JOANNA NOWAK

Two-phase modelling and experimental studies of human tissue with lymphedema for the purpose of diagnostics of hydromechanical properties

Doctoral dissertation written under the supervision of
prof. dr hab. Eng. Mariusz Kaczmarek

ABSTRACT

The presented doctoral thesis concerns a problem of modelling lymphedematous tissues in various stages of the disease, based on numerical simulations and experimental studies, to develop the assessment of hydromechanical properties.

Three methods of examination of subcutaneous tissue with edema are considered: using a skinfold caliper with ultrasound elastography function and a special holder for forming a fold, an indenter apparatus with function of mounting in a mobile or stationary holder and a two-chamber pneumatic system. Initial functional tests of the devices were carried out in laboratory conditions, on foam phantoms of various stiffness, with a 0.5 mm and 1 mm thick layer of silicone imitating skin. Clinical trials were conducted in outpatient settings and involved women struggling with the problem of lymphedema of various etiologies.

In terms of theoretical research and simulations, mathematical models were formulated and then implemented in numerical calculations. Simulations were performed for each of the previously mentioned examination methods for subcutaneous tissue , focusing on explanation of the course of mechanical process and assessing the hydromechanical properties of the tissues. Mathematical description covered two outermost layers of human tissue: skin and subcutaneous tissue. The subcutaneous tissue was treated as a biphasic material with an isotropic, resilient, permeable skeleton, fullfilled with fluid. Kinematics of (tissue) fluid and porous skeleton are independent. Balance equations were formulated for both phases. In terms of small deformations, linear model formulated by Biot was adapted for description, while for large deformations the formulation proposed by Borja was used. Physical relationships defining the mechanical properties comprised volumetric couplings, excluding effects of viscosity.

Force interactions of phases were described by a linear dependence on relative velocity of liquid flow. Skin in both cases was considered as a single-phase elastic material (in a non-linear model as a neo-Hookian material). Inertia and gravitational forces was neglected in model.

The main and original part of the work consists of numerical simulations (in terms of three considered diagnostic methods) and experimental research of lymphedematous tissue (with use of skinfold caliper with a fold-forming handle and indentation apparatus mounted in a mobile handle).

The work consists of 6 chapters. After the introduction, Chapter 1 contains a literature review in terms of experimental research and modelling of lymphedematous tissue. In discussing literature data, attention was focused on available methods of identifying lymphedema with particular emphasis on measurement methodology and nature of information obtained as a result of study. The following part of chapter describes anatomy of healthy tissues (skin and subcutaneous tissue) as well as description and etiology of oedematous tissue. The most important parameters determined for healthy, human and animal tissues, such as Young's modulus for skin and subcutaneous tissue, and subcutaneous tissue permeability, are also discussed. The final part of the chapter contains a brief review of mathematical models used to describe tissues, with particular emphasis on two-phase model. Chapter 2 contains phase balance equations and mathematical models formulated for two-phase material in terms of small deformations and for finite deformations. Chapter 3 contains a description of construction of considered diagnostic devices, along with detailed data on measurement methodology. Selected results from measurements on patients and the results of tests with an indentation apparatus on polyurethane foam phantoms are also presented. Chapter 4 contains a description of initial and boundary conditions adopted in numerical model and results from numerical simulations for the three considered test methods. This chapter also includes results of parametric analysis, focused on identifying characteristic parameters determining hydromechanical properties of lymphedematous tissue. Chapter 5 contains discussion relating to the results of experiments and simulations. The focus was on the qualitative and quantitative interpretation of experimental results, and in case of a two-chamber system, an attempt was made to identify the characteristic parameters of subcutaneous tissue with edema, Young's modulus and permeability. A summary of the measurement methodology was also made, taking into account the repeatability and objectivity of the obtained results, ease of use and patient comfort. The last, Chapter 6 contains final conclusions.

Experimental, modeling and numerical simulations carried out allowed to formulate the following conclusions:

- for three presented diagnostic methods (indentation method with a given force or a given indentation depth and chamber method) qualitative compatibility of the results for clinical experiments and numerical simulations was obtained,
- despite the use of numerous simplifications (isotropy, homogeneity, simple hyperelastic model), results of simulation allowed to explain hydromechanical processes in subcutaneous tissue,
- a key aspect of modeling was assumption of biphasic nature of subcutaneous tissue with edema and consideration of appropriate couplings between fluid and skeleton,
- parametric analysis showed that permeability and stiffness of subcutaneous tissue play a major role in understanding the hydromechanical processes occurring in the edematous tissue,
- simulation results indicate importance of size of tested area of tissue and level of pressure,
- from the point of view of ability to identify subcutaneous tissue parameters, such as stiffness and permeability, the most effective is two-chamber system (large pressure area allows to limit participation of skin in total response of system),
- in indentation methods, participation of skin in total response of system is significant, but in case of large indentation depths (so-called deep tonometry), properties of subcutaneous tissue also have a significant contribution,
- the use of the indenter apparatus does not generate limitations related to anatomy, and installation of apparatus in proposed holders improves the objectivity of measurement results,
- tests with the indenter apparatus on foam phantoms showed the sensitivity of method on local inhomogeneities, details of positioning of tested object in relation to apparatus, and presence of a silicone layer imitating skin,
- indentation method of skin fold measurement is the least effective due to limited area of operation and difficulties in implementation (fold protrusion).