Mechanical Characterization of a Positive Pressurized Alveoli-on-Chip Model

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Introduction

Alveoli-on-chip technology is an innovative approach to explore the complex mechanisms of the lung alveoli. The aims of this work were to investigate the mechanical behaviour of a new alveoli-on-chip and to develop a finite element analysis (FEA) model to represent it, while exploring the possibility of creating microvasculature on the chip membrane. The alveoli-on-chip consists of a polydimethylsiloxane (PDMS) membrane supported by pillars plasma-bonded to a glass plate. By applying pressure under the pillars, alveolar deflection during breathing can be simulated. It also has a cell culture layout with medium reservoirs and the ability to introduce a hydrogel to create a vascular network.

Materials and Methods

The membrane deflection was evaluated as a function of pressure (Fig. 1), thickness, temperature, ageing and fatigue. Two methods of measuring area strain were investigated. The first, based on images of common household sugar particles on the membrane, allows area strain to be assessed on a point-by-point basis using linear strain calculations. The second, based on confocal images of endothelial cells on the membrane (Fig. 2), provides area strain mapping. A finite element model was also constructed and compared with the experimental results. Finally, an attempt was made to grow a microvasculature on the membrane by seeding endothelial cells and fibroblasts in a hydrogel.

Results

A linear correlation was observed between membrane thickness and deflection, showing that increasing thickness reduces deflection. Post-curing time also had an effect on membrane stiffness, with a 25% drop in deflection after 10 days, which could be reduced to less than 5% with 5 days pre-conditionning at 37°C. Fatigue caused a loss of deflection of approximately 5% after 10 days. Temperature had no significant effect between 25°C and 37°C. The FEA model gives accurate overall results but overestimates deflection at low pressure. The first method of measuring area strain gave results consistent with the finite element model, but the variability of the values is high because the measurements are subject to human error and variations in particle distribution. The second method appears to be promising in providing a mapping of area strain consistent with the assumptions of the FEA model and the mechanical hypothesis. However, more and better data are required to fully evaluate this method. Attempts to create microvessels were unsuccessful due to cell non-survival and hydrogel breakage.

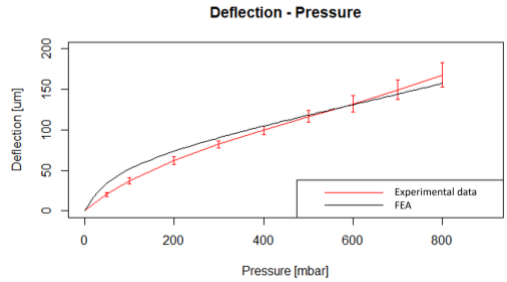

Fig. 1 Experimental measurements of deflection (red line) match FEA model data (black line).

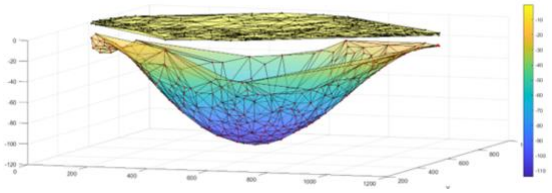

Fig. 2 3D visualisation of confocal images of the deflected and undeflected membrane. The points represent the centre of the cells and are connected by triangulation to calculate the area strain.

Discussion

Many factors influence the mechanical behaviour of the membrane, making it difficult to assess the cause of the differences observed between experiments or batches, e.g. PDMS cures at room temperature. The use of polynomial regression in the measurement area strain hides some of the data, highlighting the challenge of translating three-dimensional data into two-dimensional graphs. Attempts to create microvasculature have raised complex issues to investigate, such as fibrinogen concentration, plug removal and surface coating.

References

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