

## Tissue Fluid Pressure and Flow during Pneumatic Compression in Lymphedema of Lower Limbs

Waldemar L Olszewski, M.D., Ph.D.,<sup>1,2</sup> Pradeep Jain, M.D., Ph.D.,<sup>3</sup> Govinda Ambujam, M.D., Ph.D.,<sup>3</sup> Marzanna Zaleska, M.B.,<sup>1</sup> Marta Cakala, M.B.,<sup>1</sup> and Tomasz Gradalski, M.D., Ph.D.<sup>4</sup>

### Abstract

**Background:** Physiotherapy of edema in cases with obstructed main lymphatics of lower limbs requires knowledge of how high external pressures should be applied manually or set in compression devices in order to generate tissue pressures high enough to move tissue fluid to nonswollen regions and to measure its flow rate. **Methods:** We measured tissue fluid pressure and flow in subcutaneous tissue of lymphedematous limbs stages II to IV at rest and during pneumatic compression under various pressures and inflation timing. An 8-chamber sequential compression device inflated to pressures 50–120 mmHg, for 50 sec each chamber, with no distal deflation, was used. Pressures were measured using a wick-in-needle and electronic manometer. Fluid flow was calculated from continuously recorded changes in limb circumference using strain gauge plethysmography. **Results:** Before massage, in all stages of lymphedema, stagnant tissue fluid pressures in subcutaneous tissue ranged between  $-1$  and  $+10$  mmHg and did not differ from those measured in normal subjects. Pressures generated in tissue fluid by pneumatic compression reached 40–100 mmHg and were lower than those in inflated chambers. High pressure gradient through the skin was caused by its rigidity (fibrosis) and dissipation of applied compression force to proximal noncompressed limb regions. The calculated volumes of displaced tissue fluid ranged from 10 to 30 ml per compression cycle, to reach in some cases 100 ml in the groin region. **Conclusions:** Tissue fluid pressures generated by a pneumatic device were found lower than in the compression chambers. The obtained results point to the necessity of applying high pressures and longer compression times to generate effective tissue fluid pressures and to provide enough time for moving the stagnant fluid.

### Introduction

**P**NEUMATIC COMPRESSION OF TISSUES WITH LYMPH STASIS is, in addition to manual massage, a commonly used therapeutic modality in limb lymphedema. A number of pneumatic devices have been constructed and they are being widely used. The classification list of pneumatic compression devices includes nonsegmental and segmental home models for half or full leg without or with calibrated gradient pressure.<sup>1–9</sup> The devices differ with respect to the number of chambers, time of inflation, deflation, regulation of inflation pressure, and calibrated gradient pressure, as well as garment design. Most garments are customized for limbs; however, there are also some for the trunk and hypogastrium.

The diversity of devices and their function programs affect the treatment. Comparison of data is difficult because the

applied compression parameters vary in different centers. This is reflected in the pertinent literature by lack of reports of comparative studies determining inflation pressure levels, inflation/deflation cycle times, total pumping times in patients grouped according to the etiology of lymphedema, its duration and staging, tissue compliance and histological changes, lymphoscintigraphic evaluation, frequency of recurrent septic attacks (dermato-lymphangio-adenitis, DLA), and other parameters.

The technical parameters of pneumatic compression devices are usually based on blood rheological data derived from textbooks. These are the capillary and venous blood pressure, tissue venous blood flow and capacitance, capillary filtration rate, and laser-measured capillary flow. Unfortunately, there are no data on tissue fluid and lymph hydraulics. Basing on blood pressure/flow data, the recommended compression

<sup>1</sup>Department of Surgical Research and Transplantation, Medical Research Center, Polish Academy of Sciences, Warsaw, Poland.

<sup>2</sup>Department of Gastrointestinal and Transplantation, Central Clinical Hospital, Ministry of Internal Affairs, Warsaw, Poland.

<sup>3</sup>Indian Lymphology Centers, BHU Varanasi and TMC Thanjavur, India.

<sup>4</sup>Lymphedema Clinic, St Lazarus Hospis, Krakow, Poland.

pressures for treatment of lymphedema do not exceed 50 mmHg, time of compression by a sleeve chamber remains around 5 seconds, and it is followed by rapid deflation. Total compression time by an 8-chamber sleeve ranges between 20 and 40 seconds. Most devices have calibrated pressure gradients decreasing proximally by up to 20%.

Lack of consistency in results of treatment by pneumatic compression prompts investigation of the pathophysiological events and hydraulic parameters in the interstitial space of the massaged tissues and, in particular, the tissue fluid pressures/flows and hydraulic conductivity in normal and edematous lower limbs.

We measured tissue fluid pressures and flow under the skin of lymphedematous and control healthy lower limbs at rest and during pneumatic compression, using a specially constructed, according to our design, compression device (Biocompression, Moonachie, NJ). It was made of 8 sequentially inflated chambers, with proximal gradient pressure, time of inflation sufficient for translocation of fluid from the compressed to the proximal regions, and no deflation of distal chambers to prevent fluid back-flow and venous stasis. The obtained data are the first in the literature to show the hydraulic conditions created by pneumatic compression in the lymphedematous limb.

## Material and Methods

### Patients

The study was carried out on 15 patients of Polish and Indian ethnic origin, ages 28–56 years, mean weight 65 kg (58–72), mean height of 168 cm (161–178), BMI range 18.5–25, with diagnosis of lymphedema of one lower limb, stages II to IV, duration of 2 to 15 years (Table 1). There were no obese individuals. All patients originated from large cities. They practiced daily foot washing with antiseptic soap and were wearing shoes. Seventeen patients reported small foot skin abrasions or light foot trauma in the past, followed by development of foot and calf edema disappearing after rest. Larger edema developed months to years later and in 50% of cases was complicated by 1 to 3 attacks of dermatolymphangioadenitis. In 3 patients, edema developed without any detectable reason. Cases with acute inflammation, chronic venous insufficiency, and systemic etiology of edema were excluded from the study. Five male volunteers with healthy legs served as controls.

### Clinical staging

Staging was based on clinical evaluation: level of edema embracing limb from foot to groin, and degree of skin keratosis and fibrosis. Briefly, in stage I, pitting edema was limited to the foot; in stage II, pitting edema affected the foot and lower half of the calf; in stage III, foot and calf were involved, with hard foot and ankle area skin; in stage IV, the whole limb was edematous with foot and calf skin hyperkeratosis and papillomatosis of toes.<sup>10</sup>

### Lymphoscintigraphic staging

Evaluation of lymphatic pathways was done on lymphoscintigraphic images. They revealed in stage I spread of tracer in the foot, faint outline of superficial lymphatics and small inguinal lymph nodes. In stage II, there was spread of tracer in foot and lower part of calf, interrupted outline of a single lymphatic, and few small inguinal nodes with irregular outline. In stage III, no draining lymphatics were seen, with some inguinal nodes of irregular outline appearing after 2 hours. Stage IV was characterized by spread of tracer in the foot and entire calf without visualization of collecting lymphatics and nodes.

The consent of patients and volunteers was obtained and the study was approved by university ethics committees and a Polish–Indian intergovernmental agreement on scientific cooperation.

### Pneumatic compression appliance

A pneumatic compression device met the following conditions proposed by us: multichamber, sequential inflation, gradient inflation pressure, time of inflation sufficient for translocation of tissue fluid to proximal region, no deflation of distal chambers to prevent fluid back-flow and venous stasis in the superficial limb system. We used a device produced for us by Biocompression (Moonachie, NJ). It was composed of 8 segments 9 cm long each, sequentially inflated, inflation pressures were regulated from 50 to 125 mmHg, gradient pressures decreasing proximally by 20%, inflation time of each chamber was 50 sec, total inflation time equaled 400 sec. There was no deflation of distal chambers; deflation time of all chambers was 50 sec at the end of each cycle. The inflation pressures were measured in chambers and compared with those on pumping device manometers. The differences ranged between 2 and 5 mmHg.

TABLE 1. DEMOGRAPHIC DATA OF PATIENTS WITH LYMPHEDEMA OF LOWER LIMB UNDERGOING INVESTIGATIONS OF TISSUE FLUID PRESSURE AND FLOW DURING PNEUMATIC COMPRESSION THERAPY

M/F	Age	Group/ Stage	Level of Edema	Skin Changes	Lymphoscintigraphy
2M,3F	28–45	II	Mid-calf	None	Foot and lower calf spread, few collectors and inguinal nodes
3M, 2F	25–52	III	Knee	Foot keratosis	Foot and calf spread, single collector, inguinal node remnants
3M,2F	26–48	IV	Whole limb	Foot, calf keratosis	Foot and calf spread, no lymphatics and inguinal nodes
2M,3F	28–52		Healthy		ND

### Tissue fluid pressure measurement

The wick-in-needle technique was used. Calf and thigh skin was disinfected with isopropyl alcohol. One ml of 2% xylocaine with 5  $\mu\text{g}/\text{ml}$  adrenaline was injected intradermally and subcutaneously at 6 points of calf and thigh (Fig. 1). Adrenaline constricted arterioles and small veins preventing blood leakage at the tip of the wick. An 8 gauge injection needle with a polyethylene tubing (OD 1.34 mm) containing a glass-wool wick protruding 5 mm from the tubing tip was introduced under the skin at the depth of 5–8 mm at the level of chambers 3 to 8. The needle was withdrawn, while the wick-in-tubing remained in situ. A drop of antibiotic ointment was placed at the site of tubing entry to seal off the channel made by the needle. The outer part of tubing was fixed to the skin by adhesive tape. It was led out through an opening in the compression sleeve, then connected to the pressure transducer (Honeywell, Elblinger, Poland). Recording was done using a 3-channel device, pressure range  $-20$  to  $+150$  mmHg (Telsoft, Warsaw, Poland) and LabView software (National Instruments, Austin, TX). Calibration of pressure was done with use of an electronic device (National Instruments) and mercury and water manometers. Position of the transducer was zeroed, placing it exactly at the level of the subcutaneously located wick using a light beam device. Pressure recording was started 1 min before inflation of the sleeve and continued over the entire sequential inflation of 8 chambers. The data were collected using Microsoft Excel program and were presented graphically on a pressure/time scale.

### Continuous limb circumference measurement

Strain gauge plethysmography was used to measure circumference changes in the calf and thigh segments corresponding to the sequentially inflated chambers (Fig. 1). The obtained data served calculation of volume changes of limb, brought about by the proximally moved tissue fluid. Briefly, a plethysmograph (Hokanson, Bellevue, WA, type EC6) in a recording vein mode was applied. Six mercury strain gauges of a length of 22–53 cm were put around the limb at chamber levels 3 to 8. Elongation of the gauge was read off on the recorder graph scale in mm. It reflected the change in consecutive segments' circumference when inflation of chambers

propelled mobile tissue fluid in the proximal direction. The obtained numerical data were used for calculation of volume by multiplying the cross area of limb segments by 90 mm (length of the compressing chamber). Subtracting the volume value obtained before compression from that during compression provided data on the proximally transferred fluid volume.

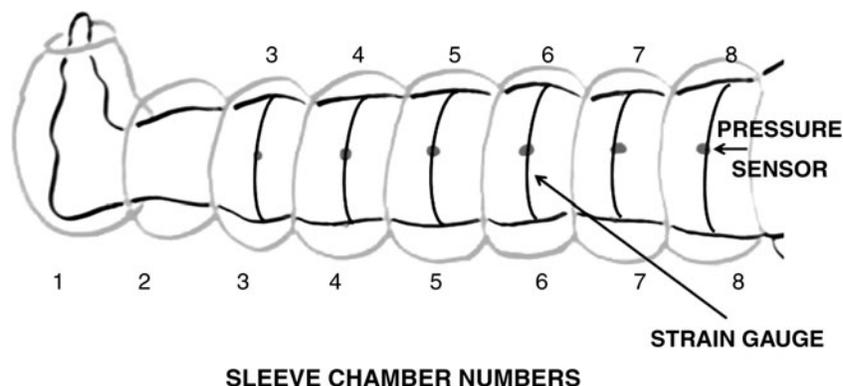
## Results

### Resting limb tissue fluid pressures

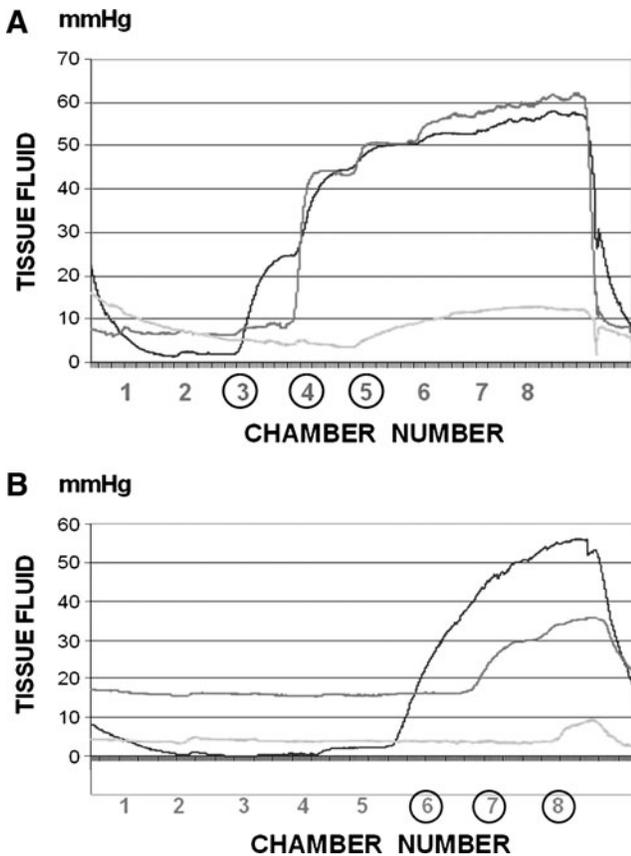
Tissue fluid pressure measured under the skin in lymphedematous calf subcutis in a horizontal position without movements ranged between  $-1.5$  and  $10$  mmHg (mean  $2.5 \pm 3.0$  SD) and in controls between  $-1.8$  and  $3.0$  mmHg (mean  $0.8 \pm 1.2$  SD). There were no statistically significant differences between the groups, although in some advanced lymphedema cases pressures were slightly above the mean value.

### Tissue fluid pressures and flow during pneumatic massage

Tissue fluid pressures during the first inflation of each sleeve chamber in all patients were lower than those in the chambers. This was observed both in the normal and edematous limbs (Figs. 2A and 2B; Fig. 3). Summarized data of 15 patients and 5 normal subjects are presented in Figure 4. The high gradient across skin was most likely caused by skin rigidity (fibrosis) and dispersion of the applied force to the proximal noncompressed regions. Unexpectedly, there was little tissue fluid pressure transmission from the compressed to the noncompressed proximal segments for a distance of 9 cm (width of the chamber) in normal as well lymphedematous limbs. For example, inflation of chamber 1 and 2 in the calf did not increase pressure at level 3. Interestingly, there was building up of pressure in the distal parts of the limb during sequential inflations of proximal chambers (Figs. 2A and 2B). This was presumably due to flow obstruction at the inguinal level that could be depicted on lymphoscintigrams. Another finding was that in the popliteal and upper thigh, tissue fluid pressures were reaching lower levels than in other limb regions. These two regions contain loose connective



**FIG. 1.** Schematic presentation of lower limb in a pneumatic sleeve with 8 chambers 9 cm wide each. 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.



**FIG. 2.** (A) Tissue fluid (TF) pressure recordings in the *normal calf* subcutaneous tissue (stage III) during pneumatic compression of 50 mmHg. Pressures recorded at chamber levels 3, above ankle (*first ascending line*), 4, mid-calf (*second ascending line*), and 5, below knee (*third ascending line*). Note that TF pressures during first inflation of chamber levels 3, 4, and 5 were lower than those in the chambers. Inflation of chamber 3 produced at level 3 pressure of 25 mmHg (*first ascending line*), stepwise rising during inflation of consecutive chambers to 55 mmHg. Inflation of chamber 4 (*second ascending line*) produced tissue fluid pressure rise at level 3 and 4 to 45 mmHg to increase during inflation of consecutive chambers to 60 mmHg. *Third ascending flat line* represents pressure in the medial aspect of calf just below the knee (level 5) usually with less edema and low flow resistance. (B) Tissue fluid (TF) pressure in the *normal thigh* subcutaneous tissue stage IV during pneumatic compression of 50 mmHg. Pressures recorded at chamber levels 6, above knee (*first ascending line*), 7, mid-thigh (*second ascending line*), and 8, upper thigh (*third ascending line*). Note that, as in the calf, tissue fluid pressures during first inflation of all chambers were lower than those in the chambers. Inflation of chambers 1–5 to 50 mmHg did not generate pressures at level 6. Inflation of chamber 6 produced at level 6 pressure of 35 mmHg (*second ascending line*), stepwise rising during inflation of consecutive chambers to 55 mmHg. Inflation of chamber 7 produced tissue fluid pressure rise at level 6 to 50 mmHg and at level 7 to 30 mmHg to increase during inflation of consecutive chambers to 55 and 35 mmHg, respectively. *Third ascending flat line* represents pressure at level 8 close to the groin, usually with less edema and low flow resistance.

tissue, are usually less swollen, and accumulate fluid translocated during sequential massage.

#### *Circumference (volume) changes during pneumatic massage*

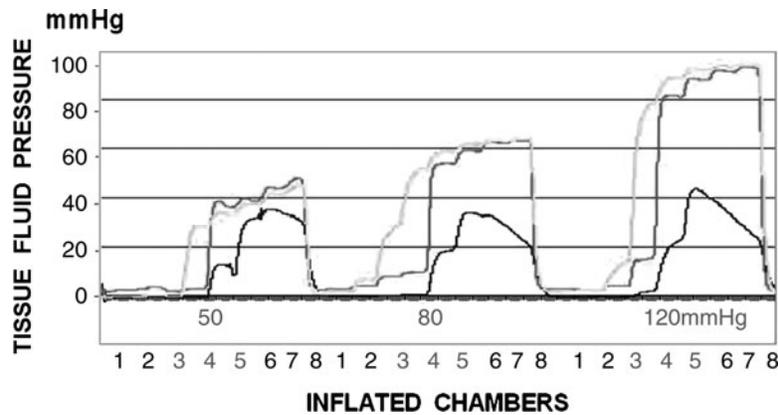
Continuous recording of circumference changes during sequential compression gave indirect insight into the volumes of fluid translocated from the compressed to the proximal segments. Following inflation of a chamber, increase of limb circumference occurred proximally to this chamber due to transfer of mobile fluid. Sequential inflations of chambers from 1 to 8 resulted in stepwise increase of circumference in the consecutive segments of the limb (Fig. 5). The increase in circumference at each level was recalculated into volume. Summarized data of 15 patients are presented in Figure 6. The transferred volume was evident in the calf, but even much more in the thigh containing larger volumes subcutaneous tissue with fluid and fat.

#### Discussion

Knowledge of the subcutaneous tissue hydraulic properties is scarce, although pneumatic compression therapy needs information about hydraulic conditions in the massaged tissues. This is indispensable for setting the massaging devices at effective pressures in order to propel the accumulated fluid toward the root of the extremity. So far, no consistent data on pressure and flow in the swollen extremities can be found in the literature. There have been some reports on pressures generated at the sleeve–skin interface, however, they give no insight into the intra-tissue physical events.

There is a general notion, so far not supported by any objective evidence, that the tissue fluid pressure in lymphedema is high. In this study, we showed that pressures were low, ranging between  $-1.5$  and  $+10$  mmHg. Moreover, we found that there were no statistically significant differences with normal limbs, although there was a slight tendency for higher pressures in lymphedema. The obtained data corroborate our previous clinical and experimental findings of low tissue fluid pressures in lymphedema.<sup>11,12</sup> The mechanism of low pressure can easily be explained by high skin compliance in the early stages of edema formation, allowing its stretching and expansion of the subcutaneous space accumulating excess of capillary filtrate not drained away by lymphatics. Accumulation of soluble proteins causes, in accordance with Starling's law, causes rise in oncotic pressure, this in turn to attraction of water and further expansion of the tissue space.

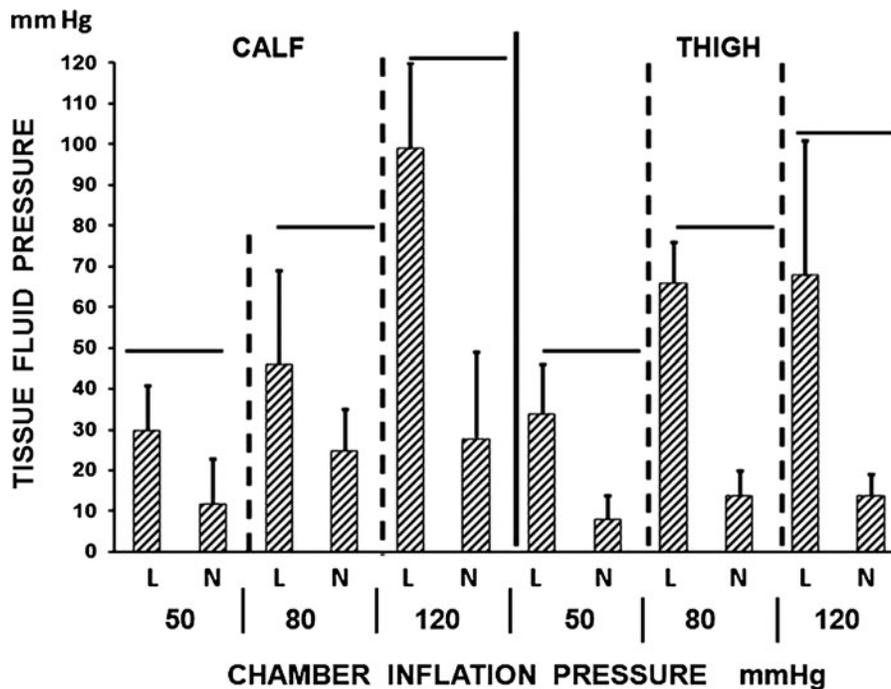
Pneumatic compression is applied in order to raise tissue fluid pressure and create a gradient between the compressed and proximal noncompressed tissues to generate physical conditions for fluid flow. The generally applied compression pressures usually range between 50 and 120 mmHg. An open question remains whether externally applied pressures generate tissue fluid pressures of the same level as in the sleeve encompassing the limb. In our studies, pneumatic compression produced tissue fluid pressures that were lower than those in the inflated sleeve. The created gradient was most likely created by low skin compliance (rigidity) caused by fibrotic process routinely ongoing in lymphedema. Another factor responsible for low pressures could be dispersion of the applied compression force in the subcutaneous tissue to the proximal noncompressed regions.



**FIG. 3.** Tissue fluid (TF) pressure recording in a lymphedematous calf subcutaneous tissue at the level of sleeve chambers 3, 4, and 5. Inflation pressures were 50, 80, and 120 mmHg, respectively. Inflation time of each chamber was 55 sec; there was no deflation of distal chambers. Numbers 1 to 8 denote consecutive sleeve chambers. Pressures were recorded under chambers 3 (*first ascending line*), 4 (*second ascending line*), and 5 (*third ascending line*). Note that TF pressures during first inflation were at all levels lower than those in chambers. Inflation of chamber 3 increased TF pressure at level 3 to 30 mmHg but not at level 4. Inflation of chamber 4 produced pressure at level 4 to 40 mmHg and at level 5 to 12 mmHg. Similar shapes of pressure curves were observed during inflation to 80 and 120 mmHg. Note that at level 5 (*third ascending line*) close to the knee with soft popliteal tissue, the TF pressures were much lower than in chamber 5. This could be explained by low resistance to flow in the popliteal fossa. However, the most important observation was lack of transmission of pressure from the compressed level to the proximal next.

Another interesting finding was a limited tissue fluid lateral pressure transmission to the noncompressed proximal segments. This could be accounted for by physiologically low hydraulic conductivity of the subcutaneous tissue both in lymphedema and normal conditions.

We also observed building up of tissue fluid pressures in the distal parts of the limb during inflation of proximal chambers. This could be explained by slow tissue fluid flow from the compressed tissues caused by low tissue hydraulic conductivity and in addition by flow obstruction at the



**FIG. 4.** Tissue fluid pressures in calf (level 4) and thigh (level 7) subcutaneous tissue in patients with lymphedema ( $n = 15$ ) and normal subjects ( $n = 5$ ) during the first inflation of pneumatic sleeve to 50, 80, and 120 mmHg. L, lymphedema, N, normal, *horizontal line* denotes pressure in the sleeve chambers, mean values in mmHg  $\pm$  SD. Note that TF pressure was in all cases lower than in the sleeve both in the lymphedema cases and healthy subjects (for explanation, see text). There were also evident differences between lymphedema and control cases.

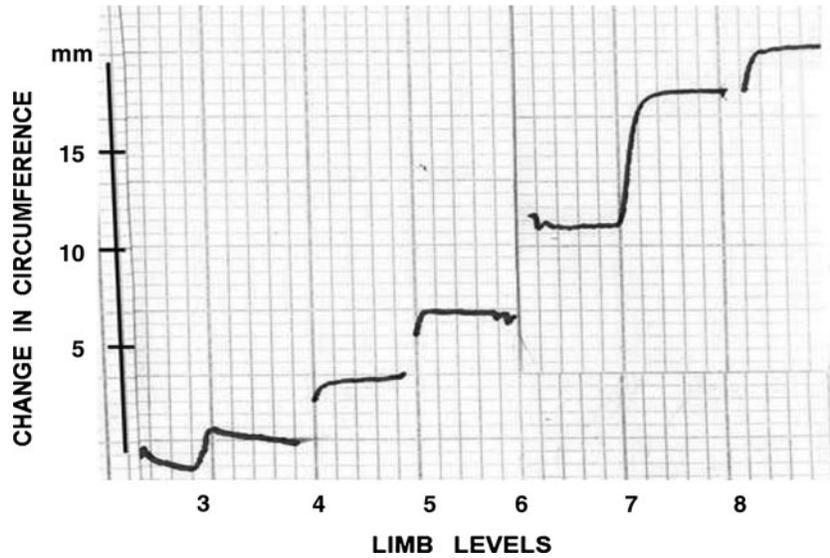


FIG. 5. Changes of limb circumference during pneumatic massage of a patient with lymphedema stage III at levels corresponding to compression chamber positions (3, 4, 5, calf; and 6, 7, 8, thigh; in mm). The measuring device was placed at 3, 4, 5, 6, 7, and 8 levels. Sequential inflation of sleeve chambers brought about consecutive increase in circumference, eventually reaching at level 8 value of 20 mm. Changes in circumference served calculation of changes in volume (sq cross area  $\times$  length of chamber 9 cm). There was no backflow of proximally pushed fluid.

inguinal level, seen on lymphoscintigrams. This last is a consequence of the ongoing fibrotic process in the groin lymphatics and nodes.

Even high generated tissue fluid pressures may remain ineffective in propelling fluid, especially in advanced stages of lymphedema. This is why, in addition to recording tissue fluid pressures, we simultaneously measured fluid flow. For

this purpose, a strain gauge was put around the limb at six levels corresponding to the level of sleeve chambers and connected to a recording device. It provided data on the continuous changes of circumference during sequential compression and allowed calculation of the approximate volume of displaced fluid by each inflated chamber. The calculated volumes ranged from 10 to 40 ml per inflated cham-

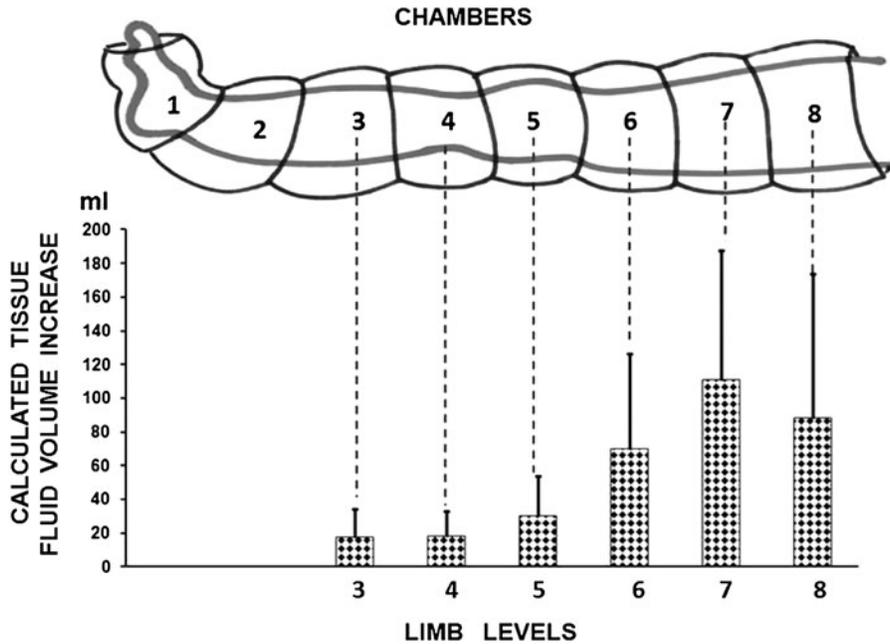


FIG. 6. Calculated volumes of tissue fluid (TF) moved sequentially from distal parts of lymphedematous limb (stages II, III, and IV) toward the groin by pneumatic compression of chambers 1 to 7. The volume increases in consecutive limb segments to reach highest values in the mid-thigh. Note that although edema is clinically most visible above the ankle level, the bulk of the fluid is moved from the thigh. Values are means  $\pm$  SD,  $n = 15$ . Note high SD caused by differences in accumulation of TF in individual patients.

ber. They were low in the calf to increase in the thigh, reaching at groin level the total volume for the entire extremity of more than 100 ml. The displaced volume was certainly of tissue fluid but not venous blood, as there was no resistance to blood flow and blood did not accumulate in the proximal segments of the limb.

This is the first published study presenting hydraulic parameters of the massaged skin and subcutaneous tissue in lymphedema. It shows that in lymphedema the resting tissue fluid pressures are low, only slightly above zero. The tissue fluid pressures generated by compression devices are lower than those in the inflated chambers. This may be due to low skin compliance, low physiological hydraulic conductivity of the subcutaneous tissue, and resistance to flow at the groin level, factors hindering tissue fluid flow to the nonswollen tissues. Our observations point to the necessity of applying high pressures and long compression times to generate effective tissue fluid pressures and to provide enough time for moving the stagnant fluid to the root of the extremity. The obtained data should be useful for physiotherapy in allowing the parameters of compression devices to be set at levels corresponding to those in the in-tissue conditions.

#### Author Disclosure Statement

Drs. Olszewski, Jain, Ambujam, and Gradalski and Ms. Zaleska and Ms. Cakala have no conflicts of interest or financial ties to report.

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Address correspondence to:

Waldemar L. Olszewski, M.D., Ph.D.

Department of Surgical Research and Transplantology

Medical Research Centre

Polish Academy of Sciences

5 Pawińskiego Str.

02-106 Warsaw

Poland

E-mail: waldemar.l.olszewski@gmail.com

