Modeling the interaction between the lymphatic capillaries and the interstitium in normal and lymphedema conditions

Introduction

The lymphatic system consists of a unidirectional network of branches that expands throughout the body. Impairment of the lymphatic transport can lead to a variation of pathologies such as lymphedema which is mainly characterized by swelling of the extremities, high susceptibility to infection, and tissue fibrosis.

Even though the lymphatic system plays a crucial role in regulating the body's fluid balance, it has been rather neglected compared to the cardiovascular system. Furthermore, there are no effective treatments for lymphedema, which severely compromises the quality of life of patients. The purpose of this study was to set some initial steps in computationally modeling the interstitial-to-lymphatic mass transport and the swelling of the interstitium, which occurs in lymphedema conditions, to gain a better understanding of the parameters influencing this phenomenon.

Methods

COMSOL Multiphysics was used to perform the computational modeling. The 2D geometry (250 by 250 µm) includes 3 different domains being the inner volume of a terminal lymph vessel (length 96 µm, diameter 24 µm), the lymphatic wall (0.6 µm thick) and the interstitium (Figure 1a). Lymph was modelled as a free fluid phase with a density of 1000 kg/m^3 and a viscosity of 1.5 cP. The lymphatic wall was considered as a linear elastic porous material and the interstitium as a poroelastic medium. For normal physiological conditions, the one-way valve function of the wall was modeled by implementing a permeability (ranging between 3.86×10^{-36} and 3.86×10^{-17} m^2) that was dependent on the pressure gradient between the inlet and outlet. For lymphedema conditions, the endothelial wall was considered as a permeable membrane with a permeability of $3.86\text{x}10^{-10}$ m^2 which allows the fluid to both enter and leave the vessel. At the inlet, a sinusoidal pressure with a magnitude of 3.5 mmHg and a frequency of 1 Hz was imposed. At the outlet, the pressure was set to 0 mmHg as in [1].

Result and discussion

These initial computational results support the strategy to model the function of the unidirectional lymphatic valves via a time- and pressure dependent permeability. In contrast to normal conditions, lymphedema results in lymph flowing back into the interstitium when the pressure gradient becomes negative, leading to swelling of the interstitium (Figure 1b and 1c). We conclude that the proposed modelling strategy is a valid first step to model lymphedema. In the next steps, we will increase the topological complexity to better match anatomical complexity, and set up validation experiments in a rodent model of lymphedema.

REFERENCES

1. Galie, P. et al., 2009. *J Biomech Eng.* 131(11).

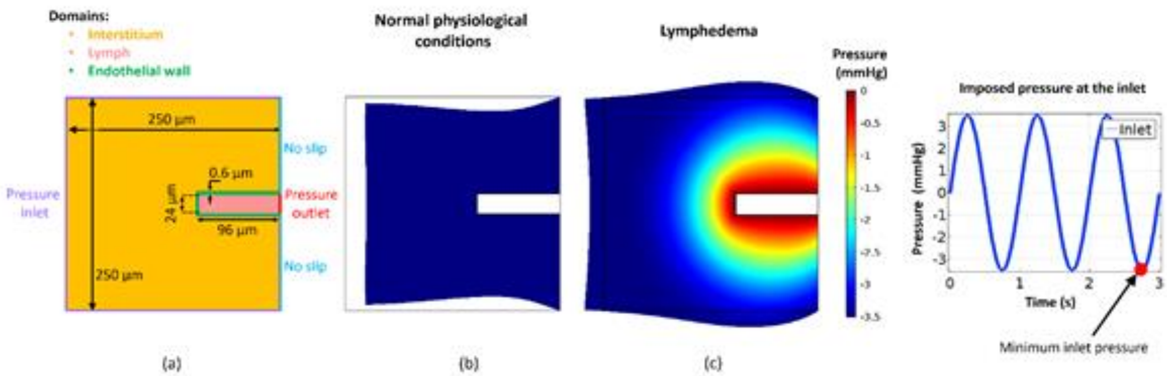

Figure 1. (a) Geometry and boundary conditions of the model, pressure contours and displacement at minimum inlet pressure (2.75 s) in case of **(b)** normal physiological conditions and **(c)** lymphedema.