Development of an in vitro branched vasculature using bioprinting technique in combination with sacrificial materials

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INTRODUCTION: Successful vascularization represents a bottleneck in the production of functional, engineered tissue constructs. The current methods of vascularization either rely on cells self-organization into the capillary network, or predesigned, biofabricated vessels that are limited in size and do not allow the replication of complex vascular networks. Proposed strategies for solving this problem include combinations of natural and synthetic hydrogels with different gelation properties, 3D bioprinting and single or multiple cell cultures with endothelial cells [1]. However, producing defined, capillary-sized hollow channels remains to be beyond reach [2].

EXPERIMENTAL: The objective of this work was to establish a procedure for obtaining a network of interconnected vascular-like channels of varying size, lined with human umbilical vein endothelial cells (HUVECs), using a bioprinting process in combination with sacrificial materials. In addition, the aim was to make the channels hollow with size comparable to the size of capillaries in vivo and to embed them into a hydrogel matrix that could be modified by cells. The method combined extrusion based 3D printing technology and double sacrificial materials- Pluronic F-127 and gelatin type A to produce a sacrificial template for the network. The produced gelatin-cell templates were embedded into a extracellular matrix (ECM)-like hydrogel composed of collagen and fibrin. After the gelatin was removed, remaining hollow structures lined with HUVECs were cultivated statically and dynamically and HUVECs state was further examined.

RESULTS AND DISCUSSION: The size of the network channels ranged from about 1000 µm to less than 20 µm. The ECM hydrogel composed of collagen and fibrin was able to support the stability of the microchannels. The exposure of cells to the inlet flow led to cell sprouting and expression of VE-Cadherin.

CONCLUSIONS: The results indicate that the developed method holds potential for the production of networks, that mimic both structural and functional characteristics of physiological capillaries. Therefore, the principle of using double sacrificial materials for fabrication of hollow vascular channels would enable downsizing of the channels achievable with 3D printing of single sacrificial materials, and that it could be used in the future to produce functional networks with predesigned structure.

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