BUTTERWORTH HEINEMANN

Med. Eng. Phys. Vol. 17, No. 2, pp. 134–140, 1995
Elsevier Science Ltd for BES
Printed in Great Britain
1350–4533/95 $10.00 + 0.00

A mathematical model of flow through the terminal lymphatics

N.P. Reddy and K. Patel

Department of Biomedical Engineering, University of Akron, Akron, Ohio 44325-0302, USA

Received 5 August 1993, accepted 18 January 1994

ABSTRACT

Proper understanding of the mechanisms of fluid absorption and flow through the terminal lymphatics is essential for the control of several pathological conditions such as edema, bedsores and cancer. A mathematical model of the terminal lymphatics was developed using the principles of mechanics. Computer simulation results substantiate the hypothesis that fluid absorption and flow through the terminal lymphatics occur due to suction mechanisms of the adjacent contractile lymphatic segments and due to periodic fluctuations in the interstitial fluid pressure. In addition, the results suggested that increasing the length of a terminal lymphatic vessel beyond a certain limit does not cause further increase in fluid flow into the terminal lymphatic.

Keywords: Lymphatic system, terminal lymphatics, mathematical model

Med. Eng. Phys., 1995, Vol. **17**, 134–140, March

INTRODUCTION

The lymphatic system plays an important role in several common pathological conditions such as edema, bedsores, cancer and interstitial fibrosis[1–4]. The lymphatic system can be considered as the drainage system consisting of a converging network of vessels which transports excess fluid, protein and metabolic waste products from the tissue spaces into the blood circulatory system[5]. Inhibition or blockage of lymph flow leads to edema and accumulation of metabolic waste products in the tissue. Prolonged edema leads to interstitial fibrosis. In particular, pulmonary edema is life threatening. Also, accumulation of metabolic waste products leads to tissue necrosis. Consequently, an understanding of the lymphatic system is essential for the control of several diseases involving interstitial fluids. Interstitial fluid is absorbed by the lymphatic capillaries which are generally referred to as the terminal lymphatics. These terminal lymphatics are delicate and fragile. They are made up of a single layer of endothelial cells. Several terminal lymphatics join to form the transporting lymphatics (also referred to as collecting lymphatics) and these join to form larger transporting lymphatics. Lymph (the fluid in the lymphatics) is filtered at the lymph nodes during its passage via the network of transporting lymphatics. There are numerous valves along the transporting lymphatic vessel network.

The interstitial fluid pressure is negative with respect to the atmosphere[1,6]. Pressure in the jugular vein, where lymph enters via the thoracic duct, is approximately 5 to 8 mmHg above the atmospheric pressure. The transporting lymphatics have smooth muscle in the wall and are intrinsically contractile. In contrast, the terminal lymphatics do not have smooth muscle in the wall and are not contractile. The mechanisms of lymph flow through the transporting lymphatics have been analysed both from physiological and biomechanical points of view[2]. Reddy *et al.*[7,8] have formulated mathematical models of a transporting lymphatic vessel and of the vessel network[9]. However, the mechanisms of fluid absorption and flow through the terminal lymphatics are poorly understood.

The purpose of the present investigation is to formulate a mathematical model and simulate lymph flow through terminal lymphatics under different physiological conditions.

MODEL DEVELOPMENT

The terminal lymphatic is made up of a single layer of endothelial cells[10]. The diameter of terminal lymphatic varies[11–14] from 10 to 30 μm. The

Address all correspondence to Narender P. Reddy, Ph.D., Professor of Biomedical Engineering, University of Akron, Akron, Ohio 44325-0302. Kandarp Patel, M.S., is now with Sekely Industries, Inc. in Alliance, Ohio

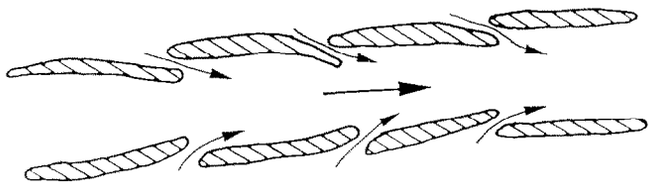

Figure 1 Inter-endothelial junctions of the terminal lymphatic act as valves and allow unidirectional motion of the fluid from the interstitial spaces into the lumen of the terminal lymphatic

main function of the terminal lymphatics is to absorb excess interstitial fluid and protein molecules from the interstitial spaces. These fluid and protein molecules are absorbed through the inter-endothelial junctions. The endothelial junctions act as valves and allow only unidirectional motion of fluid from the interstitial spaces into the lumen of the terminal lymphatic (*Figure 1*). Electron microscopic studies have revealed that the endothelial junctions are approximately 15 to 30 nm wide[15].

During edema, tissues are swollen because of excess interstitial fluid. In addition, the transluminal pressure differential across the lymphatic wall is larger due to excess interstitial fluid. This allows more endothelial junctions to open causing increased fluid flow into the lumen of the terminal lymphatic vessel. For a number of years, it has been recognized that material enters the terminal lymphatics via the large open endothelial intercellular junctions, and is retained within them during tissue compression while the open junctions temporarily remain closed[16,17].

A system of anchoring filaments keep the terminal lymphatic from collapsing during edema. One end of the filament is attached to the outer surface of the endothelial wall (*Figure 2*). The other end of the filament is attached to the tissue fibre matrix. These anchoring filaments, approximately 8 nm, help in binding the terminal lymphatics to the adjoining tissue fibres[16,18]. The filaments act as springs and exert a pulling force on the outer surface of the capillary wall[2,19].

From an engineering point of view, the terminal lymphatics can be characterized as submerged hyperplastic pressure vessels with external

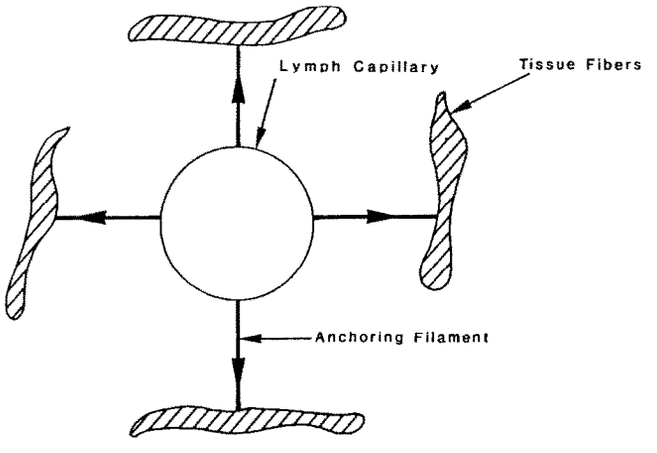

Figure 2 A diagrammatic representation of anchoring filaments in relation to the tissue matrix and terminal lymphatic wall

wall anchors. In the development that follows, the following assumptions apply.

- The terminal lymphatics are thin cylindrical vessels.
- Flow Reynolds numbers are small.
- Flow is axially symmetric.
- Lymph is a Newtonian fluid.
- Inertial forces and the shear stresses in the wall are negligible.
- Anchoring filaments are uniformly arranged along the circumference of the lymphatics so that the shear stresses in the wall can be neglected.
- No fluid slip exists at the wall.

For axial symmetry and an incompressible fluid, the continuity equation can be expressed as,

$$\frac{\partial V_z}{\partial z} + \frac{1}{r}\frac{\partial}{\partial r}(rV_r) = 0 \tag{1}$$

where, V_z is the axial velocity of the lymph, V_r is the radial velocity of the lymph, r is the radial coordinate, and z is the axial coordinate.

As axial symmetry is assumed, the radial pressure gradient within the lymphatic vessel can be neglected. As the problem is reduced to a one-dimensional case, we can integrate the momentum equation in the z direction to yield,

$$\rho\frac{\partial Q}{\partial t} = -\pi R^2\frac{\partial P}{\partial z} + \mu\left[\frac{\partial^2 Q}{\partial z^2} + 2\pi R\tau_w\right] \tag{2}$$

where, P is the pressure, τ_w is the wall shear stress, and Q is the flow rate in the terminal lymphatic vessel. It is assumed that the instantaneous wall shear stress is the same as that resulting from Poiseuille's law. Therefore,

$$\rho\frac{\partial Q}{\partial t} = -\pi R^2\frac{\partial P}{\partial z} + \mu\frac{\partial^2 Q}{\partial z^2} - \frac{8\mu}{R^2}Q \tag{3}$$

and, integrating the continuity equation (1) yields

$$\frac{\partial Q}{\partial z} = -2\pi R\, V_r|_{r=R} \tag{4}$$

But, at the wall (i.e. at $r = R$),

$$V_r|_{r=R} = \frac{\partial R}{\partial t} - \Phi\,(P_{if} - P) \tag{5}$$

where Φ is a constant which defines the conductivity of the terminal lymphatic vessel wall:

$$\Phi = K_L/(2\pi R) \text{ if } (P_{if} - P) > 0$$
$$= 0 \text{ if } (P_{if} - P) \leq 0\,.$$

Where K_L is hydraulic conductivity of the vessel wall per unit length of the wall. Thus, equation 4 can be reduced to

$$\frac{\partial Q}{\partial z} = -2\pi R\left[\frac{\partial R}{\partial t} - \Phi\,(P_{if} - P)\right] \tag{6}$$

The momentum balance for the lymphatic vessel wall can be expressed as,

$$P = P_{ext} + \frac{h}{R}\sigma_z - \frac{F}{2\pi RL} \tag{7}$$

where P_{ext} is the external pressure on the lymphatic vessel wall, σ_∞ is the hoop stress in the wall, h is the wall thickness, R is the radius of the vessel wall, and F is the force exerted by the anchoring filaments per unit length of the vessel wall.

For the purpose of the present investigation, anchoring filaments are assumed to behave like linear springs. The force exerted by the anchoring filaments per unit length of the terminal lymphatic wall (F) can be estimated by:

$$F = N_f K_1(\delta - \delta_0) \tag{8}$$

where, N_f is the number of filaments per unit length, K_1 is the constant depending on the elastic properties of anchoring filaments (similar to a spring constant), δ is the anchoring filament length, and δ_0 is the initial anchoring filament length.

Length of the anchoring filament depends on the inter-fibre distance and the instantaneous radius of the vessel wall. The amount of interstitial fluid determines the inter-fibre distance. If each terminal lymphatic is assumed to drain a concentric cylinder of tissue volume, V, the inter-fibre distance can be estimated as

$$L_f = K_2 \sqrt{\frac{V}{V_0}} \tag{9}$$

and

$$L_{f0} = K_2 \tag{10}$$

where, L_f is the length of the inter-fibre distance, L_{f0} is the initial inter-fibre distance, V is the instantaneous value of the interstitial fluid volume, V_0 is the initial interstitial fluid volume, and K_2 is a constant.

The anchoring filament length can be expressed as,

$$\delta = \frac{L_f}{2} - R \tag{11}$$

$$\delta_0 = \frac{L_{f0}}{2} - R_0 \tag{12}$$

Assuming linear elasticity, the hoop stress σ_∞ can be expressed as

$$\sigma_\infty = E\frac{R - R_0}{R_0} \tag{13}$$

where E is the modulus of elasticity in pascals.

The dynamic changes in interstitial fluid volume that occur when the normal fluid balance is altered are governed by the instantaneous rates of net trans-capillary filtration and lymph flow. Therefore,

$$\frac{dV}{dt} = Q_{filt} - Q_{tl} \tag{14}$$

where, Q_{filt} is the trans-capillary filtration rate from the blood capillary into the interstitial space, and Q_{tl} is the flow rate into the terminal lymphatics from the interstitial space.

The net filtration at the blood capillary can be expressed by the Starling–Landis relationship:

$$Q_{filt} = K_c[(P_c - P_{if}) - m(\pi_c - \pi_{if})] \tag{15}$$

where, K_c is the hydraulic conductivity of blood capillaries in $m^5/(N.s)$, P_c is the capillary pressure in Pa, P_{if} is the interstitial fluid pressure in Pa, π_c is the osmotic pressure in the blood capillary in Pa, π_{if} is the osmotic pressure of interstitial fluid in Pa, and m is the reflection coefficient. The interstitial fluid pressure is a non-linear function of interstitial fluid volume[1,20].

The flow into the terminal lymphatic can be obtained by integrating over the length of the lymphatic and multiplying by the hydraulic conductivity of the terminal lymphatic wall and the number of lymphatics:

$$Q_{tl} = N_L K_L \int_0^L (P_{if} - P)\, dz \tag{16}$$

where, Q_{tl} is the flow rate into each compartment of the terminal lymphatic vessel from the interstitial space, N_L is the number of terminal lymphatics, and K_L is the hydraulic conductivity of the terminal lymphatic wall per unit length of the wall.

The inter-endothelial junctions act as valves and present a constraint on the flow:

$$Q_{tl} \geq 0 \tag{17}$$

Another area of concern is the relationship between colloid osmotic pressure and interstitial protein concentration. Landis and Pappenheimer[21] have given equations of colloid osmotic pressure as a function of protein, albumin and globulin which closely fit experimental data:

$$\pi = 13.33\ [2.1\ C + 0.016\ C^2 + 0.00009\ C^3] \tag{18}$$

where C is the protein concentration in kg/m^3. Both π_{if} and π_c can be calculated by this expression in pascals.

The rate of change of interstitial fluid protein concentration is the difference between trans-capillary protein diffusion rate and rate of protein removal via the lymphatics.

$$\frac{\partial}{\partial t}(VC_{if}) = K_{pr}(C_c - C_{if}) - C_{if}Q_{tl} \tag{19}$$

where, K_{pr} is the capillary permeability for protein (for protein leakage into the tissue spaces), C_c is the protein concentration in the capillaries in kg/m^3, and C_{if} is the protein concentration in the interstitial fluid in kg/m^3.

Blood pressure in the capillary P_c and the protein concentration in the capillary C_c form the upstream boundary condition. Pressure in the adjacent contractile lymphatic forms the down-stream boundary condition.

PARAMETER VALUES

Quantitative anatomical data of the terminal lymphatics is scarce in the literature. Terminal lymphatics are usually about 0.5 mm long and of very irregular shape, with maximum diameters in the range of 15–75 μm when completely filled[11]. Normally, the terminal lymphatics have flattened,

uneven contours varying in diameter[10,12–14] from 10 to 30 μm. Hence, an average diameter of 20 μm was assumed. Also, the ratio of wall thickness to the radius of the vessel was assumed to be 0.1, which gave a wall thickness of 1.0 μm.

There is no data available regarding the elasticity of lymphatic vessels. Studies of Nisimaru[10] suggest that, in general, lymphatic vessels are much more (about ten times) distensible than blood capillaries. Elasticity of blood capillaries is about 0.42 MPa. Therefore, the elasticity of the lymphatic vessels was assumed to be 42 kPa. The number of terminal lymphatics (N_L) was approximated as 40,000 per kg of tissue.

Hydraulic conductivity (K_L) of the terminal lymphatic vessel wall was found as follows. Hydraulic conductivity for one pore can be calculated as:

$$\frac{q_{pore}}{\Delta P_{pore}} = \frac{\pi (R_{pore})^4}{8\mu L_{pore}} \qquad (20)$$

where, q_{pore} is the flow rate through the pore, ΔP_{pore} is the pressure difference between two sides of the wall, R_{pore} is the radius of the pore, μ is the viscosity of the fluid passing through the pore, and L_{pore} is the length of the pore.

Casley-Smith *et al.*[11] claim that tissue channels are present in the interstitial matrix. They observed channels of 30 to 70 nm. in diameter and 0.1 mm length. Therefore, the average pore size can be assumed to be 50 nm. Assuming one 50 nm pore for every 1 μm length, there are 10^4 pores for every 1 cm length and 10^8 pores for every 1 cm^2 area. These parameters can be used to calculate the hydraulic conductivity of the lymphatic vessel wall per unit length of the vessel:

$$K_L = 3.86 \times 10^{-11}\ m^4/(N.s)$$
$$[\text{or } 5.049 \times 10^{-8}\ ml/(cm.s.mmHg)] \qquad (21)$$

The lymphatic anchoring filaments are a third type of connective tissue fibrils[18], different from collagen and elastic fibres, which have a diameter averaging 8 nm. From this, a 10 nm diameter for an anchoring filament is a good assumption. Also, elasticity of the anchoring filament is assumed to be 12 MPa. Therefore, the spring constant for an anchoring filament was estimated to be $K_1 = 9.425 \times 10^{-8}$ N/m. Assuming one anchoring filament per every micron length, we have 10000 filaments (N_f) per cm length. The initial interfibre distance (I_{40}) was assumed to be 2.5 times the diameter of the terminal lymphatics; i.e., 0.005 cm.

Hydraulic conductivity of blood capillaries was assumed to be $3.86 \times 10^{-15}\ m^5/(N.s)$ or 5×10^{-7} ml/(s.mmHg). The protein concentration in blood capillaries (C_c) was assumed to be 5 kg/m^3. Reflection coefficient for protein m at the blood capillary wall was assumed to be 0.95.

Pressure at the down-stream end of the terminal lymphatic depends on the contractile nature of the lymphatic vessels. Zweifach and Prather[22] made a systematic study of collecting lymphatics in the mesentery of cat and in the omentum of rabbit using intravital microscopy. They found that contraction–relaxation cycles occurred between 10 and 18 per minute. The amplitude of pulsation ranged from 1 to 5 mmHg. in the larger vessels[22].

Table 1 Parameter values

Parameter	Value
C_c	5 kg/m^3 [0.5 g/100 ml]
C_{ai}	0.4 kg/m^3 [0.04 g/100 ml]
E	42 kPa [4.2×10^5 dyne/cm^2]
h	1 μm
I_c	5×10^{-4} m [0.05 cm]
I_{40}	5×10^{-5} m [0.005 cm]
N_L	40000/kg
N_f	10^6/m [10000/cm]
K_c	$3.86 \times 10^{-15}\ m^5/(N.s)$ [5×10^{-7} ml/(s.mmHg)]
K_L	$3.86 \times 10^{-11}\ m^4/(N.s)$ [5.049×10^{-8} ml/(cm.s.mmHg)]
K_{1p}	$10^{-13}\ m^3/s$
K_1	9.43×10^{-8} N/m [9.43×10^{-3} dyne/cm]
P_a	4 kPa [39999.0 dyne/cm^2]
P_c	2.67 kPa
R_0	10 μm
V_0	$10^{-5}\ m^3/kg$ [1 ml/100 g]
μ	10^{-3} kg/(m.s) [1 centi-poise]
ρ	980.67 $kg.m^{-3}$
m	0.95

COMPUTER SIMULATION RESULTS

Model simulation with parameters given in *Table 1* resulted in a steady state condition. The suction pressure wave generated due to the adjacent contractile lymphatic influenced only a length of 0.2 to 0.3 mm terminal lymphatic vessel adjacent to it, and only this length of the vessel was effective in fluid absorption (*Figures 3, 4*). The flow increased with increasing stiffness (elastic modulus) of the terminal lymphatic vessel wall (*Figure 5*). Increased stiffness of the anchoring filaments caused an increase in flow through the terminal lymphatics (*Figure 6*). Flow increased with increasing hydraulic conductivity of the terminal lymphatic vessel wall (*Figure 7*), and also

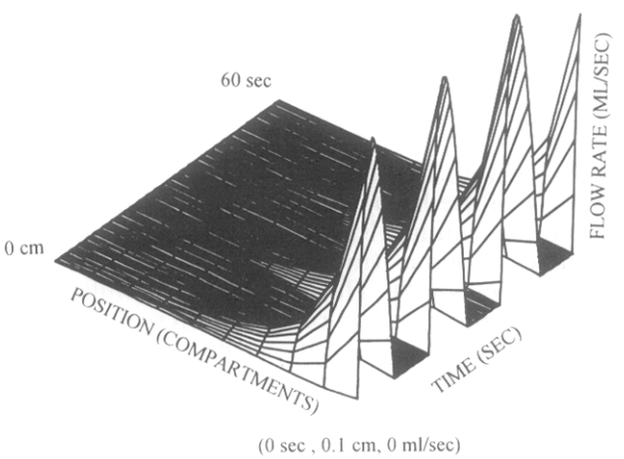

Figure 3 Flow in the terminal lymphatic plotted as a function of position and time. Extreme left (0 position) corresponds to the initial segment of the vessel and extreme right corresponds to the outlet of the terminal lymphatic where it is connected to the adjacent contractile lymphatic

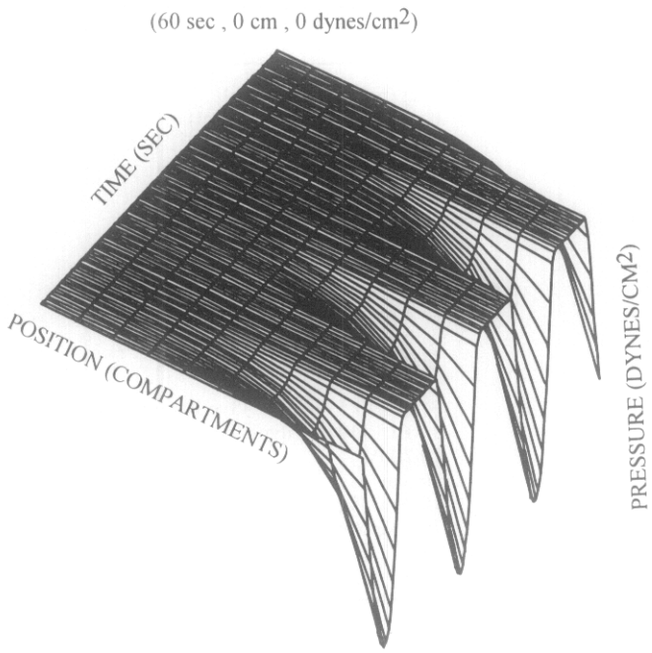

Figure 4 Pressure in the terminal lymphatic plotted as a function of position and time. Extreme left (0 position) corresponds to the initial segment of the vessel and extreme right corresponds to the outlet of the terminal lymphatic where it is connected to the adjacent contractile lymphatic

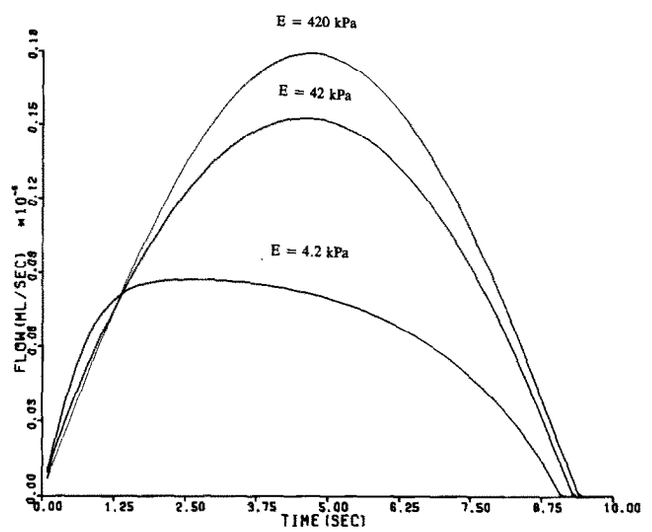

Figure 5 The flow rate increased with increasing Young's modulus of the terminal lymphatic wall

increased with increased values of hydraulic conductivity of the blood capillary wall. Also, the flow through terminal lymphatics increased during simulated edema (increase in interstitial fluid volume) (*Figure 8*). This edema was simulated by increasing the capillary pressure. Increased amplitude or frequency of contractions in the adjacent contracting lymphatic segment increased the flow.

DISCUSSION

We have established a theoretical basis for the analysis of flow through the terminal lymphatics. Principles of mechanics together with the current notions in physiology are integrated into a simple

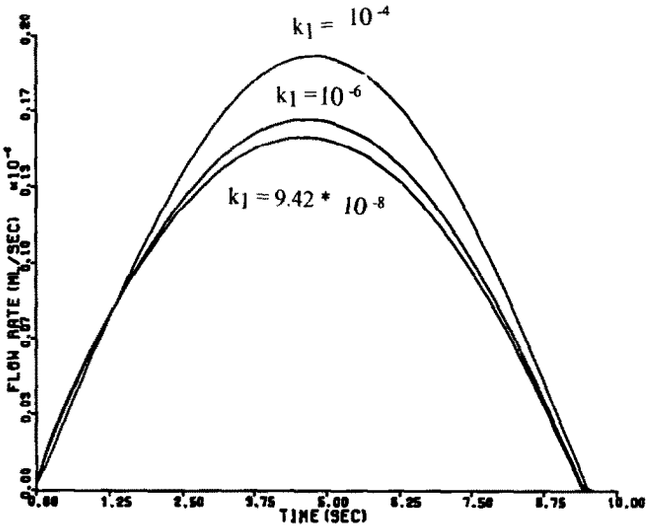

Figure 6 The flow rate increased with increasing stiffness of the anchoring filaments [K_1 is in N/m]

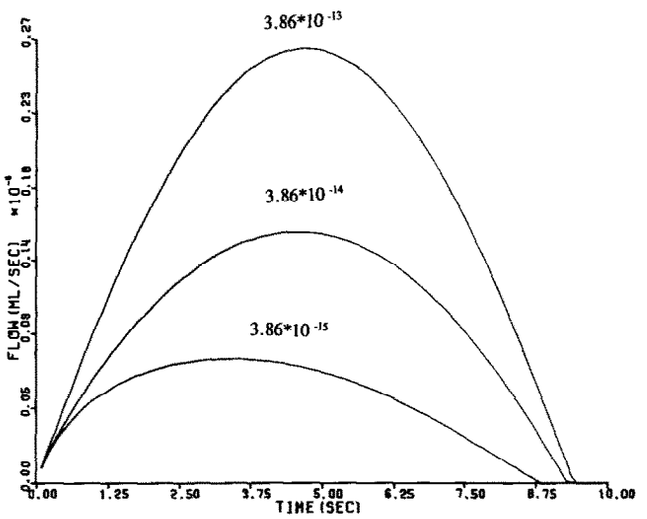

Figure 7 Out-flow rate plotted as a function of time showing the effect of hydraulic conductivity of the terminal lymphatic wall. Note the increase in flow with increasing the hydraulic conductivity [units are in $m^4/(N.s)$]

model of the terminal lymphatics. There is very little data available in the existing literature regarding the model parameters. The parameter values were estimated from known data as discussed in the section on parameter values. Model results with these parameters were consistent with available experimental results.

From the three-dimensional plots (*Figures 3,4*), it is clear that increasing the length of terminal lymphatic above a certain value does not increase the flow rate into the terminal lymphatics. This is because suction pressure is not transmitted along the entire length. The length-to-diameter ratio of the terminal lymphatic vessel was assumed to be 12.5, and the simulation results suggest that only a length of up to eight diameters of the terminal lymphatic vessel closest to the branch is effective in fluid absorption into the terminal lymphatic vessel. If the length of a terminal lymphatic vessel is larger than eight times its diameter, the excess

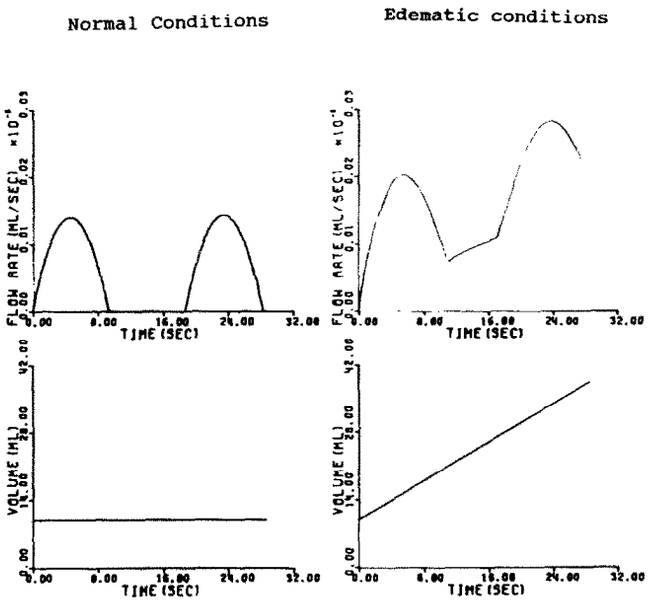

Figure 8 Lymph flow rate and interstitial fluid volume are plotted as a function of time in normal and edematic conditions. Note the increase in flow with increasing interstitial fluid volume

length may be useless for fluid absorption. However, the excess length may have loose junctions that facilitate absorption of lymphocytes and other white blood cells which are either absorbed through pinocytosis or have contractile mechanisms for self propulsion.

The contractile nature of lymphatics formed the down-stream boundary condition for the pressure. Increased amplitude of pressure pulsation in the adjacent contractile lymphatic increased the flow through the terminal lymphatics. As the vessel gets more rigid, the suction mechanisms have less effect on the vessel radius. In the present study, increasing the elastic modulus of the lymphatic vessel caused an increase in the flow through the terminal lymphatics (*Figure 5*).

Flow rate in the initial segment of the terminal lymphatic was found to be zero (*Figure 3*) because the suction pressure was not transmitted along the complete length. This might be due to our assumption that the elastic properties are constant throughout the length of the terminal lymphatics. In reality, there might be a gradient in the elastic properties along the length of the terminal lymphatics. As there is no pressure data available regarding terminal lymphatics, we assumed that the interstitial fluid pressure is independent of the position external to the terminal lymphatic wall.

Although the flow through the terminal lymphatics increased with increasing stiffness of anchoring filaments (*Figure 6*), the flow is less sensitive to anchoring filament stiffness when compared to the modulus of elasticity of the terminal lymphatic vessel wall. Anchoring filaments with increased stiffness apply a greater force on the terminal lymphatic vessel wall causing the inter-endothelial junctions to remain open for a longer period of time and thus allowing more interstitial fluid in the terminal lymphatics. There is no data in the literature regarding the mechanical properties of anchoring filaments. We assumed the stiffness of anchoring filaments to be linear and constant throughout the length of the terminal lymphatics. It is not known if these filaments have linear mechanical properties. Moreover, these properties could vary from filament to filament along the length of the terminal lymphatics.

Lymph flow, in the present simulation, increased with increasing values of hydraulic conductivity of the terminal lymphatic vessel wall. Flow also increased with increasing values of hydraulic conductivity of the blood vessel wall. This is consistent with findings of Adair and Guyton[23]. Blood capillaries with higher hydraulic conductivity allow more fluid to flow into the interstitial spaces resulting in increased interstitial fluid volume and in turn leading to increased fluid absorption and flow through the terminal lymphatic vessel.

Edema is a pathological condition characterized by an accumulation of excess fluid in the interstitial spaces. During simulated edema, lymph flow increased significantly (*Figure 8*). Increased volume leads to an increased interstitial fluid pressure, thereby increasing the trans-luminal pressure difference across the terminal lymphatic vessel wall. As a result, flow into and out of the terminal lymphatics increases. These results are consistent with experimental results reported in the literature[20]. The interstitial fluid pressure and the suction pressure oscillations created by the adjacent contractile lymphatic vessels had a significant effect on the flow.

Models are conceptual constructions which allow formulation and testing of hypotheses and in this way they simulate meaningful research. The present model results substantiate the hypothesis that fluid absorption and flow through the terminal lymphatics is due to the periodic fluctuations in interstitial fluid pressure and due to the suction mechanisms of adjacent contractile lymphatics.

CONCLUSION

A mathematical model of lymph absorption and flow through the terminal lymphatics has been developed, and simulated. Subject to the limitations discussed, the following additional conclusions can be drawn: (1) The simulation results substantiate the hypothesis that fluid absorption and flow through the terminal lymphatics is due to periodic fluctuations in interstitial fluid pressure and due to the suction mechanisms of the adjacent contractile lymphatics; (2) Only a length of up to six or eight times the diameter of terminal lymphatic vessel from the branch is effective in fluid absorption from the interstitial spaces; (3) Increased stiffness of the terminal lymphatic vessel, and increased stiffness of the anchoring filaments resulted in increased fluid absorption and flow.

REFERENCES

1. Aukland K, Reed RK. Interstitial-lymphatic mechanisms in the control of extracellular fluid volume. *Physiol Rev* 1993; **73:** 1–78.
2. Reddy NP. Lymph circulation: physiology, pharmacology, and biomechanics. *CRC Crit Rev Biomed Eng* 1986; **14:** 45–91.
3. Reddy NP. Mechanical stress and viability of skin and subcutaneous tissue, In: Hargens A, (ed) *Tissue Nutrition and Viability.* New York, Springer, 1986; 215–41.
4. Reddy, NP. Effects of mechanical stress on lymph and interstitial fluid flows, In: Bader DL, (ed) *Pressure Sores: Clinical Practice and Scientific Approach.* London, McMillan Press, 1990; 203–20.
5. Reddy NP. A note on the lymphatic vessel network design. *J Biomech* 1980; **13:** 529–31.
6. Reddy NP, Palmieri V, Cochran GVB. Subcutaneous interstitial fluid pressure during external loading. *Am J Physiol* 1981; **240:** R327–9.
7. Reddy NP, Krouskop TA, Newell PH Jr. Biomechanics of a lymphatic vessel. *Blood Vessels* 1975; **12:** 261–78.
8. Reddy NP, Krouskop TA, Newell PH Jr. A note on the mechanisms of lymph flow through the terminal lymphatics. *Microvascular Res* 1975; **10:** 214–6.
9. Reddy NP, Krouskop TA, Newell PH Jr. A computer model of the lymphatic system. *Comput Biol Med* 1977; **7:** 181–97.
10. Nisimaru Y. Summary of our studies concerning the structure and function of the lymphatic system. *Hiroshima J Med Sci* 1980; **31:** 145–92.
11. Casley-Smith JR. The fine structure and functioning of tissue channels and lymphatics. *Lymphology* 1979; **12:** 177–83.
12. Casley-Smith JR. Are the initial lymphatics normally pulled open by the anchoring filaments? *Lymphology* 1980; **13:** 120–9.
13. Casley-Smith JR. Functioning and inter-relationships of blood capillaries and lymphatics. *Experientia* 1976; **32:** 1–4.
14. Frank RM, Wiedman P, Fellinger E. Ultrastructure of lymphatic capillaries in the human dental pulp. *Cell Tissue Res* 1982; **178:** 229–35.
15. Casley-Smith JR, Foldi-Borcsok E, Foldi M. A fine structural study of the tissue channel's numbers and dimensions in normal and lymphoedematous tissues. *Lymphogie* 1979; **3:** 49.
16. Leak LV, Burke JF. Ultrastructural studies on the lymphatic anchoring filaments. *J Cell Biol* 1980; **36:** 129–62.
17. Taylor AE. Capillary fluid filtration starling forces and lymph flow. *Circ Res* 1981; **49:** 557–64.
18. Bock P. Histochemical staining of lymphatic anchoring filaments. *Histochemistry* 1978; **58:** 343–8.
19. Reddy NP, Kesavan SK. Low Reynolds number liquid propulsion in contracting tubular segments connected through valves. *Math Comput Modelling* 1989; **12:** 839–44.
20. Guyton AC. Interstitial fluid pressure and dynamics of lymph formation. *Fed Proc Fed Am Soc Exp Biol* 1978; **35:** 1861–5.
21. Landis EM, Pappenheimer JR. Exchange of substances through the capillary walls. *Handbook of Physiology (Section 2, Circulation, Vol. 2)* Am Physiol Soc, Washington, DC, 1963.
22. Zweifach BW, Prather JW. Micromanipulation of pressure in terminal lymphatics in the mesentery. *Am J Physiol* 1975; **228:** 1326–51.
23. Adair TH, Guyton AC. Lymph formation and its modification in the lymphatic system. In Johnston MG (ed) *Experimental Biology of the Lymphatic System* New York, Elsevier, 1985, 1–44.