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.

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The blood-brain barrier (BBB) strictly controls exchanges between the blood and the brain to block most external aggressions. However, glioblastoma multiforme, the most common and aggressive primary brain cancer, modifies its microenvironment and the BBB with an uncertain evolution. Organs-on-chips are innovative biotechnological tools that reproduce an organ in-vitro, helping to understand many pathological mechanisms. Developing a BBB-on-chip (BBBoC) model is particularly relevant to compare its function in healthy and tumoral contexts.

An initial BBBoC model was designed with a straight hollow channel surrounded by a hydrogel matrix containing cancer and supporting cells: astrocytes and pericytes. This channel, seeded with endothelial cells, should acts as an arteriole when perfused with nutritive medium mimicking blood flow. Complexifying the channel design is required to bring the model closer to physiological reality. Sacrificial materials were compared as templates for complex channels: carbohydrate glass, gelatin, and mixed waxes. They were evaluated regarding synthesis, molding (in a PDMS mold from 3D-printing), demolding, shape retention, and dissolution. Their biocompatibility was assessed on glioblastoma (U87-MG), brain endothelial cells (HBMEC), and astrocytes using a live-dead dyeing kit. Gelatin appeared to be the optimal choice for the BBBoC model to generate a complex channel network after its dissolution with albumin.

Capillarization assays are underway to evaluate endothelial cell organization in the channels, with emphasis on tight junctions. In parallel, different hydrogel compositions using hyaluronic acid are being tested. A dedicated chip-holding device was developed to enhance reproducibility. The model integrity will be validated using fluorescent dextran and nanoparticles before introducing cancer cells. In a longer term, this system could become an innovative tool for disease modeling and drug screening.