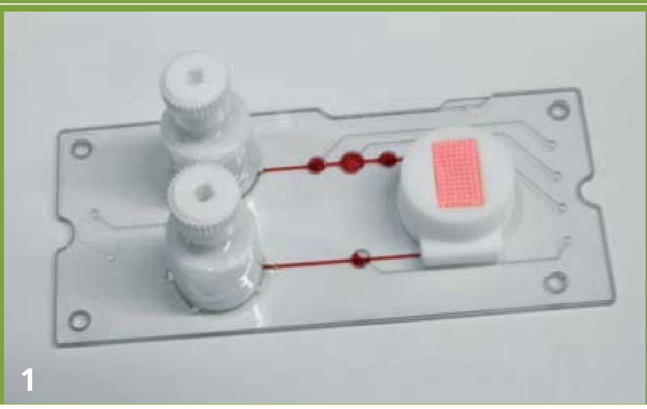

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UNIVERSAL LAB-ON-CHIP PLATFORM FOR PRINTED, COMPLEX 3D TISSUES

THE TASK

The fabrication and cultivation of three-dimensional organ-type tissues is of great importance for the pharmaceutical and cosmetic industries. Three-dimensional tissues reproduce organ-type functions much better than the classic two-dimensional cell culture models. The practical implementation, however, proves to be an interdisciplinary challenge. Complex tissues require a continuous supply of nutrients. Thus they can only be fabricated in continuously perfused lab-on-chip (LOC) systems.

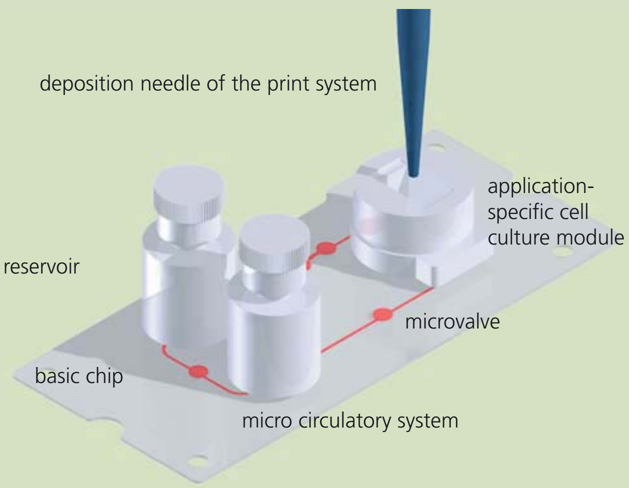
Additive manufacturing methods open fascinating possibilities for many applications including the fabrication of microsystems and the generation of complex organ-type tissues. The 3D printing of living cells (sometimes called biofabrication or 3D bioprinting) enables the fabrication of complex tissues, which consist of different cells and materials and integrate supply channels. Analogous to the human body, the tissues require permanent blood supply already during the fabrication process since the internal cells cannot be sufficiently supplied with oxygen and nutrients based on diffusion only. Nutrients need to be transported by convection to the internal cells, otherwise they die. Under sterile conditions it is possible to supply blood or a suitable solution with nutrients via the integrated supply channels.

OUR SOLUTION

Fraunhofer IWS engineers developed and established a universal and modular LOC platform that is capable of continuously supplying complex 3D printed tissues with nutrients in a sterile environment.

The platform consists of a basic chip that can be combined with application-specific cell culture modules (Fig. 1 and Fig. 2). The basic chips are made from laser microstructured polymer and elastomer foils that are assembled to form three-dimensional microfluidic systems using application specific technologies. Highly transparent polymers are used to provide optical access for non-invasive online monitoring. Integrated flexible membranes can be pneumatically deflected. This permits the integration of valves and peristaltic micropumps to transport and regulate volumetric flows.

Schematics of the LOC platform



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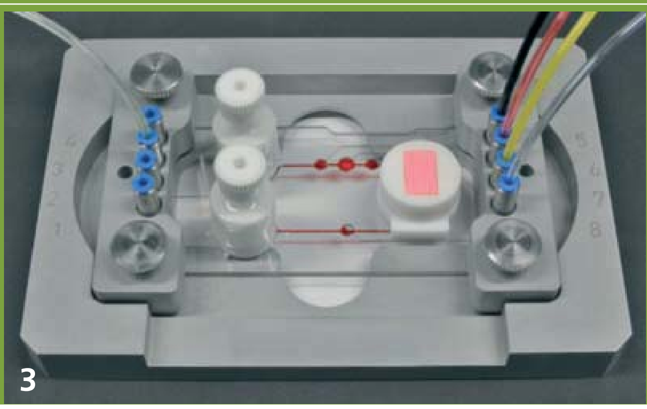

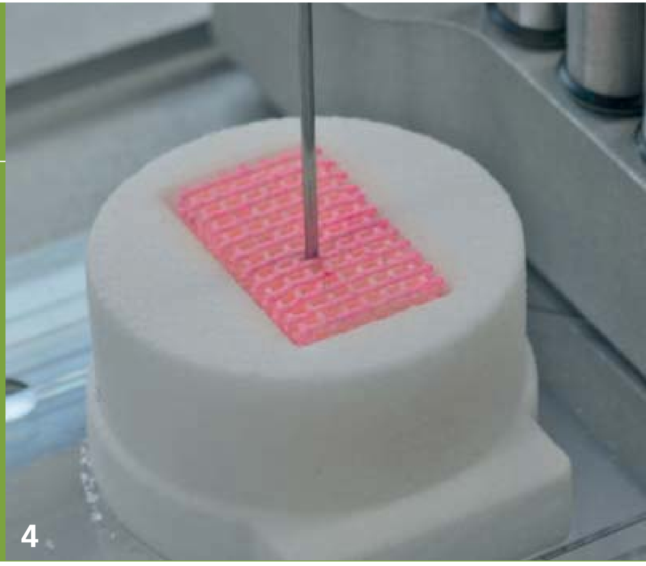

RESULTS

3D printed complex polymeric components provide the basis for the application-specific cell culture modules. Standard interfaces to connect 3D printed fluidic components and to handle the tissues are located on top and bottom surfaces (Fig. 3).

Complex three-dimensional tissues are directly printed into the cell culture modules (Fig. 4). The printing process generates at defined locations liquid-tight connections between tissue and cell culture module. This ensures that the blood or nutrient solution flows through the tissue integrated supply channels.

The versatile possibilities of the LOC platform require a complex and freely programmable embedded system based on Linux. This system provides 24 independently switchable pneumatic exit ports and enables the control of up to eight pumps. Furthermore, the system offers numerous interfaces to peripheral devices such as actors and sensors, data storage and networks. The Linux network stack offers the possibility to remote control the system and to communicate with laboratory information management and automation systems. The user interaction is handled via an integrated 7” touchscreen or corresponding PC software.

Different fabrication systems were used to print complex three-dimensional tissues with living cells directly into the cell culture modules of the LOC platform. Liquid-tight connections between tissue and cell culture module were created during the printing process enabling the nutrient solution to flow through the tissue supply channels. The tissues were supplied continuously for 28 days. The cells inside the tissue remain vital throughout the test period since they receive sufficient oxygen and nutrients.

This universal and modular LOC platform provides a sterile environment to continuously supply 3D bioprinted tissues with nutrients and oxygen for several weeks.

1 LOC system

3 LOC system when receiving

4 Tissue printing in LOC platform

CONTACT

Dr. Frank Sonntag

☎ *+49 351 83391-3259*

✉ *frank.sonntag@iws.fraunhofer.de*