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Stereolithography of poly(ethylene glycol) hydrogels produces micro-containers for cell culture and micro-channels for vascular networks.

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Three-dimensional (3D) soft biomaterial scaffolds for long-term cell culture are critical components in tissue engineering and regenerative medicine. However it is still challenging to construct such scaffolds with desired structural stability and resolution using soft hydrogel. We've developed a method to fabricate 3D biocompatible hydrogel scaffolds at sub-200 µm resolution using projection-based stereolithography to address the biomedical challenges of stem cell culture and synthetic vasculature. Poly(ethylene glycol) (PEG) hydrogels were 3D printed by spatially controlled light-induced solidification of an aqueous pre-polymer solution (PEG-diacrylate 700 Da and 5000 Da lithium acylphosphinate photoinitiator Quinoline Yellow as absorber) using a modified commercial stereolithography printing system (envisionTec Micro 405 nm illumination). Optimization of the optical properties (proximity effects) and material properties (composition of pre-polymer solution) allowed for printing of pyramid-shaped micro-containers for long-term 3D stem cell culture and cuboids with internal channels approaching arteriole dimensions (100 µm cross-section). Human mesenchymal stem cell (hMSC) culture on the pyramidal micro-containers showed that hMSC spheroids formed spontaneously after 24 h incubation and high cell viability (> 80%) was sustained in the stable cultured spheroids for 7 days of incubation. Compared to the technically delicate state-of-the-art hanging drop methodology used for spheroid formation our time- and work-efficient approach in 3D printed low cell adhesion hydrogels provides improved control of hMSC spheroid size and shape. As synthetic arteriole and venule analogs our internal channel structures could be freely designed and constructed inside a hydrogel volume at sub-200 µm resolution in a single automated process (100 µm X 100 µm square channels and <Ø200 µm circular channels) a resolution few methods can achieve in soft hydrogels with full design freedom in all three dimensions. The aim of printing micro-channels within bulk hydrogels is to further fabricate 3D microvascular scaffolds for tissue engineering since vascularization is generally considered as the most important obstacle in the field. On-going cell culture experiments show high compatibility of the printed micro-channel structures to an endothelial cell line (CRL2922) to be employed for endothelialization of the printed vascular network analogs.
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