Structuring hydrogels to enable suspended manufacture of cell-loaded constructs

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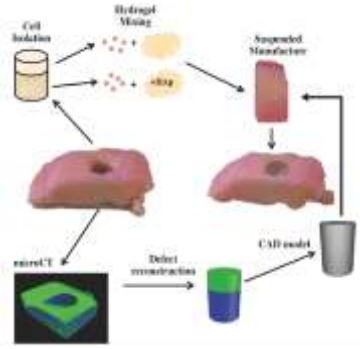
A major challenge in the 3D printing of soft tissues is that the materials that are used to support cell growth are typically too weak to support their own weight. Consequently, the soft materials must be supported by a second, more robust phase, during the manufacturing process. Researchers have used high viscosity liquids such as Pluronic F-127[1] and slurries of gelatin microparticles[2] to provide this support. There remain major drawbacks with the use of these materials, however, particularly since the supporting polymer is challenging to remove from the surface of the part. In order to address this drawback, we have generated supporting materials by applying shear to the hydrocolloids during gelation, resulting in what is known as a fluid gel. This material is formed from a mass of particles and ribbons which interact to form a structured soft solid in the absence of shear. When the material is locally deformed, it will flow and immediately heal when the shear is removed. These properties allow a secondary gelling phase to be deposited within the structure. This secondary phase may carry a population of viable cells or other sensitive entities, which may be localised within the structure. Importantly the support phase may be formed from the same compound as the gelling phase and can easily be removed from the final part using gentle agitation. We have demonstrated the utility of this process using by producing a full thickness chondral replacement using primary human osteoblast and chondrocyte cells. The cells were supported within a gellan gum matrix, which was modified with nanocrystalline hydroxyapatite within the boney region. The resulting material retained mechanical integrity over a period of 28 days of culture and importantly, the cells that were immobilised in the distinct regions of the cells retained either their predominantly osteoblastic or chondrocytic phenotype. This work demonstrates the power of the suspended manufacturing approach to produce geometrically complex cell-laden structures.



The suspended manufacture process allows for high-levels of spatial control over mechanical and chemical properties. The potential of this method for producing complicated tissues was demonstrated by manufacturing a complex hard/soft tissue interface and demonstrating that cell phenotype can be maintained over four weeks of culture.

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