

Microvessel-on-a-chip model for studying ultrasound and microbubble-mediated drug delivery

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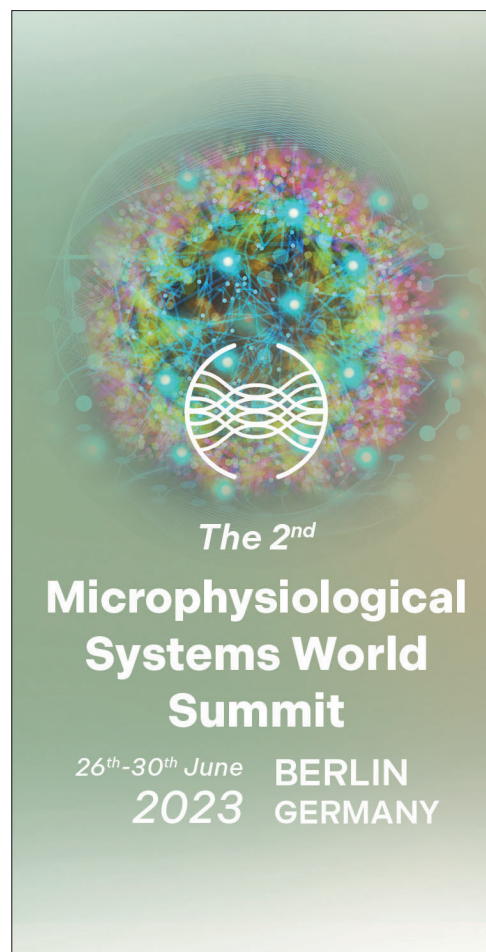


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ALTEX Proceedings

Marcel Leist, Uwe Marx
and Peter Loskill
Welcome



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Modelling, Safety Testing
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Track 4:
**MPS Highlights Across
Disciplines**



of mechanical or electrical stimuli. High-resolution CMOS-based microelectrode arrays (MEAs) are used to record the spontaneous electrical activity of CMs [3]. With these state-of-the-art techniques combined, we are able to generate CMs contraction activity propagation mechanically and electrically, revealing the cluster automaticity of hPSCs-CMs.

After mapping the in-plane and out-of-plane contraction forces and electrical activity of CMs, we focus on comparing CMs activity by inducing either an extracellular stimulus from CMOS MEAs or applying force-controlled drug delivery by FluidFM.

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Presentation: Poster

268

Microvessel-on-a-chip model for studying ultrasound and microbubble-mediated drug delivery

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The blood vessel wall creates a barrier which can impair the transport of drugs from the blood to the underlying tissue. Lipid-coated gas microbubbles (diameter 1-10 μm) oscillate upon ultrasound application which can be used to locally enhance vascular permeability. However, the mechanism underlying this effect is poorly understood. Furthermore, it is yet to be discovered what ultrasound settings maximize the treatment outcome. This study aimed to create a microvessel-on-a-chip model to investigate the effects of ultrasound and microbubble treatment on vessel permeability and cell viability.

Human microvascular endothelial cells were seeded against an extracellular matrix gel in the Organoplate[®] 3-lane and cultured for 4 days under bidirectional flow to form a 3D microvas-

cular tube (300 \times 220 \times 2200 μm). The microvessels were treated with $\alpha_v\beta_3$ -targeted microbubbles and 2 MHz ultrasound pulses of 10 \times 10 or 10 \times 1000 cycles, evenly spread over 30 s, and peak negative pressures ranging from 55-480 kPa. Controls included non-treated, microbubbles only, or ultrasound only. Permeability changes were investigated using 150 kDa FITC-dextran dye and fluorescent microscopy for 2 h. Cell viability was assessed using a WST-8 colorimetric assay which measures metabolic activity.

Two hours after treatment, vascular permeability was only significantly higher for the microbubble and 480 kPa 10 \times 10 cycles and 350 and 480 kPa 10 \times 1000 cycles ultrasound treatments in comparison to all controls. In addition, within 5 min after treatment only the microbubble and 350 and 480 10 \times 1000 cycles groups showed a clear leakage increase, suggesting an earlier onset of the treatment effect upon the 10 \times 1000 cycles. Furthermore, the plateau of the leakage approached 100% for the 10 \times 1000 cycles with microbubble groups whereas this was \sim 70% for the 480 kPa 10 \times 10 cycles, indicating that the barrier loss was less with the short cycle's treatment. The spatial leakage was unevenly distributed over the vessel which suggests that some vessel regions were more affected by the treatment than others. Finally, all treatments did not affect cell viability. These results show the potential of a microvessel-on-a-chip to investigate the mechanism and maximize the outcome of ultrasound and microbubble-mediated drug delivery treatments.

Presentation: Poster

269

Patient specific cardiac model of dilated cardiomyopathy in a beating heart-on-chip

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Dilated Cardiomyopathy (DCM) is the most common non-ischemic cardiac disease, whose current treatments only slow down its progression without repairing the produced damage (Maron et al., 2006). Elucidating the mechanism of DCM is crucial for the development of efficient therapies. Organs-on-chip (OoC) technology has emerged as a promising tool to replicate *in vitro* the human pathophysiology, allowing the integration of electromechanical stimulus and sensors (Sun et al., 2012). In this study, we generated 3D cardiac models within a heart-on-chip platform (Visone-Lozano et al., 2022) by using induced pluripotent stem cells derived cardiomyocytes (iPSC-CMs) differentiated from a patient presenting