Rapid prototyping of tough hydrogels with encapsulated stem cells for design of load-bearing tissues

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ABSTRACT

As the world’s population ages, regenerative medicine continues to rise in importance. An important aspect of this is developing the ability to reconstitute load bearing tissue such as articulating cartilage, which often cannot replenish themselves or gradually fail to do so in old age. To rectify this, much research has focused on developing hydrogels either as replacement for lost tissue or to serve as a cellular matrix encouraging the production of native tissue. However, hydrogels are naturally a weak and brittle material that cannot withstand the load demands of the human body. Tough hydrogels have been investigated in recent years to compensate for the material’s mechanical weakness. These hydrogels have the ability to dissipate deformation energy by one of several mechanisms, thus resisting loading and fracture at values similar to those of native tissue. However, no tough hydrogel has been developed that is capable of both being 3D printed and encapsulating cell culture. Here, we report a novel tough hydrogel that is biocompatible for cell encapsulation as well as a unique method of rapid prototyping allowing for complete shape control of the hydrogel. Our hydrogel is comprised of two interconnected polymer networks. The “backbone” network is a poly(ethylene glycol) diacrylate (PEGDA) matrix that forms crosslinks when exposed to ultraviolet (254 nm) light. This network works to maintain the shape of the hydrogel during deformation and gives it strength. A secondary network of alginate chains weaves throughout the PEGDA. These chains are ionically bonded via Ca²⁺ ions; these bonds easily break and reform, allowing them to dissipate energy and give the hydrogel its toughness. It should be noted that this hydrogel is completely biocompatible and we demonstrate its ability to encapsulate healthy eukaryotic cells. The other novel contribution we make is in the shaping of the hydrogel. We apply rapid prototyping technology to form this tough hydrogel into three-dimensional shapes. To do this we mix the PEGDA-alginate gel (containing eukaryotic cells) together with Ca²⁺ ions and UV crosslinking agent in a syringe that is extruded by a desktop 3D printer capable of reading standard computer-aided design files. Because of the short curing time, the cells are not harmed and give our method great promise for the production of tough hydrogels capable of regenerating load-bearing tissues.