelling lymph and tissue fluid toward the groin. However, it is directed toward the femoral canal and not to the hypogastrium. These findings point to the necessity of applying high compression pressures at the groin region and also searching for pharmacological and surgical methods that can facilitate fluid flow across the inguinal crease.

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Waldemar L. Olszewski, MD, PhD
Department of Surgical Research & Transplantology, Medical Research Centre
Polish Academy of Sciences
5 Pawinskiego Str.
02-106 Warsaw, POLAND
Tel. (48-22) 6086401; Fax (48-22) 6685334
E-mail: wlo@cmdik.pan.pl,
waldemar.l.olszewski@gmail.com