



HAL
open science

Development of an instrumented physiological microdevice to study the impact of the vascular microarchitecture and tumoral context on the brain angiogenesis and blood-brain barrier'

Thomas Sivier, Maxime Gourgues, Léo Durand, Franck Chollet, Vincent Humblot, Thérèse Leblois, Agathe Figarol

► To cite this version:

Thomas Sivier, Maxime Gourgues, Léo Durand, Franck Chollet, Vincent Humblot, et al.. Development of an instrumented physiological microdevice to study the impact of the vascular microarchitecture and tumoral context on the brain angiogenesis and blood-brain barrier'. GDR B2I, Jul 2024, Mulhouse, France. hal-04770783

HAL Id: hal-04770783

<https://hal.science/hal-04770783v1>

Submitted on 12 Nov 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Development of a complex vascular microarchitecture in a physiological microdevice to study the impact of a tumoral context on the brain angiogenesis and blood-brain barrier

Thomas Sivier^{1,*}, Maxime Gourgues¹, Léo Durand¹, Franck Chollet¹, Vincent Humblot¹, Thérèse Leblois¹, Agathe Figarol¹

¹ *Université de Franche-Comté, CNRS UMR 6174, Institut FEMTO-ST, 25000 Besançon, France*

*Correspondance : thomas.sivier@femto-st.fr

The blood-brain-barrier blocks the passage of many exogenous molecules into the brain, reducing treatment options for brain pathologies. In the case of multiform glioblastoma, the most frequent brain tumor, the evolution of the BBB remains uncertain. Developing a BBB-on-chip (BBBoC) model is particularly pertinent to compare its function in a healthy and tumoral context.

The BBB consists of a complex vascular network. The former BBBoC model was constructed with a single straight central channel seeded with endothelial cells and surrounded by a hydrogel matrix which may contains tumor and support cells. The complexification of the channel design brings the model closer to reality. Several biocompatible sacrificial materials were tested and compared: carbohydrate glass^[1], gelatin^[2], or a mixture of waxes^[3]. They were assessed in terms of ease and rapidity of synthesis, molding and demolding (in a PDMS template obtained from 3D printing), shape conservation, and triggered dissolution, taking into account the constraints of cell preservation. Around those sacrificial materials, the hydrogel is cast. After gelation of the matrix, a buffered solution dissolves the material (different temperatures and protocols were tested), making way for a more complex network of about 100-200 μm diameter channels. The biocompatibility of the materials and the dissolution processes were assessed on glioblastoma cells (U87-MG) dispersed in the hydrogel (live-dead kit).

The next step will be to check the viability of endothelial cells seeded in the channels, and of the support cells (astrocytes and pericytes) seeded within the hydrogel. The perfusion of this vascular network, with a biological fluid, will reproduce the blood flow to study the angiogenesis phenomenon and the obtention of the blood-brain barrier functions with or without cancer cells in the matrix.

References:

[1], Miller et al, « Toward Vasculature in Skeletal Muscle-on-a-Chip through Thermo-Responsive Sacrificial Templates », *Nature Materials* **2012**, volume 11, , 778.

[2], Golden et Tien, « Fabrication of Microfluidic Hydrogels Using Molded Gelatin as a Sacrificial Element », Lab on a Chip **2007**, volume 7, 720.

[3] Wan et al., « Toward Vasculature in Skeletal Muscle-on-a-Chip through Thermo-Responsive Sacrificial Templates », Micromachines **2020**, volume 11, , 907.

Keywords: microfluidic, brain cancer, sacrificial biomaterials, vascularization, tumor-on-chip