Laser-based 3D printing of hydrogels: a versatile approach for accurate 3D cellular models

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The ability to produce threedimensional structures from components that build up human tissue with tunable properties is an exciting outlook of biofabrication. Nonetheless, preserving the freedom of structuring in terms of speed, resolution and design while imitating the complexity of the native tissue architecture and function is challenging. With the currently available 3D printing methods, the realization of high resolution structures with complex architecture is cumbersome. Two photon-polymerization (2PP) is a novel 3D printing approach where the absorption of femtosecond-pulsed laser light leads to localized polymerization of photosensitive materials within the focal volume. 2PP is capable of encapsulating cells inside photosensitive hydrogels at high structural resolution in accordance to computer assisted designs (CAD). Direct cell encapsulation is a powerful tool for fabrication of 3D cell culture models in vitro, providing closer resemblance to the in vivo environment of human tissue compared to classical 2D models. Compared to cell seeding in prefabricated scaffolds, direct encapsulation provides high initial cell loading, uniform cell distribution and directed cell positioning. We report here the development of a novel biocompatible multicomponent system which has the capacity of direct cell encapsulation by printing different cells into various designs while maintaining cell viability and proliferation. The properties of the hydrogel including stiffness, degradation, and swelling can be fine-tuned by changing the concentrations of the components and/or applied energy, creating a versatile platform for in vitro modelling and tissue engineering constructs to study cell response in 3D.

Tailoring the mechanical properties of gelatin methacryloyl hydrogels through manipulation of the photocrosslinking conditions

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Photocrosslinkable hydrogels, in particular gelatin methacryloyl (GelMa), are gaining increasing importance in biofabrication and tissue engineering. While GelMa is often described as mechanically ‘tunable’, clear relationships linking the photocrosslinking conditions to reaction rates, and the resulting mechanical properties, have not been described. Meanwhile the conditions employed across the field are disparate, and difficult to compare. In this work, in situ rheological measurements were used to quantify the relative rate of reaction of GelMa hydrogels with respect to light intensity, exposure time and photo-initiator concentration. In addition the UV degradation of the photo-initiator Irgacure 2959 was measured by UV-vis spectroscopy, and used to estimate the rate of free radical production as a function of light exposure. Using these data an expression was derived which predicts the mechanical properties of GelMa hydrogels produced across a wide range of crosslinking conditions. The model was validated through fabrication of mechanical gradients which matched predicted properties. Encapsulated human mesenchymal stem cells showed high viability under the mildest crosslinking conditions, but decreased viability for conditions which generated the highest flux of photoinduced free radical formation. The expressions described may be used to aid rational design of GelMa photocrosslinking strategies, especially in cell encapsulation experiments where minimising the cytotoxic elements in the reaction is a priority.

References:

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