AN ENZYMATICALLY CLEAVABLE PHOTORESIN FOR VOLUMETRIC BIOPRINTING OF LIVING HYDROGEL CONSTRUCTS

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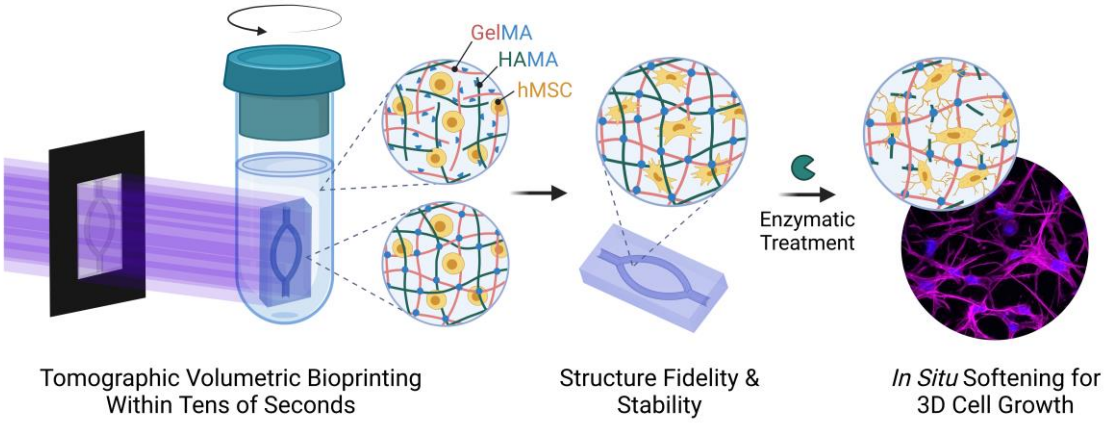
Volumetric bioprinting (VBP) is an enabling technique to rapidly fabricate complex cell-laden hydrogel constructs through tomographic photopolymerization in a single step. However, it remains a challenge to design a photoresin that combines good printability as well as the ability to support cell growth in 3D. Previous reports in VBP have predominantly used gelatin methacryloyl (GelMA) bioresins.[1-2] Yet, improving printing fidelity often comes at the cost of increasing polymer content and gel stiffness, which inevitably impedes cell spreading. Furthermore, VBP at high cell densities is difficult due to light scattering. Inspired by a recent report,[3] we employ a molecularly cleavable photoresin consisting of GelMA and hyaluronan methacrylates (HAMA), which allows for *in situ* softening of constructs after VBP by enzymatic treatment. Additionally, the refractive index of this photoresin can be fine-tuned using iodixanol to enable VBP at higher cell densities.

Multiple resin compositions were formulated and screened by *in situ* photo-rheology and mechanical testing. Among those, 5% GelMA + 0.5% HAMA + 15% iodixanol was selected as an optimal resin. Its initial compressive modulus of 10.9 kPa drops to 5.9 kPa after hyaluronidase treatment. This optically tuned photoresin enables fast VBP (23 s) of hydrogel constructs containing high densities (5×10^6/ml) of human mesenchymal stem cells (hMSCs) while retaining high viability and alkaline phosphatase activity in osteogenic culture. The bioprinted hydrogel constructs were subsequently digested by hyaluronidase, providing a softer matrix that enables faster and more pronounced cell spreading as well as enhanced expression of osteogenic biomarkers. Notably, hMSCs in the treated matrices formed a 3D cellular network on day 7. Deposition of hydroxyapatite mineral crystals in the construct was observed after 21 days of static tissue culture. Collectively, utilizing this optically tuned photoresin and enzymatic treatment presents a new methodology for fast fabrication of cm-scale 3D tissue models by photopolymerization-assisted VBP.



References

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