

Biologia vascolare

IS VESSEL-ON-CHIP COMPLEXITY WORTH IT? A QUANTITATIVE COMPARISON OF SIMPLIFIED AND COMPLEX HIGH-FIDELITY VASCULAR MODELS

V. Guadagno[1], T. Mencarini[1], F. Vicinanza[1], S. Bozzi[1], E. Raschi[2], C. Bodio[2], P. Meroni[2], A. Redaelli[1]

[1]Politecnico di Milano, Italy; [2]Istituto Auxologico Italiano, Milano, Italy

Background and Aims. Endothelial cells (ECs) are highly sensitive to biophysical and biochemical cues, including extracellular matrix (ECM) composition, vessel geometry, and shear stress. Vessel-on-Chip (VoC) platforms are widely used to study vascular biology, yet they differ substantially in structural complexity and physiological relevance. Cylindrical collagen-based microvessels closely replicate native vessel geometry and matrix conditions but involve technically demanding fabrication. Conversely, endothelialized PDMS microchannels are easier to fabricate and handle, despite their square geometry and rigid, non-physiological substrates. Although both are used extensively, few studies directly compare these architectures. This study aims to perform a controlled, side-by-side comparison of these two VoC models, systematically evaluating fabrication robustness, success rates, and the ability of the endothelial monolayer to respond to inflammation and shear stress.

Methods. Two VoC architectures were compared: (i) a cylindrical lumen (160 µm diameter) within a 3D collagen-I hydrogel formed by needle templating, and (ii) a square PDMS microchannel (170 × 170 µm) fabricated via soft lithography. Both models were seeded with human umbilical vein endothelial cells (HUVECs). PDMS channels were directly used as lumens for cell seeding after fibronectin coating, whereas hydrogel vessels required additional steps for gelation and lumen formation. Fabrication success rate and lumen geometry were quantified in both systems. Endothelial confluency, morphology, and junctional integrity were assessed by confocal microscopy using VE-cadherin staining. Inflammatory activation was evaluated via E-selectin expression. Shear stress response was analysed by measuring cell spreading, elongation, and F-actin organization under flow compared to static controls.

Results. The PDMS model demonstrated superior robustness and reproducibility, with a 100% fabrication success rate (usable lumens) and 75% of devices reaching the experimental endpoint, compared to 68% fabrication success and only 30% endpoint survival for the hydrogel model. Furthermore, the PDMS model required a significantly shorter preparation time (3 days vs. 1 week) and less operator expertise. Both models provided reliable endothelial responses to inflammatory stimuli, characterized by E-selectin expression ($p<0.01$ in PDMS channels), junctional destabilization ($p<0.01$) and partial cells loss. Response to shear flow was successfully quantified in the PDMS model, where ECs showed increased spreading ($p<0.05$) and elongation while preserving barrier integrity. Moreover, perfusion induced a shift from cortical to cytoplasmic F-actin, consistent with stress fiber formation and alignment under flow.

Conclusions. This study highlights a key trade-off between physiological relevance and experimental practicality. While collagen-based microvessels better replicate native conditions, PDMS microchannels provide greater consistency, robustness, and scalability. These findings indicate that increased biomimicry does not necessarily translate to improved experimental performance. Instead, model selection should be guided by the specific biological question and the required level of throughput and reproducibility.