The Anisotropic Permeability of Skin Determined from Inverse Analysis of Centrifugal Draining Tests

Gabriel Pulver*[1], Alexander E. Ehret[2,3], and Edoardo Mazza†[4,5]

[1]ETH Zürich, Institute for Mechanical Systems, 8092 Zürich – Switzerland
[2]ETH Zürich, Institute for Mechanical Systems, 8092 Zürich – Switzerland
[3]Swiss Federal Laboratories for Materials Science and Technology, 8600 Dübendorf – Switzerland
[4]ETH Zurich, Institute for Mechanical Systems, 8093 Zürich – Switzerland
[5]Swiss Federal Laboratories for Materials Science and Technology, 8600 Dübendorf – Switzerland

Abstract

Understanding the mechanical behaviour of human skin is crucial for medical applications such as wound healing (1), reconstructive surgery (2), automated planning of suture placement (3), skin growth using tissue expanders (4), formation of so-called stretch marks induced by abdominal skin tension during pregnancy (5), or intradermal and subcutaneous drug delivery (6). To rationalize in-vivo and ex-vivo experimental results and predict the mechanical behaviour of skin, several constitutive models were proposed. Recent studies rely on multi-layer and multiphasic modelling approaches (6), (7). In particular, quadriphasic models representing solid, liquid and ionic phases play a crucial role in modelling the biomechanics of soft biological tissue (6), (8). Thereby, tissue permeability is a crucial parameter to characterise the time-dependent mechanical behaviour of skin (9) or to analyse transport processes in drug delivery (6). Fluid permeability is often assumed to be isotropic, only accounting for changes in permeability due to volume changes (6), (7), (10). However, the collagen fibres in skin have a preferred in-plane orientation (11) which is expected to cause anisotropy of the permeability tensor. While modelling approaches accounting for anisotropic and deformation-dependent permeability properties were proposed (12), (13), there is a lack of experimental methods to accurately determine this crucial parameter and its dependence on flow direction. In fact, the range of the permeability values reported in the literature spans over a few orders of magnitude (14).
Our proposed experimental method exploits the body forces acting on all phases within a tissue sample when exposed to acceleration in a centrifuge. Centrifugal forces cause the liquid to flow out of the tissue at a rate that depends on tissue permeability. Using a porous support, liquid expelled from the tissue is rapidly transported away from the skin surface. This set of well-defined boundary conditions allows us to reliably simulate the experiment using the quadriphasic model (9) and conduct an inverse analysis, determining the permeability value based on the measured mass loss in the experiments. The new experimental setup allows us to quantify the skin's liquid flow in-plane and out-of-plane, depending on the orientation of the skin sample during the test.

First experiments were performed with porcine dermis and subcutis showing promising reproducibility. Further, the results indicate that there is indeed a measurable anisotropic

*Speaker
†Corresponding author: mazza@imes.mavt.ethz.ch

permeability. Numerical sensitivity analyses were used to tune the experimental conditions and optimise the quantitative interpretation of the results. In particular, the computations showed that the transient phase of mass reduction in the experiments is mostly governed by the hydraulic permeability, while the long-term equilibrium mass is determined by the density of fixed charges, which determines the level of osmotic pressure within the tissue. The fibre and matrix stiffness parameters were found to play a subordinate role. The mean thickness of the samples was obtained from their planar cross-sectional area and the weight in the reference state. To determine the solid and liquid content within each tested sample, the weight of each sample was measured after it was dried out in an oven at the end of the centrifuge measurement, and compared to the reference initial weight. In conclusion, the results indicate that the new measurement procedure may provide a more reproducible and accurate method to determine the hydraulic permeability and its anisotropy in soft tissues.

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